



2024

# ABSTRACTS VII ABCF CONGRESS

This compendium gathers the abstracts approved to the VII ABCF Congress, highlighting research in the pharmaceutical field.

Organizing



Sponsors



# **ABSTRACTS**

# **VII ABCF CONGRESS**

**Associação Brasileira de  
Ciências Farmacêuticas (ABCF)**

Editora Casa da Árvore

Araraquara, São Paulo  
2024

**Edição**

Editora Casa da Árvore

**Texto**

Associação Brasileira de Ciências Farmacêuticas (ABCF)

**Projeto Gráfico**

Editora Casa da Árvore

**DADOS INTERNACIONAIS DE CATALOGAÇÃO NA PUBLICAÇÃO (CIP)**

Associação Brasileira de Ciências Farmacêuticas (ABCF)

ABSTRACTS: VII ABCF CONGRESS / Associação Brasileira de Ciências Farmacêuticas (ABCF). Araraquara: Editora Casa da Árvore, 2024.

469 p.; 21cm x 29,7 cm

ISBN: 978-65-89015-10-9

1. Farmacologia 2. Divulgação I. Título

CDD 615  
CDU 615

## **Pharmaceutical sciences in promoting technological innovation to guarantee healthcare access**

Florianópolis / SC - 11 to 14 November 2024

Culture and Event Center - Universidade Federal de Santa Catarina

Florianópolis - Santa Catarina

### **National Steering Committee**

Prof. Dr. Guilherme Martins Gelfuso (UnB/DF) – Presidente da ABCF

Profa. Dra. Silvana Nair Leite (UFSC/SC) – Presidente do Congresso, Diretoria ABCF

Profa. Dra. Letícia Cruz (UFSM/RS) – Diretoria ABCF

Profa. Dra. Sandra Elisa Haas (UNIPAMPA/RS) – Diretoria ABCF

Profa. Dra. Luciana B Lopes (USP/SP) – Diretoria ABCF

Prof. Dr. Moacyr Jesus Barreto de Melo Rêgo (UFPE/PE) – Diretoria ABCF

Profa. Dra. Sandra Helena Poliselli Farsky (USP/SP) – Diretoria ABCF

Profa. Dra. Marení Rocha Farias (UFSC/SC) – Presidente da Comissão Científica

Profa. Dra. Thaís Cristine Marques Sincero (UFSC/SC) – Presidente da Comissão Local

### **Scientific Committee**

Profa. Dra. Marení Rocha Farias – UFSC – Presidente da Comissão Científica

Prof. Dr. Alexandre Macedo – UFRGS/RS

Prof. Dr. André de Oliveira Baldoni – UFSJ/MG

Profa. Dra. Andrea Diniz – UEM/PR

Profa. Dra. Clarice Madalena Bueno Rolim – UFSC/RS

Prof. Dr. Danilo Bedó – UFPE/PE

Profa. Dra. Denise Brentan da Silva – UFMS/MS

Prof. Dr. Fávero Reisdorfer Paula – UNIPAMPA/RS

Prof. Dr. Henrique Rodrigues Marcelino – UFBA/BA

Profa. Dra. Kelly Ishida – USP/SP

Profa. Dra. Letícia Scherer Koester – UFRGS/RS

Profa. Dra. Lilian Bernardes – UFSC/SC

Prof. Dr. Marcelo Campese – UFAM/AM

Prof. Dr. Marcos Luciano Bruschi – UEM/PR

Profa. Dra. Pérola de Oliveira Magalhães – UnB/DF

Prof. Dr. Ramon Pessoa – UFC/CE

Profa. Dra. Tiana Tasca – UFRGS/RS

### **Local Organization Committee**

Prof. Thaís Cristine Marques Sincero (PGFAR) – Presidente da Comissão Local

Discente Izadora Frizzo (PGFAR)

Discente Kharol Neves (PGFAR)

Discente Marina Araújo Da Silva (PGFAR)

Discente Suellen dos Reis (PGFAR)

Discente Veridiana Pacheco Goulart Martinazzo (PGFAR)

Discente Giovanna Peressoni (PGFAR)

Jenny Sumara (técnica ACL/UFSC)

Pós-doc Amanda Ellen De Athayde (PGFAR)  
Pós-doc Gabriella Da Rosa Monte Machado (PGFAR)  
Prof. Beatriz Mendes Borba (PGFAR)  
Prof. Bianca Ramos Pezzini (PGFAR)  
Prof. Fabiana Botelho De Miranda Onofre (PGFAR)  
Prof. Fabíola Branco Filippin Monteiro (PGFAR)  
Prof. Flávia Martinello (PGFAR)  
Prof. Hellen Karine Stulzer Koerich (PGFAR)  
Prof. Jussara Kasuko Palmeiro (PGFAR)  
Prof. Karin Silva Caumo (PGFAR)  
Prof. Lilian Bernardes – UFSC/SC  
Doutoranda Lívia Maria de Souza Gonçalves (PPGASFAR)  
Prof. Luciano Soares (PPGASFAR-UFSC)  
Profa. Dra. Marení Rocha Farias (PPGASFAR)  
Prof. Maria Luiza Bazzo (PGFAR)  
Prof. Marina Raijche Mattozo Rover (PPGASFAR-UFSC)  
Dr. Norberto Rech Bonetti (PPGASFAR)  
Profa. Dra. Silvana Nair Leite (PPGASFAR)  
Prof. Tatiana Herrerias (PGFAR)

# Sumário

Biotechnology, Natural Products and Food Science	7
Drug Discovery and Medicinal Chemistry	61
Quality Assurance and Analytical Chemistry	111
Pharmaceutical and Cosmetic Technology	143
Nanotecnologia	221
Pharmacology, Pharmacokinetics and Toxicology	340
Clinical Laboratory Analysis and Diagnosis	379
Pharmaceutical Policies and Care	402

**Area**

# **Biotechnology, Natural Products and Food Science**

# Probiotic formulations in cutaneous applications: A scoping review



## Author

Patricia Machado - Universidade Federal do Paraná (UFPR)  
Rodolfo Barros Leite - Universidade Federal do Paraná (UFPR)  
Fernanda Cristina Wroblewski Giublin - Universidade Federal do Paraná (UFPR)  
Marcel Henrique Marcondes Sari - Universidade Federal do Paraná (UFPR)  
Raul Edson Luna Lazo - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)  
Luana Mota Ferreira - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

No Funding



## Keywords

Topical Synbiotics/Postbiotics, Dermatological Formulations, Nanotechnology

## Abstract

Dysbiosis is the imbalance of the skin's microbiota, which can cause dermatological disorders such as rosacea, psoriasis, acne, and atopic dermatitis. Treatments include calcineurin inhibitors and corticosteroids, but prolonged use causes adverse reactions. Lactobacillus, Bifidobacterium, and other probiotics promote cutaneous health by producing antibacterial, anti-inflammatory, and immunomodulatory compounds, contributing to skin restoration. The topical application of these microorganisms is a recent innovation, although it still needs more scientific data on efficacy and safety. Due to the increasing research on innovative dermatological formulations containing probiotics, there is a need to gather scientific evidence for treating skin diseases. Given this above, the objective of this study was to conduct a scoping review of topical formulations containing pro or prebiotics, intending to treat skin disorders caused by dysbiosis. The search terms "Probiotics/prebiotics," "skin disorders," and "skin formulations" were used to search the PubMed, Scopus, and Web of Science databases. A total of 3959 articles were identified, and after removing 907 duplicates, 3052 records were screened by reading the titles and abstracts. 2919 articles that did not meet the inclusion criteria were excluded, leaving 133 studies to be read in full. After reading the full texts, 55 articles were further excluded, according to the inclusion criteria. Finally, 78 articles were assessed for eligibility. The main probiotic strain identified was Lactobacillus spp. (25) followed by mixed strains (10). Regarding prebiotics, fructo-oligosaccharides (FOS) were the most cited in the studies. The most common topical formulations were gel (17), film (15), and cream (11). These formulations were tested mainly in wound healing (34), acne vulgaris (15), and atopic dermatitis (10). The formulations containing pre or probiotics have demonstrated great efficacy in skin diseases caused by dysbiosis.



# Immunomodulatory effect of IFN- $\gamma$ licensed adipose-mesenchymal stromal cells in an in vitro model of inflammation generated by SARS-CoV-2 antigens



## Author

Elizabete Cristina Iseke Bispo - Universidade de Brasília  
Francisco de Assis Rocha Neves - Universidade de Brasília  
Enrique Roberto Argañaraz - Universidade de Brasília  
Juliana Lott de Carvalho - Universidade de Brasília  
Felipe Saldanha de Araújo - Universidade de Brasília



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Keywords

IFN- $\gamma$ -Licensed Mesenchymal Stromal cells, T-cells, SARS-CoV-2

## Abstract

In recent years, clinical studies have shown positive results of the application of Mesenchymal Stromal Cells (MSCs) in severe cases of COVID-19. However, the mechanisms of immunomodulation of IFN- $\gamma$  licensed MSCs in SARS-CoV-2 infection are only partially understood. Here we tested the effect of IFN- $\gamma$  licensing in the MSC immunomodulatory profile and established an in vitro model of inflammation by exposing Calu-3 cells to SARS-CoV-2 nucleocapsid and spike (NS) antigens and IFN- $\gamma$ . Finally, the conditioned medium (iCM) generated by Calu-3 cells exposed to IFN- $\gamma$  and SARS-CoV-2 NS antigens was used to evaluate the ability of IFN- $\gamma$ -licensed MSCs to modulate the T-cell response in this environment. We found that the exposure to IFN- $\gamma$  and SARS-COV-2 NS antigens compromised the viability of Calu-3 cells and induced the expression of the inflammatory mediators ICAM-1, CXCL-10, and IFN- $\beta$  by these cells. Importantly, despite initially stimulating T-cell activation, IFN- $\gamma$ -licensed MSCs dramatically reduced IL-6 and IL-10 levels secreted by T-cells exposed to NS antigens and iCM. Moreover, IFN- $\gamma$ -licensed MSCs were able to significantly inhibit T-cell apoptosis induced by SARS-CoV-2 NS antigens. Taken together, our data show that, in addition to reducing the level of critical cytokines in COVID-19, IFN- $\gamma$ -licensed MSCs protect T-cells from SARS-CoV-2 antigen-induced apoptosis. Such observations suggest that IFN- $\gamma$ -licensed MSCs may contribute to COVID-19 management by preventing the lymphopenia and immunodeficiency observed in critical cases of the disease.

# Polyphenol Extraction using Microwaves and Pressured Liquid Condition from Cupuaçu Seed By-product: Optimization and Comparative Study



## Author

Russany Silva da Costa - Universidade Federal do Pará (UFPA)  
Camilo Barroso Teixeira - Universidade Federal do Pará (UFPA)  
Alessandro Alberto Casazza - Universidade de Gênova (UNIGE)  
Roseane Maria Ribeiro Costa - Universidade Federal do Pará (UFPA)  
José Otávio Carréra Silva Júnior - Universidade Federal do Pará (UFPA)  
Attilio Converti - Universidade de Gênova (UNIGE)  
Patrizia Perego - Universidade de Gênova (UNIGE)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico



## Keywords

Antioxidant activity, Waste valorization, Green chemistry

## Abstract

Cupuaçu (*Theobroma grandiflorum* Schum.) is an Amazonian fruit rich in antioxidants potential due to its phenolic compounds. Recently, there has been a significant discussion in academia regarding the importance of reuse of agro-industrial biocompounds from fruits with high economic potential, such as cupuaçu. This Amazonian fruit, whose seeds are used in the production of cupulate, a chocolate-like product, is estimated to be yield over 27 thousand tons in the state of Pará, covering 8.5 thousand hectares with an average yield of 3 t/ha. This production generates approximately 30,000 tons of cupuaçu fruit husk annually in Pará. Thus, aiming to combine different waste recovery processes with sustainable techniques by applying green chemistry principles, this study aimed to optimize and compare microwave-assisted (MAE) and high pressure/temperature extraction (HPTE) of polyphenolic and flavonoid compounds from cupuaçu seed by-products. A Box-Behnken  $3^3$  factorial design assessed the influence of extraction time, solid/liquid ratio, and ethanol concentration. Responses included total polyphenol content, total flavonoid content, and anti-radical power via the ABTS+• method. In optimum conditions, MAE had the highest total polyphenol content and HPTE for flavonoids. Optimal conditions for both methods were 65% (w/v) ethanol concentration, 45 minutes extraction time, and 0.03 g mL<sup>-1</sup> solid/liquid ratio. MAE and HPTE achieved greater recovery of (-)-epicatechin and (-)-epigallocatechin-3-gallate compared to percolation. Both techniques proved viable for recovering polyphenols from cupuaçu seed by-products, in less time and with less solvent. Thus, cupuaçu by-products can be a sustainable and functional food source, with MAE and HPTE providing high yields and quality extracts rich in polyphenols.

# Optimization of extraction and partial characterization of polysaccharides produced by *Nigrospora sphaerica*



## Author

Gildomar Lima Valasques Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Edson Gabriel dos Santos - Universidade Estadual do Sudoeste da Bahia (UESB)  
Layla Matos Valasques - Universidade Estadual do Sudoeste da Bahia (UESB)  
Baraquizio Braga do Nascimento Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Pâmala Evelin Pires Cedro - Universidade Estadual do Sudoeste da Bahia (UESB)  
Alana Caese dos Anjos Miranda - Universidade Estadual do Sudoeste da Bahia (UESB)  
Aníbal de Freitas Santos Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Orlando Maia Barbosa - Universidade Estadual do Sudoeste da Bahia (UESB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Keywords

Polysaccharide, characterization, experimental planning

## Abstract

*Nigrospora* is a genus of fungal ascomycetes with a cosmopolitan distribution that can be phytopathogenic, endophytic and saprobic. The cell walls of fungi are composed of polysaccharides and proteins that may have diverse biological properties, such as antioxidant, immunomodulatory, antinociceptive. This study aimed to optimize the extraction and partially characterize the polysaccharides produced by *Nigrospora sphaerica*. The microorganism was cultivated for 5 days in liquid medium containing a nitrogen source (peptone 5g/L) and a carbon source (glucose 10g/L) in addition to other nutrients such as yeast extract (3g/L) and malt extract (3g/L). The biomass produced was subjected to an extraction process in 0.1M NaOH solution, according to the Response Surface Methodology, Doehlert experimental planning, varying the temperature at 3 levels (70, 80 and 90°C) and the time of 5 levels (1, 2, 3, 4 and 5 hours), totaling 9 experiments. The extracted polysaccharides were dried in an oven at 50°C. The polysaccharides were subjected to Infrared analysis with Fourier transform covering the region from 4000 to 500 cm<sup>-1</sup> with 20 scans. The results indicated that the conditions that generate the highest proportion of polysaccharide extraction were temperatures between 80 and 90°C and a time of around 3 hours, with the optimum point being equal to 83°C and 3.2 hours. Statistical analyzes demonstrated a generated model was well fitted with significant regression and no lack of fit. Infrared analyzes identified features compatible with polysaccharides, stretches at 3268 (O-H), 2926 (C-H), and 1020 (C-O) cm<sup>-1</sup>. Given this, it is possible to state that the methodology applied identified the optimal condition for extracting the polysaccharide (confirmed by infrared analysis) from *Nigrospora sphaerica*, and it is important to continue with the characterization tests and evaluation of the biological properties of the product obtained.

# Antimicrobial Activity of Bioactive Procyanidins from Açaí Seed



## Author

Gabriele Neuhaus Steinhauser - Universidade Federal de Santa Catarina (UFSC)  
Fabienne Antunes Ferreira - Universidade Federal de Santa Catarina (UFSC)  
Gabriel Rocha Martins Mattos - Instituto Nacional de Tecnologia do Rio de Janeiro  
Mariana Monteiro Guilherme Mattos - Instituto Nacional de Tecnologia do Rio de Janeiro  
Ayla Sant'Ana da Silva - Instituto Nacional de Tecnologia do Rio de Janeiro



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Instituto Serrapilheira



## Keywords

açaí seed, procyanidins, antimicrobial activity

## Abstract

In recent years, Brazil's production of açaí pulp from the açaí palm (*Euterpe oleracea* Mart.) has driven its increased consumption and production. However, approximately 85% of the fruit comprises non-edible seeds, leading to environmental and sanitary challenges. Previous research has identified açaí seeds as rich in procyanidins (oligomers and polymers), which possess potent antioxidant and antimicrobial properties. The hydroalcoholic crude extract was then previously fractionated using Medium-Pressure Liquid Chromatography (MPLC) on a Sephadex™ LH-20 column with varying mobile phases, yielding six fractions (1-6). Fraction 4 was identified as small procyanidins (mDP 2.6), Fraction 5 as oligomers (mDP 5.7), and Fraction 6 as procyanidins polymers (mDP 12.1), showcasing effective size-based separation. Consequently, this study aims to further explore the antimicrobial activity of these fractions. Minimum Inhibitory Concentrations (MIC) determined by broth microdilution method revealed MIC values of 0.5 mg/mL across fractions 4-6, effectively inhibiting Gram-positive bacteria (*Staphylococcus aureus* strains V329, ATCC25923, and MRSA17022) and yeast growth (*Candida albicans* ATCC10231) with  $\geq 1$ log reduction. Notably, Fraction 6 exhibited the highest antimicrobial efficacy, inhibiting 99.9% of all bacteria and yeast. Additionally, synergistic effects between Fraction 6 and the crude extract with oxacillin were investigated using the Checkerboard Assay, achieving a 1000-fold reduction in MIC against the oxacillin-resistant MRSA17022 strain. Synergy was also observed against *S. aureus* ATCC25923, highlighting Fraction 6's potential with oxacillin against beta-lactam-sensitive strains. These findings establish a foundation for exploring procyanidins chemical properties and suggest biotechnological applications for açaí seed in therapeutic and industrial settings.

# Evaluation of the technological potential of a *Bacillus* strain isolated from Umbu (*Spondias purpurea* Arruda), with antilisterial activity



## Author

Giovanni Eiji do Nascimento Ozaki - Universidade Federal do Oeste da Bahia (UFOB)  
Fabricio Luiz Tulini - Universidade Federal do Oeste da Bahia (UFOB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Fapesb and CNPq



## Keywords

Antimicrobial activity, *Listeria monocytogenes*, Probiotic

## Abstract

Probiotics are live microorganisms that can improve host health. Species from *Bacillus* genus have shown potential as probiotics in humans due to their ability to survive harsh gastrointestinal conditions and their antioxidant, immunomodulatory, and antimicrobial properties. Thus, this study aimed to characterize a *Bacillus* strain isolated from Umbu (*Spondias tuberosa* Arruda) and evaluate its technological potential. The isolate underwent identification processes, including catalase assay, gram staining, spore formation assessment, and other biochemical tests. The isolate was also evaluated for the production of antimicrobial compounds, sensitivity to antibiotics, and the ability to survive under various conditions simulating the gastrointestinal tract. The *Bacillus* strain exhibited the following traits: Catalase positive, Voges-Proskauer positive, citrate negative, motility positive, ability to grow in up to 10% NaCl BHI (Brain Heart Infusion broth), temperatures ranging from 10°C to 50°C, and pH from 5 to 10. According to Bergey's manual (2015), the isolate was identified as *Bacillus vietnamensis*, and it will be confirmed through 16S rDNA sequencing. The *Bacillus* strain demonstrated sensitivity to most tested antibiotics, with resistance observed only to amoxicillin, ampicillin, and clindamycin. Additionally, it exhibited the production of antimicrobial peptides that inhibited the growth of *Listeria monocytogenes* NCTC13627. The isolate exhibited robust survival rates in conditions simulating the gastrointestinal tract for up to 180 minutes, with survival rates of 71.2% in pepsin pH 2.0 solution, 61.4%, 66.8%, and 71.0% at BHI pH 2.0, 2.5, and 3.5, respectively, and 93.3% in BHI supplemented with 0.3% bile. The *Bacillus* strain isolated from umbu presented significant probiotic potential, and considering its antilisterial activity, it could be explored for novel food preservation strategies and the development of functional foods.

# Obtaining Saponins from *Ilex paraguariensis* by Column Chromatography and High-Performance Counter-Current Chromatography



## Author

Sara Elis Bianchi - Universidade Federal do Rio Grande do Sul - (UFRGS)  
Adriane Lindemann - Universidade Federal do Rio Grande do Sul - (UFRGS)  
Gabriela de C. Meirelles - Universidade Federal do Rio Grande do Sul - (UFRGS)  
Fábio de S. Barbosa - Universidade Federal do Rio Grande do Sul - (UFRGS)  
Valquiria Linck Bassani - Universidade Federal do Rio Grande do Sul - (UFRGS)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

FAPERGS



## Keywords

Erva-mate, matesaponin, Counter-Current Chromatography

## Abstract

*Ilex paraguariensis* St. Hill, commonly known as erva-mate, holds significant economic and cultural value in Rio Grande do Sul, Brazil. This plant species contains a variety of compounds with notable pharmaceutical and cosmetic potential, including saponins and caffeoylquinic acids, known for their pharmacological and therapeutic properties. The isolation and purification of bioactive molecules from plant sources have historically posed challenges for the pharmaceutical industry due to the complex nature of these materials. This study focuses on obtaining isolated matesaponins from aerial parts of *Ilex paraguariensis* using a combination of both column chromatography and high-performance countercurrent chromatography (HPCCC) techniques. The extraction method was optimized using factorial design, with key parameters including the drug:solvent ratio, method of maceration, and particle size. The optimized method yielded an extraction efficiency of 35.42%, calculated based on the mass of the extracted erva-mate. Fractionation using column chromatography successfully yielded a fraction enriched in saponins. The isolation of these constituents by HPCCC was conducted using a reversed-phase system. After elution in the HPCCC, the tubes obtained were analyzed by ESI-QTOF. By combining these techniques, it was possible to successfully isolate matesaponin 1. Four additional matesaponins (2, 3, 4, and 5) were identified in mixtures within the tubes following HPCCC fractionation. While HPCCC offers faster and more cost-effective isolation and purification methods, it proved insufficient for isolating matesaponins from *Ilex paraguariensis* on its own. However, by combining column chromatography with HPCCC, it was possible to isolate matesaponin 1 and obtain other fractions enriched with other matesaponins. The HPCCC method developed for separating the crude extract was found to be ineffective for the isolation and purification of saponins.

# Application of Doehlert experimental design to optimize the extraction of polysaccharides from the cell wall of *Nigrospora gorlenkoana*



## Author

Edson Gabriel Dos Santos - Universidade Estadual do Sudoeste da Bahia (UESB)  
Gildomar Lima Valasques Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Layla Matos Valasques - Universidade Estadual do Sudoeste da Bahia (UESB)  
Pâmala Evely Pires Cedro - Universidade Estadual do Sudoeste da Bahia (UESB)  
Alana Caise Dos Anjos Miranda - Universidade Estadual do Sudoeste da Bahia (UESB)  
Baraquizio Braga do Nascimento Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Aníbal de Freitas Santos Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Orlando Maia Barbosa - Universidade Estadual do Sudoeste da Bahia (UESB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES, CNPQ, FAPDF, PPGCF



## Keywords

Polysaccharides, Response Surface Methodology, characterization

## Abstract

Fungal polysaccharides are biomolecules with several properties described in the literature, including immunomodulatory, antioxidant, antinociceptive and hypoglycemic activities. Fungal sources seem to be more promising for obtaining products with pharmacological properties, since fungi are fast-growing microorganisms and many of them do not pose a risk to human health. This study aimed to optimize the extraction and partially characterize the polysaccharides produced by *Nigrospora gorlenkoana*. The microorganism was cultivated for 5 days by submerged fermentation in a medium containing peptone as a nitrogen source (5g/L), glucose as a carbon source (10g/L) in addition to other nutrients such as yeast extract (3g/L) and malt extract (3g/L). The biomass produced was subjected to an extraction process in alkaline solution pH 13 (NaOH 0.1M), in accordance with the Doehlert experimental planning of the Response Surface Methodology, with the temperature studied at 3 levels (70, 80 and 90° C) and the time of 5 levels (1, 2, 3, 4 and 5 hours). The extracted product was subjected to infrared analysis with Fourier transform covering the region from 4000 to 500cm<sup>-1</sup> with 20 scans. The results indicated that the conditions that generated the highest proportion of polysaccharide extraction were temperatures between 80 and 85°C and a time of 4.5 hours. Statistical analyzes demonstrated that the generated model was well adjusted, with significant regression and no lack of fit. Infrared analyzes identified features compatible with polysaccharides, stretches at 3086 (O-H), 2924 (C-H) and 1000 (C-O) cm<sup>-1</sup>. Given this, it is possible to state that the methodology applied identified the optimal condition for extracting the polysaccharide (confirmed by infrared analysis) from *Nigrospora gorlenkoana*, and the next steps will be the evaluation of the biological properties (antioxidant, hypoglycemic and immunomodulatory).

# Application of Doehlert experimental design in the characterization of $\beta$ -galactosidase produced by *Pleurotus ostreatus* CCMB 369 isolated in the northeastern semi-arid region



## Author

Gusttavo Moura - Universidade Estadual do Sudoeste da Bahia (UESB)  
Uanderson de Jesus Santos - Universidade Estadual do Sudoeste da Bahia (UESB)  
Bianca Maria de Jesus - Universidade Estadual do Sudoeste da Bahia (UESB)  
Rafael Borges Brito - Universidade Estadual do Sudoeste da Bahia (UESB)  
Layla Matos Valasques - Universidade Estadual do Sudoeste da Bahia (UESB)  
Baraquízio Braga do Nascimento Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Gildomar Lima Valasques Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Universidade Estadual do Sudoeste da Bahia (UESB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Not applicable.



## Keywords

Experimental planning,  $\beta$ -galactosidase, characterization.

## Abstract

The Brazilian northeastern semi-arid region is rich in environmental diversity and can be explored as a source of various studies in the area of biotechnology. Therefore, it has the potential to identify microorganisms that produce various enzymes for pharmaceutical applications, including  $\beta$ -galactosidases. This work aimed to characterize, by obtaining the optimal pH and temperature of enzymatic activity, and determining the  $K_m$  and  $V_{max}$  of  $\beta$ -galactosidases produced by *P. ostreatus*. Approximately 107 spores were inoculated into 150mL of liquid medium containing lactose as the main carbon source and the mixture was isolated at 28°C for 5 days. To eliminate the intracellular enzyme from the mycelia, 5% Triton X-100 was used for 12 hours. To determine the pH and optimum temperature of the enzyme, the Doehlert experimental design was applied, evaluating the temperature at three levels (30, 50 and 70°C) and the pH at five levels (3, 4, 5, 6 and 7). The determination of  $K_m$  and  $V_{max}$  was carried out by obtaining the regression of the Lineweaver–Burk curve. Enzymatic activity was determined by spectrophotometry, using o-nitrophenyl- $\beta$ -D-galactopyranoside (ONPG) as substrate, 1M sodium carbonate to stop the occurrence and reading at 410nm. Analysis of the results allows us to state that the optimal pH and temperature conditions for  $\beta$ -galactosidase from *P. ostreatus* were 3 to 5.5 and 40 to 55°C for pH and temperature, respectively. Statistical analyzes revealed that the generated model was well adjusted with significant regression and no lack of fit. The Lineweaver–Burk curve regression allowed calculating the  $K_m$  and  $V_{max}$  values of the enzyme, which were respectively 0.24mM and 1.25 $\mu$ mol/min. In view of this, it is possible to state that *P. ostreatus* isolated from the semiarid northeastern region produces lactases with the potential to be used to obtain delactosed products, being of pharmaceutical and industrial interest.



# Obtaining enriched fractions of phenolic acids from *Ilex paraguariensis* using Column Chromatography and High-Performance Countercurrent Chromatography (HPCCC)



## Author

Laura da Silva Machado - Universidade Federal do Rio Grande do Sul (UFRGS)  
Adriane Lindemann - Universidade Federal do Rio Grande do Sul - (UFRGS)  
Fábio de Souza Barbosa - Universidade Federal do Rio Grande do Sul - (UFRGS)  
Sara Elis Bianchi - Universidade Federal do Rio Grande do Sul - (UFRGS)  
Valquiria Linck Bassani - Universidade Federal do Rio Grande do Sul - (UFRGS)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CNPQ - Conselho Nacional de Desenvolvimento Científico e Tecnológico, 44265



## Keywords

*Ilex paraguariensis*, high-performance countercurrent chromatography, phenolic acids

## Abstract

This project aimed to obtain fractions rich in phenolic acids and to isolate specific compounds from the leaves and stems of *Ilex paraguariensis*, using high-performance countercurrent chromatography (HPCCC) in the final separation phase. The solvent system was optimized using a simplex-centroid design with ternary mixtures of water, ethanol, and methanol. Once the optimal solvent was determined, the extraction conditions were refined through a factorial design involving five variables at two levels. The optimal extraction conditions (50% v/v ethanol heated to 80 °C, maceration with mechanical stirring for 60 min, a drug/solvent ratio of 10 g/50 mL, and a particle size of 0.025 mm) were applied, yielding a crude extract with a yield of 35.42% (relative to the mass of yerba mate used in the extraction). High-performance liquid chromatography (HPLC) analysis showed a content of 56.00% caffeoylquinic acids, 5.00% caffeine, and 1.50% rutin. Among the caffeoylquinic acids, 3,5-dicaffeoylquinic acid (19.00%) and 5-O-caffeoylquinic acid (16.00%) had the highest contents. The extract was fractionated by column chromatography, packed with Diaion® HP-20 resin, and eluted with water mixtures in decreasing polarity. This process successfully yielded ten less complex fractions, with fractions 3 to 6 containing caffeoylquinic acid compounds derived from phenolic acids. For the separation of caffeoylquinic acids, tests were performed using HPCCC with a reverse-phase system. This process yielded three fractions, which were analyzed by HPLC and identified using high-resolution mass spectrometry. The analysis revealed the presence of caffeine, dicaffeoylquinic acids (3,4-dicaffeoylquinic, 3,5-dicaffeoylquinic, and 4,5-dicaffeoylquinic), and monocaffeoylquinic acids (5-O-caffeoylquinic, 3-O-caffeoylquinic, and 4-O-caffeoylquinic). This study showed that combining column chromatography and HPCCC yields enriched fractions, proving the method's efficiency.

# Anti-CD123 monoclonal antibodies as therapy for acute myeloid leukemia: an ongoing systematic review



## Author

Vitória Vito - Universidade Federal de Santa Catarina (UFSC)  
Vinícius André Boff- Universidade Federal de Santa Catarina (UFSC)  
Ana Carolina Rabello de Moraes - Universidade Federal de Santa Catarina (UFSC)  
Izabel Galhardo Demarchi - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Not applicable



## Keywords

Acute Myeloid Leukemia, anti-CD123, immunotherapy

## Abstract

$\beta$ -galactosidase (lactases) can be obtained from various sources, however, the sources fungi are very promising, since fungi are capable of producing  $\beta$ -galactosidase with optimal pHs and temperatures compatible with use in production of lactose-free foods. The objective of this work was to characterize, from the identification of the optimum pH and temperature for enzymatic activity, and the determination of kinetic parameters of  $\beta$ -galactosidases produced by *P. camemberti*. Approximately  $10^7$  spores of the microorganism were inoculated into 150mL of medium liquid containing lactose as the main carbon source, and fermentation was conducted for 5 days at 28°C. The extraction of the intracellular enzyme was carried out using the mycelium with 5% Triton X-100 for 12 hours. To determine the optimal pH and temperature of the enzyme, the Doehlert experimental design was applied studying the temperature at three levels (30, 50, 70°C) and pH at five levels (3, 4, 5, 6, 7). The determination of  $K_m$  and  $V_{max}$  was performed based on the regression of the Lineweaver–Burk plot. The reaction medium consisted of 150  $\mu$ L of crude enzymatic extract, 750  $\mu$ L of ONPG (5 mM) subjected to 50°C for 30 min, followed by the addition of 500  $\mu$ L of 1M sodium carbonate and reading at 410 nm in a spectrophotometer. The analysis of the results allows to state that the optimal conditions for pH and temperature for  $\beta$ -galactosidase from *P. camemberti* were pH 5 to 7 and 45 to 60°C for pH and temperature, respectively. Statistical analyses demonstrated that the generated model was well adjusted with significant regression and absence of lack of adjustment. The regression of the Lineweaver–Burk plot allowed the calculation of the enzyme's  $K_m$  and  $V_{max}$  values, which were 0.84 mM and 0.328  $\mu$ mol/min, respectively. Therefore, it is possible to affirm that *P. camemberti* produces lactases with the potential to be used in the production of lactose-free products, important for individuals with lactose intolerance.

# Antioxidant and hepatoprotective effects of a protein isolate from Brazil nuts (*Bertholletia excelsa* H.B.K.)



## Author

João Lucas Rufino - Universidade Federal do Amazonas (UNEB)  
Bárbara Janaína Paula da Silva - Universidade Federal do Amazonas (UNEB)  
João Pedro Cezário Brandão - Universidade Federal do Amazonas (UNEB)  
Laura Beatriz Souza e Souza - Universidade Federal do Amazonas (UNEB)  
Anibal de Freitas Santos Júnior - Universidade Federal do Amazonas (UNEB)  
Emersom Silva Lima - Universidade Federal do Amazonas (UNEB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Fundação de Amparo à Pesquisa do Estado do Amazonas - FAPEAM



## Keywords

Brazil nut, selenium, antioxidant

## Abstract

The Brazil nut (*Bertholletia excelsa*) has a high economic relevance for the Amazon. It is rich in fibers, proteins and lipids, and also contains vitamins and minerals, especially selenium. These aspects position Brazil nuts as an alternative source of protein, for example, in contrast to animal protein, whose production becomes scarcer and less sustainable every day. Brazil nuts can positively influence events resulting from oxidative stress, due to their possible antioxidant activities and due to their selenium content, and they can also have a hepatoprotective effect. The present study aimed to characterize, in terms of antioxidant and hepatoprotective effects, a protein isolate (PI) from Brazil nuts. The PI was obtained by via precipitation of proteins using different pHs and then drying in a spray dryer. In the analysis, it presented humidity of  $1.96 \pm 0.16\%$ , water activity of  $0.24 \pm 0.001$  AW,  $6.32 \pm 0.005\%$  of total phenols and  $7.03 \pm 1.0\%$  of total lipids. In vitro antioxidant activity was determined by the ability to scavenge ABTS or DPPH free radicals, in which the PI did not show significant activity. The selenium content found in the PI was  $16.63 \pm 0.63$   $\mu\text{g}/100$  g. As for the aminogram, the following values were obtained for selenated amino acids: Se-methionine 6.01 g/100 g and Se-cysteine 2.05 g/100 g. HepG2 cells, subjected to oxidative stress with carbon tetrachloride, were also treated with the PI or the standard silymarin. Treatment with the isolate protected cells from oxidative aggression when monitored via TGO, LDH or alkaline phosphatase activities. These results demonstrate a possible hepatoprotective effect of the Brazil nut PI, probably due to the selenium content and effect on glutathione peroxidase activity. These data justify the use of the Brazil nut PI as a possible nutraceutical active ingredient to be explored in food or medicines.

# Characterization of $\beta$ -galactosidase produced by *Penicilium camemberti* ATCC 4845



## Author

Isanna Carvalho - Universidade Estadual do Sudoeste da Bahia (UESB)  
Gildomar Lima Valasques Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)  
Uanderson de Jesus Santos - Universidade Estadual do Sudoeste da Bahia (UESB)  
Bianca Maria de Jesus - Universidade Estadual do Sudoeste da Bahia (UESB)  
Vanessa Ribeiro dos Santos - Universidade Estadual do Sudoeste da Bahia (UESB)  
Rafael Borges Brito - Universidade Estadual do Sudoeste da Bahia (UESB)  
Layla Matos Valasques - Universidade Estadual do Sudoeste da Bahia (UESB)  
Baraquízio Braga do Nascimento Júnior - Universidade Estadual do Sudoeste da Bahia (UESB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Not applicable.



## Keywords

Response Surface Methodology, Lactases, Characterization.

## Abstract

$\beta$ -galactosidase (lactases) can be obtained from various sources, however, the sources fungi are very promising, since fungi are capable of producing  $\beta$ -galactosidase with optimal pHs and temperatures compatible with use in production of lactose-free foods. The objective of this work was to characterize, from the identification of the optimum pH and temperature for enzymatic activity, and the determination of kinetic parameters of  $\beta$ -galactosidases produced by *P. camemberti*. Approximately 107 spores of the microorganism were inoculated into 150mL of medium liquid containing lactose as the main carbon source, and fermentation was conducted for 5 days at 28°C. The extraction of the intracellular enzyme was carried out using the mycelium with 5% Triton X-100 for 12 hours. To determine the optimal pH and temperature of the enzyme, the Doehlert experimental design was applied studying the temperature at three levels (30, 50, 70°C) and pH at five levels (3, 4, 5, 6, 7). The determination of  $K_m$  and  $V_{max}$  was performed based on the regression of the Lineweaver–Burk plot. The reaction medium consisted of 150  $\mu$ L of crude enzymatic extract, 750  $\mu$ L of ONPG (5 mM) subjected to 50°C for 30 min, followed by the addition of 500  $\mu$ L of 1M sodium carbonate and reading at 410 nm in a spectrophotometer. The analysis of the results allows to state that the optimal conditions for pH and temperature for  $\beta$ -galactosidase from *P. camemberti* were pH 5 to 7 and 45 to 60°C for pH and temperature, respectively. Statistical analyses demonstrated that the generated model was well adjusted with significant regression and absence of lack of adjustment. The regression of the Lineweaver–Burk plot allowed the calculation of the enzyme's  $K_m$  and  $V_{max}$  values, which were 0.84 mM and 0.328  $\mu$ mol/min, respectively. Therefore, it is possible to affirm that *P. camemberti* produces lactases with the potential to be used in the production of lactose-free products, important for individuals with lactose intolerance.

# Effects of conditioned medium obtained from breast cancer cells on macrophage proliferation and differentiation



## Author

Felipe de Lara Janz - Universidade Estadual de Ponta Grossa (UEPG)  
Gabriela Ruva Fagundes - Universidade Estadual de Ponta Grossa (UEPG)  
Paulo Roberto Costa de Almeida - Universidade Estadual de Ponta Grossa (UEPG)  
Giovani Marino Favero - Universidade Estadual de Ponta Grossa (UEPG)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Not applicable.



## Keywords

Macrophages, Tumor microenvironment, Conditioned medium

## Abstract

The tumor microenvironment is composed not only of neoplastic cells but also of stromal cells, immune system cells, and various other non-tumoral types. Macrophages are cells known for their phagocytic capability; additionally, they present antigens to T cells and initiate inflammation by releasing cytokines that attract and activate other immune cells. A subpopulation of macrophages, tumor-associated macrophages (TAMs), are part of the microenvironment in most tumors. In some malignant neoplasias, such as breast cancer, TAMs can represent more than 50% of the tumor mass. This study aimed to evaluate the toxicity and proliferative effects of the conditioned medium (CM) from breast cancer cells on macrophage cultures. All cell samples were cultivated in RPMI 1640 medium supplemented with 20% fetal bovine serum and maintained in a CO<sub>2</sub> incubator at 37°C. To evaluate proliferation and cytotoxicity, the MTT assay was achieved. CM was obtained from pre-established 4T1 cell cultures (breast cancer cell line), filtered, and applied in different concentrations to J774 cell cultures (macrophage cell line) for 48 hours. After this time, a solution of MTT 5 mg/mL was added, and the cells were incubated for additional 3 hours. Afterwards, all medium was removed, and formed crystals were solubilized in DMSO. The absorbance was evaluated using an optical spectrophotometer at 570 nm. J774 cells showed a significant difference of approximately 60% above the control group ( $p < 0.05$ ; t-test/GraphPad Prism), indicating higher proliferation when treated with the CM. Possibly, CM contains pro-mitotic substances in its composition that increased the division rate of 4T1 cells. This study found that the CM from breast cancer tumor cells increased the proliferation of macrophages. Further studies are needed to assess the composition of the CM and to study other possible modulations, such as pro or anti-tumorigenic differentiation undergone by the macrophages.

# Exploring the potential of coffee leaves extract for wound healing treatment



## Author

Fernanda Maria Pinto Vilela - Universidade Federal de Juiz de Fora (UFJF)  
Valéria De Mello - Universidade Federal de Juiz de Fora (UFJF)  
Wanderleya Toledo dos Santos - Universidade Federal de Juiz de Fora (UFJF)  
Ana Cláudia Chagas de Paula Ladvocat - Universidade Federal de Juiz de Fora (UFJF)  
Fernanda Brito Leite - Universidade Federal de Juiz de Fora (UFJF)  
- Universidade Federal de Juiz de Fora (UFJF)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), project number APQ-02555-18



## Keywords

Coffee leaves, cytotoxicity, wound healing

## Abstract

Coffee leaves are considered by-products, however, they are sources of bioactive compounds such as mangiferin, which is not found in the coffee bean, chlorogenic acids, and caffeine. These compounds give the extract antioxidant, antityrosinase, anticollagenase, antielastase, anti-inflammatory, antimicrobial, emollient, and antilipogenic properties. In this study, an ethanolic extract was prepared from *Coffea arabica* leaves, and the amounts of 5-caffeoylquinic acid (5-CQA), caffeine, and mangiferin were determined using HPLC. The extract's cytotoxicity was assessed at doses ranging from 3.9 to 2000  $\mu\text{g}/\text{mL}$  in the human fibroblast cell line 1059SK using the MTT test. Then, the cell migration test was conducted using the in vitro wound healing assay using the scratch test with extract doses of 50, 500, and 2000  $\mu\text{g}/\text{mL}$ . The contents of 5-ACQ were 20.82 mg/g of extract, caffeine was 51.2 mg/g, and mangiferin was 21.705 mg/g. The cells remained viable at all concentrations tested. The extract induced cell migration 24 hours after treatment. At 50  $\mu\text{g}/\text{mL}$ , migration rates were 68.1% after 24 hours and 92.45% after 48 hours of treatment. At 500  $\mu\text{g}/\text{mL}$  of extract, the migration rate increased to 93% and 95.08% after 24 and 48 hours of treatment, respectively. Based on the findings, it was feasible to underscore the therapeutic potential of the coffee leaves, a byproduct, encouraging the development of new therapeutic approaches, such as topical formulations, for skin healing.

# Effectiveness of Liposomal Coffee Canephora Stem Cell Extract for Melasma Management



## Authors

Marcio Fronza - PPGCF - Universidade Vila Velha (UVV)  
Marcia Paula de Oliveira Sales Gabrieli - PPGCF - Universidade Vila Velha (UVV)  
Victor Paulo Mesquita Aragão - PPGCF - Universidade Vila Velha (UVV)  
Mariana Magalhães Marchesi Ribeiro Celestino - PPGCF - Universidade Vila Velha (UVV)  
Misleini de Oliveira Sales Gabriel - PPGCF - Universidade Vila Velha (UVV)  
Marcio Guidoni - PPGCF - Universidade Vila Velha (UVV)  
Iana Soares Pessoa - PPGCF - Universidade Vila Velha (UVV)  
Flavia Vitorino de Araujo Porto - PPGCF - Universidade Vila Velha (UVV)  
Antônio Domingos de Souza Junior - PPGCF - Universidade Vila Velha (UVV)  
Samara Peixoto Rodrigues - PPGCF - Universidade Vila Velha (UVV)  
Marcela Gonçalves Santana - PPGCF - Universidade Vila Velha (UVV)  
Tamires Cruz dos Santos - PPGCF - Universidade Vila Velha (UVV)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Fundação de Amparo à Pesquisa do Espírito Santo (FAPES) under Grants 2021-NBD7G and 2023-L72KT, by the National Council for Scientific and Technological Development (CNPq) under Grant 312015/202



## Keywords

Plant stem cells, Coffea canephora, Melasma

## Abstract

Aging is a continuous and complex process influenced by extrinsic and intrinsic factors. In this sense, exposure to ultraviolet radiation is the main cause of the appearance of blemishes on the skin, including melasma. Plant stem cell extracts may represent an effective alternative to improve skin quality. Therefore, this study aimed to evaluate the in vivo effects of a liposomal stem cell extract formulation from Coffee canephora (LSCECC) for the treatment of melasma. For this purpose, the clinical efficacy of LSCECC was studied in 23 patients for 60 days. The liposome was developed and characterized through the dynamic light scattering technique, atomic force microscopy and transmission electron microscopy. Clinical improvements in the treatment of melasma were evaluated using a sociodemographic questionnaire, assessment of improvement in quality of life with the MELASQOL (Melasma Quality of Life Scale), calculation of reduction in melasma area, assessment of improvement in severity index using the MASI (Melasma Area and Severity Index), and photographic records. The sociodemographic data showed that the patients with different lifestyles and histories of blemishes. After treatment, patients self-declare a significant improvement in quality of life, including mental health and social interaction. The LSCECC demonstrated to be effective in reducing the area affected by melasma in treated patients. In addition, the MASI value decreased linearly at the end of the study, demonstrating the effectiveness of the product in reducing skin blemishes. Thus, the study demonstrated the high therapeutic efficacy of the plant stem cell extract of *C. canephora* in the treatment of melasma by reducing the area and severity of skin manifestations and, consequently, improving the quality of life of the patients.

# Study of the Pectin Extraction Process From Renewable Resources



## Author

Patricia Dias - Universidade Federal Fluminense (UFF)  
Mourão, S. C. - Universidade Federal Fluminense (UFF)  
Muri, E. M. F. - Universidade Federal Fluminense (UFF)  
Falcão, M. A. L. - Universidade Federal Fluminense (UFF)  
Santos, S. V. S. - Universidade Federal Fluminense (UFF)  
Spitz, O. - Universidade Federal Fluminense (UFF)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Universidade Federal Fluminense



## Keywords

Pectin, Acid Citric, Waste

## Abstract

Biodegradable polymeric materials, decomposing through microbial activity or sunlight, are gaining attention for their renewable resource base and diverse industrial applications such as food, cosmetics, textiles, pharmaceuticals, and bioengineering. This study aims to optimize the pectin extraction process for better economic viability and quality using response surface analysis and Central Composite Design (CCD). Three independent variables were assessed: pH, citric acid concentration, and reaction time, with temperature fixed at 90°C. These variables were tested at five levels, evaluating extraction yield, galacturonic acid content, and degree of esterification using titration and infrared spectroscopic analysis. Statistical analysis with Statistica software identified significant factors affecting pectin yield and quality. Results showed wide variation in pectin yield, consistent with the experimental design, suggesting citrus fruit peels could be viable for pectin extraction using organic acids. The Pareto Chart showed pH and citric acid concentration positively affected yield, with significant linear effects and interactions (pH-concentration and pH-time) having p-values below 0.05. Reaction time and quadratic effects did not significantly impact yield. The response surface graph indicated higher yield with increased pH and citric acid levels. These variations highlight challenges in industrial-scale pectin extraction. Higher pH values (>5) are less explored, and potential interactions between citric acid and ethanol might cause interference during extraction, possibly leading to Fischer Esterification. Methoxyl content varied (1.55%-9.92%) but was acceptable within a regression model. In conclusion, extracting pectin from citrus fruit peels using organic acid is feasible, but further testing is needed to refine parameters significantly impacting yield. pH, ideally between 1.3-2.7, appears critical, supported by scientific literature.



# Establishment of bacterial bioprocesses with potential for biodegradation of polyethylene and production of PHA



## Author

Bruno Melo - Universidade de Brasília (UNB)  
Beatriz de Oliveira Lobo - Universidade de Brasília (UNB)  
Barbara de Oliveira Moura - Universidade de Brasília (UNB)  
Gabriela Bispo Rosa - Universidade de Brasília (UNB)  
Micaelle França da Rocha - Universidade de Brasília (UNB)  
Serena Pireneus Oliveira Borges de Pina - Universidade de Brasília (UNB)  
Talita Fernandes Nunes - Universidade de Brasília (UNB)  
Mariana Mattioli Portugal - Universidade de Brasília (UNB)  
Ricardo Henrique Krüger - Universidade de Brasília (UNB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding



## Keywords

Bioprocess, biodegradation, PHA

## Abstract

Current post-consumer plastic management strategies are insufficient, leading to substantial ecological damage and the release of toxic compounds, which have resulted in the mortality of various animal species. Polyhydroxyalkanoate (PHA) is a biopolymer produced via bioprocesses, notable for its biocompatibility and biodegradability, making it suitable for numerous industrial applications and a viable alternative to petroleum-based plastics. However, PHA production encounters significant challenges, including high costs and environmental impacts. Therefore, developing efficient industrial processes for managing post-consumer plastics and exploring biodegradation products is crucial to address global sustainability issues. Experiments were conducted to assess the plastic degradation capacity of the bacteria *Comamonas* sp. and *Alcaligenes* sp., and to determine optimal conditions for PHA production. Biomass production data for these bacterial strains were obtained through experiments conducted in Erlenmeyer flasks and bioreactors, evaluating three temperatures (25°C, 30°C, and 37°C) and three pH levels (5, 7, and 9) for each bacterium. To establish optimal conditions for bacterial biomass production, various temperatures were assessed, and a bacterial growth curve was constructed by evaluating optical density (OD<sub>600</sub>) and performing cell counts on plates. Inocula were added to Erlenmeyers with culture medium and sampled every 2 hours to monitor cell growth and metabolite production. At 30°C, both *Comamonas* sp. and *Alcaligenes* sp. exhibited a significant increase in growth rate. Conversely, at 37°C, both species demonstrated a decline in growth after 12 hours of incubation. The results indicate that 30°C is the optimal temperature for maximizing growth rate and potential PHA production. Based on these findings, future experiments will focus on evaluating the capacity of these bacteria to degrade polyethylene, produce PHA, and perform other biotechnological activities.

# Safety and antimutagenic potential of *Leonotis nepetifolia* leaf extract.



## Author

Antônio João Viana Batista - Universidade Vila Velha (UVV)  
Lauro Bendel Junior - Universidade Vila Velha (UVV)  
Karynna Alcantara Dutra - Universidade Vila Velha (UVV)  
Antônio Ricardo Alexandre Brasil - Universidade Vila Velha (UVV)  
Girlandia Alexandre Brasil Amorim - Universidade Vila Velha (UVV)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CNPq



## Keywords

Friar's cord; Bioinformatics; Cytotoxicity; Anticancer.

## Abstract

*Leonotis nepetifolia* (*L. nepetifolia*), known as lion's ear, is a plant whose tea is traditionally used to treat inflammatory diseases such as asthma and bronchitis, and is also used as a uterine anti-hemorrhagic. However, few studies have evaluated its safety and the potential anti-mutagenic properties of its aerial parts extract. Therefore, this work aims to assess the biological potential through bioinformatics and determine the chemical composition, toxicity, antioxidant activity, and anti-mutagenic properties of the ethanolic extract of the leaves and inflorescences of *L. nepetifolia*. Protein and peptide prospecting was conducted using UNIPROT and BIOPEP databases with Python. Phytochemical prospecting was carried out using thin-layer chromatography (TLC), and the total phenolic content was quantified by the Folin-Ciocalteu method. Flavonoids were quantified through their reaction with aluminum chloride, and antioxidant activity was evaluated using ABTS, DPPH, and FRAP techniques. In vivo tests involved male Swiss mice (CEUA-471/2018), divided into two assays: acute toxicity (OECD-420) and micronucleus (mutagenic and anti-mutagenic). Bioinformatics prospecting revealed peptides with anti-diabetic, anti-hypertensive, and antioxidant activities. TLC analysis demonstrated the presence of flavonoids and terpenes in all extracts. Both extracts exhibited antioxidant activity, with no toxic effects, and showed cytoprotective and anti-mutagenic activities. Thus, the extracts of *L. nepetifolia* proved to be a good source of phenolic compounds and bioactive peptides with strong antioxidant activity, safe for use even at high doses (2000 mg/kg), and with notable cytoprotective and anti-mutagenic properties. Further studies should be conducted to investigate their biological actions and potential use in traditional medicine.

# Antioxidant, antiglycant, antityrosinase and antibacterial activity of *Eugenia brasiliensis* extract and fractions for potential application as phytocosmetics



## Author

Raquel Oppermann- Universidade do Vale do Itajaí (UNIVALI)  
Mayra Alice Corrêa Pitz - Universidade Regional de Blumenau (FURB)  
Carlos Rafael Vaz - Universidade do Vale do Itajaí (UNIVALI)  
Isabel Daufenback Machado - Universidade Regional de Blumenau (FURB)  
José Roberto Santin - Universidade do Vale do Itajaí (UNIVALI)  
Michele Debiasi Alberton - Universidade Regional de Blumenau (FURB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding



## Keywords

antioxidant, tyrosinase, phenolic compounds

## Abstract

Skin care is an important topic to health and well-being and natural compounds have become targets of research on new actives. The aim of this study was to evaluate the crude hydroalcoholic extract (CHE) and fractions of *E. brasiliensis* leaves as a potential application for skincare phytocosmetic. CHE was obtained by maceration and partitioned in hexane fraction (HF), dichloromethane fraction (DF), ethyl acetate fraction (EAF) and aqueous fraction (AF). They were analyzed for total phenolic compounds, total flavonoids, total flavanols, anthocyanins and total contents of  $\beta$ -carotene and lycopene by spectrophotometric method in addition to their antioxidant, antiglycant and antityrosinase in vitro activity. In vitro wound healing activity was evaluated by Scratch assay and the toxicity was evaluated by MTT and Agarose overlay in murine fibroblast, hemolysis assay in human erythrocytes and HET-CAM assay. Antibacterial activity against *S. aureus* and *S. epidermidis* was performed by MIC assay. CHE and AF had the highest levels of total phenolics and total flavanols. CHE, EAF and AF showed lower IC<sub>50</sub> for DPPH test, higher superoxide anion scavenging capacity when compared to the standard gallic acid and higher cooper reducing potential. AF had a greater capacity to scavenging nitric oxide when compared to the standard gallic acid. For antiglycant activity, EAF showed a higher percentage of oxidative glycation inhibition. AF and EAF demonstrated better IC<sub>50</sub> in tyrosinase enzymatic inhibition assay. All fractions, except for DF, had a score of 0 (non-irritant) on HET-CAM assay, CHE and AF had absence of cytotoxicity in L929 cells and hemolysis absence at tested concentration. The EAF showed moderate antibacterial activity against *S. aureus* and *S. epidermidis*. CHE, AF and EAF of *E. brasiliensis* leaves showed promising biological activities, and these results seem to be related partly to their constitution in phenolic compounds.

# Feeding with different concentrations of green banana flour shows a neuroprotective effect against iron-induced oxidative stress in *Drosophila melanogaster*



## Author

Vitória Tadeu - Universidade Federal do Pampa (UNIPAMPA)  
Caroline Lacerda Nogueira - Universidade Federal do Pampa (UNIPAMPA)  
Murilo Ricardo Sigal Carriço - Universidade Federal do Pampa (UNIPAMPA)  
Rafael Roehrs - Universidade Federal do Pampa (UNIPAMPA)  
Elton Luis Gasparotto Denardin - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding



## Keywords

Iron, Stress, *Drosophila melanogaster*

## Abstract

Stress factors generate metabolic and behavioral adaptation, which triggers an increase in energy supply. In invertebrates, the main stress response pathway is mediated by octopamine. Iron (Fe) is an essential micronutrient in the biological processes of living beings, but excess iron in the body is extremely harmful and pathological to cells and can lead to stress. Green banana flour (GBF) has been studied in the prevention and treatment of many diseases. The objective of this study was to evaluate octopamine levels in *D. melanogaster* after intoxication by feeding with green banana flour and subsequent acute exposure to Fe. A total of 720 flies were divided into six groups of 120 flies each, and treated with Fe for eight days, according to the following groups: 1. control (8 days with agar); 2. Fe (4 days in agar and 4 days of exposure to 10 mmol Fe); 3. GBF10 (4 days with 10 mg/mL GBF and 4 days with agar); 4. GBF50 (4 days with 50 mg/mL GBF and 4 days with agar); 5. GBF10 Fe (4 days with 10 mg/mL GBF and 4 days of exposure to 10 mmol Fe); 6. GBF50 Fe (4 days with 50 mg/mL GBF and 4 days of exposure to 10 mmol Fe). After treatment, octopamine levels of flies were analyzed by HPLC-DAD. The values were analyzed using GraphPad Prism and Tukey post-test. The results showed an increase in octopamine concentrations for the group exposed to iron, while the groups fed with flour and Fe GBF10 Fe and GBF50Fe did not show an increase in octopamine levels when compared to the control. These results show that in situations of iron overload the body can release octopamine in response to stress. The GBF10 Fe and GBF50 Fe groups were effective in protecting flies against increased stress caused by Fe poisoning. In conclusion, the results showed that green banana flour has components that help keep octopamine levels low in flies exposed to iron.

# PhotoMetrix PRO: utilizing a smartphone app as an alternative tool for protein quantification in spectrophotometric analysis



## Author

Caroline Betim Beralde - Universidade Federal do Pampa (UNIPAMPA)  
Marina Diaz Rodrigues - Universidade Federal do Pampa (UNIPAMPA)  
Murilo Ricardo Sigal Carriço - Universidade Federal do Pampa (UNIPAMPA)  
Thainá Silva Perez - Universidade Federal do Pampa (UNIPAMPA)  
Maria Eduarda Cebage Ferreira - Universidade Federal do Pampa (UNIPAMPA)  
Vitória Joaquina Tavares Resende - Universidade Federal do Pampa (UNIPAMPA)  
Elton Luis Gasparotto Denardin - Universidade Federal do Pampa (UNIPAMPA)  
Rafael Roehrs - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES



## Keywords

PhotoMetrix PRO, spectrophotometric analysis, smartphone app

## Abstract

Spectrophotometry is a technique utilized for measuring color intensity to quantify substances across different light wavelengths. Widely applied in pharmaceutical, chemical, and food sectors, this method led to the development of the PhotoMetrix PRO smartphone application. This app enables colorimetric analysis through image capture, offering ease of use for various tests, including total protein quantification. Calibration involved creating a curve using albumin concentrations of 5, 10, 15, 20, and 25 mg/L. The analysis, involving comassie brilliant blue reaction in a 96-well microplate, required adding 20  $\mu$ L of sample and 160  $\mu$ L of 0.01% comassie blue. Tests were conducted in quintuplicate using PhotoMetrix PRO in univariate mode, with a 16x16 setting to avoid microplate wall interference, and a SpectraMax® M5 plate reader at 595 nm. Comparison criteria included linearity, repeatability, LOD, and LOQ. The plate reader's curve parameters were:  $y=0.0161x+0.1959$ ;  $R^2= 0.9780$ ,  $RSD = 7.45\%$ ,  $LOD 4.07$  mg/L, and  $LOQ 5$  mg/L. PhotoMetrix PRO results showed:  $y = 3.5199x + 108.169$ ;  $R^2= 0.9752$ ;  $RSD = 0.38\%$ ;  $LOD$  of 0.44 mg/L and  $LOD$  of 5 mg/L. The Photometrix PRO method proves to be a cost-effective, sensitive, and reliable alternative for protein quantification analysis, as evidenced by the validation parameters.

# Development and assessing an antioxidant bioinput from dry coffea arabica grounds extract



## Author

Ana Carolina de Oliveira - Universidade do Vale do Itajaí (UNIVALI)  
Ruth Meri Lucinda da Silva - Universidade do Vale do Itajaí (UNIVALI)  
Gizelle Inácio Almerindo - Universidade do Vale do Itajaí (UNIVALI)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES e CNPQ



## Keywords

Coffee (Coffea arabica), Solid waste, Spray dryer

## Abstract

Coffee is one of the most important raw materials in the agro-industry worldwide, with the highest commercial value. According to the latest report released by National Supply Company, in May 2023, arabica coffee production totaled 37,93 million bags, representing a gain of 15,9% compared to the same period of the previous harvest. The Brazilian Association of Public Cleaning and Special Waste Companies report revealed that 81,8 million tons of urban solid waste (USW) were generated in Brazil in 2022. In this context, coffee grounds have been the subject of significant research aimed at extracting their antioxidant compounds, due to their composition containing caffeine, tannins, and polyphenols such as chlorogenic acid (CGA). Thus, the present research aimed to develop a dry extract of Coffea arabica grounds as an active pharmaceutical ingredient with antioxidant potential. The coffee grounds used in this research originate from 100% arabica beans, specifically Catuaí 62 yellow and Catuaí 44 red varieties, grown in Serra do Caparaó-MG. The coffee grounds were obtained from Sun Coffee Cafeteria, located in Itajaí – SC, resulting from the accumulation of different brewing methods using 100% arabica beans. For obtaining the dry extract, spray drying was employed using a binary mixture of modified starch and microcrystalline cellulose (60:40) as drying adjuvant, with assays according to the Box-Behnken experimental design. Characterization of the dry extracts included analyses of dry residue, total phenolic content (TPC), antioxidant activity (EC50), chlorogenic acid content by HPLC-DAD, thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), and scanning electron microscopy (SEM). Thus, for use as an active pharmaceutical antioxidant ingredient, the system composed of modified starch and microcrystalline cellulose showed promising physical properties, chemical composition, and antioxidant activity.

# Evaluation of in vitro enzymatic inhibition of bioactive compounds from Brazilian medicinal plants with therapeutic potential for SARS-CoV-2 infection, selected from an antiviral database - avMpNp DB.



## Author

Daniela Quadros de Azevedo - Universidade Federal de Minas Gerais (UFMG)  
Mateus Sá Magalhães Serafim - Universidade Federal de Minas Gerais (UFMG)  
Thaís Helena Maciel Fernandes - Universidade Federal do Rio Grande do Sul (UFRG)  
Ellen Gonçalves de Oliveira - Universidade Federal de Minas Gerais (UFMG)  
Rachel Oliveira Castilho - Universidade Federal de Minas Gerais (UFMG)  
Vinícius Gonçalves Maltarollo - Universidade Federal de Minas Gerais (UFMG)  
Anthony J. O'Donoghue - University of San Diego (UCSD)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES. 88887.595578/2020-00.



## Keywords

medicinal plant, bioactive compound, database

## Abstract

**Introduction:** Results from medicinal plants (MPs) and bioactive compounds (BCs) with antiviral activity have been obtained by different research groups. With this in mind, avMpNp DB (Antiviral Medicinal Plants and Natural Products database) has been developed to play a relevant role as a source for organising and disseminating knowledge about antiviral BCs and to solve problems such as the search for new antiviral drugs. **Objective:** Demonstrate in vitro enzymatic inhibition (EI) of phenolics by avMpNp DB, against SARS-CoV-2 Mpro. **Methodology:** Recombinant SARS-CoV-2 Mpro was expressed and purified in *E. coli*. The EI of phenolic compounds was evaluated at a concentration of 10 or 20  $\mu\text{M}$ . The IC<sub>50</sub> was determined for BCs that inhibited the enzyme activity by 50% or more and values were calculated by non-linear regression. **Results:** Analysis of the in silico and in vitro studies of BCs stored in avMpNp DB, selected caffeic acid, gallic acid epicatechin, that inhibited at least 50% of the activity of SARS-CoV-2 Mpro at 20  $\mu\text{M}$ . IC<sub>50</sub> for caffeic acid, gallic acid and epicatechin was promising, with values of  $15.795 \pm 0.155 \mu\text{M}$ ,  $6.308 \pm 0.296 \mu\text{M}$  and  $8.078 \pm 0.364 \mu\text{M}$ , respectively. Caffeic acid is part of the chemical matrix (CM) of *Lippia alba* (Mill.) N.E. Br. ex Britton & P. Wilson, which has been shown anti-Zika and anti-Dengue virus activity. In a second step, a new evaluation about BCs was made. Among the selected compounds, galocatechin, epigallocatechin and epigallocatechin gallate inhibited at least 50% of the activity of SARS-CoV-2 Mpro at 10  $\mu\text{M}$  and the IC<sub>50</sub> values obtained were  $2.33 \pm 0.59 \mu\text{M}$ ,  $0.096 \pm 0.01 \mu\text{M}$  and  $0.05 \pm 0.004 \mu\text{M}$ , respectively. These CBs, epicatechin and gallic acid are part of the CM *Stryphnodendron adstringens* (Mart.) Coville, a plant with potential antiviral activity against poliovirus type 1. **Conclusions:** After evaluated of 205 BCs stored in avMpNp DB, phenolic compounds showed potential promise for the development of new drugs against SARS-CoV-2.

# Chemical profile and wound healing in vitro property of *Calophyllum brasiliensis*



## Authors

Luciana Rabelo Quintela Iunes Araújo - Universidade Federal do Espírito Santo (UFES)  
Jéssica Raquel Borges Monteiro - Universidade Federal do Espírito Santo (UFES)  
Rodrigo de Almeida Romagna- Universidade Federal do Espírito Santo (UFES)  
Mahyara Rodrigues Dias Schultz - Universidade Federal do Espírito Santo (UFES)  
Rita de Cássia Ribeiro Gonçalves - Universidade Federal do Espírito Santo (UFES)  
Ricardo Pinto Schuencka - Universidade Federal do Espírito Santo (UFES)  
Ricardo Machado Kuster - Universidade Federal do Espírito Santo (UFES)  
Rodrigo Rezende Kitagawa - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

FAPES (Edital nº20/2022), CNPq (Edital nº04/2021), CAPES and UFES



## Keywords

Guanandi, wound healing, L929 human fibroblast

## Abstract

Every year, millions of people around the world develop scars in response to skin injuries following surgery, trauma or burns. In this context, the study of natural products as healing agents has been intensifying due to the substances that can influence one or more phases of healing. *Calophyllum brasiliense* Cambess (Clusiaceae), popularly known as guanandi, is found in the tropical rain forests in Brazil and it has been shown to be a rich source of bioactive compounds, including coumarins, xanthonones, triterpenoids and bioflavonoids. It has been widely used in folk medicine to treat a variety of maladies including pain, inflammation, and rheumatism. Despite its extensive use, only a few biological activities have been reported in the scientific literature including wound healing. In the present study, we evaluated the chemical profile, antioxidant, antibacterial and wound healing properties of methanol extract from *C. brasiliense* fruit peels. Chemical profile was analyzed by mass spectrometer (ESI FT-ICR MS). The antibacterial activity was performed with *Staphylococcus aureus* by broth microdilution test. The antioxidant potential was evaluated by scavenging of DPPH. In vitro scratch assay using L929 human fibroblast cell line was performed to evaluate the wound healing properties of *C. brasiliense* methanol extract. Phytochemical data from ESI FT-ICR MS analysis suggest the presence of coumarins (5) like mamea A/BA, cromanonones (3) and xanthonones (5), jacareubin. The antioxidant result showed low inhibition potential of DPPH with CE50 of 228 µg/ml. The MeOH extract was effective against *S. aureus* at 2,5 mg/ml (CIM e CBM). In the scratch assay, MeOH extract with non-toxic concentrations of 3.125µg/ml (22.4%) and 6.25 µg/ml (26.03%) showed significant effect on L929 cells compared to the control. Considering the presented results *C. brasiliensis* peels fruit can be promising in future studies to developing of new herbal medicine to treat tissue scars.



# Comparison Of The Chemical Profile Of Probable Chemotypes Of *Lippia alba* (Mill.) N. E. Brown, Using Gas Chromatography Coupled Mass Detector (GC-MS)



## Author

Natalia Koehler - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Capes and Fundação Araucária



## Keywords

*lippia alba*, gc-ms, Verbenaceae

## Abstract

**Introduction:** *Lippia alba*, also known as Melissa, Salva, and Sana-lo-todo, is a plant species belonging to the Verbenaceae family. It is native to Central and South America. Its leaves are aromatic and used in herbal infusions due to their variety of traditional medicinal uses, such as digestive, for colic, and as an anxiolytic. It is also indicated for migraines, colds, and flu. This study aimed to compare the chemical profile of extracts obtained from the leaves of different individuals of *Lippia alba* (Mill.) N. E. Brown with different sensory characteristics. **Methods:** The plant material was collected at the Medicinal Plants Didactic Garden of the Federal University of Santa Catarina and at Porto da Lagoa in the municipality of Florianópolis, Santa Catarina. These leaves were subjected to the following extraction processes: leaf washing, infusion with subsequent fractionation in solid phase (SPE-C18), and headspace. These were chemically characterized by gas chromatography coupled to a mass detector with liquid injection and headspace injector, using the NIST library for compound identification. **Results:** The results suggest the chemical variability of the *L. alba* specimens. It was found that the individuals known as Salva, collected at Porto da Lagoa and the Garden, presented the same chemotype, with the presence of linalool and beta-copaene, and linalool in the infusion. For the individuals known as Melissa, collected at the same locations, a chemotype with the presence of citral and carveol was observed, and citral also in the infusion. The Sana-lo-todo had a different chemotype, with the presence of major carvone. **Conclusion:** The study demonstrated the chemical variability among individuals of *Lippia alba*, highlighting the presence of different compounds in the popular chemotypes Salva, Melissa and Sana-lo-todo. These results can contribute to the appropriate use of each *Lippia alba* chemotype in medicinal and therapeutic applications.

# Extracts From The Processing Of Litchi (*Litchi chinensis*) By-Products: Antioxidant Potential And Application In Facial Masks.



## Author

Juliana Olivato - Universidade Estadual de Ponta Grossa (UEPG)  
Anna Caroline Lopes - Universidade Estadual de Ponta Grossa (UEPG)  
Ana Beatriz Klosowski - Universidade Estadual de Ponta Grossa (UEPG)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Capes and Fundação Araucária



## Keywords

Bioactives; cosmetic; natural extracts

## Abstract

The by-products from fruit processing represents an unexplored source of bioactives which are mostly discarded or underutilized. Lychee (*Litchi chinensis*) peel and seeds are an interesting source of phenolic compounds with antioxidant properties, which can reduce oxidative damage to cells and making them useful in cosmetic products such as anti-aging formulations. This work aimed to develop a peel-off facial mask using the extract from by-products of lychee processing. The by-products were collected, dried, standardized, and submitted to maceration and Soxhlet techniques to obtain the lychee by-product extract. (LBE). The total phenolic content of LBE, obtained by the Folin Ciocalteu method, was  $401.2 \pm 0.5$  mg EAG/g. A high antioxidant efficacy was exhibited by the antioxidant activity of LBE, with an IC<sub>50</sub> of 0.93 for the ABTS method and an IC<sub>50</sub> of 3.97 for the DPPH method. It is suggested that LBE is effective in neutralizing free radicals and preventing oxidative stress. LBE was then added to a peel off mask formulation, based on poly (vinyl alcohol), in a concentration of 5% (wt) (LBE5). A control formulation, without LBE (LBE0), was also produced and their physicochemical characteristics were evaluated. The LBE5 formulation demonstrated stability, spreadability and viscosity similar to that of LBE0. The spreadability of the samples LBE5 and LBE0 was adequate, allowing for easy and uniform application on the skin. The drying time of the LBE5 formulation was 32 min and for LBE0 was 17 min, which indicates that LBE increased the drying time of the mask. The centrifugation test resulted in a precipitate formation for the LBE5, which was absent in the LBE0. The viscosity of both samples was similar, and no influence of the LBE on the viscosity was observed. The LBE5 formula presents a promising sustainable solution for peel-off masks, increasing the value of the by-product and promoting a circular economy.

# Chemical description and evaluation of the antioxidant power of an ethanolic *Curcuma longa* Linn extract



## Author

Claudia Masrouah Jamal - Universidade Federal do Espírito Santo (UFES)  
Bernardo de Jesus Pavuna - Universidade Federal do Espírito Santo (UFES)  
Christopher William Fagg - Universidade Federal do Espírito Santo (UFES)  
Damaris Silveira - - Universidade Federal do Espírito Santo (UFES)  
Marcos André de Paula Pinheiro - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES



## Keywords

*Curcuma longa*, Curcuminoids, HPLC-DAD

## Abstract

*Curcuma longa* Linn (Zingiberaceae) has been used in different ways to treat multiple illnesses. The rhizome is the most used organ of the plant. Curcuminoids are the main markers for the genera with the highest expression of curcumin, desmethoxycurcumin, and bisdesmethoxycurcumin. Curcuminoids are known for presenting antioxidant properties. Therefore, this work aimed to determine the chemical profile and evaluate the antioxidant capacity of a *C. longa* extract. The rhizomes were subjected to Soxhlet extraction using ethanol as solvent. A forced degradation assay was carried out in the ethanolic extract solution with acid, alkaline, heat, and oxidative degradation. The chromatographic profile was obtained by High-Pressure Liquid Chromatography (HPLC) and Liquid Chromatography coupled to quadrupole time of flight mass LC/(-)ESI-Q-TOF MS. The antioxidant activity was evaluated by DPPH• radical scavenger method. In the forced degradation assay, curcuminoids undergo a slower degradation in acidic conditions than in alkaline conditions. The HPLC-DAD analysis identified curcuminoids by comparing them with a standard. The quantification showed  $437.73 \pm 1.11$  mg curcumin/g extract, resulting in yield values of curcumin of 40 - 45%. LC/(-)ESI-Q-TOF MS analysis allowed the identification of several compounds such as sesquiterpenes, monoterpenes, diphenylheptanoids, simple phenolic compounds, sugars, phenylpropanoids, flavonoids. The antioxidant activity was expressed as IC<sub>50</sub> of  $24.49 \pm 1.69$  µg/mL. However, it is important to note that the use of curcuminoids as antioxidants in formulations depends on strict pH control to guarantee the stability and hydrogen donor properties of the active.

# Bright horizons: Unveiling safe biocolorant from fungi with *C. elegans* as experimental model



## Author

Talita Cristina Mena Segato - Universidade de Sorocaba (UNISO)  
Francisco Javier San Miguel Novoa - Pontifícia Universidad Católica de Chile (UC Chile)  
Vicente André Araya Salcedo - Pontifícia Universidad Católica de Chile (UC Chile)  
Erika Leão Ajala Caetano - Universidade de Sorocaba (UNISO)  
Maria Fernanda Hornos Carneiro - Pontifícia Universidad Católica de Chile (UC Chile)  
Denise Grotto - Universidade de Sorocaba (UNISO)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES



## Keywords

*C. Elegans*, Biocolorants, Avaliação de segurança

## Abstract

Synthetic dyes are widely used in the food industry due to their low cost and high availability. However, growing evidence of their adverse health and ecological effects has driven the search for safer alternatives. In this context, the production of dyes from microorganisms, such as ascomycete fungi, emerges as a promising solution. This study evaluated the safety of a new azaphilone biocolorant, obtained from the fungus *Talaromyces amestolkiae*, using the alternative model *Caenorhabditis elegans*. The nematodes were cultured on agar plates with a layer of *Escherichia coli*, which served as a food source. The biocolorant's toxicity was determined through a dose-response survival curve (ranging from 31.2 to 500 mg/mL of the biocolorant) and behavioral tests represented by area, length, and motility. Data were reported as mean and standard deviation, and differences were demonstrated by one-way ANOVA, followed by Scheffé's post hoc test. The results showed that the nematodes had 100% survival when exposed to all doses of the biocolorant. There was a significant increase in length at the highest dose, but no significant changes in the area parameter. On the other hand, all doses significantly increased the nematodes' motility compared to the control group. This increase in motility may be associated with a disturbance in dopamine receptors, potentially related to neurodegenerative diseases. However, it is worth noting that the biocolorant contains 1.54% glucose, a substance to which nematodes may be sensitive. In conclusion, although the azaphilone biocolorant did not exhibit lethal toxicity, the observed behavioral change highlights the need for further studies to assess its neurotoxic impact and ensure its safety for commercial use, especially at lower concentrations.

# Manilkara salzmannii (A.DC.) H.J.Lam. from Atlantic Forest biome: ultrasound-assisted extraction and anti-Trichomonas vaginalis activity.



## Author

Larissa Silva - Universidade Federal da Bahia (UFBA)  
Fernanda Gomes Cardoso - Universidade Federal da Bahia (UFBA)  
Ingrid Caroline da Silva - Universidade Federal da Bahia (UFBA)  
Joseane Cardoso Gomes de Alencar - Universidade Federal da Bahia (UFBA)  
Bruno Nicolau Paulino - Universidade Federal da Bahia (UFBA)  
Tiana Tasca - Universidade Federal da Bahia (UFBA)  
Glória Narjara Santos da Silva - Universidade Federal da Bahia (UFBA)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

NCT 3D Saúde: This study is part of the National Institute of Science and Technology in 3D printing and Advanced Materials Applied to Human and Veterinary Health - INCT\_3D-Saúde, funded by CNPq, Brazil (Grant #406436/2022-3)



## Keywords

Atlantic Forest plant, Trichomoniasis, Environment-friendly extraction

## Abstract

*Manilkara salzmannii* (A.DC.) H.J.Lam. (Sapotaceae), also known as “maçaranduba”, is native and endemic specie to Brazil and occurs in the Atlantic Forest (Resting area). *Manilkara* species have already been described as antiparasitic, antimicrobial and antitumor. These activities may be attributed to the presence of secondary metabolic, such as an uncommon bidesmosic saponin from *Manilkara rufula* (Miq.) H.J.Lam described as antitrichomonal. The trichomoniasis is caused by *Trichomonas vaginalis*, the most common non-viral sexually transmitted disease worldwide. Considering the treatment of trichomoniasis relies on one class of drugs, 5-nitroimidazoles, and the increasing of drug resistance is the main cause of treatment failure, new drugs are urgently needed. Then, the aim of this study was to evaluate the activity against *T. vaginalis* of *M. salzmannii*, plant still unexplored in the field of pharmacological. In order to carry out the investigation, the crude hydroalcoholic extract (CHE) of the dried leaves (35g, 150mL of EtOH 80%) was achieved by using ultrasound-assisted extraction (UAE) in SONICS VCX505 for 10min. UAE is a green efficient alternative to traditional extraction techniques since the extraction time and temperature are reduced, preserving the stability of extracted compounds. CHE (yield = 17.4%) was partitioned by the liquid-liquid extraction resulting in the dichloromethane (DF; yield = 1.91%) and ethyl acetate (EAF; yield = 11.29%) fractions. Anti-*T. vaginalis* assay was performed in vitro, by treating the trophozoites with 1.0mg/mL for 24h. DF reduced the parasite viability to 9.20%. Then it was evaluated DF in a concentration range from 1.0 to 0.25mg/mL, displaying IC<sub>50</sub> 0.626mg/mL. Overall, the results demonstrated for the first time the pharmacological investigation of *M. salzmannii*, and revealed the nonpolar fraction as a new perspective to obtain compounds, from an eco-friendly extraction technology, to treat the infection caused by *T. vaginalis*.

# Unveiling the Antibacterial Potential and Cyclopeptide Diversity of *Metarhizium anisopliae*



## Author

Caroline de Moura Costa - Universidade Federal de Mato Grosso do Sul (UFMS)  
Fernanda Motta Ribeiro DA SILVA - Universidade Federal de Mato Grosso do Sul (UFMS)  
Amanda Galdi BOARETTO - Universidade Federal de Mato Grosso do Sul (UFMS)  
Denise Brentan DA SILVA - Universidade Federal de Mato Grosso do Sul (UFMS)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CNPQ, CAPES, FUNDECT



## Keywords

liquid chromatography-mass spectrometry (LC-MS/MS), biotechnological potential, destruxins

## Abstract

*Metarhizium anisopliae*, an entomopathogenic fungus, has been extensively applied for biological control of pests across various agricultural crops. Cyclopeptides are produced by *Metarhizium spp.* strains, such as destruxins. This compound exhibits insecticidal activity and functions as an immunosuppressant. Its multifaceted action on cellular structures has the potential to provide valuable insights into antibacterial activity. According to the World Health Organization (WHO), new antibiotics are continuously required. However, the vast and largely unexplored variety of cyclopeptides produced by the fungal species represents a significant source for these active compounds. The aim of this study is to evaluate the antibacterial activity of secondary metabolites produced by the fungal species *M. anisopliae*. This strain was cultivated in Potato Dextrose Agar medium and the crude extract (CE) was obtained from extraction with ethyl acetate containing 1% formic acid applying an ultrasonic bath (10 min). The CE was evaluated against the bacteria *Staphylococcus aureus* and *Pseudomonas aeruginosa* and the minimum inhibitory concentration (MIC) was determined. The extract CE was analysed by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) and the molecular networking was obtained by GNPS platform. CE demonstrated promising antimicrobial activity against *S. aureus*, with a minimum inhibitory concentration (MIC) of  $\leq 32.125 \mu\text{g/mL}$ . Cyclopeptides from extract CE were annotated, such as destruxins. The production of cyclopeptides were also optimized from submerge medium using OSMAC (one strain many compounds) strategy. In conclusion, several metabolites were annotated, among them different destruxins. The compounds produced by the *M. anisopliae* strain expanded the understanding of the chemical diversity of this fungus. The results indicate a promising biotechnological potential for antibacterial properties.

# Morphoanatomical and histochemical study of a European mistletoe: *Viscum album* subsp. *austriacum* (Wiesb.) Vollm



## Authors

Irailson Thierry Monchak - PPGCF - Universidade Estadual de Ponta Grossa (UEPG)  
Valter Paes de Almeida - PPGCF - Universidade Estadual de Ponta Grossa (UEPG)  
Jane Manfron - PPGCF - Universidade Estadual de Ponta Grossa (UEPG)  
João Vitor da Costa Batista - Society for Cancer Research, Hiscia Institute Arlesheim  
Carla Holandino - Multidisciplinary Laboratory of Pharmaceutical Sciences, Faculty of Pharmacy, Universidade Federal do Rio de Janeiro (UFRJ)  
Stephan Baumgartner - Society for Cancer Research, Hiscia Institute Arlesheim  
Mirio Grazi - Society for Cancer Research, Hiscia Institute Arlesheim  
Vijayasankar Raman - National Center for Natural Products Research, School of Pharmacy, University of Mississippi (NCNPR)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior do Brasil (CAPES; Código Financ 001; 88887.569108/2020-00), Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPE BPP 201.004/2022).



## Keywords

Microscopy, *Pinus sylvestris*, *Viscum album*

## Abstract

The genus *Viscum* (Santalaceae) comprises hemiparasitic plants that develop in tropical and temperate regions of Europe, Africa and Asia. In Europe, the species *Viscum album* L. is an important medicinal plant traditionally used in the treatment of various diseases, including the treatment of cancer. It grows on more than 450 species of trees, with *V. album* subsp. *austriacum*, one of its three subspecies. This work aimed to provide morphoanatomical and histochemical characteristics of the leaves, stems, fruits and seeds of *V. album* subsp. *austriacum* growing on *Pinus sylvestris* L., began to assist in the identification and botanical characterization of species and in the quality control of plant medicines. To this end, the usual techniques of optical microscopy, scanning electron microscopy and histochemical reagents were used. Macroscopically, the plant has articulated, glabrous and green stems, leaves that vary from green to yellowish-green and globular, whitish and translucent berries. In the transverse section, a microscopy revealed isomilateral and amphistomatic leaves, with paracytic stomata. Thick cuticles were observed on leaves and stems, and thin cuticles on fruits and seeds. The midrib is flat with a central vascular bundle and a concave-convex piece with five vascular bundles. The stem is circular, ranging from eight to nine bundles around the pith. A histochemical analysis showed the presence of phenolic and lipophilic compounds in the cuticles of the leaves and stem. Oil bodies were also transmitted into different organs of the plant. This is the first histochemical analysis of *V. album* subsp. *austriacum* growing as a hemiparasite on *P. sylvestris* L. Starch grains and calcium oxalate crystals have also been described in different parts of the plant. The results of this study convey new microscopic information that can aid in the authentication of mistletoe raw material.

# Critical priority *Enterobacterales* in clinical samples from *Procellariiformes* in Brazil: A warning for ocean health



## Author

Sabrina Carvalho Suominen - Universidade Federal de Santa Catarina (UFSC)  
Mateus Rocha Ribas - Universidade Federal de Santa Catarina (UFSC)  
Gustavo Rocha - Universidade Federal de Santa Catarina (UFSC)  
Victor Felipe Wolleck - Universidade Federal de Santa Catarina (UFSC)  
Rafael Meurer - Associação R3 Animal Florianópolis  
Cristiane Kiyomi Miyaji Kolesnikovas - Associação R3 Animal Florianópolis  
Jussara Kasuko Palmeiro - Universidade Federal de Santa Catarina (UFSC)  
Thais Cristine Marques Sincero - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

no funding



## Keywords

Epidemiological Surveillance, Wild Birds, One Health

## Abstract

*Procellariiformes* are an order of seabirds with pelagic behavior, spending most of their lives in the oceans. The increasing pollution of the oceans has become a significant challenge to their survival. This study aimed to assess the presence of critically prioritized *Enterobacterales* in clinical samples from *Procellariiformes* rescued and treated at the R3 Animal Association, a Wildlife Rehabilitation Center in Florianópolis, southern Brazil. Samples from R3 Animal Association were collected as part of The Santos Basin Beach Monitoring Project (PMP/BS). This project is a requirement set by Brazilian Institute of the Environment (IBAMA) for the environmental licensing of oil and natural gas production and transport by Petrobras in the pre-salt province under ABIO N° 640/2015. We conducted a screening of **Enterobacterales** from clinical samples of *Procellariiformes* at the strain collection of Associação R3 Animal, resulting in 20 isolates of interest from 11 animals belonging to eight species of *Procellariiformes*. Antimicrobial susceptibility testing was performed using the disk diffusion method to identify resistance to  $\beta$ -lactams, aminoglycosides, fluoroquinolones, and tetracycline. Additionally, we screened for Extended-Spectrum Beta-Lactamases (ESBLs) using the disk approximation method. Subsequently, PCR was performed to identify resistance genes in these isolates. Among the critical priority *Enterobacterales* isolates, we identified one isolate resistant to carbapenems and producing New Delhi Metallo-beta-lactamase, eight isolates producing ESBLs harboring the blaCTX-M1 gene (8) and the blaCTX-M9 gene (1), and one isolate producing AmpC beta-lactamases, which harbored the blaCMY-2-like gene. This study demonstrates the presence of critically prioritized bacteria in seabirds, confirming their role as sentinels of anthropogenic impacts. This underscores the fragility of marine ecosystem health, which may be contaminated with bacteria of pollution origin.



# Clove Tincture Incorporated in Cellulose Nanocrystal for Bread Preservation: An Experimental Study



## Author

Joana Magalhães - Universidade de Sorocaba (UNISO)  
Érika Leão Ajala Caetano - Universidade de Sorocaba (UNISO)  
Angela Faustino Jozala - Universidade de Sorocaba (UNISO)  
Denise Grotto - Universidade de Sorocaba (UNISO)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Pipe FAPESP 23/01989-8



## Keywords

bacterial cellulose, natural actives, antifungal

## Abstract

Food preservation is a major challenge faced by the food industry, and it is typically achieved through the use of chemical additives, which are capable of inhibiting the growth of microorganisms in finished products. However, hypersensitivity reactions, allergies, and neuromodulatory effects have been reported due to the excessive consumption of artificial preservatives. In this context, natural products can stand out for their antimicrobial properties and, most importantly, for being healthier. However, natural compounds degrade easily and therefore require protective delivery systems. This study investigated the the preservation of bread using clove tincture loaded into bacterial cellulose nanocrystals. The Minimum Inhibitory Concentration (MIC) of clove tincture was determined using the microdilution method in 96-well plates. Each well contained Sabouraud broth, fungi inoculum from food (10<sup>6</sup> Colony Forming Units/g), and clove tincture ranging from 0.02 to 20%. Nanocrystals of cellulose were incorporated with clove tincture at concentrations of 5% and 7% (the best concentration in MIC test), and than they were applied to bread, alongside a control sample for standardization. Bread deterioration was monitored daily and documented with photographs to observe fungal colony formation. Fungal growth was observed on the control bread on the sixth day, while bread with 5% clove tincture deteriorated by the eighth day and that with 7% by the tenth day. These findings indicate that the 7% concentration of clove tincture incorporated in nanocrystals was more effective, highlighting the potential of the bacterial cellulose techonology and the natural extracts as alternatives to synthetic preservatives in the food industry.

# Evaluation of cytotoxic and antimigratory properties of *Baccharis* species



## Author

Maria Eduarda Sedrez - Universidade Federal de Santa Catarina (UFSC)  
Isabella Dai Prá Zuchi - Universidade Federal de Santa Catarina (UFSC)  
Maria Beatriz De Oliveira Rabelo - Universidade Federal de Minas Gerais (UFMG)  
Alessandra Caroline Montes Frade - Universidade Federal de Minas Gerais (UFMG)  
Rodrigo Maia de Pádua - Universidade Federal de Minas Gerais (UFMG)  
Geraldo Wilson Afonso Fernandes - Universidade Federal de Minas Gerais (UFMG)  
Izabella Thaís da Silva - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Pronem / FAPESC / Termo de Outorga: 2020TR715 SIGPEX UFSC: Ação de Extensão Sigpex: 20191794



## Keywords

*Baccharis*, cancer, cytotoxic activity

## Abstract

Cancer is one of the most significant public health problems worldwide. Data published in 2022 by the International Agency for Research on Cancer (IARC) indicate 20 million new cases, with lung cancer being the most prevalent. Current drug treatments often exhibit severe and frequent adverse effects, demonstrating a lack of selectivity. Therefore, the search for new treatments is necessary, with natural products offering a diverse source for bioactive compounds. In Latin America, species of the genus *Baccharis* have shown several biological activities, including cytotoxic and anti-migratory actions against tumor cells, making them a promising research focus. This study evaluated the cytotoxic activity of *Baccharis* species on human lung cancer cell lines (A549 and H460) using the sulforhodamine B (SRB) colorimetric assay. The most active samples were also evaluated on non-tumoral human fibroblasts (HGF) to determine the selectivity index (SI). The *Baccharis megapotamica* extracts showed significant cytotoxic activity with IC<sub>50</sub> values of 4.27 µg/mL in A549 and 1.36 µg/mL in H460, and a CC<sub>50</sub> value of 85.72 µg/mL in HGF. *Baccharis retusa* extracts also demonstrated promising cytotoxic activity with IC<sub>50</sub> values of 36.90 µg/mL in A549 and 45.62 µg/mL in H460, and a CC<sub>50</sub> value of 337.10 µg/mL in HGF. The SI values of *B. megapotamica* were 20.80 in A549 and 63.03 in H460, while *B. retusa* showed SI values of 9.10 in A549 and 8.27 in H460. These promising samples were further investigated for their anti-migratory action using the scratch assay technique. *Baccharis retusa* at 50 µg/mL inhibited half of the cell migration, similar to the positive control, paclitaxel, demonstrating satisfactory anti-migratory potential. Therefore, the bioprospecting of *Baccharis* species could lead to the discovery of compounds capable of selectively acting against tumor cell lines, potentially leading to the development of more effective and selective cancer treatments.

# Bread preservation with natural antimicrobials and cellulose nanocrystal: An effective and healthy alternative.



## Author

Erika Leão Ajala Caetano - Universidade de Sorocaba (UNISO)  
Joana Garrossino Magalhães - Universidade de Sorocaba (UNISO)  
Angela Faustino Jozala - Universidade de Sorocaba (UNISO)  
Denise Grotto - Universidade de Sorocaba (UNISO)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Pipe FAPESP 23/01989-8



## Keywords

Clove tincture, Cinnamon Tincture, cellulose nanocrystal

## Abstract

The growing demand for safe, healthy, and durable foods drives the search for innovative and sustainable preservation methods. In this context, the use of natural agents stands out for their efficacy and safety. Natural ingredients, combined with bacterial cellulose nanocrystal, can enhance antifungal activity and prolong the shelf life of foods. In this way, the purpose of this study was to explore the benefits of natural antimicrobials as preservative agents in baking. The antimicrobial efficacy of clove and cinnamon tinctures was investigated by determining the Minimum Inhibitory Concentration (MIC) using the microdilution method in 96-well plates. Each well contained Sabouraud broth, a fungal from food inoculum (106 CFU/g), and clove and cinnamon tincture in concentrations ranging from 0.02% to 20%. The ideal MIC was determined to be 5%. Subsequently, the tinctures were incorporated with cellulose nanocrystal in a 1:1 ratio using a shaker for 4 hours. Tests were then conducted on baked products, focusing on bread. The bread formulation for 500 g included wheat flour, water, powdered milk, margarine, salt, sugar, and yeast as the control, and the test bread incorporated 5% of the active ingredients in synergy. The results showed that the addition of 5% of the incorporated active ingredients provided antimicrobial properties without compromising the sensory quality of the bread. The synergy between the tinctures and cellulose nanocrystal effectively inhibited fungal growth, with the control bread showing fungal activity in 5 days, while the test bread resisted up to 7 days. Although the shelf life was only two days longer than the control, the study suggests that the incorporation of tinctures into bacterial na cellulose nanocrystal nocellulose can be an effective and healthy strategy. For future tests, the tinctures incorporated into the cellulose nanocrystal will be sprayed on the bread, rather than incorporated into the dough.

# Evaluation of the cytotoxic action of new semisynthetic cardenolides and their effect on the clonogenic potential of prostate tumor cells.



## Author

Luíse Schulte - Universidade Federal de Santa Catarina (UFSC)  
Iara Zanella Guterres - Universidade Federal de Santa Catarina (UFSC)  
Flaviano Melo Ottoni - Universidade Federal de Minas Gerais (UFMG)  
Ricardo José Alves - Universidade Federal de Minas Gerais (UFMG)  
Rodrigo Maia de Pádua - Universidade Federal de Minas Gerais (UFMG)  
Izabella Thaís da Silva - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

PRONEN / FAPESC / Termo de Outorga: 2020TR715; SIGPEX UFSC: Ação de Extensão Sigpex: 201917940



## Keywords

Cardenolides, Prostate tumor, Clonogenic potential

## Abstract

Cancer is the second leading cause of death worldwide, with prostate cancer accounting for 13.5% of all cases. This issue has become increasingly urgent due to both the rising number of affected individuals and the current pharmacological treatments, which lack specificity and often induce serious adverse effects. Natural products are significant sources of biologically and pharmacologically active compounds, offering substantial potential for the development of new antitumor drugs. Cardenolides, traditionally used to treat congestive heart failure and atrial arrhythmias, are one example of these compounds. Recently, several studies have demonstrated the potential cytotoxic and antitumor potential of certain molecules within this class. In this context, the goal of this study was to evaluate the cytotoxic activity of eight new semisynthetic cardenolide analogues, using sulforhodamine B assay to determine their 50% cytotoxicity concentration (CC50) in healthy (HGF) and prostate tumor cells (DU145 and PC3). Based on the obtained results, the selectivity indices (SI) were calculated to identify the most promising compounds. Two compounds, 6b and 6d, stood out, presenting the lowest CC50 values: 3.66 and 3.38 for DU145 cells, and 2.23 and 2.56 for PC3 cells, respectively. The two compounds demonstrated low cytotoxicity towards HGF cells, indicating selectivity for tumor cells and resulting in the highest SI among the tested compounds (between 12 and 45). Considering these promising results, the two compounds were selected for evaluation of their long-term cytotoxic action using clonogenic assay. The results show that both compounds, at different concentrations, significantly reduced colony growth on DU145 and PC3 cells treated with the CC50 and 2x CC50, compared to untreated cells. Further assays will be conducted to fully elucidate their mechanism of action.

# Evaluation of the nutritional and antimicrobial potential of the cladodes of *Opuntia ficus-indica* and *Cereus jamacaru*



## Author

Fabicio Luiz Tulini- Universidade Federal do Oeste da Bahia (UFOB)  
Itana Vivian Rocha Santana - Universidade Federal do Oeste da Bahia (UFOB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

FAPESB (Fundação de Amparo à Pesquisa da Bahia) PPF 0017/2021



## Keywords

Natural antimicrobials, Semi-arid regions, Functional products

## Abstract

*Opuntia ficus-indica* (forage cactus) and *Cereus jamacaru* (mandacaru) are cacti whose flat stem segments (cladodes) are commonly used as livestock feed, especially in semi-arid regions during dry periods. However, there is a lack of research exploring their antimicrobial properties and their potential use in human food. Thus, this study aimed to analyze the proximal composition of the cladodes of forage cactus and mandacaru and to assess their antimicrobial activity. Moisture, ash, lipids, proteins, fibers, and carbohydrates, was determined through various tests. The cladodes were dried, cut, and then placed in a circulation oven at 55°C for 48 hours. Subsequently, 60% hydroalcoholic extracts were prepared using a shaker for 48 hours, and filtered. The antimicrobial activity was tested using disk diffusion method against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Listeria monocytogenes*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, and *Salmonella enterica*. The moisture content of the mandacaru and forage cactus cladodes did not differ significantly ( $92.44 \pm 0.629\%$  and  $91.73 \pm 0.775\%$ , respectively), nor did the ash content ( $0.99 \pm 0.075\%$  and  $0.89 \pm 0.041\%$ ) and lipids ( $0.010 \pm 0.0\%$  and  $0.01 \pm 0.0\%$ ). However, there was a statistical difference in the fiber content ( $5.56 \pm 0.3736\%$  and  $4.47 \pm 0.473\%$ ) and proteins ( $3.090 \pm 0.027\%$  and  $0.623 \pm 0.005\%$ ) between the two species. The hydroalcoholic extracts demonstrated significant antimicrobial activity against the tested bacteria, with inhibition zones larger than those of the negative control used, except against *E. faecalis*. The proximal composition indicates a rich supply of macromolecules and highlights the potential application of these species in the development of functional products. The extensive antimicrobial activity observed underscores the potential of these cacti as valuable sources of natural antimicrobials, with potential biotechnological applications.

# Development of an HPLC-DAD fingerprint method for four *Phyllanthus* species



## Authors

Lucas Pereira - Universidade do Vale do Itajaí (UNIVALI)  
Adrielli Tenfen Voltolini - Universidade do Vale do Itajaí (UNIVALI)  
Gabrieli Zollet - Universidade do Vale do Itajaí (UNIVALI)  
Priscila de Souza - Universidade do Vale do Itajaí (UNIVALI)  
Luis Adriano Funez - Herbarium Navegantes  
Valdir Cechinel Filho - Universidade do Vale do Itajaí (UNIVALI)  
Luiz Carlos Klein Junior - Universidade do Vale do Itajaí (UNIVALI)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CNPq - 404926/2023-1



## Keywords

Fingerprint, HPLC, *Phyllanthus*

## Abstract

The genus *Phyllanthus* L., known as "stone breaker," is used in traditional Brazilian medicine for treating urolithiasis. The Brazilian Pharmacopoeia (FB) provides monographs for *P. niruri* and *P. tenellus*. Other species are also popularly used due to their similar botanical characteristics. Thus, the RENISUS emphasizes research into additional native species like *P. amarus* and *P. urinaria*. Consequently, ensuring quality control of *Phyllanthus* products proves challenging because current standardization methods, focusing on tannins and gallic acid, don't cover all commonly used species or account for potentially active compounds. Understanding the chemical complexity of these species is crucial for addressing both quality control and therapeutic considerations. In this study, a method of analysis by HPLC-DAD to define fingerprints of the different species of *Phyllanthus* was developed. The *Phyllanthus* samples from March 2023 to May 2024 were dried, ground, and extracted twice with 70% ethanol for three hours. After concentration at 40°C in a rotaevaporator, the aqueous extract was frozen and lyophilized. HPLC-DAD used 0.1% formic acid as the aqueous phase and MeOH and/or ACN as the organic phase. Various MeOH/ACN mixtures (75:25, 50:50, 25:75) were tested, with extracts analyzed at 2.0 mg/mL at 274 nm. The method yielding the highest peak number and resolution was selected. We found that the pharmacopoeial method didn't provide satisfactory separation. The ACN method revealed 77 peaks, but with insufficient separation. ACN:MeOH 50:50 and 25:75 showed 46 and 56 peaks, respectively, with a low degree of separation. ACN:MeOH 75:25 showed 90 peaks with satisfactory resolution. The ACN:MeOH 75:25 method effectively separated *Phyllanthus* compounds, establishing a fingerprint representative of the chemical complexity of the species. Future work includes *in vitro* studies on kidney stone models and using chemometric techniques to link the fingerprint with biological activity.

# The efficacy of *Baccharis dracunculifolia* essential oil in wound healing and its irritating potential



## Author

Carine Cedrola - Universidade Federal de Juiz de Fora(UFJF)  
Carolina Sousa Ponciano - Universidade Federal de Juiz de Fora(UFJF)  
Fernanda Brito Leite - Universidade Federal de Juiz de Fora(UFJF)  
Ana Cláudia Chagas de Paula Ladvocat - Universidade Federal de Juiz de Fora(UFJF)  
Thais Nogueira Barradas - Universidade Federal do Rio de Janeiro (UFRJ)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) e Fundação de Amparo Pesquisa do Estado de Minas Gerais (FAPEMIG)



## Keywords

Keywords: *Baccharis dracunculifolia* oil, Cell migration, Irritation.

## Abstract

Wound healing is a complex and dynamic process that includes several biological and molecular stages. *Baccharis dracunculifolia* essential oil (BDO) contains bioactive components with antibacterial, antioxidant, and anti-inflammatory effects that can aid in wound healing. Firstly, the aim of this study was to identify and quantify the main components present in the oil. Furthermore, BDO's effectiveness in wound healing was investigated by the cell migration (scratch assay) using CCD1059Sk human fibroblasts treated with different concentrations (250, 500, and 1000 µg/mL) for 72 hours to measure the rate of wound closure. Subsequently, aiming for the incorporation of the oil into topical formulations, the hen's egg test-chorioallantoic membrane (HET-CAM) was carried out in order to evaluate the ocular irritation potential of pure BDO or diluted in olive oil. (1:1) and estimate the oil's security. HPLC analysis detected the presence of *t*-nerolidol and  $\beta$ -caryophyllene in BDO, at concentrations of 138.40 mg/mL and 26.82 mg/mL, respectively. The Scratch Assay showed that concentrations of 500 µg/mL of BDO promoted an area coverage of 93%, whereas 1000 µg/mL resulted in 87% coverage, indicating cytotoxic effects at higher concentrations. The HET-CAM test showed that pure BDO was moderately irritating. However, the mixture of BDO and olive oil (1:1) did not show warning signs, being classified as non-irritating. BDO has been proven to promote cell migration at non-cytotoxic doses. This could be due to the existence of *t*-nerolidol and  $\beta$ -caryophyllene, which have previously reported therapeutic effects. Furthermore, when diluted in olive oil (1:1), BDO did not show significant irritating potential. These findings are encouraging for the development of new therapeutic approaches to wound therapy, highlighting the potential of BDO as an active ingredient in dermatological formulations.

# Investigating the presence of antibiotic-resistant bacteria through microbiological surveillance in the oyster supply chain



## Author

Gustavo Rocha - Universidade Federal de Santa Catarina (UFSC)  
Luany de Oliveira Hinkel - Universidade Federal de Santa Catarina (UFSC)  
Mateus Rocha Ribas - Universidade Federal de Santa Catarina (UFSC)  
Juliana Lemos dal Pizzol - Universidade Federal de Santa Catarina (UFSC)  
Julia Raimundo de Jesus - Universidade Federal de Santa Catarina (UFSC)  
Gabriel Sanabria da Silva - Universidade Federal de Santa Catarina (UFSC)  
Jussara Kasuko Palmeiro - Universidade Federal de Santa Catarina (UFSC)  
Thais Cristine Marques Sincero - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

FAPESC



## Keywords

ESBL, Multidrug-resistant, One Health

## Abstract

Oysters are fresh foods often consumed *in natura*, where the presence of antibiotic resistant bacteria represents a health problem directly impacting the quality of these products. In this way, the objective of this work was to conduct microbiological surveillance in the oyster supply chain. During summer and winter, samples of one liter of sea water and 15 adult oysters were collected from oyster farmers located in the north bay (n=3) and south bay (n=3) of Florianópolis/SC, as well as from the establishments (restaurants and fish markets) where these producers supply. In total, 175 bacteria with antimicrobial resistance profiles were isolated, 49 isolated directly from the sea water, 62 isolated in oysters collected directly from the sea and 64 from commercially available oysters. Regarding the oysters collected directly from the sea, 17 resistant isolates were obtained in the North Bay of 7 different bacterial species, where 5.88% of the isolates were classified as multidrug-resistant, and 29.41% exhibited the Extended-Spectrum Beta-Lactamase (ESBL) phenotype. Meanwhile, 20 isolates were collected from commercial oysters supplied by producers in the same region, from 8 different species, of which, 10% were multidrug-resistant and 45% ESBL. In the South Bay, 45 resistant isolates of 10 species were collected from the sea oysters. Among these isolates, 48.88% were multidrug-resistant and 46.66% exhibited the ESBL phenotype. Additionally, 44 resistant isolates of 13 different species were obtained from the oysters supplied by these producers, of which 54.54% were multidrug-resistant and 52.27% ESBL. Our results demonstrate that oysters concentrate contaminants from the water, which remain in the oysters until they reach final consumers. The number of antimicrobial-resistant isolates is more influenced by water quality during production than by storage or handling itself.



# Purification of a fungal L-asparaginase using aqueous biphasic systems



## Author

Marina Borges Guimarães - Universidade de Brasília (UNB)  
Pérola de Oliveira Magalhães - Universidade de Brasília (UNB)  
Jorge Fernando Brandão Pereira - University of Coimbra



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Capes and FAPDF (193.000919-2020-07)



## Keywords

L-asparaginase, aqueous biphasic system, leukemia

## Abstract

L-asparaginase (L-ASNase) is used mainly to treat acute lymphoblastic leukemia (ALL). Currently, only bacterial L-asparaginase is available in the market, obtained from *Escherichia coli* and *Erwinia chrysanthemi*. Hypersensitivity reactions are frequent in both treatments, due to the high levels of immunogenicity of bacterial L-ASNase. Eucaryotic sources of L-ASNase are being studied to minimize these effects because their enzymes are expected to be more similar to mammal proteins than prokaryotic proteins. Considering that L-asparaginase is a tetramer, and quite unstable, aqueous biphasic systems (ABS) are eco-friendly and biocompatible for its purification. This work aimed to evaluate the purification of an L-ASNase aqueous extract from *Penicillium sizovae* in a polymer/salt-based (or ionic liquids) ABS. The systems, including PEG (with different molecular weights)/phosphate buffer and PPG/[Ch]Cl, could separate the enzyme in one phase. The most promising systems were PEG-2000/phosphate and PPG/[Ch]Cl with an extraction efficiency of 100 % and 93.6%, a purification factor of 1.63 and 0.50, a relative activity of 28.7 % and 21.8%, and specific activity of 0.66 U/mgprotein and 0.23 U/mgprotein, respectively. The polymer/salt-based ABS promoted the partition of L-ASNase. They revealed its potential as a low-cost and environmentally friendly method for the purification and recovery of a fungal L-ASNase.

# Preliminary In Vitro Cytotoxicity of *Agrimonia eupatoria* L. Ethanol Extract (Rosaceae) in RAW 264.7 and L929 Cell Lines



## Author

Yris Bazzo - Universidade de Brasília (UNB)  
Lilian Santana Coelho - Universidade de Brasília (UNB)  
Omar Enrique Estrada Semprun - Universidade de Brasília (UNB)  
Dâmaris Silveira - Universidade de Brasília (UNB)  
Pérola de Oliveira Guimarães - Universidade de Brasília (UNB)  
Yris Maria Fonseca-Bazzo - Universidade de Brasília (UNB)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES, CNPq and FAPDF



## Keywords

*Agrimonia eupatoria* L., cytotoxicity, flavonoids.

## Abstract

*Agrimonia eupatoria* L. (Rosaceae) is a perennial herb traditionally used in the treatment of various diseases. Despite historical reports supporting its benefits, contemporary scientific evidence remains limited. To advance research on *A. eupatoria*, understanding the safety profile of extracts or fractions derived from this plant is crucial. This study aimed to investigate the in vitro cytotoxicity of an ethanol extract from the aerial parts of *A. eupatoria* in RAW 264.7 and L929 cell lines. Additionally, TLC analysis was performed. RAW 264.7 and L929 cell lines were sourced from the Rio de Janeiro Cell Bank and cultured in DMEM supplemented with 10% fetal bovine serum, 3.7 g/L sodium bicarbonate, 1 mM sodium pyruvate, and 1% antibiotic solution at 37 °C with 5% CO<sub>2</sub>. Cytotoxicity assessment involved seeding cells (2.5x10<sup>4</sup> cells/well for RAW 264.7 and 10<sup>4</sup> cells/well for L929) in 96-well plates with 200 µL of medium per well. Cell viability was determined using the MTT assay. TLC analysis utilized ethyl acetate, acetic acid, formic acid, and water (100:11:11:26) as the mobile phase, with 10% ceric sulfate in methanol as the revealing reagent. Preliminary findings indicated no cytotoxic effects at concentrations up to 250 µg/mL of *A. eupatoria* ethanol extract in L929 cells (91% viability) and up to 500 µg/mL in RAW 264.7 cells (86% viability). Non-cytotoxic concentrations will be further investigated in subsequent experiments using RAW 264.7 and L929 cell lines. TLC analysis revealed two prominent yellow spots suggesting the presence of flavonoid compounds (R<sub>f</sub> 0.88 and 0.61). This study provides initial insights into the cytotoxicity and chemical composition of *A. eupatoria* ethanol extract, underscoring its potential for further pharmacological investigations.

# Convenient extractions for maximizing content of bioactive compounds from *Dysphania retusa*



## Author

Heloísa Sommer - Universidade Federal de Santa Catarina (UFSC)  
Carla Roana Moraes Monteiro - Universidade Federal de Santa Catarina (UFSC)  
Igor Vivian Roberto - Universidade Federal de Santa Catarina (UFSC)  
Rodrigo Teixeira Destro - Universidade Federal de Santa Catarina (UFSC)  
Christiane Meyre da Silva Bittencourt - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CNPq 406855/2023-4



## Keywords

Bioinsecticide, Phytochemical investigation, *Chenopodium retusum*

## Abstract

The genus *Dysphania* is known for its high bioactive potential, including pharmacological and agrochemical activities. Considering the bioinsecticidal potential of components present in *D. ambrosioides*, mainly the terpen ascaridole epoxide, and the novelty of the species *D. retusa*, the aim of this work was evaluate the extraction procedures with *D. retusa* aerial parts to obtain extracts enriched with substances that may exhibit biodefensive potential. The dried aerial parts were submitted to theunderwent pressurized liquid extraction (PLE), supercritical fluid extraction (SFE), and Soxhlet apparatus extraction. Extracts were analyzed by gas chromatography-mass spectrometry (GC-MS), and the compounds were identified using the NIST library and specialized literature. Among the major compounds identified by the PLE method were: hexadecanoic acid (14.04 %), 3-methyl-6-(propan-2-yl)-7-oxabicyclo[4.1.0]heptan-2-one (13.38 %), and aromadendrene oxide (12.72 %). From SFE were identified 3-methyl-6-(propan-2-yl)-7-oxabicyclo[4.1.0]heptan-2-one (14.48%), thymol (13.61 %), and ascaridole epoxide (10.81 %). Soxhlet extraction yielded ascaridole epoxide (22.10 %), carvacrol (13.52 %), and 3-methyl-6-(propan-2-yl)-7-oxabicyclo[4.1.0]heptan-2-one (9.35 %). The study highlights several monoterpenes as secondary metabolites, with Soxhlet extraction being the most efficient for obtaining the desired bioactive compounds as ascaridole epoxide known to exhibit repellent activity. These results highlight the chemical potential of the extract obtained by soxhlet and direct the continuation of studies to evaluate the biorepellent property.

# Evaluation of fibroblast migration in biomaterial applied as a scaffold



## Author

Ana Carolina Souza Chacon - Universidade de Sorocaba (UNISO)  
Érika Leão Ajala Caetano - Universidade de Sorocaba (UNISO)  
Thais Jardim Oliveira - Universidade de Sorocaba (UNISO)  
Jéssica Asami - Universidade Católica de Sorocaba (PUCSP)  
Thaísa Borim Pickler - Universidade de Sorocaba (UNISO)  
Gabriel Pereira Machado - Universidade de Sorocaba (UNISO)  
Larissa Oliveira Simões - Universidade de Sorocaba (UNISO)  
Joana Garrossino Magalhães - Universidade de Sorocaba (UNISO)  
Denise Grotto - Universidade de Sorocaba (UNISO)  
Moema de Alencar Hausen - Universidade Católica de Sorocaba (PUCSP)  
Angela Faustino Jozala - Universidade de Sorocaba (UNISO)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

PROBIC, University of Sorocaba (UNISO)



## Keywords

fibroblast migration, scaffold, bacterial cellulose

## Abstract

Regenerative engineering in biomedical studies is a field with many advancements. The need for the development of new tissue regeneration techniques is significant, as is the innovation to prevent tissue rejection or transplant rejection. Biomaterial scaffolds are becoming increasingly relevant, and their associations with different cell types are expanding the field of regenerative medicine. The objective of this work is to evaluate the migration of fibroblasts in bacterial cellulose membranes, given that their production is sustainable and applicable for future development. Migration evaluations were performed by immersing the membrane in a cell solution, followed by a colorimetric test for the accurate quantification of viable cells in proliferation assays using MTS dye, read on a microplate reader at 490 nm. Additionally, scanning electron microscopy (SEM) analyses were performed after the material was lyophilized. As a result of the colorimetric test, high cell viability was observed, consistent with the incorporation time in the cell solution and the number of cells in the solution, meeting expectations. Furthermore, in SEM, it was possible to observe the structures of fibroblasts among the fibers of the bacterial cellulose membrane, proving the possibility of migration; however, their morphology may indicate a lack of cell adhesion or cell death. These results expand the potential application of the product as a future scaffold. However, the study of new methodologies is necessary to ensure cell viability and success in its medical application.

# Development of a Biodegradable Polymer-Based Biomaterial for Antimicrobial Treatment of Antibiotic-Resistant Wound Infections



## Author

Gabriel Pereira Machado - Universidade de Sorocaba (UNISO)  
Thaís Jardim Oliveira - Universidade de Sorocaba (UNISO)  
Larissa Oliveira Simões - Universidade de Sorocaba (UNISO)  
Ana Carolina Souza Chacon - Universidade de Sorocaba (UNISO)  
Thaís Borin Pickler - Universidade de Sorocaba (UNISO)  
Denise Grotto - Universidade de Sorocaba (UNISO)  
Angela Faustino Jozala - Universidade de Sorocaba (UNISO)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES



## Keywords

Biodegradable Polymers, Wound Treatment, anti-bacterial

## Abstract

The use of biodegradable polymers is essential for environmental preservation, offering a promising alternative to fossil fuel-derived polymers. In drug delivery, these polymers provide several advantages, including wide applicability, easy excretion, biocompatibility, and low cytotoxicity. With this in mind, this study aims to develop a biomaterial containing polymers and natural actives to treat wounds contaminated by antibiotic-resistant bacteria. The formulation of the biomaterial was made using gelatin, citric acid, PEG 400, bacterial cellulose, and sericin as excipients, and nisin as the active agent. The antimicrobial potential was assessed using the minimum inhibitory concentration (MIC) method and agar diffusion against standard *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*, as well as antibiotic-resistant bacteria *Pseudomonas aeruginosa*, *Serratia marcescens*, *Enterobacter cloacae*, *Escherichia coli*. Results indicated that the film with the best characteristics contained 15g of gelatin, 0.48g of citric acid, 0.2g of PEG 400, 3g of bacterial cellulose, 0.5g of sericin, and 0.1g of nisin. The concentration of nisin was determined through MIC testing. The antimicrobial activity of the film without the active agent showed no inhibition zone against any of the bacteria tested. However, the film containing nisin exhibited antimicrobial activity against standard bacteria of 3 log<sub>10</sub>AU for *S. aureus* and *E. coli*; 2 log<sub>10</sub>AU for *P. aeruginosa*. For antibiotic-resistant bacteria, the activity was 2 log<sub>10</sub>AU for *S. marcescens*, *E. cloacae*, *E. coli*, and *P. aeruginosa*. The optimal film composition included specific quantities of these components, leading to significant antimicrobial activity against both standard and antibiotic-resistant bacteria, showcasing its potential for addressing challenging bacterial infections. With the results being promising, future tests should be conducted to evaluate its broader applicability.

# Evaluation of the minimum inhibitory concentration of the antibiotic amoxicillin in association with curcumin and nisin



## Author

Patricia Alves - Universidade De Sorocaba (UNISO)  
Larissa Oliveira Simões - Universidade De Sorocaba (UNISO)  
Érika Leão Ajala Caetano - Universidade De Sorocaba (UNISO)  
Joana Garrossino Magalhães - Universidade De Sorocaba (UNISO)  
Gabriel Pereira Machado - Universidade De Sorocaba (UNISO)  
Érika Leão Ajala Caetano - Universidade De Sorocaba (UNISO)  
Denise Grotto Universidade De Sorocaba (UNISO)  
Angela Faustino Jozala Universidade De Sorocaba (UNISO)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

FINEP número 01.22.0214.00



## Keywords

amoxicillin, antibiotic, minimum inhibitory concentration

## Abstract

The COVID-19 pandemic has increased the use of antibiotics, exacerbating microbial resistance. The focus is on finding methods to control amoxicillin-resistant microorganisms. This preliminary study evaluates the minimum inhibitory concentration (MIC) of amoxicillin in combination with curcumin and the peptide nisin, aiming to provide an alternative for combating exacerbated microbial resistance due to the pandemic. The MIC test was conducted using 96-well plates, where each well initially received 100  $\mu$ L of Tryptone Soya Broth, except well 1 which received 200  $\mu$ L of the antimicrobial agent. From well 1, 100  $\mu$ L was serially diluted into wells 2 to 11. Subsequently, 10  $\mu$ L ( $10^6$ CFU) of the microorganism was added to wells 1 through 12, except well 11. The plate was then incubated overnight at 37°C. Next, 5  $\mu$ L from each well was transferred to Petri dishes containing Tryptone Soya Agar with *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* for MIC evaluation. The combination of amoxicillin and curcumin was initially tested at concentrations of 6 mg/mL and 4 mg/mL, respectively, while the combination of amoxicillin and nisin was tested at 12 mg/mL and 2.5 mg/mL, respectively. Results showed that the MIC of the amoxicillin-curcumin combination was 0.37 mg/mL and 0.25 mg/mL against *E. coli*, with effective inhibition against *S. aureus* at all tested concentrations but no inhibition against *P. aeruginosa* at any concentration. In the amoxicillin-nisin combination, *E. coli* exhibited inhibition starting from 0.09 mg/mL and 0.009 mg/mL, while *S. aureus* was inhibited at all tested concentrations and *P. aeruginosa* from 1.25 mg/mL and 0.31 mg/mL. Based on the MIC results, it was concluded that the combination of amoxicillin with nisin demonstrated potential synergistic antimicrobial activity against the tested microorganisms. This combination will be further evaluated against amoxicillin-resistant microorganisms in future studies.

# Voltammetric analysis and ex vivo inhibition of lipid peroxidation in rat cerebral tissue by *Solanum lycocarpum* St. Hil



## Author

Renata Anastacia De Oliveira Batista - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJ)  
Eva Edvaniely Ribeiro Gonçalves - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)  
Andrea Renata Malagutti - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)  
Eduardo de Jesus Oliveira - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)  
Ana Paula Rodrigues - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)  
Roseâmely Angélica de Carvalho Barros - Universidade Federal de Catalão (UFCat)  
Thiago Sardinha de Oliveira - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES



## Keywords

Plantas Medicinais, atividade antioxidante, neuroproteção

## Abstract

Oxidative damage, often caused by reactive oxygen species (ROS), is known to contribute to neuronal damage and neurodegenerative disorders, which can result in lipid peroxidation. In this sense, this study aimed to evaluating antioxidant activity and prevention of lipid peroxidation of *S. lycocarpum* leaves hydroalcoholic extract (SLHE). SLHE was prepared according to Thomaz DV (2018), SisGen n° A88B22D, escicata UFVJM HDJF 10535. For the voltammetric experiments, electrochemical cells were used with reference electrodes (Ag/AgCl), counter electrode (Pt) and working electrode (GCE). DPPH was determined spectrophotometrically for antioxidant analysis. Lipid peroxidation was measured by TBA-RS, by the reaction between malondialdehyde (MDA) and thiobarbituric acid (TBA). Brain tissue homogenates were incubated with SLHE (1, 3 and 10 mg/mL), analyzed by spectrophotometry at 535 nm. The level of lipid peroxides was expressed as nmoles of MDA released/mg of protein. Gallic acid was used as standard. Protocol CEUA/UFVJM n° 14/2020. Data are presented as mean±SEM of 7-9 experiments analysed by Student's t-test or one-way ANOVA. The cyclic voltammogram recorded peaks with  $E_{pa1} = 0.22$  V and  $E_{pa2} = 0.62$  V for SLHE and with  $E_{pa1} = 0.36$  V for gallic acid. The low  $E_{pa}$  measured for SLHE indicates high antioxidant power of the species present in the extract. SLHE inhibited the DPPH oxidation, showing  $IC_{50}$  values of  $51.14 \pm 1.07$  µg/mL. As the concentration of SLHE is increased the levels of MDA decrease proportionally at concentrations of 1, 3 and 10 mg/mL ( $0.220 \pm 0.007$ ,  $0.121 \pm 0.003$  and  $0.105 \pm 0.004$  TBA-RS per mg of protein, respectively). Taken together, these results indicate that SLHE represent a prospective approach to neuroprotective assays and a possible candidate to reverse neuronal death.

# Voltammetric analysis and ex vivo inhibition of lipid peroxidation in rat cerebral tissue by *Solanum lycocarpum* St. Hil



## Author

Isabella Dai Prá - Universidade Federal de Santa Catarina (UFSC)  
Douglas Santos Porto - Universidade Federal de Santa Catarina (UFSC)  
Bianca da Costa Bernardo Port - Universidade Federal de Santa Catarina (UFSC)  
Débora Fretes Argenta - Universidade Federal de Santa Catarina (UFSC)  
Thiago Caon - Universidade Federal de Santa Catarina (UFSC)  
Izabella Thaís da Silva - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Financial support: Pronem / FAPESC / Termo de Outorga: 2020TR715 SIGPEX UFSC: Ação de Extensão Sigpex: 201917940



## Keywords

$\beta$ -caryophyllene, Herpes simplex viruses, nanotechnology

## Abstract

Herpetic infections constitute a global public health challenge, with millions of individuals estimated to be infected with the Herpes Simplex Virus Type 2 (HSV-2). This infection increases vulnerability to HIV and complicates treatment with conventional drug therapies. Given the limitations of current treatments, natural products such as  $\beta$ -caryophyllene, a sesquiterpene present in plant essential oils, have garnered attention due to their antimicrobial, antitumor, and antiviral properties. Nanotechnology has facilitated advances by allowing the manipulation of these compounds at nanometric scale, overcoming solubility and bioavailability issues, protecting against degradation, and enabling controlled release. These developments have led to the creation of more effective delivery systems, reduced side effects, and the potential for revolutionizing personalized therapeutic approaches. This study aimed to evaluate the in vitro antiviral potential of  $\beta$ -caryophyllene by developing an optimized nanoformulation against HSV-2. The antiviral activity was assessed using the plaque assay. The results demonstrated that isolated  $\beta$ -caryophyllene showed approximately 97% viral inhibition at a concentration of 2.0 mM, with an IC<sub>50</sub> value of 0.734 mM. Following formulation, the viral inhibition was maintained at a lower concentration of approximately 0.2 mM, with an IC<sub>50</sub> value of 0.080 mM, which is nearly ten times lower than that of the isolated compound. Due to the promising findings, further tests will be carried out to elucidate the mechanism of antiviral action.



# Emergence of carbapenemase-producing *Escherichia coli* isolated from Magellanic penguins in Southern Brazil



## Author

Victor Felipe Wolleck - Universidade Federal de Santa Catarina (UFSC)  
Mateus Rocha Ribas - Universidade Federal de Santa Catarina (UFSC)  
Gustavo Rocha - Universidade Federal de Santa Catarina (UFSC)  
Sabrina Carvalho Suominen - Universidade Federal de Santa Catarina (UFSC)  
Rafael Meurer - Associação R3 Animal  
Cristiane Kiyomi Miyaji Kolesnikovas - Associação R3 Animal  
Jussara Kasuko Palmeiro - Universidade Federal de Santa Catarina (UFSC)  
Thais Cristine Marques Sincero - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

No Funding



## Keywords

Carbapenem resistance, One Health, Epidemiological surveillance

## Abstract

Magellanic penguins (*Spheniscus magellanicus*) are known for their seasonal migrations between Patagonia and Brazil. During these journeys, the penguins encounter anthropized and contaminated aquatic environments, which can make them reservoirs of antibiotic resistance. This study phenotypically and genotypically characterized the antimicrobial resistance of *Escherichia coli* isolates obtained from penguin. Samples were collected between 2016 and 2020 from various anatomical sites, including blood cultures, pericardial fluid, trachea, coelomic cavity, air sac, and lung, by the R3 Animal Association through the Beach Monitoring Project (PMP/BS). The PMP-BS is an activity developed to meet the conditions of the federal environmental licensing, conducted by Ibama, for Petrobras' oil and gas production and flow activities in the Santos Basin (ABIO 640/2015). The disk diffusion method was used to identify resistance to  $\beta$ -lactams, aminoglycosides, fluoroquinolones, and tetracycline. Furthermore, we utilized the disk approximation method to screen for Extended-Spectrum Beta-Lactamases (ESBLs). PCR was conducted to detect resistance genes in these isolates. Among the 55 isolates, 83.5% were classified as MDR (Multidrug-Resistant). The proportion of isolates with an ESBL phenotype was 20%. Additionally, the proportion of isolates resistant to carbapenems was 30.9%. The genes blaTEM (8), blaSHV (2), blaCTX-M-1 (17), blaNDM (16), and blaKPC (1) were detected. This study indicates a temporal increase in the presence of the blaNDM in Magellanic penguins and is also the first to report the blaKPC in these animals. The results show the interconnection of environmental, animal, and human health and the necessity for collaborative efforts in addressing antibiotic resistance globally. They also indicate that Penguins can act as sentinels for the impact of antibiotic resistance, providing crucial insights into the spread and evolution of resistant bacteria across different ecosystems.

# Effect of different extraction techniques on the yield, and profile by gc-ms of eugenia umbelliflora leaves



## Author

Rodrigo Destro - Universidade Federal de Santa Catarina (UFSC)  
Heloísa Fontana Sommer - Universidade Federal de Santa Catarina (UFSC)  
Carla Roana Moraes Monteiro - Universidade Federal de Santa Catarina (UFSC)  
Igor Vivian Roberto - Universidade Federal de Santa Catarina (UFSC)  
Christiane Meyre-Silva - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

No Funding



## Keywords

*Eugenia astringens*, Baguaçu, Monoterpens

## Abstract

The genus *Eugenia*, belonging to the family *Myrtaceae*, is widely recognized for its high bioactive potential, with various species containing a broad range of compounds with pharmacological and cosmeceutical activities. The species *E. umbelliflora* is notable for its antimicrobial, anti-inflammatory, and antioxidant properties, making it a valuable object of study in these areas. This study aims to investigate the influence of extraction methods on the yield and phytochemical composition of *E. umbelliflora* leaves. Dried and crushed leaves were subjected to two distinct extraction methods: pressurized liquid extraction (PLE), a modern technique known for its efficiency, and Soxhlet apparatus extraction, a traditional and widely used procedure in phytochemistry. Extracts were analyzed by gas chromatography-mass spectrometry (GC-MS), and the compounds were identified using the NIST library and specialized literature. PLE (yield: 10.1%) extraction revealed the major presence of aloraromadendrene (23.45%), caryophyllene (17.76%), and viridiflorol (14.36%). In contrast, Soxhlet extraction (yield: 15.34%) yielded aloraromadendrene (32.18%), guaiol (10.56%), and  $\beta$ -gurjunene (6.37%). The significant presence of aloraromadendrene suggests a considerable impact, though other compounds like caryophyllene and viridiflorol are also known for their antibacterial properties. This study highlighted the presence of various sesquiterpenes as secondary metabolites, with aloraromadendrene standing out due to its high concentration. The results demonstrate that the phytochemical profile of *Eugenia umbelliflora* leaves varies significantly depending on the extraction method used, indicating that different methods may be more appropriate depending on the compounds of interest and desired applications.

# Chlorella vulgaris IBL-C 105 as a source of Extracellular Vesicles



## Author

Yasmin Passos - Núcleo de Estudos em Biotecnologia e Nanotecnologia Universidade Federal da Bahia (UFBA)  
Miguel de Jesus Oliveira Santos - Núcleo de Estudos em Biotecnologia e Nanotecnologia Universidade Federal da Bahia (UFBA)  
Milena Botelho Pereira Soares - Instituto Gonçalo Moniz, Fundação Oswaldo Cruz  
Henrique Rodrigues Marcelino - Núcleo de Estudos em Biotecnologia e Nanotecnologia Universidade Federal da Bahia (UFBA)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

Universidade Federal da Bahia - 402782/2023-2



## Keywords

Extracellular vesicle, *Chlorella vulgaris*, Pharmacological Approved

## Abstract

Extracellular Vesicles (EVs) are fundamental in intra and intercellular communication. The use of microalgae to obtain EVs may have potential advantages such as biocompatibility, low toxicity, and scalability at a low cost (compared to cell cultivation). The biomass of the *Chlorella vulgaris* species has already been studied for its therapeutic effects, which suggests that the EVs they produce also have pharmacological effects. In this context, this work aimed to obtain EVs by cultivating *C. vulgaris* IBL-C 105 with a view to the possible pharmacological application of EVs. We carried out batch cultivation at constant temperature and aeration. The culture was monitored daily for pH and optical density (UV-Vis Spectrophotometer) for 22 days. The isolation of EVs was carried out by low-speed centrifugation and filtration with a 0.22 $\mu$ m membrane. We performed Nanoparticle Tracking Analysis (NTA, Nanosight® NS300, Malvern) for the EV characterization process to check the average particle size and concentration. EVs were visualized by Transmission Electron Microscopy (TEM, JEM-2800, JEOL). From the obtained results, daily pH analysis showed that the samples had characteristic alkaline pH with an average of  $9.11 \pm 0.15$ . Through a standard curve of *C. vulgaris* IBL-C 105, we ascertained the maximum biomass yield in  $0.44 \pm 0.01$  g/L. The NTA detected the presence of particles with sizes ranging from 50 to 200 nm regardless of the sampling day. Images obtained through TEM showed structures with a circular shape and size similar to those previously seen in the NTA. Thus, the obtention of *C. vulgaris* IBL-C 105 EVs on our process can be indicated. A biomarkers assay is underway to confirm the biochemical nature of the obtained nanoscale particles. Confirmation of the obtention of *C. vulgaris* EVs can lead to standardization protocols and in-vitro assays to ascertain their pharmacological potential.

# Biocompatibility and potential of PLGA membrane with bovine corneal extracellular matrix for limbal stem cell therapy in ocular tissue regeneration



## Author

Ana Karulline Garcia Ungaratti - Universidade Federal de Goiás (UFG)

Paula Letícia de Melo Souza - Universidade Federal de Goiás (UFG)

Aliny Pereira de Lima - Universidade Federal de Goiás (UFG)

Jordana Andrade Santos - Universidade Federal de Goiás (UFG)

Marize Campos Valadares - Universidade Federal de Goiás (UFG)



## Knowledge Area

Biotechnology, Natural Products and Food Sciences



## Funding

CAPES



## Keywords

Biodegradable Scaffolds, Ocular Regeneration, PLGA Membranes

## Abstract

Membrane-shaped scaffolds are promising for stem cell therapies in ocular tissue regeneration, offering easy manipulation, differentiation, and localized cell delivery. The biodegradable copolymer PLGA is widely used, and adding bovine corneal extracellular matrix (ECM) hydrogel, rich in collagen, laminin, and fibronectin, enhances biocompatibility. This improves stem cell interaction, adhesion, proliferation, and differentiation, making it ideal for ocular tissue engineering. Our objective was to develop a biocompatible and biodegradable membrane designed for use in cell therapies aimed at regenerating tissues damaged by eye diseases. Suspended 24 mm inserts were used to mold 10% PLGA biomembranes coated with bovine corneal ECM hydrogel. Limbal stem cells were cultured on the biomembrane, and 24-hour biocompatibility was assessed with LIVE/DEAD™ Kit. Cellular behavior was examined using 3D confocal microscopy, and ocular progenitor markers (PAX-6 and RX) were evaluated via immunofluorescence. After viability monitoring, limbal stem cells on the biomembrane retained typical morphology. A predominance of live cells (green with calcein AM) over dead cells (red with ethidium homodimer-1) was observed. 3D confocal microscopy showed cell permeation into the biomembrane up to 40 μm within the ECM framework. Immunofluorescence confirmed continued expression of ocular progenitor markers PAX-6 and RX. Our data show that the developed biomembrane is biocompatible, non-toxic, and supports limbal stem cell adhesion, proliferation, and maintenance. Cell permeation within the ECM layer and continued expression of PAX-6 and RX confirm functional competence and potential for differentiation into specialized ocular cells. These findings suggest the biomembrane has strong potential for regenerating or repairing damaged ocular tissues.

**Area**

# **Drug Discovery and Medicinal Chemistry**

# Revealing MAC1 as a promising target for SARS-CoV-2 drug discovery: Crafting novel antiviral inhibitors via in silico tools.



## Author

Eduardo Willian de Alencar Pereira - Universidade de São Paulo (USP)  
Naomí Crispim Tropéia - Universidade de São Paulo (USP)  
Gabrielle Motta Fernandes - Universidade de São Paulo (USP)  
Vanessa Barbosa Malaquias - Universidade de São Paulo (USP)  
Laura Razzo de Moraes Almeida - CEUMA Universidade  
Claúdia Quintino da Rocha - CEUMA Universidade  
Lídio Gonçalves Lima Neto - CEUMA Universidade  
Alcindo Aparecido dos Santos - Universidade de São Paulo (USP)  
Gláucio Monteiro Ferreira - Universidade de São Paulo (USP)  
Mário Hiroyuki Hirata - Universidade de São Paulo (USP)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES 88887.714991/2022-00



## Keywords

SARS-CoV-2, drugs, MAC1

## Abstract

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that emerged in late 2019 in China, spreading worldwide. Besides the various targets known to treat SARS-CoV-2, one of the most promising new targets described lately is the non-structural protein 3 (NSP3) formed with a Macrodomain 1 (MAC1), Macrodomain 2 (MAC2) and Macrodomain 3 (MAC3). The MAC1 composed of 7  $\beta$ -sheets flanked by 6  $\alpha$ -helices that is fundamental for viral replication and pathogenicity. Here, we evaluate using in silico strategies the potential activity of new compounds LQPN05, IQ1, IQ2 e IQ3 against MAC1. Initially, the MAC1 structure was created by the Maestro edition tool (PDB:6W02). Then, ligand docking was performed by Chimera 1.17.3 software. We have assembled MAC1 complexes, including LQPN05, IQ1, IQ2 and IQ3, including two controls: Z8539 and GS-441524. Subsequently, conducted molecular simulations lasting 3.5  $\mu$ s (all systems) using Desmond software, OPLS-2005 force field. The compounds investigated here interact with some residues in common with the controls (GS441524 and Z8539). Specifically, GS441514 interacts with residues PHE156 (67.80%), LEU126 (67.80%), and GLY130 (67.80%) through hydrogen bonds. In these residues LQPN05 presents a frequency of 97.12%. IQ1 shares residue PHE156 (46.40%), while IQ2 interacts with GLY130 (54.36%) and IQ3 with PHE156 (43.47%) and LEU126 (47.39%). Z8539 shares the ILE23 (67%) residue with similar frequency to GS441524 and PHE156 (73%). In addition, LQPN05 (-7.0 kcal/mol), IQ1 (-7.2 kcal/mol), IQ2 (-6.8 kcal/mol) presented higher binding free energy than GS441524 (-6.3 kcal/mol). Interestingly, IQ3 with -8.7 kcal/mol has a higher affinity than Z8539 (-8.1 kcal/mol). Our findings indicate promising activity of LQPN05, IQ2, IQ1 and IQ3, respectively, against SARS-CoV-2 via MAC1 and could represent an advance in the development of new anti-COVID-19 drug candidates.

# Identification of potential selective caspase-3 inhibitors using virtual screening and molecular docking



## Author

Márcia Evangelista Borges - PCF - Universidade Estadual do Oeste do Paraná (UNIOESTE)  
Paula Beatriz Jesus Santos - PCF - Universidade Estadual do Oeste do Paraná (UNIOESTE)  
Eduardo Borges de Melo - PCF - Universidade Estadual do Oeste do Paraná (UNIOESTE)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Fundação Araucária



## Keywords

Caspase-3, Alzheimer, Molecular modeling

## Abstract

Caspase-3 participates in the regulation of apoptosis, and its dysregulation is related to Alzheimer's disease. Selective inhibitors of this enzyme may aid in treating this disease. Virtual screening (VS) of molecules may be a promising and efficient approach to identifying potential inhibitors. Therefore, this study aimed to perform a VS to identify possible inhibitors of caspase-3, which are selective about its main homolog, caspase-7. Thus, a pharmacophore model based on a potent and selective ligand for caspase-3 was used for screening using the CrossMiner program (CCDC). Hit searching was performed in the Cambridge Crystallographic Database (CSD), using internal structural constraints and selecting only small molecules. One hundred hits of interest were identified. By visual inspection, molecules that were too large, complex, or lacked drug-like structural characteristics were removed. Thus, 12 hits were selected for the molecular docking stage in the GOLD program (CCDC) using the Chemplp algorithm. Scores ranged from 50.49 to 71.16 in caspase-3 (PDB 1GFW), while in caspase-7 (PDB 3IBC) there was a variation from 42.82 to 62.64. All hits formed bonds with Tyr 204 and Trp 206. Interaction analysis was consistent with the literature. The ligand with the highest score interacted with residues Tyr204, Trp206, Trp214, and Phe256, located in pockets S1 and S2, which are considered necessary for potency and selectivity of caspase-3 inhibition compared to 7. The molecule with the highest score (NUSQUP\_1) extends throughout the cavity, a characteristic of good selective inhibition, as the caspase-7 cavity is too narrow for ligand extension. As concluded, the obtained molecules are promising candidates for further in silico and subsequent in vitro studies.

# Exploring a new organoselenium: admet properties and in vitro cytotoxicity



## Authors

Bianca Maia - Universidade Federal de Santa Maria (UFSM)  
Bruna Fracari do Nascimento - Universidade Federal de Santa Maria (UFSM)  
Juan Pedro Burnett da Luz - Universidade Federal de Santa Maria (UFSM)  
Gabriele Cogo Carneosso - Universidade Federal de Santa Maria (UFSM)  
Sidne Rodrigues da Silva - Universidade Federal de Santa Maria (UFSM)  
Oscar Endrigo Dorneles Rodrigues - Universidade Federal de Santa Maria (UFSM)  
Clarice Madalena Bueno Rolim - Universidade Federal de Santa Maria (UFSM)  
Daniele Rubert Nogueira-Librelotto - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES and FAPERGS (Project 21/2551-0002067-9)



## Keywords

Tumor cell lines, in silico, selenium compounds

## Abstract

**Background:** Cancer is a deadly disease that claims around 8.2 million lives every year worldwide. Chemotherapy, the current cancer treatment, still acts in a non-specific manner. Therefore, innovative molecules, such as the organoselenium 5'-Se-(phenyl)-3'-(benzo-thiadiazol-amido)-thymidine (SP01), may be interesting alternatives in the search for new compounds with anti-tumor activity. **Objectives:** The aim is to use in silico platforms to estimate the pharmacokinetic properties of the compound SP01, and to evaluate its in vitro anti-tumor activity using a sensitive (A549, lung cancer) and a resistant/MDR (NCI/ADR-RES, ovarian cancer) tumor cell lines. **Methods:** In silico data from platforms like Molinspiration, pkCSM, admetSAR, and SwissADME were used. Additionally, the MTT assay was applied to evaluate cell viability in both cell lines. **Results:** Lipinski's rule was slightly violated only in terms of molecular weight, making it a good candidate for oral administration therapy. The evaluation of pharmacokinetic processes suggested that this organoselenium would be well absorbed by the intestine, but would not have access to the brain. Furthermore, it may be a substrate/inhibitor of P-glycoprotein and CYP3A4, and pulmonary, reproductive, and liver toxicity were also suggested. The MTT assay showed anti-proliferative activity, with the A549 cell line presenting around 60% cell viability at the highest tested concentrations of 60  $\mu\text{g}/\text{mL}$  and 40  $\mu\text{g}/\text{mL}$ . At the lowest concentration of 1  $\mu\text{g}/\text{mL}$ , slight cytotoxicity was observed, with around 70% cell viability. The compound also proved to be cytotoxic even in the resistant tumor cell line, with around 65.2% and 66.1% cell viability at the highest treatment concentrations and non-cytotoxic at the lowest treatment concentration (cell viability ~93%). **Conclusion:** The in silico and in vitro results suggest a promising compound for anti-tumor therapy, requiring further studies to confirm this premise.



# Native Brazilian plants with potential antifungal properties against *Candida auris*, a WHO critical priority fungal pathogen



## Author

Henrique Santos Moure - Instituto de Biociências da Universidade de São Paulo (USP)  
Marcello Vittorio Bertachini de Ferrari - Instituto de Biociências da Universidade de São Paulo (USP)  
Rodrigo dos Anjos Miguel - Instituto de Biociências da Universidade de São Paulo (USP)  
Juliana C. S. Carvalho - Instituto de Biociências da Universidade de São Paulo (USP)  
Cinthia I. Tamayose - Instituto de Biociências da Universidade de São Paulo (USP)  
Letícia V. Costa Lotufo - Instituto de Biociências da Universidade de São Paulo (USP)  
Marcelo J. Pena Ferreira - Instituto de Biociências da Universidade de São Paulo (USP)  
Miriam Sannomiya - Instituto de Biociências da Universidade de São Paulo (USP)  
Kelly Ishida - Instituto de Biociências da Universidade de São Paulo (USP)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPESP (grant 2023/12190-0 and scholarship 2023/12793-7), CAPES (finance code 001) and CNPq (306041/202



## Keywords

*Candida auris*, Native Brazilian Plants, Fungal Priority Pathogens

## Abstract

*Candida auris* is considered by WHO one of the most critical priority fungal pathogens to research, along with *Cryptococcus neoformans*, *Candida albicans*, and *Aspergillus fumigatus*, mainly due to its multidrug resistance profile, high mortality, and fast worldwide spread. With the rise of superbugs, new treatment and disinfection options must be found to increase the fungus eradication strategies. In this study, we screened plant extracts and fractions (n=54) and some isolated compounds (n=25) obtained from native Brazilian species from Asteraceae, Bignoniaceae, and Malpighiaceae against fungal pathogens. Eighteen extracts or fractions displayed anti-*C. auris* action (2-128 µg/mL), as well as against other yeasts (*C. albicans* and *C. neoformans*), but none showed activity against *A. fumigatus*. Notably, *C. auris* clade II isolate was more susceptible while clade I and IV isolates often showed higher tolerance. The most prominent samples, with MIC values below 64 µg/mL for at least one species, were the n-butanol fraction of *Moquiniastrium oligocephalum*, ethyl acetate fraction of *Baccharis oblongifolia* and methanolic extract of *Byrsonima fagifolia*. This last one and some of its isolated galloylquinic acid derivatives showed the best antifungal activity on *C. auris* (1-32 µg/mL). Cytotoxicity assays on mammal cell lines indicated that *B. fagifolia* extract had low to no cytotoxicity up to 100 µg/mL on CCD18Co and J774A1 cells but reached CC50 values at 6.8-19.4 µg/mL on HCT-116 and MCF-7 tumor cell lines, while extracts and fractions from *M. oligocephalum* and *B. oblongifolia* were less toxic at the same values, but less effective on tested fungal species. Taken together, *Byrsonima* genus and the galloylquinic derivatives are already described in literature with action against *C. albicans* and *C. neoformans*, and now, in this research, we described *B. fagifolia* extract and the galloylquinic derivatives as an important candidate for further studies of antifungal anti-*Candida auris*.

# Bayesian Ensemble Optimization of Molecular Docking Protocols for the Discovery of Cruzain Inhibitors



## Author

Blasco Quefi - Universidade Federal de Goiás (UFG)  
Vinícius Alexandre Fiaia Costa - Universidade Federal de Goiás (UFG)  
Bruno Junior Neves - Universidade Federal de Goiás (UFG)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Fundação de Amparo à Pesquisa do Estado de Goiás (FAPEG)



## Keywords

Trypanosoma cruzi. SBVS. predictive modeling machine learning.

## Abstract

Chagas disease is a severe endemic morbidity caused by the flagellated protozoan *Trypanosoma cruzi*, affecting approximately 8 million people, primarily in Latin America. The current treatment, centered on benznidazole, faces challenges such as low efficacy, adverse effects, and parasitic resistance, underscoring the need for new therapeutic approaches. In this context, the cysteine protease cruzain of *T. cruzi* has emerged as a promising drug target since it plays a crucial role in vital processes of the parasite's biological cycle, including proliferation, differentiation, cell invasion, and evasion of the host immune system. This study aims to analyze the structure of cruzain and optimize molecular docking protocols to rank and discover new inhibitors. Initially, 26 structures of cruzain were collected from the Protein Data Bank (PDB) and analyzed using the Bio3D package. These analyses included identifying conserved regions and significant conformational variations through covariance analysis. Additionally, hotspot analysis was conducted to identify energetically favorable binding pockets and critical areas for protein stability and function. These investigations provided fundamental insights into the structural dynamics of the cruzain catalytic site, essential for selecting six representative conformations for developing molecular docking protocols. A large benchmark dataset, comprising 30 known inhibitors and 1,261 decoys, was compiled from the literature for validating an ensemble docking protocol. The energy terms from docking were then used to train a Bayesian scoring function. Using this score, we achieved enrichment rates with AUC = 0.87, EF > 40.74, and BEDROC > 0.85 in the top 1% of the ranked list, demonstrating the potential of protocol for candidate ranking. This study, therefore, opens new avenues for optimizing the discovery workflows of cruzain inhibitors, emphasizing the importance of innovation in computational strategies.

# In silico approaches supporting drug repurposing for leishmaniasis: A scoping review



## Author

Gustavo Scheiffer - Universidade Federal do Paraná (UFPR)  
Karime Zeraik Abdalla Domingues - Universidade Federal do Paraná (UFPR)  
Daniela Gorski - Universidade Federal do Paraná (UFPR)  
Alexandre de Fátima Cobre - Universidade Federal do Paraná (UFPR)  
Raul Edison Luna Lazo - Universidade Federal do Paraná (UFPR)  
Helena Hiemisch Lobo Borba - Universidade Federal do Paraná (UFPR)  
Luana Mota Ferreira - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES (Finance Code 001); CNPq (Proc.: 444941/2023-1; N° 21/2023)



## Keywords

Computational Drug Discovery, Leishmaniasis, Drug repurposing

## Abstract

The shortage of treatment options for leishmaniasis, especially those easy to administer and viable for deployment in the world's poorest regions, highlights the importance of employing strategies to investigate repurposing candidates cost-effectively. This scoping review aims to map the studies using in silico methodologies for drug repurposing against leishmaniasis. The study was conducted and reported according to the JBI guidelines for scoping reviews and the PRISMA-ScR checklist, respectively. Articles were systematically searched on PubMed, Scopus, and Web of Science databases (October/2023, updated in Apr/2024), without publication date restrictions. Studies that employed at least one computational method and aimed to repurpose an approved molecule against leishmaniasis were included. Information about methodologies, obtained data, and outcomes was extracted from the selected articles. Studies were discussed in the form of narrative synthesis, and data was analyzed through descriptive statistics and presented in tabular and graphical formats. After duplicate removal, 3316 articles were screened, of which 60 were fully appraised, resulting in 34 studies included in this review. Eighteen computational techniques were identified, with molecular docking being the most frequently used method (n=25). Studies reported 154 unique ligands and 72 different targets, and 14- $\alpha$  demethylase and trypanothione reductase were the most explored. In silico screening was able to correctly pinpoint some known active drug classes and propose previously untested drugs. Fifteen drugs investigated in silico exhibited low micromolar inhibition ( $IC_{50} < 10 \mu M$ ) of *Leishmania* spp. in vitro. In conclusion, several in silico repurposing candidates remain to be investigated in vitro and in vivo. Future research could expand the number of targets screened and employ advanced methods to optimize drug selection, offering new starting points for treatment development.

# Exploring Global phytochemicals and drug repurposing using machine learning and QSAR for leishmaniasis treatment



## Author

Raul Edison Luna Lazo - Universidade Federal do Paraná (UFPR)  
Lais Salvador do Amaral - Universidade Federal do Paraná (UFPR)  
Marcelino Marcos Agostinho - Universidade Federal do Paraná (UFPR)  
Dile Pontarolo Stremel - Universidade Federal do Paraná (UFPR)  
Luana Mota Ferreira - Universidade Federal do Paraná (UFPR)  
Alexandre de Fátima Cobre - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

No funding



## Keywords

Machine Learning, Drug Discovery, Drug Repurposing

## Abstract

Leishmaniasis, a neglected tropical disease, affects over 1 billion people worldwide. The World Health Organization reporting ~30,000 new cases of visceral leishmaniasis and over 1 million cases of cutaneous leishmaniasis annually. This study introduces an innovative approach that integrates machine learning, QSAR, and polypharmacology to identify new drug candidates derived from natural products and repurpose already approved medications for leishmaniasis treatment. Using a dataset of 12,072 compounds with IC<sub>50</sub> values against nine *Leishmania* species (*L. infantum*, *L. mexicana*, *L. tropica*, *L. chagasi*, *L. amazonensis*, *L. aethiopica*, *L. major*, *L. braziliensis*, and *L. donovani*) from ChEMBL database, described by PubChem fingerprints, we trained and evaluated Random Forest and XGBoost models. For predictions we use world biodiversity natural products databases including the five continents, and for drug repurposing we use ZINC, Drug Bank, and ChEMBL in clinical trial drugs databases. The models achieved R<sup>2</sup> scores of 0.80-0.84 during training and 0.70-0.71 in prediction, with RMSE metrics of 0.34 and 0.46-0.47, respectively. Among the promising natural products identified are Amphotericin B and Nystatin, along with PubChem compounds CID 11632231 and CID 11702226 in Africa. In Asia, we identified dihydrocyclobuxine D, 12-methyl-E,E-2,13-octadecadien-1-ol, dehydrocholesterol, veratrozine, falcarinol, and an additional compound not registered in the PubChem Database. In Oceania, notable compounds include nonadec-5-en-1-ol, cryptocariol, 12-methyl-E,E-2,13-octadecadien-1-ol, and dehydrocholesterol. Drug repurposing efforts highlighted significant anti-leishmania activity in nystatin, stamycin, spiramycin, solamargine, and plicamycin. These findings underscore the potential of natural products and drug repurposing in the fight against leishmaniasis and demonstrate the effectiveness of combining machine learning and QSAR in accelerating the discovery of new treatments.

# Predicting potential targets of two Amaryllidaceae alkaloids through network pharmacology and molecular docking



## Author

Gustavo Neves - Universidade Federal do Rio Grande do Sul (UFRGS)  
Luciana Ruschel Tallini - University of Barcelona  
Maria Helena Vendruscolo - Universidade Federal do Rio Grande do Sul (UFRGS)  
Paula Rezende-Teixeira - Universidade Federal do Rio Grande do Sul (UFRGS)  
Warley Borges - Universidade Federal do Espírito Santo (UFES)  
Jaume Bastida - University of Barcelona  
Letícia Costa-Lotufo - Universidade de São Paulo (USP)  
Vera Lucia Eifler-Lima - Universidade Federal do Rio Grande do Sul (UFRGS)  
José Angelo Zuanazzi - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES and CNPq



## Keywords

Medicinal Chemistry, Natural products, Molecular docking

## Abstract

**Background:** The Amaryllidaceae is known for producing unique alkaloids with diverse biological activities, including anticancer. Over 650 compounds have been isolated from this family. In medicinal chemistry, identifying targets is essential for discovering disease-relevant proteins. Modern methods use disease-related databases, artificial intelligence, and visualization techniques to explore new targets. **Objectives:** This work aims to identify potential anticancer targets combining network pharmacology with molecular docking for lycorine and montanine. **Methods:** The target prediction was performed through target-fishing based on the structure of the alkaloids. The results were associated to disease-related databases. The common targets were curated and plotted on a Venn diagram. Then they were mapped through protein-protein interaction network built in STRING database. Cytoscape 3.9.1 was used for network visualization. The enrichment analyses were performed at ShinyGo and KEGG. The top ten pathways were evaluated and related targets were selected for molecular docking, which was performed by GOLD 5.2 with ChemPLP and default parameters. The docking protocol was validated by redocking. The best ranked pose of each ligand was selected and visually inspected. **Results:** The network pharmacology highlighted PI3K-Akt as a potential pathway. Based on target prediction results four targets were selected for docking: CDK8, EGFR, ER-alpha, and dCK. The docking scores revealed two promising targets for the alkaloids, CDK8 and dCK, with scores similar to the co-crystallized compounds. Visual inspection suggests that the alkaloids interact with key residues from both targets. **Conclusion:** The computational studies suggested PI3K-Akt as a potential pathway to be further analyzed. The docking performed for the alkaloids indicated that CDK8 and dCK could be associated to the anticancer activity observed. **Acknowledgements:** The authors thank to CNPq and CAPES for the financial support.

# A scoping review of in silico, in vitro, and in vivo approaches in drug repositioning for lung cancer



## Author

Wellington Ragassi - Universidade Federal do Paraná (UFPR)  
Fernando Miguel Stelmach Alves - Universidade Federal do Paraná (UFPR)  
Raul Edson Luna Lazo - Universidade Federal do Paraná (UFPR)  
Fernanda Stumpf Tonin - Escola Superior de Tecnologia da Saúde de Lisboa  
Luana Mota Ferreira - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)  
Ednéia Peres Machado - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES (Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior)



## Keywords

Keywords: Lung cancer, oncology, drug repositioning

## Abstract

Recent data from GLOBOCAN show that lung cancer was the most incident neoplasm, with the highest number of deaths, totaling 2.48 million new cases and 1.81 million deaths. The development of new drugs for cancer treatment requires several stages, including the identification and optimization of molecules with potential effects on the disease, followed by preclinical and clinical studies to determine the pharmacokinetic, pharmacodynamic characteristics, and toxicity of the new drug. This process is costly and takes several years to complete. Drug repositioning has emerged as a strategy that allows for the investigation of the action of drugs with characteristics already described for diseases that require new treatments. In the field of oncology, this approach can save time and human, technical, and financial resources related to the development and market launch of a new antineoplastic. Given this, the aim of this study is to map the characteristics of current in silico, in vitro, and in vivo approaches and clinical trials for drug repositioning in oncology, focusing on lung cancer, as well as to identify molecular targets for the treatment of the disease. The search terms "Lung cancer" and "Drug repositioning" were used to search the PubMed, Embase, and Web of Science databases. A total of 1249 articles were identified, and after removing 525 duplicates, 724 records were screened by reading the titles and abstracts. A total of 637 articles that did not meet the inclusion criteria were excluded, leaving 87 studies for full reading. In an initial data analysis, it was found that the drugs metformin, itraconazole, propranolol, celecoxib, sertraline, and atorvastatin are the most cited to have potential to be repurposed for treating lung cancer. The next steps involved discussing their main molecular targets and their effectiveness in vitro and in animal studies.

# Machine Learning-Based QSAR for Multitarget Drug Discovery in Alzheimer's Disease



## Author

Thales Jung - Universidade Federal do Paraná (UFPR)  
Helena Hiemisch Lobo Borba - Universidade Federal do Paraná (UFPR)  
Alexandre de Fatima Cobre - Universidade Federal do Paraná (UFPR)  
Raul Edison Luna Lazo - Universidade Federal do Paraná (UFPR)  
Henrique Gabriel Wuchryn Martins - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Agency CAPES



## Keywords

Alzheimer's Disease, Drug Discovery, Machine Learning

## Abstract

Alzheimer's disease is the most prevalent neurodegenerative disorder worldwide, characterized by the progressive loss of cognitive function. Current therapeutic approaches, based on acetylcholinesterase inhibitors and NMDA receptor antagonists, have not demonstrated satisfactory efficacy in slowing or halting the progression of the disease. This study focused on using machine learning algorithms to build a structure-activity relationship model capable of identifying new drug candidates for the treatment of Alzheimer's disease. To construct the model, bioactivity data available from the ChEMBL database were used, targeting  $\beta$ -Amyloid,  $\gamma$ -secretase, NEDD8 activating enzyme,  $\beta$ -secretase 1, and  $\beta$ -secretase 2, adopting a multitarget approach. The individual datasets for each target were combined into a single final dataset, which underwent a data selection step to retain the most relevant data, keeping molecules based on the type of bioactivity assay and IC<sub>50</sub> value as the bioactivity parameter. At the end of the data filtering stage, a total of 16,194 compounds were maintained. PubChem Fingerprint descriptors were used to represent the structure of the compounds. In total, 42 algorithms were screened, of which only five were selected for model construction. The selected algorithms were HistGradientBoosting Regressor, Random Forest, Extreme Gradient-Boosting Regressor, Extra Trees Regressor, and LightGBM. Among all the models, the most promising was the one built with the Extreme Gradient-Boosting Regressor algorithm, which achieved the following performance metrics: R<sup>2</sup> of 0,75, RMSE of 0,52, MSE of 0,65, and MAE of 0,42. The next step will be to apply the model to an external database to identify promising molecules as multitarget drug candidates. In conclusion, machine learning algorithms allow the generation of complex models from the analysis of large volumes of data, aiding in the discovery of new treatments for Alzheimer's disease.

# Combining Computational and Experimental Strategies to Discover a Novel Inhibitor of *Schistosoma mansoni* Dihydroorotate Dehydrogenase (SmDHODH)



## Author

Kamilla Alves - Universidade de São Paulo (USP)  
Marina Sena Mendes - Universidade de São Paulo (USP)  
Miguel de Menezes Vaidergorn - Universidade de São Paulo (USP)  
Aline Dias da Purificação - Universidade de São Paulo (USP)  
Flavio da Silva Emery - Universidade de São Paulo (USP)  
Maria Cristina Nonato - Universidade de São Paulo (USP)  
Carolina Horta Andrade - Universidade de São Paulo (USP)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

National Council for Scientific and Technological Development – CNPq grant #441038/2020-4;  
CAPES - 88887.809238/2023-00



## Keywords

Schistosomiasis, computational drug discovery, Inhibitor discovery

## Abstract

Schistosomiasis is caused by trematode parasites of the genus *Schistosoma* and is a neglected tropical disease. Praziquantel is the only available drug, safe and effective against adult worms. However, it lacks activity against juvenile worms, and cases of resistance have been documented. Therefore, the development of new therapeutic options for treating the disease is crucial. The metabolic pathways responsible for pyrimidine synthesis in *S. mansoni* are functional. A key enzyme in this process is the dihydroorotate dehydrogenase (SmDHODH), which catalyzes the stereospecific conversion of dihydroorotate to orotate. Hence, this study aims to identify new SmDHODH inhibitors that directly affect the parasite's survival, using computational and experimental approaches. The crystallographic structure of SmDHODH (PDB: 6UY4) and the inhibitor 2-hydroxy-3-isopentyl-naphthalene-1,4-dione were used as starting points. Shape-based models were developed using 13 active and 8 inactive compounds against SmDHODH. The best model was obtained using the FitTverskyCombo function, with an area under the curve (AUC) of 0.946, enrichment factor (EF) of 8.46, and the BEDROC of 0.76 for the top 10% of ranked compounds. The validated model was subsequently employed as a filter for a virtual screening campaign utilizing the ChemBridge library. This was followed by molecular docking and ADME property predictions. Ultimately, 18 compounds were selected and purchased for experimental validation. The enzymatic activity of SmDHODH in the presence of the compounds was assessed by monitoring DCIP consumption at 610 nm without a pre-incubation step. Notably, compound LabMol-525 demonstrated an IC<sub>50</sub> of 0.76  $\mu\text{M} \pm 0.06$ . These results highlight the significant potential of LabMol-525 against SmDHODH, thereby validating the employed methodology. Future steps will involve the optimization of this hit through a multiparametric approach to enhance its pharmacological and pharmacokinetic properties.



# In silico target fishing of dipeptidyl nitrile derivatives



## Authors

Edwin Leonel Bonilla Rozo - Instituto de Química de São Carlos | Universidade de São Paulo(USP)  
Andrei Leitão - Instituto de Química de São Carlos | Universidade de São Paulo (USP)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CNPq (312086/2023-7), FAPESP (2023/16111-8)



## Keywords

Target fishing, molecular docking, covalent inhibitors.

## Abstract

The research group has made a significant stride in the ongoing search for new bioactive molecules to inhibit cysteine proteases with nanomolar potency. By combining computational techniques and in vitro assays, we designed over 500 dipeptidyl nitrile compounds. However, some chemicals do not inhibit any of the enzymes of this family, necessitating the exploration of new molecular targets for these molecules. In this study, three target fishing programs were used: PBB2D, SwissTarget, and COMET-PDB+. This comprehensive search identified potential macromolecular targets. Based on a consensus scoring, it was observed that 14 out of 44 compounds showed promising binding profiles for the metalloproteinase and histone deacetylase families, which are associated with tumoral processes. Subsequently, molecular docking was conducted to evaluate their binding properties further. These compounds are now under in vitro evaluation against the target proteins. This study opens new avenues in medicinal chemistry and pharmacology, contributing to the advancement of human well-being.

# Antifungal activity of Ebselen against *Cryptococcus gattii* and virulence factors



## Authors

Letícia S. da Costa - Instituto de Ciências Biomédicas da Universidade de São Paulo (ICB-USP)  
Kelly Ishida - Instituto de Ciências Biomédicas da Universidade de São Paulo (ICB-USP)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, finance code 001), CNPq (306041/2022-7) and Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, grant 2023/12190-0; scholarship 2023/13608-9)



## Keywords

*Cryptococcus*, antifungal, ebselen

## Abstract

*Cryptococcosis* is an invasive fungal infection caused by *Cryptococcus* spp., an encapsulated yeast, manifesting pulmonary disease and/or meningitis. Both species share important virulence factors, such as polysaccharide capsule, titan cells and melanin production, but *C. gattii* presents additional features to evade host's immune system and establish the infection in healthy patients. These features can contribute to failure on drug therapy, besides to resistance and high toxicity of antifungal. In front of these facts, the need to search and prospect new molecules with potential antifungal becomes a priority. Thus, the aim of this study is to evaluate the action of Ebselen (EBS) against *C. gattii* and its virulence factors. To determine the minimum inhibitory concentration (MIC) of EBS, broth microdilution technique was performed on *C. gattii* R265 strain and clinical isolates (n=8) and on in vitro morphotypes, such as enlarged capsule and titan cells. Yeast morphometry, determination of capsular permeability and melanization assay were performed. Time kill curve was performed after exposure to EBS and amphotericin B (AMB) at several concentrations. *C. gattii* strains were susceptible to both AMB and EBS at low concentrations (0.03–2 µg/ml) leading cell death in the initial 2 h of treatment. The reduced capsular thickness and higher capsular permeability were observed after EBS treatment. Finally, melanin production was totally inhibited in *C. gattii* yeasts treated with EBS. Together, these data highlight the antifungal potential of EBS against *C. gattii* strains, suggesting that EBS could be a promising molecule to be further explored and improved in more in vitro but also in vivo studies.

# Development of CODOC and CODIN interfaces: Open-source tools for automation and increasing the performance of molecular docking and molecular dynamics methods in structure based drug design (SBDD).



## Author

Moisés Neto - Universidade Federal do Paraná (UFPR)  
Gustavo Scheiffer - Universidade Federal do Paraná (UFPR)  
Raul Edison Luna - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES



## Keywords

molecular docking, molecular dynamics, virtual screening

## Abstract

SBDD methods are widely employed in the drug research and development pipeline, enhancing success rates compared to traditional high-throughput screening (tHTS) approaches. They enable the ranking of extensive compound databases through virtual HTS (vHTS). A broader screening scope increases the structural diversity of the tested chemical population, thereby raising the chances of identifying promising compounds. Consequently, working with extensive ligand libraries is desirable, but this can be limiting for research groups lacking high-performance computing (HPC) resources. Available tools, both local and online, do not combine key features such as being open-source, having a graphical interface, allowing parameter configuration via the interface, automating ligand preparation, organizing output files by target and ligand library in multitarget approaches, generating result spreadsheets, performance logs, and end-time predictions. Addressing these needs, this study aimed to develop two tools, CODOC and CODIN, for molecular docking and molecular dynamics methods, respectively. These tools, written in Shell, manage other open-source applications (e.g., Open Babel, AutoDock Vina, Vina-GPU, GROMACS), redirect to online platforms when necessary (e.g., CHARMM-GUI and CGenFF), and automate many time-consuming procedures requiring computational expertise. Multithread tools were included to enable CPU and GPU parallelism, significantly boosting performance even on low-cost workstations. Our tests demonstrated over a 70% reduction in execution time using parallelism, with no significant alterations in ligand ranking parameters, as evidenced by Spearman coefficient. The software will be made available to the scientific community on an open-access platform (GitHub) and will receive updates to include Machine Learning classification models for bioactivity prediction, contributing to future in silico approaches.

# In silico study of cavities and compounds with potential allosteic modulation of GSK3 $\beta$



## Author

João Lucas Anglada Fernandes - Universidade Federal do Pampa (Unipampa)  
Fávero Reisdorfer Paula - Universidade Federal do Pampa (Unipampa)  
Sabrina Bairros Witczak - Universidade Federal do Pampa (Unipampa)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPERGS, UNIPAMPA, CAPES



## Keywords

GSK3B, In silico, Allosteric

## Abstract

The enzyme glycogen synthase kinase 3-beta (GSK3 $\beta$ ) plays a critical role in various metabolic and cellular signaling pathways. Recent research establishes an association between GSK3 $\beta$  and tumor proliferation and metastasis formation. Given this connection, investigating potential GSK3 $\beta$  inhibitors becomes a relevant strategy for developing new agentes to target tumors associated with this enzyme. In drug discovery, in silico tools like Cavity Search, Bioisosterism, and Prediction of Biological Targets are widely used. These methods help identify potential active and allosteric sites for ligand interactions and explore allosteric modulators of enzymes. Our study aimed to investigate allosteric binding sites in the GSK3 $\beta$  protein (PDB model code 7U36) and search for bioisosteric analogues of tideglusib. The computational program Cavity Plus was employed to calculate potential protein cavities, and MolOpt to generate the bioisosteric analogues, and the Self-Ensemble Approach (SEA) Search for predicting biological targets. When searching for cavities/molecular sites using subunits A and B, it was identified 30 molecular cavity proposals, with 5 considered strong or "druggable." Three of these were confirmed as allosteric sites based on Cavity Plus results and served as prototypes for searching similar cavities in the PDB database. Among 1000 cavity models in the PDB, 19 had fit-values above 0.3. Bioisosteric studies led to the generation of 804 analogues. Both studies suggest that 11 compounds resulting from cavity search and bioisosteric application exhibit predictive activity against GSK3 $\beta$  and could be candidate for potential inhibitors. Investigating allosteric sites and their inhibitors is crucial for proposing new e GSK3 $\beta$  modulators.

# Predicting Adverse Outcome Pathways of Endocrine-Disrupting Environmental Contaminants Using Artificial Intelligence



## Author

Eder Santos - Faculdade de Farmácia | Universidade Federal de Goiás (UFG)  
Eufrásia de Sousa Pereira Faculdade de Farmácia | Universidade Federal de Goiás (UFG)  
Bruno Junior Neves Faculdade de Farmácia | Universidade Federal de Goiás (UFG)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ); Fundação de Amparo à Pesquisa do Estado de Goiás (FAPEG)



## Keywords

QSAR, Endocrine-Disrupting Chemicals, Predictive Modeling

## Abstract

In recent years, thousands of chemicals with endocrine-disrupting properties have been identified as emerging contaminants, raising significant concern due to their potentially harmful effects on the human reproductive system. These chemicals negatively impact the signaling of estrogen receptors (ERs) and androgen receptors (ARs) either through direct interactions with the receptors or indirectly via transcription factors and modulation of critical metabolic enzymes involved in hormone synthesis and metabolism. Currently, studies on the reproductive toxicity of chemical substances can be conducted through *in vitro* and *in vivo* approaches. However, implementing these experimental assays faces numerous challenges, including the limited data processing capacity given the enormous volume of commercial chemicals, the operational complexity of the tests, and the ethical concerns associated with the use of animal models. Therefore, this work aims to develop artificial intelligence models as alternative methods to predict endocrine disruptors chemicals and adverse outcome pathways potentially harmful to the male and female reproductive systems. Initially, datasets of compounds tested *in vitro* were compiled from the Tox21 and ToxCast databases, and single-task models (Random Forest, Support Vector Machine, LightGBM) and multi-task models (MT-DNN) were developed using ECFP4 fingerprints as molecular descriptors. The results demonstrated predictive models, particularly the MT-DNN, which showed an accuracy rate of 87% and balanced values of recall and specificity (~75%) after in-house developed task2task calibration. In summary, this study offers promising methods for identifying reproductive toxicants, representing a valuable alternative or complement to *in vitro* and *in vivo* assays, highlighting the relevance and potential impact of the developed modeling tools in advancing toxicological research and minimizing the reliance on animal models.

# Integration of Machine Learning, QSAR, and Polypharmacology for Identifying Novel Phytochemicals as Drug Candidates Against Schistosomiasis



## Author

Gustavo Corrêa - Universidade Federal do Paraná (UFPR)  
Alexandre de Fátima Cobre - Universidade Federal do Paraná (UFPR)  
Allan Michael Junkert - Universidade Federal do Paraná (UFPR)  
Eric Luiz Domingos - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ)



## Keywords

Anti-schistosomal, Machine learning, Natural products.

## Abstract

Schistosomiasis, caused by *Schistosoma* sp., ranks as the second most pathogenic human parasitic infection after malaria. Recognized by WHO among 20 neglected tropical diseases, global initiatives aim for eradication. Endemic in low-income regions lacking basic amenities, it causes 280,000 deaths annually in Sub-Saharan Africa. New treatments are urgently needed due to praziquantel's limitations and resistance issues. Natural products offer diverse bioactive compounds for screening. This study aimed to integrate machine learning, QSAR, and polypharmacology approaches to predict compounds with anti-schistosomal bioactivity. To achieve this goal, compounds with anti-schistosomal bioactivity linked to three Target IDs were selected from ChEMBL. Subsequently, using Python, we removed compounds lacking IC<sub>50</sub> values, SMILES codes, or duplicates. We preprocessed the data using the Padelpy library and screened 40 machine learning algorithms with LazyPredict. Five algorithms were selected for bioactivity prediction, and Scikit-Learn was employed to predict bioactivity from five external databases: African, Asian, Australian, Brazilian, and worldwide against schistosomiasis. Preliminary results showed that initially 3,490 compounds were retrieved from ChEMBL, and after preprocessing, we obtained 669 non-redundant compounds. The five selected algorithms were: Extra Trees Regression, Histogram-based Gradient Boosting, Light Gradient Boosted Machine, Random Forest, and XGBoost. Regarding performance metrics, the R<sup>2</sup> values ranged from 0.8957 to 0.9330, MSE between 0.2642-0.3648, RMSE between 0.5140-0.6040, and MAE between 0.3522-0.4141. The next steps are to validate these models on independent datasets and optimize them for better accuracy and robustness. Further analysis with external databases is necessary to predict the bioactivity of natural products. Concluding, this study provided insights into the use of machine learning models to propose new drug candidates.

# Synthesis, characterization, and photodynamic evaluation of alginate-photosensitizer conjugates



## Author

Jaqueline Carneiro - Universidade Federal do Paraná (UFPR)  
Danielly Caetano - Universidade Federal do Paraná (UFPR)  
Miguel Daniel Nosed - Universidade Federal do Paraná (UFPR)  
Maria Eugênia Duarte Nosed - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CNPq, CAPES



## Keywords

Polysaccharides, photosensitizers, photodynamic inactivation.

## Abstract

The development of biomaterials integrating biopolymers with photosensitizers presents promising new therapeutic agents for a variety of applications, including wound dressings with photodynamic properties. Alginate is already explored in wound care due to its excellent physicochemical properties and biocompatibility. Chlorins, porphyrinoid photosensitizers, are well-researched for their roles in photodynamic therapy (PDT) and photodynamic inactivation (PDI). This study focused on chemically modifying alginate by attaching chlorin-type photosensitizers, which were derived from pheophytin a, extracted from the biomass of *Spirulina* sp., and used as a precursor for the semi-synthesis of methyl-pheophorbide a. The exocyclic ring of methyl-pheophorbide a was opened with diamines to produce different chlorins. The chlorins were then covalently bonded to alginate by amidation, resulting in amide alginate conjugates. Spectroscopic and spectrometry analyses confirmed the chemical modifications. Soret and Q-bands similar to those of the free chlorins, indicating successful conjugation. Photodynamic evaluation revealed that the conjugates had higher photostability compared to free chlorins. Singlet oxygen generation studies showed that the conjugates kept their efficiency. These findings suggest that the new chlorin-alginate conjugates hold significant potential as biomaterials for future applications in photodynamic inactivation and other therapeutic areas. The use of a natural polymer coupled with a photosensitizer extracted from microalgae underscores this study's alignment with the United Nations' Sustainable Development Goals (SDGs). It addresses objectives related to health, sustainability, and responsible consumption and production. This approach not only advances health outcomes by providing effective therapeutic options but also promotes sustainable practices in biopolymer and biopharmaceutical applications.

# Chemical Diversity of LaSOM Chemical Library: Insights from Density Based Clustering and ADME Analysis



## Author

Carolina Ritter - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CNPq, CAPES



## Keywords

Virtual screening, Chemical space, Computational techniques

## Abstract

**Background:** Antitumorals are crucial in cancer therapy, inhibiting malignant cell growth and enhancing treatment efficacy for multimodal treatment strategies. The Laboratório de Síntese Orgânica Medicinal (LaSOM) possesses a chemical library rich in compounds mostly designed to target anticancer and antioxidant mechanisms, aligning with the antitumoral molecular targets currently under investigation. **Objectives:** This study aims to characterize the chemical diversity, predict the drug-likeness, and evaluate the compound's ADME properties. These analyses seek to provide critical insights for advancing early-stage drug discovery efforts. **Methods:** A total of 435 compounds were drawn and converted to SMILES. Subsequently, drug-likeness and ADME properties were predicted using the open-source web server SwissADME. A set of 47 descriptors, including Lipinski parameters (molecular weight, Consensus logP, number of hydrogen bond donors and acceptors), Veber's rules, rotatable bonds, and topological polar surface area (tPSA), were then evaluated using descriptive statistics. Uniform Manifold Approximation and Projection for Dimension Reduction (UMAP) was employed to visualize distinct clusters within the dataset. **Results:** Compliance evaluation indicated that over 95% compounds had no infractions. Most molecules exhibited acceptable log P values, indicating favorable gastrointestinal absorption and blood-brain barrier permeability. Interquartile range (IQR) of 2.68 (1.95-3.49) confirmed this consistency across the dataset. The UMAP analysis effectively explained a sizable portion of the data variance, highlighting distinct clusters associated with specific pharmacological activities. **Conclusion:** Most screened compounds adhered to drug-likeness rules. The clustering analysis identified chemical patterns, highlighting the utility of density based clustering in understanding compound relationships. **Acknowledgments:** The authors thank CAPES, CNPq and FAPERGS for financial support.



# Evaluation Of The Antitumoral Activity Of New Compounds Derived From Chromanones



## Author

Diogo Pilger - LABC - Universidade Federal do Rio Grande do Sul (UFRGS)  
Júlia Biz Willig - LABC - Universidade Federal do Rio Grande do Sul (UFRGS)  
Bruna Stedile - LABC - Universidade Federal do Rio Grande do Sul (UFRGS)  
Nicolas Gouault - Laboratório de Modelagem Molecular, Pharmacie, Université de Rennes 1  
Patrícia de Aguiar Amaral - LaPlaM - Universidade do Extremo Sul Catarinense(UNESC)  
Simone Gnoatto - Laboratório de Fitoquímica e Síntese Orgânica (LaFIS)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

PPGCF/UFRGS and CAPES (Finance Code 001)



## Keywords

Chromanones; anticancer; cytotoxic

## Abstract

Chromanones are a class of flavonoids characterized by a chemical structure composed of benzene fused to a 2,3-dihydro- $\gamma$ -pyranone ring. Considering the necessity of new alternative treatments for cancer, the objective of this study was to evaluate the cellular viability of eight chromanones-derivatives compounds in cancer cell lines. The anticancer activities of the Chromanones-derivatives were evaluated in cervical cancer cell lines (SiHa and HeLa), breast cell lines (MCF-7), and chronic myeloid leukemia cell line (K-562). Non-tumorigenic Vero cells were also used. The cytotoxic effect of the compounds was performed using the MTT assay and cell counting. Cells were treated with different concentrations of compounds (10-100 $\mu$ M) and incubated for 48 hours. After 48 hours, the medium containing the treatment was removed and the cells were incubated with MTT solution (0.5mg/ml) or cell counting. Results were expressed as a percentage of control and IC<sub>50</sub> values. The degree of selectivity of compounds was expressed for each tumor cell line according to the equation  $SI = CC_{50} / IC_{50}$ . For evaluation of the mechanism by apoptosis, cells were treated with the concentration of the corresponding IC<sub>50</sub> of the compound for 48 hours and Annexin V-FITC/PI Staining Phosphatidylserine. The results show that NG400-1 compound was the most selective for cancer over normal cells. The NG400-1 molecule showed cytotoxicity in K-562 (IC<sub>50</sub>=41.65 $\mu$ M  $\pm$  1.87 and SI=8.54), MCF-7 (IC<sub>50</sub>= 54.02 $\mu$ M  $\pm$  1.21 and SI=6.58), HeLa (IC<sub>50</sub>= 38.88  $\mu$ M  $\pm$  1.22 and SI=9.15) and SiHa (IC<sub>50</sub>= 36.22  $\pm$  1.15 and SI=9.82) cells. The other compounds were also cytotoxic in relation to tumor cells with IC<sub>50</sub> ranging from 5 to 94 $\mu$ M, however they had a lower SI compared to the NG400-1 molecule. Regarding the mechanism of action, the NG400-1 molecule induces apoptosis. In this context, we showed that the NG400-1 compound is a promising candidate for cancer treatment, however studies other mechanisms of action need to be carried out.

# Virtual screening of natural products as *Helicobacter pylori* urease inhibitors



## Author

Dalila Loose - Universidade Federal do Espírito Santo (UFES)  
Rodrigo Rezende Kitagawa - Universidade Federal do Espírito Santo (UFES)  
Rita de Cássia Ribeiro Gonçalves - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Capes, Ufes, Fapes.



## Keywords

*Helicobacter pylori*, Urease, Natural Products

## Abstract

*Helicobacter pylori* infect over 40% of the world's population, being the major cause of gastric cancer. In this context, the emergence of resistant strains reveals the need for new therapies and new drug targets, as urease, an enzyme that is essential for pathogen survival in the acidic environment of the stomach. Furthermore, natural products have been traditionally used to treat gastric disorders for centuries, and the employment of bioinformatics is able to reduce time and cost required for drug discovery. Therefore, this study aimed to perform the virtual screen of substances from natural sources which can be candidates to urease inhibitors. A bibliographic screening was carried out to identify compounds inhibitors of urease from natural sources. The compounds with the best results were submitted to a virtual screening including Tanimoto's similarity in BindingDB, prediction of activity spectra for biologically active substances (PASS) in Way2Drug, prediction of physicochemical properties in SiwssADME and molecular docking in AutoDock. The structural comparison with standard inhibitors from literature indicated similarities from 0.00 up to 0.09 (very low). In addition, PASS revealed the best probability of activity (Pa) in urease inhibition for protocatechuic acid (0.747), anacardic acid (0.614) and atranorin (0.416). The prediction of physicochemical properties showed that all three substances follow Lipinski rule of 5 and do not inhibit metabolism's enzymes as CYP3A4 and CYP2D6. Molecular docking performed with *H. pylori* urease (PDB 1E9Y) and validated by acetohydroxamic acid redocking resulted in binding free energy equals to -3.44; -4.06 and -4.07 kcal/mol for protocatechuic acid, anacardic acid and atranorin, respectively, and the interactions were mainly stabilized by hydrogen bonds involving oxygens from the ligands. Hence, these substances have potential in urease inhibition, which stand in need of confirmation by further in vitro and in vivo studies.

# Molecular Dynamics Simulations And Mm/Pbsa Calculations Of Two Potential Inhibitor Of P-Glycoprotein Identified By Virtual Screening.



## Author

Eduardo de Melo - Universidade Estadual do Oeste do Paraná (UNIOESTE)  
Marcia Evangelista Borges - Universidade Estadual do Oeste do Paraná (UNIOESTE)  
Fernando Berton Zanchi - Fiocruz Rondônia -Rio Branco  
Patrícia Rijo - CBIOS ULHT Lisboa - Portugal  
Gabrielle Bangay - CBIOS ULHT Lisboa - Portugal  
Daniel J. V. A. dos Santos - CBIOS ULHT Lisboa - Portugal  
Vera M. S. Isca - CBIOS ULHT Lisboa - Portugal  
Florencia Z. Brauning - Institute "Siniša Stanković" Belgrado - Serbia  
Jelena Dinic - Institute "Siniša Stanković" Belgrado - Serbia  
Milica Pesic - Institute "Siniša Stanković" Belgrado - Serbia  
Bernardo Brito Palma - CBIOS ULHT Lisboa - Portugal  
Ana M. Díaz-Lanza - Universidad de Alcalá de Henares Madrid - Spain



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Araucaria Foundation; FAPERO; CAPES; CNPQ; EPIAMO; FCT/Portugal; Calouste Gulbenkian Foundation



## Keywords

Cancer, P-gp protein, Molecular modeling

## Abstract

Cancer is the second cause of mortality worldwide. A severe associated problem is that the majority of cancer patients can develop tumors that are resistant to multiple drugs (MDR: multidrug resistance). P-glycoprotein (P-gp), an efflux pump, is one of the most responsible for the emergence of MDR. In this context, inhibitors of this protein can be interesting adjuvants for cancer chemotherapy. Thus, this study aimed to perform molecular dynamics simulations of P-gp complexes with two promising ligands previously identified in the ZINC database in a pharmacophoric screening and molecular docking study. The P-gp complex (PDB ID: 3G60) with the ligands ZINC9418354 (1) and ZINC15842390 (2) was simulated in the GROMACS 2024.1 program using the Amber99 force field. The ligand was prepared in the Acpype program. The simulations were carried out in a cubic box with a side length of 2 Å using the TIP3 water solvation model. The system was neutralized with 0.15 M NaCl. The system was minimized using the Steepest Descent and Conjugate Gradient methods and equilibrated at NVT and NPT. The simulation was performed for 150 ns. In the end, the complex proved to be highly stable. A vital characteristic of this protein is its very hydrophobic binding site; the stability of the complex was mainly due to a large number of van der Waals bonds, as expected. The protein had an RMSD of 0.6 for 1 and 0.73 for 2, while the ligand-protein complex had a value of 0.20 and 0.11, respectively. The MM/PBSA method obtained a  $\Delta G_1 = -35$  Kcal/mol and  $\Delta G_2 = -52$  Kcal/mol. These in silico results show that both compounds are promising candidates for in vitro studies to confirm their abilities to block P-gp activity in tumor cells.

# Characterization Of The Aqueous Solubility Profile Of The 1,3,4- Oxadiazole Derivative (Lmm6)



## Author

João Marcos Barbosa Piai - Universidade Estadual de Maringá (UEM)  
Amanda Antunes Herling - Universidade Estadual de Maringá (UEM)  
Victor Nery Machado Lippa - Universidade Estadual de Maringá (UEM)  
Gustavo Finatti Sakamoto - Universidade Estadual de Maringá (UEM)  
Maria Sueli Soares Felipe - Pontifícia Universidade Católica de Brasília (UCB)  
Andrea Diniz - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES; FAPDF 00193-00001743/2022-64.



## Keywords

biopharmaceutical study, solubility, biorelevant media

## Abstract

**Introduction:** Fungal infections are a growing concern in medicine by increasing incidence and resistance to antifungal treatments, recognizing their severity is crucial, especially with the rise in immunosuppressive therapies and advancements in intensive care medicine. Recently, a new compound, 1,3,4-oxadiazole derivative (LMM6), showed promising antifungal activity against the thioredoxin system. However, its potential is hindered by limited biopharmaceutical data, particularly regarding its aqueous solubility. **Objectives:** The goal of this work was the solubility and lipophilicity characterization of the LMM6 molecule to guide the development of formulations. **Methods:** To perform the aqueous solubility study, a chromatographic methodology in high-performance liquid chromatography was developed and validated, using a HPLC Shimadzu Prominence-i LC-2030C photodiode array detector (PAD) following the guidelines established by the International Conference on Harmonization (ICH Q2-R1 and Q2-R2) and by RDC N° 166 of 2017 of the Brazilian National Health Surveillance Agency (ANVISA). The thermodynamic solubility analysis was conducted using the shake-flask method at 37 °C and 200 rpm for 24 hours. Various media were tested, including pharmacopoeial and biorelevant media. Additionally, experimental investigations were carried out to determine the log P (octanol-water partition coefficient) and melting point of LMM6. **Results:** In pharmacopoeial media, solubility ranged from 2.70 to 4.94 mg/L, while in biorelevant media, it ranged from 3.80 to 12.95 mg/L. In the analyses of melting point and log P, the following results were obtained: 222.53 °C and 2.11, respectively. **Conclusions:** These findings indicate that LMM6 exhibits low aqueous solubility across pH ranges. Biorelevant media slightly enhanced aqueous solubility compared to pharmacopoeial media. Moreover, the obtained log P value confirms its hydrophobic nature, crucial for understanding its pharmaceutical behavior.

# Synthesis and evaluation of antibacterial activity of ferulic acid derivatives



## Author

Alfredo José do Nascimento Neto - Universidade Federal do Oeste da Bahia (UFOB)  
Fabrício Luiz Tulini - Universidade Federal do Oeste da Bahia (UFOB)  
Stefânia Neiva Lavorato - Universidade Federal do Oeste da Bahia (UFOB)  
Pedro Lucas do Nascimento Bezerra Souza - Universidade Federal do Oeste da Bahia (UFOB)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

PDPG III 38/2022, ACT 294/2023, funding contract PPF00042023



## Keywords

antibacterials, ferulic acid, bacteria

## Abstract

Infections caused by microorganisms, mainly bacteria, are a public health problem due to the bacterial ability to develop resistance mechanisms to antimicrobial drugs, which generates a recurring demand for new agents. Alternatively, natural products with already known antibacterial activity, like ferulic acid, can be explored as hit compounds for novel antibacterials development. In this work, ferulic acid and four derivatives were synthesized and their activities against several bacteria of clinical interest were evaluated. Ferulic acid and its analogues *p*-coumaric acid, cinnamic acid and 4-hydroxy-3-nitrocinnamic acid were obtained by Doebner-Knoevenagel condensation, reacting malonic acid with the corresponding aromatic aldehydes in the presence of aniline and pyridine, under heating. The isopropyl ferulate ester was obtained by Fischer esterification, reacting ferulic acid with isopropanol in an acidic medium. The antibacterial activity of the synthesized compounds was evaluated against *Escherichia coli*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Staphylococcus aureus* and *Salmonella enteritidis* using a growth-inhibition assay by microplate method at a concentration of 50 µg/mL. The compounds were obtained with yields ranging from 52-75% and characterized by their melting points and infrared and <sup>1</sup>H and <sup>13</sup>C NMR spectra. It was observed that temperatures above 70°C, in the Doebner-Knoevenagel condensation, favor the formation of a vinyl contaminant derived from a double decarboxylation. Except for *Enterococcus faecalis*, at least one of the evaluated compounds showed inhibition activity against the listed bacteria, with a predominance of action against Gram-positive bacteria, indicating that the proposed modifications retain the biological activity already documented for ferulic acid.

# Neolignan Grandisin shows neuroprotective activity against memory impairment on a $\beta$ -amyloid induced Alzheimer's disease mouse model



## Authors

Herbert Patric Kellermann Cleveland - Universidade Federal de Mato Grosso do Sul (UFMS)  
Victor Hugo Bittencourt Andrade - Universidade Federal de Mato Grosso do Sul (UFMS)  
Gabrielle Teixeira Machado - Universidade Federal de Mato Grosso do Sul (UFMS)  
Ana Beatriz Nogueira da Silva - Universidade Federal de Mato Grosso do Sul (UFMS)  
Caroline Dorneles Pereira Portes - Universidade Federal de Mato Grosso do Sul (UFMS)  
Daniele Barboza Miranda Guimarães - Universidade Federal de Mato Grosso do Sul (UFMS)  
Diego Bento de Carvalho - Universidade Federal de Mato Grosso do Sul (UFMS)  
Paola Mayara valente coronel - Universidade Federal de Mato Grosso do Sul (UFMS)  
Egidi Mayara Silva Firmino - Universidade Federal de Mato Grosso do Sul (UFMS)  
Luiz Fernando Polizelli Pereira - Universidade Federal de Mato Grosso do Sul (UFMS)  
Albert Schiaveto de Souza - Universidade Federal de Mato Grosso do Sul (UFMS)  
Adriano Cesar de Morais Baroni - Universidade Federal de Mato Grosso do Sul (UFMS)  
Leonardo Resstel Barbosa Moraes - Universidade Federal de Mato Grosso do Sul (UFMS)  
Eduardo Benedetti Parisotto - Universidade Federal de Mato Grosso do Sul (UFMS)  
Everton do Nascimento Alencar - Universidade Federal de Mato Grosso do Sul (UFMS)  
Davi Campos La Gatta - Universidade Federal de Mato Grosso do Sul (UFMS)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) , finance code 01



## Keywords

Grandisin, Neuroprotection, Alzheimer's Disease

## Abstract

Alzheimer's disease (AD) is a multifactorial neurodegenerative disorder with complex etiology and the most common form of dementia. Although some drugs are available for treatment, they show limited efficacy and expressive collateral effects. Some neolignans showed neuroprotective properties against  $A\beta$  in vitro and recently Triazole Grandisin, an analogue of the neolignan Grandisin extracted from *Virola surinamensis*, was found to prevent memory impairment and neuroinflammation in vivo. However, the original compound, grandisin (GRA), despite presenting anti-inflammatory and antioxidant activity, has never been tested in an AD animal model. To evaluate the neuroprotective effect of GRA, male C57/Bl6 mice (CEUA protocol: 1.272/2023) underwent stereotaxic surgery for intracerebroventricular (i.c.v.) injection of  $A\beta$  oligomers or vehicle (V.). A seven days treatment protocol initiated twenty four hours after surgery by intraperitoneal (i.p.) administration of GRA (1 mg/kg) or V. according experimental groups: (V. i.c.v./V. i.p.), ( $A\beta$  i.c.v./V. i.p.) and ( $A\beta$  i.c.v./GRA i.p.). Object recognition test with 24 h between acquisition and retention was used to calculate the discrimination index (d2) and assess long-term memory formation. The test started one day after the last i.p. injections. Immediately after the test, animals were euthanized for cortex (Ctx) and Hippocampus (Hpc) dissection. Tiobarbituric acid reactive species (TBARS) test was performed in both structures to measure malondialdehyde (MDA) levels, as a parameter of lipoperoxidation. GRA reduced recognition memory loss caused by  $A\beta$  injection ( $P < 0.01$ ). Moreover,  $A\beta$  injection increased MDA levels in HPC ( $P < 0.05$ ) but not in CTX. GRA was able to prevent MDA increase in Hpc. These results show that GRA has potential neuroprotective effects by antioxidant mechanisms, as it prevents long-term memory disruption and reduced lipoperoxidation induced by  $A\beta$  injection.

# Characterization Of Melting Point And The Aqueous Solubility Of Ebselen



## Author

Victor Nery Machado Lippa - Universidade Estadual de Maringá (UEM)  
João Marcos Barbosa Piai - Universidade Estadual de Maringá (UEM)  
Amanda Antunes Herling - Universidade Estadual de Maringá (UEM)  
Gustavo Finatti Sakamoto - Universidade Estadual de Maringá (UEM)  
Maria Sueli Soares Felipe - Universidade Católica de Brasília (UCB)  
Fernanda Belincanta Borghi Pangoni - Universidade Estadual de Maringá (UEM)  
Érika Kioshima Cotica - Universidade Estadual de Maringá (UEM)  
Andrea Diniz - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

This study was supported by Fundação Araucária and FAPDF 00193-00001743/2022-64.



## Keywords

biopharmaceutical study, solubility, biorelevant media

## Abstract

**Introduction:** Ebselen is a selenorganic compound, originally synthesized in 1984. Since then, ebselen has shown potential for numerous applications, including: antifungal, antiviral and antibacterial, as well as a neuroprotector after brain stroke. The evaluation of aqueous solubility could immensely impact the approaches during development phases of ebselen-containing drugs as the solubility is a critical parameter for the adequate absorption of drugs in vivo. **Objectives:** The goal of this work was to evaluate the experimental physicochemical parameters aqueous solubility in different media and melting point to guide drug development. **Methods:** The thermodynamic solubility assay was conducted using the shake-flask method at 37 °C and 200 rpm for different aqueous media. The melting point was determined by a capillary tube method using a fusion point FISATOM model 430. All quantification analysis were performed using a validated HPLC-MS/MS method. **Results:** For water and the pharmacopeial media, solubility was 14.78  $\mu\text{g/mL}$  phosphate buffer (pH 6.8), 24.42  $\mu\text{g/mL}$  for acetate buffer (pH 4.5), 13.06 for HCl solution (pH 1.8) and 18.95  $\mu\text{g/mL}$  for water (pH 6.4). In biorelevant media, the solubility was 20.09  $\mu\text{g/mL}$  for FaSSiF (pH 6.8), 11.05  $\mu\text{g/mL}$  and 41.62  $\mu\text{g/mL}$  for FeSSGF (pH 4.5). The melting point was found to be 169.0 °C. Albeit there was a significant difference between the solubility in different aqueous media, the major increase in solubility was observed for the media simulating gastric fluid in fed state. These characteristics are fundamental during the development of ebselen-containing drugs as they could be a limitation especially during the absorption process. **Conclusions:** The overall aqueous solubility of ebselen was considered low.

# Machine learning models based on QSAR and polypharmacology reveal repurposing drug candidates to inhibit *Trypanosoma cruzi* and *Trypanosoma brucei*



## Author

Karime Domingues - Universidade Federal do Paraná (UFPR)  
Laís Salvador do Amaral - Universidade Federal do Paraná (UFPR)  
Gustavo Henrique Scheiffer - Universidade Federal do Paraná (UFPR)  
Allan Michael Junkert - Universidade Federal do Paraná (UFPR)  
Luana Mota Ferreira - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Capes - Finance code 001



## Keywords

Machine Learning, QSAR, Neglected Tropical Diseases

## Abstract

**Background** African and American trypanosomiasis, known as sleeping sickness and Chagas disease, respectively, are defined by WHO as neglected tropical diseases (NTD), necessitating increased research and investment in more effective, and safer therapies. In this scenario, *in silico* studies, combined with Artificial Intelligence (AI), are proving to be robust and optimized approaches for mapping potential new treatments. In this context, leveraging drug repositioning, which explores approved compounds for new applications, is particularly promising due to its cost and time efficiencies, along with the enhanced safety profiles. **Methodology** This study integrates machine learning, QSAR (Quantitative Structure-Activity Relationship) models, and polypharmacology to repurpose FDA-approved drugs for trypanosomiasis treatment. We analyzed 21,605 compounds with inhibitory bioactivity (expressed as IC<sub>50</sub>) against *Trypanosoma brucei* and *Trypanosoma cruzi* from the ChEMBL database using PubChem fingerprints. Forty multi-target machine learning algorithms were evaluated using regression metrics such as R<sup>2</sup>, MSE, RMSE, MAE, and training time. The top models were used to screen the ZINC database for repurposing candidates. **Results** For prediction calculations, two ensemble models using decision trees were implemented due to their applicability in drug discovery, and superior metrics results: Random Forest and Extreme Gradient Boosting. Pentamidine isethionate served as a positive control, and 39 repurposing candidates were identified (pIC<sub>50</sub> > 6 and coefficient of variation < 5%), primarily antineoplastic (28%) and antifungal drugs (29%). **Conclusion:** The machine learning models used for ligand-based virtual screening (LBVS) analysis were able to rapidly identify an already approved drug for sleeping sickness treatment, as well as other compounds with potential inhibitory effects against *T. brucei* and *T. cruzi*, which can be tested in further *in vitro* and *in vivo* studies.



# Synthesis and antitumor potential of $\beta$ -lapachone triazole derivative



## Author

Rhanna Amaral da Silva - Universidade Federal do Amazonas (UFAM)  
Fernanda Guilhon-Simplicio - Universidade Federal do Amazonas (UFAM)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPEAM (062.00931/2013)



## Keywords

Synthesis, Metalloproteinase, in silico

## Abstract

Conjugation with triazoles in drug synthesis has been a promising approach, originating stable derivatives with low binding energy against metalloproteinases, key enzymes in the degradation of components of the extracellular matrix (ECM), and in the process of carcinogenesis. Of the prototype molecules,  $\beta$ -lapachone has various pharmacological properties, including antitumor. Therefore, the objective was to synthesize a triazole derivative of  $\beta$ -lapachone in order to enhance its antitumor activity. The synthesis occurred with 50 mg of  $\beta$ -lapachone (0.21 mmol) and 138.1 mg of 1,2,4-triazole (2 mmol) and 1 mL of trietholamine in 10 mL of ethanol stirred at 70 °C for 24 hours, being monitored by thin layer chromatography. Next, 20mL of water was added, extracted with dichloromethane, which was evaporated, resulting in 12.2mg (24%) of product, purified on a silica gel 60 column, using hexane: ethyl acetate (8:2) as a mobile phase. The structure was confirmed by <sup>1</sup>H Nuclear Magnetic Resonance, in addition to anchoring the derivative to Matrix Metalloproteinase 2 (MMP2), using the GOLD software, validated by redocking (1.369 Å). <sup>1</sup>H NMR indicated multiplet signals at  $\delta$  8.10 ppm and 7.55 ppm referring to the aromatic ring A, multiplet signal at  $\delta$  7.70 ppm referring to the triazole hydrogen, triplet signal at 7.36 ppm (J= 2, 2 Hz) referring to aromatic ring A and a doublet doublet signal at 7.14 ppm (J= 2.4; 8.6Hz) also referring to aromatic ring A. A triplet signal was observed at 2.63 ppm (J=6.6 Hz) and doublet at 2.05 ppm (J=7.5 Hz). Triplet at 1.83 ppm (J=6.7 Hz) of H-3 of ring C and a simplet at 1.26 ppm referring to two methyls, which confirm the structure of 1,2,4- triazole-  $\beta$ -lapachona. In molecular docking, the fitness score of the generated derivative was 59.37, compared to 30.09 for  $\beta$ -lapachone, indicating a higher binding affinity of the derivative. Thus, an unprecedented triazole derivative of  $\beta$ -lapachone was obtained with potential activity against tumor cells.

# Synthesis and Cytotoxicity of Nor- $\beta$ -Lapachone and Aminopyrimidine Derivative



## Authors

Angel Yasmin Maia da Cruz - Universidade Federal do Amazonas (UFAM)  
Rhanna Victória Amaral Silva - Universidade Federal do Amazonas (UFAM)  
Fernanda Guilhon Simplicio - Universidade Federal do Amazonas (UFAM)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CNPQ



## Keywords

Aminopyrimidine,  $\beta$ -Lapachone, In Silico

## Abstract

Numerous studies associate pyrimidines with the ability to enhance the affinity of molecules toward various proteins, a fact demonstrated by molecular docking. Thus, to potentiate the antitumor activity of nor- $\beta$ -lapachone, this molecule was conjugated with aminopyrimidine. Its cytotoxic capacity was evaluated in vitro, and molecular docking analysis was performed against the BRAFV600E, MMP-2, and MMP-9 proteins using the GOLD software. For the synthesis, 4 mL of pyridine and 10 mL of dichloromethane (DCM) were added to nor- $\beta$ -lapachone, along with 3 mmol of I2, under stirring at room temperature for 24 hours, monitored by TLC. Cold water was then added, and the solution was washed with 10% Na<sub>2</sub>CO<sub>3</sub> (3x) and distilled water (3x). The resulting solution was dried with anhydrous sodium sulfate, filtered, and the solvent was evaporated at room temperature. The product was purified by silica gel column chromatography, using hexane/ethyl acetate 8:2 as the eluent. Subsequently, 20.7 mg of the iodinated derivative in ethanol and 4 eq. of aminopyrimidine reacted in ethanol/acetic acid 1:1. Finally, a saturated NaCl solution was added. The mixture was extracted with DCM, and the organic phase was dried with anhydrous sodium sulfate. The cytotoxicity evaluation at 24, 48, and 72 hours was conducted on MRC-5 cell lines. The reaction yielded 65% of an orange solid substance. Its characterization by <sup>1</sup>H and <sup>13</sup>C NMR is being finalized. The docking results showed fitness scores of 61.9155 (BRAF), 36.3172 (MMP-2), and 38.8528 (MMP-9), higher than  $\beta$ -lapachone, which had scores of 56.5421 (BRAF), 30.0952 (MMP-2), and 26.2199 (MMP-9). The viability results in MRC-5 cells were below 20% after 48 hours, indicating its potential in anticancer stimulation.

# A recollection of the work with dipeptidyl nitrile derivatives as anticancer chemicals.



## Authors

Andrei Leitão - NEQUIMED-IQSC-USP



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPESP 23/16111-8; CNPq 312086/2023-7.



## Keywords

drug discovery, cathepsin inhibitors, cell-based assays

## Abstract

Cysteine cathepsins (CTS) are involved in many pathophysiological processes, including cancer progression, and many reviews point to their activity in distinct instances of cancer. However, despite the description of potent and selective chemicals against CTS, not much was achieved for the inhibitors in a drug discovery pipeline. Here, a recollection is made regarding our finding for the study of dipeptidyl nitriles against different cancer cell lines and the putative mechanisms of action. The novel results will be presented for the cell migration inhibition and apoptotic and autophagic pathway modulation (primarily focused on breast, pancreatic, and liver cancer cell lines). The assessment of novel macromolecular targets and physical-chemical properties using many in vitro studies will also be mentioned. Altogether, these results will outline a path toward the coming years of research efforts in the field.

# Investigation of the effect of triazole glycosides of digitoxigenin against lung cancer cells and Herpes Simplex Virus



## Authors

Iara Zanella Guterres - Universidade Federal de Santa Catarina (UFSC)  
Flaviano Melo Ottoni - Universidade Federal de Minas Gerais (UFMG)  
Isabella Dai Prá - Universidade Federal de Santa Catarina (UFSC)  
Luíse Gauer Schulte - Universidade Federal de Santa Catarina (UFSC)  
Maria Eduarda Sedrez - Universidade Federal de Santa Catarina (UFSC)  
Gislaine Fongaro - Universidade Federal de Santa Catarina (UFSC)  
Ariadne Cristine Cabral - Universidade Federal de Santa Catarina (UFSC)  
Ricardo José Alves - Universidade Federal de Minas Gerais (UFMG)  
Rodrigo Maia de Pádua - Universidade Federal de Minas Gerais (UFMG)  
Izabella Thaís Silva - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Pronem / FAPESC / Termo de Outorga: 2020TR715. SIGPEX UFSC: Ação de Extensão Sigpex: 201917940.



## Keywords

cardenolides, cytotoxic activity, anti-herpetic activity

## Abstract

Natural products are essential sources in the research and development of novel drugs due to their abundant and complex structural diversity, which holds vast potential for biological and pharmacological effects. These natural compounds serve as models for synthesizing new pharmaceutical agents. Traditionally used to treat cardiac diseases, Cardenolides have recently garnered attention for their remarkable cytotoxic, antitumor, and antiviral properties. Herpes Simplex Virus type 1 (HSV-1) infects approximately 70% of the global population, posing a significant health problem worldwide. Meanwhile, cancer, with its high mortality rate, represents another global health challenge, requiring the exploration of new treatment alternatives. In this context, the cytotoxic and anti-herpetic activities of semisynthetic cardenolide analogs were evaluated. The sulforhodamine B assay was employed to assess cytotoxicity (CC50) in human lung tumor cells (A549), and the plaque reduction assay (IC50) was used to evaluate antiviral activity against HSV. Two compounds, 6b and 6d, emerged as particularly promising and were selected for mechanistic studies. These studies involved evaluating the primary pathway of cell death, the impact on cell cycle progression, and the clonogenic potential of the compounds. To investigate the antiviral mechanism of the most active compounds, their effects on HSV-1 viral adsorption and penetration were examined. Additionally, the interference of cardenolides with the protein expression in herpesviruses was analyzed using the HSV-1 29-R strain, which is resistant to acyclovir. Therefore, these semisynthetic cardenolides deserve attention as bioactive molecules with potential for drug development. Their study contributes to increasing knowledge in the field and offers promising new therapeutic alternatives.

# Innovative therapeutic approaches for neuroprotection in Alzheimer's Disease



## Author

Maria Paula Faccin Huth - Universidade Federal do Rio Grande do Sul (UFRGS)  
Thais Carine Ruaro - Universidade Federal do Rio Grande do Sul (UFRGS)  
Murillo Orsatto Haas - Universidade Federal do Rio Grande do Sul (UFRGS)  
Grace Gosmann - Universidade Federal do Rio Grande do Sul (UFRGS)  
Aline Rigon Zimmer - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPERGS, CNPq



## Keywords

Alzheimer, neuroprotective, chalcone

## Abstract

Alzheimer's disease (AD) is a progressive and multifactorial neurodegenerative disease that still has no cure. Different pathological processes contribute to the disease's development, such as amyloid beta (A $\beta$ ) plaques, neurofibrillary tangles, glutamatergic excitotoxicity, oxidative stress, and neuroinflammation, highlighting the need to investigate new targets for AD. In this study, we evaluated the cytotoxicity and neuroprotective effects of a series of natural and synthesized molecules using *in silico* methods, where virtual platforms determined and predicted the drug-like characteristics of compounds and their permeation capacity by the BBB, and *in vitro* assays, in cell lines. Chalcones, polyphenolic compounds of natural origin with a wide range of biological activities, and emerging studies have reported neurotrophic activity, anti-inflammatory and antioxidant effects, and the inhibition of A $\beta$  aggregation. *In vitro* assays of 19 compounds were performed in C6 astroglial and VERO cell lines to assess cytotoxicity, followed by evaluation of their neuroprotective effects against oxidative and glutamatergic insults in C6 astroglial cells. The 3 most promising compounds were tested in a primary culture of astrocytes from the cerebral cortex of a neonatal Wistar rat, and their ability to protect the cell from neuroinflammatory insult was evaluated. The *in silico* results indicated that all compounds presented satisfactory drug-like properties and low or no cytotoxicity. Among tested compounds in *in vitro* assays, the most promising candidate was CHA 16. It showed a suitable oral bioavailability and a high potential to cross the BBB, low cytotoxicity, and a neuroprotective effect against the oxidative and glutamatergic insults in C6 astroglial cells and against the inflammatory insult in primary astrocyte cells. CHA 16 displayed significant astro-trophic effects in both cells tested, showing that it is a promising candidate for clinical testing targeting AD treatment.

# Virtual screening of *Persea americana* Mill. seed compounds for potential effects on oncogenic proteins CagA and VacA of *Helicobacter pylori*



## Author

Amanda Cavalcante Gonzaga Nunes - Universidade Federal do Espírito Santo (UFES)  
Leonardo Bruno Federico - Universidade Federal do Espírito Santo (UFES)  
Lorena Carnielli Queiroz - Universidade Federal do Espírito Santo (UFES)  
Rodrigo Rezende Kitagawa - Universidade Federal do Espírito Santo (UFES)  
Rita de Cássia Ribeiro Gonçalves - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Fundação de Amparo à Pesquisa e Inovação do Espírito Santo (FAPES), 28/2022 (UNIVERSAL)  
Nº 2023-93PSM



## Keywords

*Helicobacter pylori*, *Persea americana*, Virtual screening

## Abstract

Studies with *Persea americana* Mill. seed extract have shown its satisfactory effect in inhibiting *Helicobacter pylori*, a bacterium that infects approximately 40% of the world's population and is directly related to the development of gastric cancer. Two virulence factors are important in the carcinogenic potential, CagA and VacA proteins, which cause inhibition of pro-apoptosis signaling and activation of inflammatory pathways, respectively, so they can be promising targets for new therapies. This work aimed to select, *in silico*, compounds from avocado seed extract with potential to interact with CagA and VacA proteins and a suitable profile to become a drug. The prediction of pharmacokinetic and toxicity properties was performed in SwissADME and ADMETlab, analyzing Lipinski's rule, Caco-2 permeability, nephrotoxicity and hepatotoxicity. The prevision of "Anti-*Helicobacter pylori*" activity was performed in "PASS Online". Molecular docking was performed in GOLD and AutoDock Vina. From the thirteen compounds, nine showed good properties of gastrointestinal absorption and toxicity. The prevision of anti-*H. pylori* effect was indicated for seven compounds, which were subjected to molecular docking. GOLD results proposed more stable complexes between Kaempferol, Luteolin and Quercetin, with ChemPLP score 29.92, 31.81, 33.61 for CagA and 23.17, 22.59, 23.58 for VacA, respectively. Vina indicated better interaction to the same ligands, providing binding energies (kcal/mol) of -7.1, -6.7, -7.2 for CagA and -5.5, -5.8, -5.8 for VacA, respectively. The three substances interact with the following amino acids from the binding site: Phenylalanine<sup>114</sup> and Valine<sup>107</sup> of CagA and Asparagine<sup>289</sup> and Tyrosine<sup>375</sup> of VacA. Therefore, the flavonoids Luteolin, Quercetin and Kaempferol were the compounds that provides the best interaction, *in silico*, with the oncogenic proteins CagA and VacA of *H. pylori*, presenting adequate preliminary pharmacokinetic parameters.

# Co-crystals Design of Potent P2X7 Receptor Inhibitors

## Applying Molecular Modeling



### Author

Guilherme Eduardo Martins Mendes - Universidade Federal Fluminense (UFRJ)  
Robson Xavier Faria - FIOCRUZ  
Murilo Lamim Bello - Universidade Federal Fluminense (UFRJ)



### Knowledge Area

Drug Discovery and Medicinal Chemistry



### Funding

FAPERJ; CNPq



### Keywords

P2X7 receptor, crystalline polymorphs, Computational Chemistry

### Abstract

Inflammatory diseases result from multiple biological systems, and their treatment often involves inhibiting the purinergic P2X7 receptor, which is abundant in inflammation-modulating cells. In recent decades, there has been a significant search for safe and effective anti-inflammatory molecules due to treatment failures caused by side effects and interactions with existing drugs. Four potent compounds - velpatasvir (VEL), itacitinib (ITA), narirutin (NAR), and lithospermic acid (LIT) - were selected through our previous analysis of thousands of molecules for their high affinity for P2X7. VEL and ITA, both approved drugs, are classified as class IV in the biopharmaceutical classification system, indicating difficult bioavailability. NAR and LIT are natural products. One strategy to modulate a drug's pharmacokinetic properties is to apply co-crystals with suitable co-formers. Molecular modeling and computational chemistry techniques for co-crystal drug design continue to lack comprehensive rationalization in optimizing experimental design. This study aimed to provide significant theoretical information utilizing advanced quantum calculations to investigate crystalline systems. First, Avogadro, MOPAC2016, Mercury, and Molegro Virtual Docker programs were used for virtual screening a molecule library of 10<sup>7</sup> co-formers. Next, USPEX and Quantum Espresso were employed for crystal structures optimization. Preliminary results suggest that VEL could form a co-crystal with LIT or NAR, providing an improved dual-action product, while ITA could form stable co-crystals with lactobionic acid. The most stable ratios and symmetries will be proposed for re-crystallization and dissolution studies. The development of novel co-crystals is important to pharmaceutical research, as it involves optimizing bench experiments, exploring new patents, and mitigating risks in high-cost formulations, providing insights for selecting methods to scale up production on an industrial level.

# Development of amoebic biofilm and evaluation of the antibiofilm activity of phendione-derived metallocomplexes with potential for the treatment and prevention of amoebic keratitis



## Author

Karin Silva Caumo - Universidade Federal de Santa Catarina (UFSC)  
Gabriella da Rosa Monte Machado - Universidade Federal de Santa Catarina (UFSC)  
Gabrieli Eduarda Israel - Universidade Federal de Santa Catarina (UFSC)  
Dayara Corrêa Matiola - Universidade Federal de Santa Catarina (UFSC)  
Luis Gabriel Wagner - Universidade Federal de Santa Catarina (UFSC)  
Christiane Fernandes - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPESC AND CNPQ



## Keywords

Acanthamoeba keratitis; metal complexes; synergism.

## Abstract

Amoebic keratitis is a serious corneal infection caused by species of *Acanthamoeba*. Most cases progress to the need for corneal transplantation and loss of vision. Amoebic keratitis treatment involves complex treatment protocols to eliminate trophozoites and cystic forms. Furthermore, several cases of *Acanthamoeba* x fungus co-infection; and *Acanthamoeba* x bacteria are reported and worsened by the high potential of *Acanthamoeba* spp. in the constitution of microbial biofilms. The biofilm on the cornea during the infectious process and on cases and contact lenses makes it difficult to eradicate forms of *Acanthamoeba* spp. and other microorganisms. The lack of active ingredients with amoebicidal potential highlights the need to develop new compounds for eye drops and cleaning solutions for contact lens cases. The present study aimed to develop an amoebic biofilm and evaluate the ability of phendione-derived metallocomplexes to inhibit adhesion and eradicate biofilms of *Acanthamoeba* spp. The adhesion capacity of the protozoan was evaluated on polystyrene microplates using the ATCC 50492 strain and a regional clinical isolate of the genus *Acanthamoeba*. After 48 hours of incubation, trophozoites were stained with 1% crystal violet and the adhesion rate was measured by absorbance at 570 nm. Concomitantly, the phendione-derived metallocomplexes (200 and 100  $\mu\text{Mol}$ ) were incubated with *A. castellanii* trophozoites and the regional isolate for 48 hours. Subsequently, crystal violet (1%) was added and absorbance was measured at 570 nm. Phendione metallocompounds containing copper(II) and silver(I) showed anti-adhesion efficacy of 60% to 80% against the strains and isolates evaluated, presenting great potential for the development of new ocular formulations and agents for multipurpose solutions for contact lens cases.



# Anti-Candida and anti-Fusarium prospecting of metallocomplexes as new options for the treatment of severe keratomycosis



## Author

Gabriella da Rosa Monte Machado - Universidade Federal de Santa Catarina (UFSC)  
Dayara Corrêa Matiola - Universidade Federal de Santa Catarina (UFSC)  
Gabrieli Eduarda Israel - Universidade Federal de Santa Catarina (UFSC)  
Heveline Silva - Universidade Federal de Minas Gerais (UFMG)  
Karin Silva Caumo - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPESC



## Keywords

metallocomplexes, fungal resistance, keratomycosis

## Abstract

*Candida* and *Fusarium* species are important pathogens and responsible for keratomycosis. These infections are of treat difficult, mainly due to the fungal resistance, which leads to therapeutic failures, and to the corneal transplantation, affecting the public health system. The antifungal therapy is scarce and associated with high rates of toxicity, which makes the keratomycosis treatment of even more problematic. The search for new chemical entities with a greater antifungal spectrum and no toxicity to the patient is urgent. This study evaluated the antifungal efficacy of different metallocomplexes against *Candida* and *Fusarium* species resistant, together with in vitro cytotoxicity parameters on rabbit corneal cells and an ex vivo irritation model on the chorioallantoic membrane of the egg. Antifungal susceptibility evaluated was carried out according to documents M27-A3 (*Candida* spp.) and M38-A2 (*Fusarium* spp.) - Clinical & Laboratory Standards Institute (CLSI, 2008) between 128 – 0.25 µg/mL. The metallocomplexes cytotoxicity against the SIRC lineage (ATCC – CCL 60) was evaluated by the OECD n°491/2018 method, and the cell viability was determined by the MTT dye at 570 nm. The metallocomplexes were active against *Candida* spp. - compound M5.14, M5.16, M5.3 and M5.4 with the lowest minimum inhibitory concentrations (MIC 0.25 - 64 µg/mL). The compounds M5.3, M5.4 (8 - 128 µg/mL), and M5.14 (16 µg/mL) were the most effective against *Fusarium*. At 10 µMol, the compounds M5.2 (99.24%), M5.3 (62.03%), M5.4 (61.46%), and M5.15 (71.75%) maintained a high corneal cell survival, indicating a possible safety profile. The results demonstrate the excellent potential of metallocomplexes for the development of new ophthalmic formulations for keratomycosis.

# Validation of a Microscale Parallel Synthesis (MPS) Platform Combined with a Medium-Throughput Screening (MTS) for Accelerated Hit-to-lead Optimization of Anti-Infective Agents



## Author

Daniel Gedder Silva - FCFRP Universidade de São Paulo (USP)  
An Matheeußen - University of Antwerp - Flandres - Belgium  
Guy Caljon - University of Antwerp - Flandres - Belgium



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Research Grants - Young Investigators Grants: #2023/11804-5; 2024/08271-8



## Keywords

Anti-infectives, heterocyclic, medicinal chemistry

## Abstract

A large number of new heterocyclic compounds having different ring systems were synthesized using condensation, Mannich and C-H activation reactions. Following, the fused rings were decorated with many functional groups, giving rise to a structurally diverse set of analogs, which demonstrate high antitrypanosomal activities on parasite cultures and show significant promise for trypanosomiasis drug discovery.<sup>1</sup> However, guiding structural modification through structure-activity relationships (SARs) is essential, but laborious using conventional synthesis methods. A Microscale Parallel Synthesis (MPS) approach allows rapid access to libraries of compounds. This platform linked with Medium-Throughput Screening (MTS) was explored using the urea bond formation reactions in a 96-well plate using imidazopyrimidine core. The compounds' libraries are composed of the core ring (fragment FR1) and amine derivatives (fragment FR2). They were assembled in a microscale coupling reaction in a 96-well plate. The amine derivatives can be represented by linear aliphatic, unsaturated, cycloaliphatic, aromatic, heteroaromatic and phenylpiperazines groups. The LCMS and semi-q<sup>1</sup>H-NMR methods were used to allow the determination of the conversion rate of each of the reactions. To test whether unpurified reaction mixtures can give useful screening results against parasite panels, identified hits were resynthesized, purified and further characterized and retested. By exploring the introduction of various ureas groups into the imidazopyrimidine core, SAR study by means of cell assays against *T. cruzi*, *T. brucei*, and mammalian cells were built. The implementation and validation of the MPS method show that large compound libraries can be produced without purification to an initial biological screening and guide the enlargement of the chemical space of heterocycles as potential antitrypanosomal agents.

# Novel acylamide-benzilpiperidines are potent and selective anti-*Trypanosoma cruzi* drug-like agents



## Author

Thaiane Santos - Dep de Ciências Farmacêuticas, Universidade Federal de São Paulo (Unifesp)  
Mariana S. Breno - Dep de Ciências Farmacêuticas, Universidade Federal de São Paulo (Unifesp)  
Fernanda F. Ramos - Dep de Ciências Farmacêuticas, Universidade Federal de São Paulo (Unifesp)  
Marina T. Varela - Dep de Ciências Farmacêuticas, Universidade Federal de São Paulo (Unifesp)  
Flavia B. Lopes - Dep de Medicina, Universidade Federal de São Paulo (Unifesp)  
Andre G. Tempone - Butantan Instituto de São Paulo  
João Paulo S. Fernandes - Dep de Ciências Farmacêuticas, Universidade Federal de São Paulo (Unifesp)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CNPq (grant 307829/2021-9); CAPES (financial code 001)



## Keywords

antiparasitic agent, acylamide benzilpiperidine, neglected disease

## Abstract

The absence of effective chronic treatment, expansion to non-endemic countries and the significant burden in public health caused by the parasite *Trypanosoma cruzi* have stimulated the search for novel antiparasitic agents. Nonetheless, no new drug was approved for the treatment of Chagas disease. Considering this scenario, our research group has identified naturally-inspired compounds as effective anti-*T. cruzi* agents, which were developed to improve the drug-likeness and solubility. In previous work, we identified benzoyl and cinnamoyl piperazine/piperidine compounds with interesting anti-amastigote activity allied to adequate drug-likeness. In this work, we prepared novel substituted derivatives to investigate whether the activity could be improved with higher solubility. Six compounds with polar substituents were synthesized by reacting the benzoic or cinnamic acid derivatives with appropriate piperazines/piperidines to give the target compounds with good yields. The compounds were assessed for their antiparasitic activity against *T. cruzi* trypomastigotes and amastigotes, as well as the cytotoxicity profile. The benzylpiperidine derivatives showed potent anti-amastigote activity (IC<sub>50</sub> 7.3-16.9  $\mu$ M), with high selectivity toward the parasite cells (SI 6-42) and good anti-trypomastigote activity (IC<sub>50</sub> 10-63  $\mu$ M), while the piperazine-containing compounds were inactive. The SAR analysis suggest that substitution in the eastern basic moiety and the presence of a basic nitrogen were detrimental to the activity, while the catechol motif is important to increase the antiparasitic activity along with better solubility. Moreover, the absence of a substituent in 3-position in the western ring is associated to loss of activity. In summary, potent and selective anti-*T. cruzi* compounds were identified, with highlights to compound 2b as the most potent and selective in the series.

# Preliminary studies of the antimicrobial activity of tetra-cationic zinc trimethylamino-porphyrins in clinical isolates of *Klebsiella pneumoniae*



## Author

Vitória Fernanda Novais - Universidade Federal de Santa Maria (UFSM)  
Arthur Guglielme Correa - Universidade Federal de Santa Maria (UFSM)  
Franciane Batista Nunes - Universidade Federal de Santa Maria (UFSM)  
Bernardo Almeida Iglesias - Universidade Federal de Santa Maria (UFSM)  
Roberto Christ Vianna Santos - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Research Grants - Young Investigators Grants: #2023/11804-5; 2024/08271-8



## Keywords

Antimicrobial resistance; Photodynamic therapy; Porphyrins.

## Abstract

Antimicrobial resistance is a significant threat to public health, resulting in prolonged infections, increased mortality, and economic impacts, especially in underdeveloped countries. By 2050, it is estimated that around 10 million deaths a year could be attributed to this cause. In addition, the formation of biofilms increases microbial resistance, highlighting the need for new therapies. One promising alternative is the photodynamic therapy (PDT), a non-invasive and low-cost procedure that uses photosensitizing agents, such as porphyrins, and light. The PDT involves two stages: the administration of a photosensitizer and later irradiation with light, which promotes a state of electronic excitation that generates reactive oxygen species, causing damage to the cellular structures of microorganisms, inactivating them. This study evaluated the *in vitro* activity of new porphyrins synthesized by the Laboratory of Bioinorganic and Porphyrinic Materials at Universidade Federal de Santa Maria (UFSM) against clinical isolates of *K. pneumoniae*. The minimum inhibitory concentrations (MIC) of the porphyrins were determined using the broth microdilution technique, according to protocol M27-A3 of the Clinical Laboratory Standards Institute (CLSI). A 96-well plate was exposed to white light for 60 minutes and then incubated for 24 hours at 37°C. Another plate was kept in the dark for the same incubation period at 37°C. The MIC was the lowest concentration capable of visually inhibiting microbial growth. The porphyrin studied showed moderate antimicrobial activity *in vitro* when irradiated with white light (MIC 0.11 µM), resulting in photoinactivation of the microorganism. The application of these photosensitizers has significant potential against resistant infections. Therefore, photodynamic therapy can be an effective alternative in antimicrobial treatments, helping to reduce resistance and improve clinical outcomes.

# Metal complexes with high anti-Acanthamoeba potential: antitrophozoite activity, evaluation of synergistic effect, cytotoxicity and characterization of cell death mechanisms



## Author

Gabrieli Eduarda Israel - Universidade Federal de Santa Catarina (UFSC)  
Dayara Corrêa Matiola - Universidade Federal de Santa Catarina (UFSC)  
Gabriella da Rosa Monte Machado - Universidade Federal de Santa Catarina (UFSC)  
Heveline Silva - Universidade Federal de Santa Catarina (UFSC)  
Karin Silva Caumo - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

Fundação de Amparo à Pesquisa e Inovação do Estado de Santa Catarina (Fapesc) e Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq)



## Keywords

Acanthamoeba spp, metal complexes, amoebicidal activity

## Abstract

Acanthamoeba spp. have gained medical interest in recent years because they act as emerging pathogens in cases of Amoebic Keratitis and Granulomatous Amoebic Encephalitis. Both infections are considered serious, as they have an unfavorable prognosis due to the lack of specific and effective treatment. Currently, treatment protocols are based on combinations of antimicrobial medications, which are nonspecific and toxic, often ineffective for treating the infection. Considering the need to develop drugs for the treatment of infections caused by free-living amoebae of the Acanthamoeba genus, the present study aimed to evaluate the anti-Acanthamoeba activity of metal complexes (CM), their potential synergistic effect when associated with chlorhexidine by the checkerboard test on Acanthamoeba castellanii trophozoites (ATCC 50492), as well as the evaluation of the cytotoxic potential against rabbit corneal cells (SIRC - ATCC CCL-60). In viability assays with A. castellanii, the most active CM were MP2 and MP4, which showed high amoebicidal activity, with a 50% inhibitory concentration (IC<sub>50</sub>) of 3.1  $\mu$ M and 6.3  $\mu$ M, respectively. When associated with chlorhexidine, MP2 and MP4 showed synergistic activity at concentrations 4x lower than the concentrations defined as 90% inhibitory concentration (IC<sub>90</sub>). MP2 and MP4 proved to be little cytotoxic at concentrations corresponding to the IC<sub>50</sub>. Furthermore, previous studies with protozoa, such as Leishmania spp., demonstrated death by apoptosis of the same CM evaluated in the present work and with action on the enzymes thioredoxin reductase and cysteine protease, which suggests that MP2 and MP4 may act in a similar way against Acanthamoeba spp.

# Prospects Of Potential Metallocomplexes And Synergistic Interaction With Chlorhexidine As A Therapeutic Strategy For Treating Acanthamoeba Keratitis



## Author

Dayara Matiola - Universidade Federal de Santa Catarina (UFSC)  
Gabriella Rosa Monte Machado - Universidade Federal de Santa Catarina (UFSC)  
Gabrieli Eduarda Israel - Universidade Federal de Santa Catarina (UFSC)  
Heveline Silva - Universidade Federal de Santa Catarina (UFSC)  
Karin Silva Caumo - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPESC/CNPQ N° 202310069



## Keywords

Acanthamoeba keratitis, metal complexes, synergism

## Abstract

Acanthamoeba keratitis (AK), is a severe and progressive corneal infection, frequently associated with contact lens use. Treating this infection is particularly challenging due to the lack of specific drugs and the pathogens' resistance to standard therapies. Consequently, the combination of different antimicrobials is often necessary to attempt to eradicate the corneal infection. Recent studies have shown the effectiveness of metal-based compounds against protozoa, suggesting a new therapeutic approach. This study aimed to evaluate the amoebicidal activity of metallocomplexes in combination with chlorhexidine and the cytotoxicity to topical ocular application. Eight metallocomplexes were screened against *Acanthamoeba castellanii* trophozoites (ATCC 50492). The cytotoxicity on rabbit corneal cell line (ATCC—CCL 60) was performed. The compounds showed high amoebicidal potential, with inhibition of trophozoite viability above 80%. Observational analysis of the combinations through optical microscopy revealed the presence of cellular debris and hypervacuolated, granular, and rounded trophozoites, indicative of cellular stress. The MT3 and MT4 compounds showed mean inhibitory concentration (IC<sub>50</sub>) of 2  $\mu$ M and 4  $\mu$ M, respectively, and lower than chlorhexidine, which is close to 10  $\mu$ M. The results showed that all prospective compounds exhibited synergistic interaction with chlorhexidine by the Checkerboard method. In vitro evaluation with corneal cells demonstrated low cytotoxicity of the metallocomplexes evaluated. Compounds MT3 and MT4 have potential for future application in developing ophthalmic formulations against *Acanthamoeba keratitis* and its use in multipurpose solutions is highlighted.

# Prospects Of Potential Metallocomplexes And Synergistic Interaction With Chlorhexidine As A Therapeutic Strategy For Treating Acanthamoeba Keratitis



## Author

Dayara Corrêa Matiola - Universidade Federal de Santa Catarina (UFSC)  
Gabriella Rosa Monte Machado - Universidade Federal de Santa Catarina (UFSC)  
Gabrieli Eduarda Israel - Universidade Federal de Santa Catarina (UFSC)  
Heveline Silva - Universidade Federal de Santa Catarina (UFSC)  
Karin Silva Caumo - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES, CNPq, FAPESC and PGFAR



## Keywords

Acanthamoeba keratitis, metal complexes, synergism

## Abstract

Acanthamoeba keratitis (AK), is a severe and progressive corneal infection, frequently associated with contact lens use. Treating this infection is particularly challenging due to the lack of specific drugs and the pathogens' resistance to standard therapies. Consequently, the combination of different antimicrobials is often necessary to attempt to eradicate the corneal infection. Recent studies have shown the effectiveness of metal-based compounds against protozoa, suggesting a new therapeutic approach. This study aimed to evaluate the amoebicidal activity of metallocomplexes in combination with chlorhexidine and the cytotoxicity to topical ocular application. Eight metallocomplexes were screened against *Acanthamoeba castellanii* trophozoites (ATCC 50492). The cytotoxicity on rabbit corneal cell line (ATCC—CCL 60) was performed. The compounds showed high amoebicidal potential, with inhibition of trophozoite viability above 80%. Observational analysis of the combinations through optical microscopy revealed the presence of cellular debris and hypervacuolated, granular, and rounded trophozoites, indicative of cellular stress. The MT3 and MT4 compounds showed mean inhibitory concentration (IC<sub>50</sub>) of 2  $\mu$ M and 4  $\mu$ M, respectively, and lower than chlorhexidine, which is close to 10  $\mu$ M. The results showed that all prospective compounds exhibited synergistic interaction with chlorhexidine by the Checkerboard method. In vitro evaluation with corneal cells demonstrated low cytotoxicity of the metallocomplexes evaluated. Compounds MT3 and MT4 have potential for future application in developing ophthalmic formulations against *Acanthamoeba* keratitis and its use in multipurpose solutions is highlighted.

# Exploring the CB2 receptor: a molecular docking study of $\beta$ -caryophyllene derivatives.



## Author

Roberto Gomes de Carvalho Filho - Universidade Federal de Santa Catarina (UFSC)  
Lucas Pradi - Universidade Federal de Santa Catarina (UFSC)  
Lílian Sibelle Campos Bernardes - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES, CNPq, FAPESC and PGFAR



## Keywords

Molecular Docking, Type II Cannabinoid Receptor,  $\beta$ -caryophyllene.

## Abstract

The type II cannabinoid receptor (CB2) receptor has emerged as a promising molecular target in the development of new drugs for diseases associated to inflammatory processes and CB2 agonists have analgesic and anti-inflammatory properties.<sup>1</sup> With the acquisition of the crystal structure of the CB2, in silico molecular docking techniques bring a promising perspective for structure-activity relationship studies using a target-based. Given this, this research aimed to apply molecular docking analysis to diverse chemical libraries, which include known CB2 agonists,  $\beta$ -caryophyllene derivatives, and hypothetical  $\beta$ -caryophyllene analogs. The results were obtained using the crystallized CB2 receptor (PDB: 6pt0)<sup>2</sup>, in order to explore the chemical space associated with the target and identify interaction patterns between critical amino acids in the binding site and ligands. Molecular docking of known agonists showed that PHE183, TRP194 and PHE87 interacted by  $\pi$ -stacking and  $\pi$ -T interactions, while ILE110, SER285, THR114, SER90 and LEU182 via hydrogen bonds. Additionally, PHE117, HIS95, ILE186, PHE94, VAL113, VAL261 and TRP258 interacted mainly through hydrophobic bonds. These interaction patterns are consistent with the literature.<sup>3</sup> Furthermore, a specific binding pose of  $\beta$ -caryophyllene was proposed from the docking of active derivatives<sup>4</sup>, which may guide the development of hypothetical analogs in a rational way. Understanding the structural bases of how agonists exert activity is a crucial step in developing more selective and potent CB2 hits.

## REFERENCES:

1. GERTSCH, Jü, et al. Proc. Natl. Acad. Sci., 26, 9099-9104, 2008.
2. XING, Changrui, et al. Cell, 180, 645–654, 2020.
3. LI, Xiaoting, et al. Nat. Commun., 14, 1447, 2023.
4. CHICCA, Andrea, et al. Chem. Biol., 7, 1499-1507, 2014.



# Drugs approved by the FDA and ANVISA developed using Artificial Intelligence: a systematic review.



## Author

Vinicius dos Santos Machado - Universidade Federal de Santa Catarina (UFSC)  
Leonardo Bruno Federico - Universidade Federal de Santa Catarina (UFSC)  
Lílian Sibelle Campos Bernardes - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

PPGFAR, UFSC



## Keywords

artificial intelligence, drug discovery, Regulatory agencies

## Abstract

Artificial intelligence (AI) has been revolutionizing the development of drugs due to its ability to improve and optimize the process of drug discovery as a whole, reducing costs and speeding up the launch on the market.<sup>1,2</sup> The objectives of this study were to identify the AI tools employed in development process of the drugs approved by both the Food and Drug Administration (FDA) and the Agência Nacional de Vigilância Sanitária (ANVISA). Hence, a systematic review with bibliometric analysis was conducted using regulatory documents available in the databases of these agencies. An algorithm was developed in the Python programming language for screening the data and the period analyzed was from 2015 to 2024. During this period, 435 drugs were approved, out of which 166 were screened using the algorithm to detected potential uses of AI. Two drugs were identified after conducting manual file analysis, Veklury® (remdesivir), approved by both the FDA and ANVISA, utilized machine learning, while Brenzavvy® (bexagliflozin), approved only by the FDA, employed natural language processing.

1. SCHLANDER, M. et al. How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. *Pharmaco Economics*, v. 39, n. 11, 9 Ago 2021.

2. RASHID, A. Artificial Intelligence Effecting a Paradigm Shift in Drug Development. *SLAS TECHNOLOGY*, v. 26, n. 1, p. 3–15, 17 Set 2020.

# Affinity Of Lupeol Derivatives To Globulin As Part Of Their Anti-Inflammatory Mechanism



## Author

Douglas Emanuel Mota de Souza - Universidade Federal do Amazonas (UFAM)  
Guilhon-Simplicio, F. - Universidade Federal do Amazonas (UFAM)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding



## Keywords

lupeol, derivatives, docking

## Abstract

The structural similarity of lupeol and its derivatives with corticoids could explain their anti-inflammatory activity. However, the mechanism of action of corticoids depends on binding to various proteins such as globulin, which transports corticoids during an inflammatory response. The aim of this work was to investigate the affinity of five lupeol derivatives with globulin, among other pharmacokinetic and toxicological parameters *in silico*, as a contribution to studies on their anti-inflammatory activity. The five derivatives are molecules with C2 (1 and 2) and C30 (3, 4 and 5) modifications of lupeol, which were designed and had their energy minimized in Chem3D®. AutoDock Vina®, Discovery Studio® and the PDB 2V95 protein were used for docking, using a method validated by redocking (0.4326 Å) with the cocrystallized hydrocortisone ligand. PreADMET® was used to predict pharmacokinetic parameters and PROTOX® was used to predict toxicological parameters. The molecules did not meet Lipinski's rules, but showed high skin permeability and could be indicated for topical or transdermal application. In molecular docking, hydrogen, pi-alkyl and alkyl bonds were observed between the derivatives and the amino acids Trp362, Val17, Ala13, Arg252, Ile255, Phe234 and Lys359. The binding energy was -11.2, -9.4, -10.8, -10.5 and -9.4 kcal/mol, respectively, while that of hydrocortisone was -11.4 kcal/mol. Derivatives 3 and 4 showed inhibition of CYP2C9 and 2C19, which may have an impact on the metabolism of other substances. The inhibition of P-glycoprotein suggests that they may affect the pharmacokinetics of other molecules. No algal toxicity or mutagenicity was observed, but derivatives 1, 2 and 3 showed carcinogenic activity in rats and mice. Despite the potential for drug interactions, the derivatives showed good affinity with globulin, which reinforces that their anti-inflammatory action may be related to their steroid-mimetic structure.

# In silico evaluation of Silymarin compounds as potential inhibitors of BabA, CagA and VacA proteins of *Helicobacter pylori*



## Authors

Vitor Zorzal Majeski - Universidade Federal do Espírito Santo (UFES)  
Amanda Cavalcante Gonzaga Nunes - Universidade Federal do Espírito Santo (UFES)  
Dalila Nickel Loose - Universidade Federal do Espírito Santo (UFES)  
Rodrigo Rezende Kitagawa - Universidade Federal do Espírito Santo (UFES)  
Rita de Cássia Ribeiro Gonçalves - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

FAPES and UFES



## Keywords

lupeol, derivatives, docking

## Abstract

**BACKGROUND:** Silymarin is a mixture of flavonolignan isomers extracted from the seeds of *Silybum marianum*, and was shown to have anti-*Helicobacter pylori* properties in-vitro. *H. pylori* is a bacteria that infects the stomach of approximately 40% of the world's population and is considered to be the greatest risk factor for developing stomach cancer. Such infection is related to its virulence factors such as BabA (an adhesin), VacA and CagA (two known carcinogenic toxins), therefore, the inhibition of these factors could potentially mean new treatment options against such bacteria and must be investigated. **OBJECTIVES:** The present study aimed to evaluate the molecular interactions established between Silymarin compounds and *H. pylori*'s BabA, CagA and VacA virulence factors through molecular docking. **METHODS:** Molecular docking was performed in GOLD with crystallographic structures 4ZH7 (BabA), 4IRV (CagA) and 2QV3 (VacA) obtained from Protein Data Bank (PDB) and six compounds present in Silymarin: Silybinin, Isosilybinin, Silycristin, Isosilycristin, Taxifolin and Silydianin. **RESULTS:** It was found that the highest ChemPLP scores were obtained by the compounds capable of interacting with the following residues: Gly191 and Ser244 present in the active site of BabA; Val107, Phe219 present in the active site of CagA; Val266 and Pro323 of VacA. The compounds with the highest ChemPLP scores were: Isosilybinin (57.75) for BabA, Silycristin (63.08) for CagA and Isosilybinin (54.58) for VacA, furthermore, Silybinin, which is the compound present with the highest concentration in Silymarin, was shown to have the second highest score for all three targets: 57.61, 63.01 and 53.47 respectively. **CONCLUSION:** The compounds present in Silymarin, mainly Isosilybinin, Silycristin and Silybinin, were shown to interact with the active site of both BabA and CagA virulence factors of *H. pylori*.

# Analysis Of The Anthelmintic Potential Of $\alpha$ -Thujone In *Caenorhabditis Elegans*



## Authors

Julia de Souza Esteves - Universidade Federal do Pampa (UNIPAMPA)  
Matteus Teixeira Guerra - Universidade Federal do Pampa (UNIPAMPA)  
Natália da Silva Jardim - Universidade Federal do Pampa (UNIPAMPA)  
Daiana Silva de Ávila - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES



## Keywords

Parasites, GABA, Natural Products

## Abstract

Intestinal parasite infections are a major public health issue that, in addition to clinical manifestations, weaken the immune system, increasing susceptibility to other diseases. As parasites develop resistance to existing medications, there is a growing need to study new molecules. In this context, plants like *Artemisia absinthium* and *Salvia officinalis* are used in traditional medicine for parasitic diseases and their majority compound is  $\alpha$ -thujone. Studies have shown that  $\alpha$ -thujone inhibits the gamma-aminobutyric acid A (GABAA) receptor, affecting chloride channel properties and inhibiting post-synaptic frequency. The free-living nematode *Caenorhabditis elegans* is a promising model for studying inaccessible larval stages in the parasite's life cycle due to its genetic and anatomical similarities. Wild-type worms (N2) were divided into treated and control groups, with the control group exposed to 2% DMSO and the treated group to  $\alpha$ -thujone at concentrations of 0.5 mM, 0.75 mM, 1 mM, and 1.5 mM. After synchronization using a lysis solution, approximately 1500 L1 stage worms were treated for 30 minutes in M9 buffer, then transferred to NGM plates with 200  $\mu$ L of *E. coli* OP50 bacteria as a food source and maintained for 48 hours at 20°C. One-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test indicated decreased survival, egg production, and brood size in the treated  $\alpha$ -thujone groups at concentrations of 1.0 mM and 1.5 mM. The swimming assay was analyzed using repeated two-way ANOVA followed by Tukey's multiple comparisons test, showing significantly decreased activity at the concentration of 1.5 mM. Apoptosis of germline cells was evaluated using the MD701 strain, revealing an increase in apoptosis at concentrations of 0.5 mM, 0.75 mM, and 1.0 mM of  $\alpha$ -thujone. Our data indicate that  $\alpha$ -thujone has potential against parasitic nematodes, but further studies are needed to understand its mechanisms and therapeutic potential.

# Molecular modeling study of the conformational changes in mGluR5 allosteric modulation and their influence on substance use disorder (SUD)



## Author

Gustavo Henrique Goulart Trossinii - Universidade de São Paulo (USP)  
Witor Ribeiro Ferraz - Universidade de São Paulo (USP)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

CAPES, CNPq and FUSP



## Keywords

Computational Chemistry, Substance Use Disorder, Glutamate Receptor

## Abstract

Stigma and discrimination against individuals with Substance Use Disorder (SUD) have remained constant over the past decades. Furthermore, this issue has been increasing in Brazilian urban and rural areas and is mainly linked to the abuse of products derived from *Erythroxylum coca*, such as cocaine and crack cocaine. In this context, the Metabotropic Glutamate Receptor 5 (mGluR5) is an important molecular target for combating this disorder, and understanding the mechanism of allosteric activation and inhibition of its seven transmembrane domain (7TM) is essential for the rational design of more selective and safe drugs for SUD treatment. To evaluate the conformational changes of mGluR5 complexed with a negative allosteric modulator (NAM) and a positive allosteric modulator (PAM) through molecular dynamics (MD) simulations, verifying significant changes in residues and protein motifs to generate structural insights that will aid in the development of drug candidates for human SUD treatment. Starting from a structure obtained by Cryo-EM (PDB:6N52) of the 7TM, designing, optimizing, and docking PAM and NAM into the apo structure and placing the best poses in an MD simulation to evaluate the obtained conformational changes. After obtaining a satisfactory docking, MD simulation showed distinct changes in the 7TM structure, both in simulations with PAM and NAM. The conformational changes observed here confirm results obtained in other experimental and theoretical works and increase the robustness of the hypothesis of developing allosteric modulators for SUD treatment.

# Miltefosine and amphotericin B cause membrane rigidity in *Leishmania amazonensis* and Leishmania-infected macrophages



## Author

Ellyêssa do Nascimento Borges - Universidade Federal de Goiás (UFG)  
Antonio Alonso - Universidade Federal de Goiás (UFG)



## Knowledge Area

Drug Discovery and Medicinal Chemistry



## Funding

This study was financially supported by grants from the Brazilian research funding agencies CNF (445666/2014-5 and 406521/2016-6), CAPES and FAPEG (201210267001110)



## Keywords

Leishmania;, miltefosine;, amphotericin B;

## Abstract

Leishmaniasis is a neglected tropical disease that affects the world's poorest populations. Currently, therapeutic options are highly toxic, require long treatment regimens, and have an undefined mechanism of action. Understanding these mechanisms will aid in the discovery of new drugs. Spin label EPR spectroscopy was used to show that the drugs approved for the treatment of leishmaniasis, miltefosine (MTF) and amphotericin B (AmB), cause membrane rigidity in the *L. amazonensis* parasite at the same drug concentrations as inhibit the growth of the parasite. Membrane rigidity was associated with lipid peroxidation and/or oxidation of membrane proteins, resulting from increased formation of ROS promoted by drugs. The membrane rigidity induced by MTF is not the result of its direct interactions with the membrane because for short incubation periods its MTF causes fluidity. For measurements immediately after treatment, where the incubation period is insufficient for oxidative stress to occur, AmB also causes membrane rigidity, but this effect was only observed for drug concentrations 100x higher. However, membrane rigidity induced by oxidative stress was not observed in J774A.1 macrophage, suggesting that its production of nitric oxide can intercept oxidative stress. On the other hand, both drugs induced membrane rigidity in the Leishmania-infected macrophage system for drug concentrations slightly above the reported IC 50 values for amastigotes. The EPR data suggest that the membranes of the macrophage-amastigote system can also undergo oxidative processes even without treatment. This work also suggests that the mechanisms of antileishmanial activity of the two membrane-active drugs are associated with their primary effects on the cell membrane. Membrane alteration may likely result in ionic imbalance, which in turn should affect mitochondrial membrane potential and thus increase ROS formation.

**Area**

# **Quality Assurance and Analytical Chemistry**

# Bioanalytical Method By Lc-MS/MS For Simultaneous Quantification Of Pioglitazone, Amphotericin B And Fluconazole In Human Plasma



## Author

Camila Machado Brêtas - Universidade Federal de Minas Gerais (UFMG)  
Mateus Araújo Castro e Souza - Universidade Federal de Minas Gerais (UFMG)  
Juliana Machado Brêtas - Universidade Federal de Minas Gerais (UFMG)  
Daniel de Assis Santos - Universidade Federal de Minas Gerais (UFMG)  
Christian Fernandes - Universidade Federal de Minas Gerais (UFMG)  
Isabela da Costa César - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Fundação de Amparo à Pesquisa do Estado de Minas Gerais and Coordenação de Aperfeiçoame de Pessoal de Nível Superior



## Keywords

antifungals, cryptococcosis, LC-MS/MS.

## Abstract

Cryptococcosis is an invasive systemic fungal infection with high mortality. The combination of amphotericin B (AMP) and fluconazole (FLU) is the most common anticytotoxic therapy, despite the high rates of toxicity and resistance development. In a drug repositioning study of pioglitazone (PIO) for the treatment of cryptococcosis in a murine model, animals treated with this drug showed a reduction in morbidity, nephrotoxicity related to amphotericin B and fungal burden. Due to these promising results, a clinical study has been carried out, in which patients undergoing treatment for cryptococcosis are receiving PIO associated with antifungal standard therapy. The clinical study was approved by the Research Ethics Committee from UFMG (CEP-UFMG) and by the National Research Ethics Commission (CONEP), protocol n° 17377019.0.0000.5149. A bioanalytical method using high-performance liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) was developed for the simultaneous quantitation of PIO, AMP and FLU in human plasma. Sample preparation was carried out by protein precipitation, which is a simple and fast technique. The separation was performed on C18 column (150 mm × 4.6 mm, 5 µm) at 35 °C, with a gradient mobile phase containing 2 mM ammonium acetate with 0.1% formic acid and methanol:acetonitrile mixture (70:10 v/v), at a flow rate of 1 mL/min. Ions were monitored in positive electrospray mode by Multiple Reaction Monitoring with transitions  $m/z$  357.133 → 134.108 for PIO,  $m/z$  924.290 → 743.300 for AMP,  $m/z$  307.134 → 220.100 for FLU e  $m/z$  366.066 → 132.074 for Indapamide (internal standard). The bioanalytical method showed to be fast and robust and allowed the simultaneous quantitation of all analytes within 11 minutes. After validation, patient plasma samples will be analyzed. The study aims to correlate drug plasma concentrations with patients clinical and laboratory indicators and to contribute to the evaluation of proposed therapeutic schemes.



# Quality by Design approach in RP-UHPLC-ToF-MS method development for simultaneous analysis of peptides from *Tityus stigmurus*



## Author

Ana Roberta Johnson - Universidade Federal do Rio Grande do Norte (UFRN)  
Márcia Natália da Silveira Pinto - Universidade Federal do Rio Grande do Norte (UFRN)  
Cícero Flávio Soares Aragão - Universidade Federal do Rio Grande do Norte (UFRN)  
Dayanne Lopes Porto - Universidade Federal do Rio Grande do Norte (UFRN)  
Matheus de Freitas Fernandes Pedrosa - Universidade Federal do Rio Grande do Norte (UFRN)  
Fábio Santos Souza - Universidade Federal do Rio Grande do Norte (UFRN)  
Rui Oliveira Macêdo - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

CNPQ



## Keywords

peptides, simultaneous analysis, UHPLC- MS/TOF

## Abstract

The peptides present in the venom and their synthetic analogues of the scorpion species (*Tityus stigmurus*) have been evaluated for different therapeutic actions with highlights for their antimicrobial (Stigmurin, StigA-8, and TsAP-2) and hypotensive properties (TistH), which demonstrates potential for the development of new drugs. Consequently, the development of chromatographic methods for their analysis in different stages of drug development becomes of interest. Thus, the objective of this work is the usage of the Quality by Design (QbD) approach for the simultaneous analysis of 4 peptides from *Tityus stigmurus* through Ultra-High Performance Liquid Chromatography combined with Time-of-Flight Mass Spectrometry (UHPLC-ToF-MS). A full  $3^3$  factorial design was performed, in which the independent variables consisted of the length of the analytical column, flow rate, and percentage of organic mobile phase, resulting in 27 methods to be evaluated. From the parameters obtained from each experiment, statistical analyses were developed using Pareto diagrams and response surface graphs, which allowed for investigating the influence of the independent variables on factors such as retention time (RT), resolution ( $R_s$ ), and number of theoretical plates (N), allowing the determination of the best chromatographic condition capable of providing a number greater than 2,000 theoretical plates for all four peptides, indicating the efficiency of the analytical column. Higher  $R_s$  values  $>3$  were found for all critical pairs (1-2, 2-3, 3-4). The proposed method allows simultaneous analysis in  $<10$  minutes. The RP-UHPLC-ToF-MS method is a tool of potential applicability for the technological innovation of peptide-based drugs.

# Chromatographic method validation for finasteride and melatonin determination in skin samples



## Authors

Marianne Costa - Universidade de Brasília (UNB)  
Marcilio Cunha-Filho - Universidade de Brasília (UNB)  
Taís Gratieri - Universidade de Brasília (UNB)  
Guilherme Martins Gelfuso - Universidade de Brasília (UNB)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

FAPDF (Grant n. 00193-00002389/2023-76) and CAPES for providing doctor scholarship.



## Keywords

Alopecia, HPLC, Topical delivery.

## Abstract

**Introduction:** Finasteride (FNS) is a 5-alpha-reductase enzyme inhibitor used to treat alopecia, while melatonin (MLT) is a hormone secreted by the pineal gland, which has been extensively studied due to its antioxidant effect. Thus, combining FNS and MLT in a topical formulation shows advantages in alopecia treatment. **Objective:** The study proposes to validate a chromatographic method to simultaneously determine FNS and MLT in skin samples to support the development of topical formulations to treat alopecia. **Methodology:** The HPLC method used a mobile phase of ultrapure water and acetonitrile at 70:30 (v/v), which flowed at 0.6 mL/min in a C18 column (reversed-phase). The oven was kept at 30 °C, and UV detection was set at 220 and 240 nm for FNS and MLT, respectively. The validation parameters analyzed were selectivity against skin samples, linearity, precision, accuracy, and limits of detection and quantification, according to the guidelines of ICH Q2 (R1) (2005). **Results:** The chromatographic analysis showed a retention time of 11.1 and 13.6 min for FNS and MLT, respectively. The chromatographic method was selective against skin interferences and linear in a concentration range of 2.5 – 15.0 µg/mL (linear correlation coefficient = 0.99). The technique was also precise, with a variation coefficient of less than 5%, meeting the acceptance criteria of ICH. The limits of detection and quantification were, respectively, 0.62 and 0.20 µg/mL for FNS and 0.02 and 0.01 µg/mL for MLT. Recovery rates of FNS and MLT from the skin samples (following drug extraction with methanol under 24 h of stirring) were 100.4% and 99.6%, 98.1% and 93.9%, and 99.6% and 99.9% from the stratum corneum, follicular casts, and remaining skin, respectively. **Conclusion:** The chromatographic method was straightforward and suitable for simultaneous quantifying FNS and MLT in skin samples.

# Eco-friendly capillary electrophoresis method for the quantification of Apixaban in oral dosage form



## Authors

Amanda Mohr - Universidade do Rio Grande do Sul (UFRGS)  
Manoelly Oliveira Rocha - Universidade do Rio Grande do Sul (UFRGS)  
Jacqueline Arguello da Silva - Universidade do Rio Grande do Sul (UFRGS)  
Martin Steppe - Universidade do Rio Grande do Sul (UFRGS)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

CAPES



## Keywords

apixaban, capillary zone electrophoresis, green chemistry

## Abstract

Apixaban (APX) is a direct, selective, and reversible factor Xa anticoagulant used to prevent and treat venous thromboembolic events. The present work describes for the first time an eco-friendly capillary zone electrophoresis (CZE) methodology for determining APX in oral dosage form. The electrophoretic conditions were optimized according to the following parameters: concentration and pH value of the electrolyte solution, applied voltage, and capillary temperature. The method was validated as recommended by ICH, establishing selectivity, linearity, precision, accuracy, and robustness. The analytical procedure was linear in the range of 10 - 125  $\mu\text{g mL}^{-1}$ , with correlation coefficients higher than 0.999. Moreover, the green profile of the method was evaluated by the National Environmental Methods Index (NEMI), Analytical Eco-Scale, Green Analytical Procedure Index (GAPI), and Analytical GREENness Metric (AGREE) assessment tools. The results suggest that the CZE method aligns with the principles of green chemistry, offering a greener alternative for routine analysis of drug quality control. Also, the method presents a low-cost analysis, using fewer organic solvents and minimizing waste generation, when compared to techniques commonly used in routine analysis.

# Application of Tools using Quality by Design in the Development of a UHPLC-ToF-MS Method for Analyzing the TsAP-2 Peptide



## Authors

Márcia Natália da Silveira Pinto - Universidade Federal do Rio Grande do Norte (UFRN)  
Ana Roberta Pereira Johnson dos Anjos - Universidade Federal do Rio Grande do Norte (UFRN)  
Dayanne Lopes Porto - Universidade Federal do Rio Grande do Norte (UFRN)  
Artur de Santana Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Lilian Grace da Silva Solon - Universidade Federal do Amapá (UNIFAP)  
Fernando Henrique Andrade Nogueira - Universidade Federal do Rio Grande do Norte (UFRN)  
Matheus de Freitas Fernandes Pedrosa - Universidade Federal do Rio Grande do Norte (UFRN)  
Cícero Flávio Soares Aragão - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

This study was financially supported by grants from the Brazilian research funding agencies CNPq (445666/2014-5 and 406521/2016-6), CAPES and FAPEG (201210267001110)



## Keywords

TsAP-2 peptide, Box-Behnken, time of flight mass spectrometry

## Abstract

TsAP-2 is a peptide isolated from *Titius serrulatus* that has an important antimicrobial action, composed of the amino acid sequence FLGMIPGLIGGLISAFK-NH<sub>2</sub> with a molecular mass of 1734.0022 Da, making it promising for a new peptide-based drug. The study aims to develop an Ultra-High Performance Liquid Chromatography combined with Time-of-Flight Mass Spectrometry (UHPLC-ToF-MS) method using tools such as QbD where experiments were conducted using the Box-Behnken 3<sup>3</sup> design, resulting in a total of 15 experimental conditions. The independent factors selected for the experiments were the chromatographic column with different technologies, the mobile phase flow rate and the percentage of organic mobile phase. The columns selected were Zorbax RRHD (dp 1.8 μm), Kinetex (dp 2.4 μm) and Zorbax Extend 300 (dp 3.5 μm). The mobile phase varied between 30, 40 and 50%, while the flow rate varied between 0.1, 0.3 and 0.5 ml min<sup>-1</sup>. The data was statistically analyzed using response surface methodology (RSM) and Pareto diagrams for the dependent variables retention time, number of theoretical plates, tailing factor and retention factor. Making it possible to determine the best chromatographic condition for analyzing the TsAP-2 peptide by UHPLC-MS/TOF.

# Statistical Treatment Of Linearity Of A Spectrophotometric Method To Quantify Ascorbic Acid



## Author

Thais Cristina dos Santos - Universidade Federal de São João Del-Rei (UFSJ)  
Mariana Alves Souza - Universidade Federal de São João Del-Rei (UFSJ)  
Whocely Victor de Castro - Universidade Federal de São João Del-Rei (UFSJ)  
Frank Pereira de Andrade - Universidade Federal de São João Del-Rei (UFSJ)  
Ana Julia Pereira Santinho Gomes - Universidade Federal de São João Del-Rei (UFSJ)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Supported by PIBIC/UFSJ (code 26800)



## Keywords

method validation, ordinary least squares analysis, linear model

## Abstract

The statistical treatment of linearity is the first step in conducting the validation of an analytical method according to the criteria available in national and international documents. From these analyses, the most suitable conditions can be established for obtaining other parameters such as detection and quantification limits, precision, and accuracy. This study aims to evaluate the linearity of a spectrophotometric method to quantify ascorbic acid (C<sub>6</sub>H<sub>8</sub>O<sub>6</sub>). The analytical curve was obtained using 5 concentration levels (10 to 45 µg/mL), independently prepared (n = 3) in methanolic medium, and measured randomly at 243 nm. Regression parameters were obtained using the Ordinary Least Squares Method (OLSM). After evaluating extreme values using the Jackknife Standardized Residual (JSR) test, the following assumptions were assessed: normality (Ryan-Joiner test), homoscedasticity (Brown-Forsythe test), and independence of residuals (Durbin-Watson test). According to the JSR test, an outlier was identified that could influence the slope of the analytical curve, and thus it was removed to improve the fit of the first-obtained curve ( $y = 0.0558x - 0.1526$ ). Upon evaluating the assumptions, it was found that the residuals follow a normal distribution ( $R_{eq} = 0.977 > R_{crit} = 0.935$ ), are independent ( $d = 1.43 > d_U = 1.35$ ), and exhibit homoscedastic behavior ( $t_L = 0.33 < t_{crit} = 0.75$ ). After evaluating the assumptions required by OLSM, an analysis of variance was conducted, revealing that the regression is significant ( $F_{calc} = 186.6 > F_{crit} = 4.7$ ) and that there was no deviation from linearity ( $F_{calc} = -2.82 < F_{crit} = 3.86$ ) upon verification. A new regression equation was obtained as  $y = 0.0576x - 0.1854$ , with improved residual fitting of  $R^2 = 0.992$  to  $R^2 = 0.999$ , resulting in a more accurate curve after statistical treatment. In conclusion, the analytical method demonstrated good linearity for the determination of C<sub>6</sub>H<sub>8</sub>O<sub>6</sub> in the proposed range and shows potential for validation.

# Characterization of Levothyroxine Sodium API for application in formulation development studies.



## Author

Brendha Lang Camboim - Universidade Federal do Rio Grande do Sul (UFRGS)  
Cassia Virginia Garcia - Universidade Federal do Rio Grande do Sul (UFRGS)  
Martin Steppe - Universidade Federal do Rio Grande do Sul (UFRGS)  
Andreas Mendez - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

CAPES - 88887924117202300



## Keywords

Levothyroxine sodium, Characterization, Quality control

## Abstract

Levothyroxine sodium (LT<sub>4</sub>) is the sodium salt of the thyroid hormone thyroxine (T<sub>4</sub>), being indicated as replacement therapy in hypothyroid disease, where T<sub>4</sub> levels are insufficient. The aim of this work is to characterize the active pharmaceutical ingredient (API) levothyroxine sodium for subsequent development of a formulation. To achieve this, different techniques were applied: Mass Spectrometry (MS), Nuclear Magnetic Resonance (<sup>1</sup>H and <sup>13</sup>C NMR) Spectroscopy, Ultraviolet (UV) Spectrophotometry, Fourier-transform Infrared Spectroscopy (FTIR) and High-performance Liquid Chromatography (HPLC). The MS sample at 50 µg/mL was prepared in methanol, and the spectrum showed a molecular ion at 777 m/z, corresponding to levothyroxine molecular weight. NMR was performed in d-DMSO, and both <sup>1</sup>H and <sup>13</sup>C spectra corresponded to the literature data. The FTIR performed using attenuated total reflectance (ATR) device, scanned between 400 and 4000 cm<sup>-1</sup>, resulted in a spectrum where it was possible to visualize the characteristic bands of the functional groups present in the LT<sub>4</sub> molecule. The HPLC chromatography used a mobile phase of water + phosphoric acid : acetonitrile (70:30), rate of flow 1.0 mL/min, injection volume 50 µL, samples concentration 5 µg/mL and a L10, 4.6 mm × 250 mm column (at 25 °C). The chromatograms showed similar retention time for the API and standard samples (10.09 and 10.28 min, respectively), with the same tailing factor (1.2). The UV spectrophotometry, scanning in the 200 to 400 nm range, with the API and standard samples 50 µg/mL prepared in water with pH 6, demonstrated an API spectrum very similar to the standard, with maximum absorption at 225 nm, which matches the literature data. Based on the data obtained, it was possible to conclude that the API is the levothyroxine sodium, and it is suitable within the quality standards to be used in the formulation development stage.

# Development of a Stability-Indicating Method for Quantifying Haloperidol in Oral Solution among its Degradation Products using the Analytical Quality-by-Design Approach



## Author

Allan Junkert - Universidade Federal do Paraná (UFPR)  
Naomi Gerzolf - Universidade Federal do Paraná (UFPR)  
Karime Zeraik Domingues - Universidade Federal do Paraná (UFPR)  
Gustavo Torres - Universidade Federal do Paraná (UFPR)  
Moisés Maia - Universidade Federal do Paraná (UFPR)  
Luana Mota Ferreira - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

This study was financially supported by grants from the Brazilian research funding agencies CNF (445666/2014-5 and 406521/2016-6), CAPES and FAPEG (201210267001110)



## Keywords

haloperidol, stability-indicating method, AQbD

## Abstract

**Objective:** Develop a stability-indicating method for haloperidol oral solution using the Analytical Quality-by-Design (AQbD) approach. **Methodology:** Haloperidol was subjected to forced degradation under acidic, basic, thermal, oxidative, and photolytic conditions. The development of a HPLC-DAD method with AQbD approach included the following steps: establishing the analytical profile; applying risk analysis to identify critical method attributes and parameters (CMAs and CMPs); selection of categorical and numerical CMPs using factorial designs; fitting the regression model; and determining the Method Operable Design Region (MODR), while proposing strategies for process control. **Results:** Stability tests identified two degradation products of haloperidol and methylparaben under acidic and alkaline conditions. Significant variables in the method included flow rate, gradient elution slope, column temperature, and mobile phase pH, affecting nine chromatographic CMPs such as resolutions, symmetries, and capacity factors. The normal operating conditions (NOC) were defined using a Waters Symmetry C18 column (3.9 mm x 150 mm, 5  $\mu$ m) and a mobile phase of 100 mM pH 3.8 formate buffer (A) and acetonitrile (B) with the following gradient: 0 to 4 minutes - 10% to 50% B, 4 to 6 minutes - 50% B, 7 minutes - 10% B, and 12 minutes - 10% B. Detection was at 246 nm, with an injection volume of 20  $\mu$ L. The MODR includes flow rates between 1.2 and 1.35 mL/min (NOC = 1.3 mL/min), a gradient slope of 10% B/min, a temperature range of 8 to 20  $^{\circ}$ C (NOC = 15  $^{\circ}$ C), and mobile phase pH variations from 3.3 to 4.3 (NOC = 3.8). **Conclusion:** The stability-indicating method for haloperidol oral solution was developed, resulting in a robust method with a clear development plan. This approach, combining statistical methods with risk analysis, enhances experimental planning and provides a comprehensive understanding of the method to ensure the quality of the results within the MODR.

# Development of a Digital Imaging-Based Colorimetric Method for the Determination of Metoclopramide in Pharmaceutical Dosage Forms



## Author

Betania Nascimento - Universidade Federal do Pampa (UNIPAMPA)  
Bruna Machado Escobar - Universidade Federal do Pampa (UNIPAMPA)  
Fabiana Ernestina Barcellos da Silva - Universidade Federal do Pampa (UNIPAMPA)  
Marcelo Donadel Malesuik - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

CAPES



## Keywords

Metoclopramida. Colorimetria. Imagens digitais.

## Abstract

In scientific literature and official compendia, various analytical methods can be found to assess the quality of metoclopramide (MCP) pharmaceutical preparations. However, concerns arise regarding the use of large quantities of toxic reagents harmful to the environment, as well as the extended analysis time and high cost of equipment. In this context, there is a growing demand for simple and low cost analytical methodologies based on sustainable parameters in accordance to green analytical chemistry (GAC) principles. Based on GAC, this study aimed to develop a digital imaging-based colorimetric (DIC) method for the determination of MCP in pharmaceutical dosage forms. The method is based on the colour reaction produced between MCP and p-dimethylaminobenzaldehyde (p-DMAB) under acidic conditions, in a miniaturized system using microplates. Image acquisition utilized a portable system comprising a light-controlled box and a smartphone. Image processing was performed using the PhotoMetrix PRO® app, decoding colour via the RGB system. Method optimization was conducted by Design of Experiments using a Central Composite Design (CCD) model. The following factors were evaluated: MCP:p-DMAB ratio, p-DMAB concentration, and final well volume. Optimal conditions determined were: MCP:p-DMAB 1:1, p-DMAB concentration at 1.0 mol/L, and final well volume of 2.0 mL. The proposed method was validated in accordance with official guidelines, and showed linearity, precision, accuracy, and robustness. The developed method proves to be a promising tool aligned with GAC principles, offering rapid analyses, low cost, high analytical frequency, and accessible equipment.



# Development and validation of a simple and rapid HPLC/UV-Vis method for the quantification of gabapentin: assessment of its aqueous thermodynamic solubility



## Author

Gustavo Finatti Sakamoto - Universidade Estadual de Maringá (UEM)  
Nathalia Aiko Kawamura - Universidade Estadual de Maringá (UEM)  
João Marcos Barbosa Piai - Universidade Estadual de Maringá (UEM)  
Fernanda Belincanta Borghi Pangoni - Universidade Estadual de Maringá (UEM)  
Andréa Diniz



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Coordination for the Improvement of Higher Education Personnel (CAPES), Process Number: 88887.684929/2022-00



## Keywords

Gabapentin, Thermodynamic solubility, HPLC/UV-Vis

## Abstract

Introduction: Solubility is a key parameter in pharmaceutical research and represents one of the main causes of failure in drug discovery and development programs. According to the Biopharmaceutical Classification System (BCS), gabapentin (GBP) is considered a BCS class III drug, and its aqueous solubility has been reported as > 100 mg/mL. However, comprehensive information on its thermodynamic solubility in saline is not readily available for practical applications in preclinical pharmacokinetic/biopharmaceutical studies. Aim: This study aimed to develop and validate an analytical method to quantify GBP by HPLC/UV-Vis and determine its thermodynamic solubility in saline solution. Materials and Methods: Analytical method validation was carried out according to the ICH Q2(R2) guideline. The analyses were conducted using a Phenomenex Gemini® C18 column (150x4.6 mm, 3 µm) (Torrance, USA) at 30 °C on a Shimadzu® LC-20A Prominence with UV-Vis detection (Tokyo, JP). The mobile phase was composed of aqueous trifluoroacetic acid 0.05% (pH 2.4):acetonitrile (86:14 v/v) and eluted under isocratic mode (1.0 mL/min). GBP was quantified using  $\lambda = 210$  nm. The thermodynamic solubility of GBP was determined by the shake-flask method using an orbital incubator (Thoth® 6420B) at temperatures of  $37.2 \pm 0.2$  and  $20.5 \pm 1.5$  °C for 24 h (250 rpm). The samples were then centrifuged (12000 rpm, 4 °C) for 15 min and the supernatant was diluted (1:200) before injection in quintuplicate. Results: The method was linear in the concentration range of 0.2-0.8 mg/mL, selective, accurate, precise, and robust to small changes in column temperature. The thermodynamic solubility of GBP was  $121.5 \pm 3.5$  mg/mL (37.2 °C) and  $99.4 \pm 1.5$  mg/mL (20.5 °C). GBP was stable in saline for up to 7 days at room temperature ( $28.1 \pm 2.0$  °C). Conclusion: An increase in temperature enhanced the thermodynamic solubility of GBP in saline, which may have an impact on the outcome of future studies using GBP in saline.

# The Effect of Ozone Dosage of Vegetable Oils on Their Biological Activities and Chemical Properties



## Author

Gabriel Serpa Jacinto - Universidade do Vale do Itajaí (UNIVALI)  
Larissa Benvenutti - Universidade do Vale do Itajaí (UNIVALI)  
Angela Malheiros - Universidade do Vale do Itajaí (UNIVALI)  
Alexandre Bella Cruz - Universidade do Vale do Itajaí (UNIVALI)  
Luiz Carlos Klein-Junior - Universidade do Vale do Itajaí (UNIVALI)  
Rilton Alves de Freitas - Universidade Federal do Paraná (UFPR)  
Rogério Corrêa - Universidade do Vale do Itajaí (UNIVALI)  
Tania Mari Bellé Bresolin - Universidade do Vale do Itajaí (UNIVALI)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

FAPESC (grant 2021TR1823 and 2021TR1241), CNPq (grant 304799/2021-1-TMBB; 310326/2020-6-JR; 305768/2021-2-RAF; 310804/2020-5-AM)



## Keywords

Ozonation standardization, Ozonized vegetable oil, Peroxide value

## Abstract

The use of ozonated oils in dermo-cosmetic and therapeutic applications has grown, especially due to their antibacterial and antifungal effects. However, ozonation of vegetable oils occurs without standardization using just the peroxide value (PV) as quality parameter, adapted from vegetable oils, with divergences in the analytical protocols applied to ozonated vegetable oils. In addition, there are few studies on the minimum ozone dosage necessary to ensure biological activity. This work aimed to optimize the PV methodology applied to sunflower oil with different ozone dosages (A, B and C). Vegetable oils of sunflower (SO) and olive (OO) and ozonated (OSO and OOO, respectively), in three ozone dosages, were supplied by the Philozon Co. The samples were analyzed for their chemical characteristics: PV, acidity value (AV), iodine value (IV), and gas chromatography (GC-MS). Viscosity, and density, as well as, the in vitro biological activities of antimicrobial and anti-inflammatory effects were also analyzed. The PV optimization was carried out using the Box-Behnken design, and the optimized conditions (40 °C, 10 min, 0.9 mL of KI, 0.15 g of oil, 30% of chloroform) showed better discrimination of the ozone dosages compared to the original method. The PV, AV, density and viscosity were directly proportional to the ozone dosages, and the IV was inversely proportional. The formation of oxygenated compounds, by the ozonation reaction, monitored by GC-MS, showed the presence of aldehydes (hexanal and nonanal) and carboxylic acids (hexanoic acid and nonanoic acid), among the major compounds. The intermediary ozone dosage (B, about 90 and 140 g O<sub>3</sub>/L for OOO and OSO, respectively) resulted in a similar MIC (Minimum Inhibitory Concentration) and maximum anti-inflammatory effect of the highest ozone dosage (C, about 100 and 200 g O<sub>3</sub>/L for OOO and OSO, respectively), highlighting the importance of standardizing the ozonation process and the analytical methodology.

# Kinetic release of 3D-printed allopurinol based on model-dependent and model-independent techniques



## Author

Bruna Machado Escobar - Universidade Federal do Pampa (UNIPAMPA)  
Angélica Inês Kaufmann - Universidade Federal de Santa Maria (UFSM)  
Juliano Smanioto Barin - Universidade Federal de Santa Maria (UFSM)  
José Luiz Ribeiro Portela - Universidade Federal do Pampa (UNIPAMPA)  
Marcelo Donadel Malesuik - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES, code 001)



## Keywords

Dissolution profiles, 3D printing, Allopurinol (ALO)

## Abstract

3D printing has emerged as a promising tool for the customization of medications, aiming to meet the demand for dosage forms tailored to patient needs, such as dose adjustments for pediatric or geriatric populations or even formulation adaptations for veterinary use. However, in the development of 3D-printed medications, aspects related to solubility, dissolution, and release profiles must be considered in the proposed formulations to ensure their safety and efficacy. Allopurinol (ALO) is an anti-gout drug with various reports in the literature highlighting the need for dose adaptation in human and veterinary medicine. Therefore, this study aims to compare the dissolution profiles of 3D-printed ALO 50 mg obtained by semi-solid extrusion (SSE) with commercially available tablets (reference drug – ALORef and generic drug – ALOGen) to elucidate the API release mechanism. The drug release profiles of the 3D printed solid forms were evaluated using a USP II-apparatus (Varian Dissolutor) under the following conditions: 75 rpm; 900 mL of 0.01M HCl;  $37\pm 0.5$  °C. Samples were collected between 2-60 min, and the concentration of ALO was determined by UV spectrophotometry (250 nm). The analysis was conducted using statistical, model-independent ( $f_2$  – similarity factor), and model-dependent techniques for the dissolution profile comparison and fitting, respectively. Model equations, including zero- and first-order, Hixson-Crowell, Higuchi, and Korsmeyer-Peppas were employed to match the experimental data. 3D-printed ALO demonstrated similarity to the profiles of the commercial tablets ( $f_2$  3D-Ref = 57,  $f_2$  3D-Gen = 60) and Dissolution Efficiency (DE, %) values above 70. The Korsmeyer-Peppas was the kinetic model that best described the release of the active ingredient for all formulations studied. The results show that the 3D-printed ALO, despite differences in dosage, excipients, and size, did not modify the release rate pattern when compared to ALOGen and ALORef.

# Adulteration of dried extracts of *Citrus sinensis* (L.) Osbeck juice marketed in compounding pharmacies.



## Author

Maria Izabel Lamego Neta - Universidade do Vale do Itajaí (UNIVALI)  
Tania Mari Bellé Bresolin - Universidade do Vale do Itajaí (UNIVALI)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES, code 001)



## Keywords

cyanidin-3-O-glucoside, *Citrus sinensis* (L.) Osbeck, Quality

## Abstract

The extract of Moro orange juice (*Citrus sinensis* (L.) Osbeck) has been consumed in the form of dryextract in hard capsules, claiming to aid in weight loss, reduce abdominal fat, lower cholesterol and triglycerides, among other benefits. Its composition includes carotenoids, ascorbic acid, hydroxycinnamic acids, and anthocyanins, which are responsible for the juice's color, such as cyanidin-3-O-glucoside(C3G), an active marker. Due to the high demand for this product, patented by an Italian company and distributed in Brazil, other manufacturers have started commercializing the dry extract, which is sold by compounding pharmacies in hard capsule, withoutauthenticity analysis. The samples used in this study were obtained from a compounding pharmacy in Itajaí-SC, from four different suppliers (A, B, C, andD). A Thin Layer Chromatography (TLC) method wasdeveloped, using sílica Gel GF254 plates, butanol:water:acetic acid (3:1:1 v/v) as the mobile phase, with detection at 254 nm and with 1%(w/v) ferric chloride. Also, the total anthocyanin content(AMT) expressed as cyanidin-3-O-glucoside (C3G) was determined by spectrophotometry. The samples from suppliers A and B showed a reddish-purple color at pH 1.0 and became almost colorless at pH 4.5, the sample from supplier C maintained a red color at both pH values, and the sample from supplier D remained green at both pH values. ByTLC, the presence of C3G, which presented an Rf of0.76, was only detected in samples A and B, inagreement with the pH differential test. Therefore, 50% of *C. sinensis* samples sold in magistral pharmacies do not meet the requirement for thepresence of anthocyanins. These methodologiess that are easy to perform and lof ow cost have provento be useful for detecting anthocyanins in samples fo*C. sinensis* extracts. Lack of quality controlrequirements, leads to this lack of standardization ofproducts and consequently it is not possible togua antee reproducibility of the therapeutic effect.

# Development and Validation of a Chromatographic Method for Acetaminophen Quantification in Water Phytoremediated by *Salvinia auriculata*.



## Author

Marina Diaz Rodrigues - Universidade Federal do Pampa (UNIPAMPA)  
Murilo Ricardo Sigal Carriço - Universidade Federal do Pampa (UNIPAMPA)  
Caroline Betim Beralde - Universidade Federal do Pampa (UNIPAMPA)  
Elton Luis Gasparotto Denardin - Universidade Federal do Pampa (UNIPAMPA)  
Rafael Roehrs - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

CAPES



## Keywords

metabolites, Acetaminophen, water

## Abstract

Acetaminophen (ACE) is frequently detected in wastewater, which is concerning due to the potential formation of toxic metabolites (1,4-benzoquinone and N-acetyl-p-benzoquinone imine) during water treatment. These metabolites pose a risk because of their high biological activity. This study proposes using phytoremediation (PR) with *S. auriculata* as a strategy to remove ACE. The primary objective is to develop and validate a chromatographic method using high-performance liquid chromatography coupled with a diode array detector (HPLC-PDA) to assess ACE phytoremediation. Seedlings of *S. auriculata* were exposed to ACE solutions (300 mL) at concentrations of 20 and 60 mg/L for 28 days to evaluate PR efficacy. A degradation control was also included to monitor natural compound breakdown at both concentrations (n=5). Water samples (500 µL) were collected on days 0, 14, and 28 for ACE analysis using HPLC (Young Lin 9100). The separation method employed an isocratic approach with a 50:50 mixture of water pH 3 (phosphoric acid) and methanol over 13 minutes, utilizing an C18 Inertsil ODS-3 column (40.6 x 250 mm), a flow rate of 0.5 mL/min, and an injection volume of 20 µL. ACE detection occurred at 245 nm, and a calibration curve ranging from 0.25 to 10 mg/L was established with 8 points. Method validation included parameters such as linearity, selectivity, repeatability, (LOD), and LOQ. The chromatographic curve equation was  $y=179.93x-35.654$ , demonstrating linearity ( $R^2=0.9964$ ) and selectivity without interference from the matrix ( $107.8 \pm 0.8\%$ ). The method exhibited sensitivity with an LOD of 0.03 mg/L and LOQ of 0.25 mg/L. Furthermore, the plant efficiently reduced ACE levels to below 80% within 14 days and 40% within 28 days for both concentrations, while the control group showed minimal degradation. This research underscores the promising potential of *S. auriculata* in ACE phytoremediation and advocates for the adoption of a reliable HPLC method for ACE detection.

# Experimental lurasidone hydrochloride solubility in compendial and biorelevant media



## Author

Márcia Nunes da Silva - Universidade Estadual de Maringá (UFM)  
Fabio Pinheiro de Souza - Universidade Estadual de Maringá (UFM)  
Andrea Diniz - Universidade Estadual de Maringá (UFM)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

The authors thank Prati-Donaduzzi Pharmaceutical Industry for the analytical supply.



## Keywords

Solubility, Lurasidone, Biopharmaceutics

## Abstract

**Introduction:** Lurasidone (LUR) is indicated for the treatment of schizophrenia and depressive episodes associated with bipolar disorder. It is classified as a class II drug in the Biopharmaceutical Classification System (BCS), where the dissolution rate is a critical factor for bioavailability (BA). The BA of LUR increases with concomitant food intake. Understanding the factors contributing to this increase is essential to elucidate the mechanistic absorption of formulations. **Objectives:** This study aims to evaluate the aqueous solubility of LUR hydrochloride in different media to assess the impact of food on its solubility. **Methods:** The thermodynamic solubility assay was conducted using the shake flask method at 37 °C and 150 rpm in various aqueous media (compendial and biorelevant). The quantification was performed in a validated method in UHPLC. **Results:** LUR exhibited poor solubility in media with higher pH in compendial medium (potassium phosphate buffer at pH 6.8) or biorelevant mimicking the fasted state intestinal condition (FaSSIF) at pH 6.5, and the solubility was measurable only for FaSSIF (3 µg/mL). In contrast, for media with lower pH the solubility increased significantly. In the compendial 0.1 M hydrochloric acid medium was 95 µg/mL, and fasting state-simulated gastric fluid (FaSSGF) at pH 1.6, was 110 µg/mL. For the intermediate pH level in sodium acetate buffer at pH 5.0, the solubility was 5 µg/mL. Conversely, in biorelevant media mimicking fed state conditions, there was a substantial improvement in solubility: 199 µg/mL in fed state-simulated gastric fluid (FeSSGF) at pH 5.0 and 51 µg/mL in fed state-simulated intestinal fluid (FeSSIF). **Conclusions:** These findings confirm that the positive food effect on the bioavailability for LUR could be attributed to an enhancement in its solubility. This information helps understanding in vivo performance, supporting formulation development, and predicting the outcomes of bioequivalence studies.

# An HPLC-DAD method developed and validated to study the pharmacokinetics of a new leishmanicidal drug candidate in rat plasma



## Author

Flávia Elizabete Guerra Teixeira - Universidade Federal do Pampa (UNIPAMPA)  
Taiane Ciocheta - Universidade Federal do Pampa (UNIPAMPA)  
Sandra Elisa Haas - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

This study was funded by CAPES, Fundação de Amparo à Pesquisa do Rio Grande do Sul FAPERJ (n° 88881.506652/2020-01 and 19/2551-0001970-0) and CNPQ (n° 309401/2020-8).



## Keywords

Leishmanicidal, Pharmacokinetic, Bioanalytical method

## Abstract

LASSBio17-36 (LB) was developed to be a drug candidate for the treatment of Leishmaniosis and have been demonstrated efficacy against the promastigote forms of *L. major*. LB pharmacokinetic (PK) in rats was described in a previous study in our group and demonstrated the terminal half-life, clearance, and tissue distribution, showing characteristics PK agree to other leishmanicidal drugs, although presented low oral bioavailability. Here, formulations are developing to improve the aqueous solubility. This work aims to perform the bioanalytical validation of LB and show its application in a pharmacokinetic pilot study in rats. A reverse phase high-performance liquid chromatography method has been developed using C18 column (Waters) using an isocratic mobile phase composed of water with triethylamine 0.4% (pH3), methanol, and acetonitrile grade (45:15:40, v/v/v) at a flow rate of 1mL/min. UV-Visible detector was used at wavelength of 289 nm. Liquid-liquid extraction was employed to extract LB and IS from 100 µL of plasma previously basified with NaOH 0.1 M. The parameters evaluated were linearity, precision, and accuracy. A new formulation was administered by intravenous administration (8 mg/kg) in three rats and a non-compartmental analysis of PK was performed (PKanalix software) (Ethics Committee Approval Number 027/2023).. The accuracy of the method was >99%. The relative standard deviations intra and interday were <6.58 and <12.13%, respectively. It was possible to quantify LB for 72 h in rat plasma with good accuracy and precision. The compartmental analysis demonstrated adequate results for the area under curve ( $49.82 \pm 23.72$  (µg.h/mL)) and clearance ( $0.48 \pm 0.18$  (mL/h)) after intravenous administration. The bioanalytical method proposed was able to describe the plasma versus time observations in rats. Moreover, this method will be used in studying the pharmacokinetics of new formulations, after that.

# Development And Validation Of An Hplc Method To Assay Tretinoin In Soft Gel Capsules Using Multivariate Analysis



## Author

Emanuele Saul Saraiva - Universidade Federal de Santa Maria (UFSM)  
Bruna Rafaela Fretag de Carvalho - Universidade Federal de Santa Maria (UFSM)  
Laura Correa de Moraes - Universidade Federal de Santa Maria (UFSM)  
Andréa Inês Horn Adams - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

CAPES; FIPE



## Keywords

Tretinoin; validation, análise multivariada

## Abstract

Tretinoin (TTN) is a drug used topically to treat skin disorders, as well as orally for managing acute promyelocytic leukemia. Despite being approved by the FDA in 1995, there are still no official methods or other reported method for the assay of soft gel capsules, which is the only available oral dosage form. The objective of this study was to develop and validate an HPLC method to assay TTN capsules, using the DoE (Design of Experiments) approach. The pH, mobile phase rate, and column temperature were optimized using the Central Composite Rotatable Design (CCRD). The analytical conditions were a mobile phase composed by methanol and acidified water, pH 3.0 (90:10, v/v), at 1.2 mL/min, detection at 353 nm using a PDA detector, and an RP-C18 column. The sample preparation was optimized by the Central Composite Design (CCD), where different levels of surfactant, temperature, and extraction times were tested. The usual sample concentration was defined as 10 µg/mL, and the method was validated by the ICH guidelines. The optimized conditions resulted in a chromatographic run of 12 minutes. The method was linear in the range of 2.5-30 µg/mL; accuracy values was within the range of 98 to 102% (n=9) and the RSD values in the precision study were < 2%. Stress test was used to assess the method specificity, and the TTN peak remained pure and it was not affected by the degradation products, by the excipients or by isotretinoin, demonstrating the method's specificity. The robustness was evaluated using the CCD and the results indicated that minor alterations in the analytical factors did not affect the results. In conclusion, a stability-indicating HPLC method to assay TTN soft gel capsules was successfully developed and the DoE approach was crucial in determining the best analytical conditions. To the authors best knowledge, this is the first method provided in the literature to assay this product and can be used in routine and in stability studies.



# Application of Forced Degradation in Beta-Blockers: Comparison of Different Structures and In Silico Studies



## Author

José Luiz Portela - Universidade Federal do Pampa (UNIPAMPA)  
Bruna Machado Escobar - Universidade Federal do Pampa (UNIPAMPA)  
Favero Reisdorfer Paula - Universidade Federal do Pampa (UNIPAMPA)  
Marcelo Donadel Malesuik - Universidade Federal do Pampa (UNIPAMPA)  
Fabiana Ernestina Barcellos da Silva - Universidade Federal do Pampa (UNIPAMPA)  
Clésio Soldateli Paim



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Program Capes - 88887.807804/2023-00



## Keywords

Forced Degradation, Beta-Blockers, In Silico Studies

## Abstract

**Introduction:** Degradation processes play a crucial role in the decomposition of pharmaceutical compounds, revealing molecular stability under adverse conditions beyond accelerated tests. Beta-blockers exhibit variations in degradation under physical and chemical stress conditions, highlighting the need to understand their different reactivities. In silico tools can be used to elucidate reactivity that may influence the stability of these drugs. This study aimed to deepen the understanding of chemical structure changes in 5 beta-blockers (Atenolol, Carvedilol, Metoprolol, Nadolol, and Propranolol) during degradation under the influence of UVA light, acidic and basic hydrolysis. **Methodology:** The beta-blockers (12.5 mg) were weighed and dissolved in a 25 mL volumetric flask with methanol, obtaining a concentration of 500 µg/mL. Then, the degradation of the drugs was performed for photolytic tests (UVA) and acidic (0.1 mol/L HCl) and basic (0.1 mol/L NaOH) hydrolysis, which were analyzed by high-performance liquid chromatography (HPLC). **Results and Discussion:** The beta-blockers CARV and NAD showed high susceptibility to UVA photodegradation, indicating that exposure to UVA radiation results in significant degradation of these. This finding underscores the importance of protecting these medications from light to maintain their efficacy. On the other hand, when subjected to degradation by acidic (0.1 mol/L HCl) and basic (0.1 mol/L NaOH) hydrolysis, the drugs were susceptible to this forced degradation but showed greater stability, indicating higher robustness under extreme pH conditions, which is essential for formulation and storage. In silico studies allowed the identification of specific degradation sites in each molecule, elucidating the observed effects. This data is crucial to understanding the behavior of beta-blockers under different degradation conditions and to developing more stable formulations.

# Inclusion Complexes of Dillapiole with Cyclodextrins: In Silico Studies, Physicochemical Characterization, and Antibiotic Modulation



## Author

Simone Carneiro - Universidade Federal do Amazonas (UFAM)  
Micael Davi Lima de Oliveira - Universidade Federal do Amazonas (UFAM)  
Jonathas Nunes da Silva - Universidade Federal do Amazonas (UFAM)  
Thalita Sévia S. de Almeida Magalhães - Universidade Federal do Rio Grande do Norte (UFRN)  
Valdir Florêncio da Veiga Júnior - Instituto Militar de Engenharia Rio de Janeiro  
Emersom Silva Lima - Universidade Federal do Amazonas (UFAM)  
Ádley Antonini Neves de Lima - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Fundação de Amparo à Pesquisa do Estado do Amazonas - FAPEAM e Conselho Nacional de Desenvolvimento Científico e Tecnológico-CNPq



## Keywords

dillapiole, cyclodextrin, Antibiotic Modulation

## Abstract

Dillapiole is the major substance in the essential oil of the Amazonian species *Piper aduncum*. The oil from this species has antifungal, antibacterial, insecticidal, and anti-inflammatory activity. Despite its bioactive potential, dillapiole has limitations due to low solubility, bioavailability, and high volatility. Inclusion complexes with cyclodextrins may be an alternative to reduce these factors that hinder the development of a pharmaceutical product. The aim of the study was to prepare inclusion complexes of dillapiole with  $\beta$ -cyclodextrin ( $\beta$ -CD) and Hydroxypropyl- $\beta$ -cyclodextrin (HP- $\beta$ -CD), evaluate the physicochemical properties, and antibacterial and antibiotic-modulating action. Inclusion complexes were prepared with  $\beta$ -CD and HP- $\beta$ -CD by physical mixing, kneading method, and slurry method. In silico studies of inclusion complexes were performed by molecular dynamics and binding free energy calculations. Physicochemical characterization was done by Fourier-transform infrared spectroscopy, scanning electron microscopy, X-ray diffraction, thermogravimetry, and differential scanning calorimetry. The antibacterial activity was expressed as minimum inhibitory concentration (MIC), and the antibiotic-modulating activity with subinhibitory concentration against *Escherichia coli*, *Streptomyces aureus*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*. The results revealed that dillapiole with cyclodextrins were able to successfully form inclusion complexes with higher interaction energy between dillapiol and  $\beta$ -CD of -18.99 kcal/mol. MIC values showed higher antibacterial activity of the complexes. In combination with antibiotics, it was possible to observe a potential synergistic effect of inclusion complexes mainly against *S. aureus* and *E. faecalis* when combined with ampicillin and vancomycin. Inclusion complexes with dillapiole represent an interesting alternative in efforts to combat infectious diseases and bacteria resistant to current antibiotics.

# Plant Micro-Nanoparticles Obtained From The Leaves Of Ziziphus Joazeiro: Physical And Morphological Characterization



## Author

Rui Oliveira Macêdo - Universidade Federal da Paraíba (UFPB)  
Naara Felipe Da Fonseca - Universidade Federal da Paraíba (UFPB)  
Maraiana Rilo Sato - Universidade Federal da Paraíba (UFPB)  
Rael Alves Nobre - Universidade Federal da Paraíba (UFPB)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq- Programa MAI – DAI),  
Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES – PDPG/PÓS-DOC).



## Keywords

Micro-nanotechnology, Phytomedicine drugs, Analytical Techniques

## Abstract

**Introduction:** The notorious growth and innovations in technology applied to micro and nanoparticles, focused on medicinal plants and green chemistry, are contributing to the development of new materials aimed at the herbal medicine industry.

**Objectives:** To characterize plant particles from the leaves of Ziziphus joazeiro (juazeiro). **Methods:** The micro and nanoparticulate plant sample was supplied by the Foundation for the Support of Biotechnology and Technological Innovation in Health. The physical and morphological characterization of the sample was carried out using a DTA-60 simultaneous analyzer (Shimadzu), microscopic analysis by Morphologi (G3SE, Malvern) and nanoparticle tracking analysis (NTA, NanoSight NS300, Malvern). **Results:** The thermal analyses were carried out at a heating rate of 5 °C/min. The Differential Thermal Analysis curve showed three exothermic peaks at 338.23, 447.09 and 496.17 °C with energies of 5.14, 1.15 and 3.24 kJ/g, respectively. In the thermogravimetric curve, the three peaks showed mass losses of 1.709, 0.434 and 0.380 mg, corresponding to 79.74%. The analyses obtained by Morphologi revealed a total of 19861 particles, highlighting the sizes of <6.25 µm (41.10%) and >150 µm (0.73%), with volumes of 0.02% and 44.91%, respectively. Regarding the number of particles in the dispersion (19mm<sup>3</sup>), the morphology presented was 3063 circular particles, 5946 convex and 14157 elongated. For evaluation by NTA, a 3 mg/ml solution of the previously filtered sample (1.6 µm membrane) was prepared, in which three distinct populations could be highlighted in the size ranges of 103, 229 and 409 nm, with a prevalence of particles in the average size of 229 nm at a concentration of 2.71 x10<sup>07</sup> particles/ml. **Conclusions:** The analytical data obtained allowed for the characterization of the micro and nanoparticles of the juazeiro plant drug, with a view to establishing its quality specifications and traceability.

# Comparative Study Of The In Vitro Dissolution Profile Of Veterinary And Human Oral Commercial Forms Of Meloxicam



## Author

Bianca Ramos - Universidade Federal do Pampa (UNIPAMPA)  
Augusto Cezar Dotta Filho - Universidade Federal do Pampa (UNIPAMPA)  
Fabiana Ernestina Barcellos da Silva - Universidade Federal do Pampa (UNIPAMPA)  
Clésio Soldateli Paim - Universidade Federal do Pampa (UNIPAMPA)  
Sandra Elisa Haas - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding



## Keywords

quality control, computational modeling, absorption

## Abstract

In the contemporary socio-family sphere, there has been a vertiginous increase in households with pets. This scenario raises questions about the care and safety of these animals. As a result, innovation in the provision of services is essential in order to establish standards to regulate the sector and guarantee the quality and safety of products and pharmaceutical forms. This includes medicines used to treat diseases and pre- and post-operative situations in pets, such as antibiotics, antimicrobials and anti-inflammatories. Within this last class are the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), of which we can highlight meloxicam. Meloxicam (MLX) belongs to class II in the Biopharmaceutical Classification System, which corresponds to drugs with low solubility and high permeability. This low solubility gives MLX limitations in terms of absorption in the gastrointestinal tract. In order to evaluate and simulate the behavior of drugs in vivo, in vitro studies are carried out, dissolution assay. The scope of this study is to evaluate the dissolution of the MLX commercial oral veterinary and human form of MLX in compendial media. To do this, we used the US Pharmacopoeia (USP) which describes the dissolution test for MLX and quantification by Ultraviolet/Visible Spectrophotometry. Our preliminary results show that the dissolution of MLX veterinary form was in the 80% range in 30 min, a value that compares with human commercial forms of the drug. Prospects include expanding the human and veterinary commercial forms of MLX and carrying out PBPK/PBBM modeling.

# Quantification of Methylene Blue: A Validated Analytical Approach for Veterinary Product Stability Evaluation



## Author

Jamyly Martins - Universidade de Santa Catarina (UFSC)  
Hellen Karine Stulzer Koerich - Universidade de Santa Catarina (UFSC)  
Giovana Carolina Bazzo - Universidade de Santa Catarina (UFSC)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES, code 001)



## Keywords

Dissolution profiles, 3D printing, Allopurinol (ALO)

## Abstract

Stability studies aim to verify possible variations in the quality attributes of products, under different conditions, as well as establish the expiration date and appropriate storage conditions. Carrying out stability studies has recently become a requirement of the Ministry of Agriculture, Livestock and Food Supply (MAPA) for requesting and renewing the registration of some products for veterinary use. Hence, many companies are adjusting to new regulations and must conduct stability tests on their products. This study aims to develop and validate a visible spectrophotometric method for quantifying methylene blue in a veterinary product. The analytical conditions used were: ethanol as solvent, detection at 663 nm and working concentration of 2.5 ug/mL. The analytical validation parameters evaluated were: linearity, detection and quantification limits, selectivity, precision (repeatability) and accuracy, as recommended by RDC 166/2017 (ANVISA). The method proved to be linear in the range of 0.25 to 5.0 ug/mL (linear correlation coefficient of 0.9996), with detection and quantification limits of 0.22 and 0.67 ug/mL, respectively. Precision (repeatability) was demonstrated by a relative standard deviation of 3.0 %, from analyzes performed in sextuplicate, at the same concentration. The other components present in the product formulation did not show absorption at 663 nm, demonstrating selectivity. Recovery values in the range of 96 to 104% were obtained for three different concentrations, showing the accuracy of the method. Thus, it is concluded that the proposed methodology has been validated and can be applied to quantify methylene blue in stability studies of products containing this substance, as its degradation can be evidenced by the decrease in its color intensity at the specific wavelength used.

# Performance assessment based on measurement uncertainty to estimate risk of false decision as part of AQbD implementation in a stability indicating method for primaquine 5 mg tablets



## Author

Rayza Adrielle Dias de Almeida - Farmanguinhos/Fiocruz  
Felipe Rebello Lourenço - Universidade de São Paulo (USP)  
Livia Deris Prado - Farmanguinhos/Fiocruz



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Farmanguinhos/Fiocruz



## Keywords

Measurement uncertainty, risk of false decision, Analytical Quality by Design

## Abstract

Stability indicating methods (SIM) are used in quality assessment of medicines since they quantify the content of active pharmaceutical ingredients and their impurities. SIM must be suitable for intended purpose, which includes appropriate measurement uncertainty (MU). In compliance assessment, MU play a critical role since it can lead to unacceptable risks of false decision. This can translate in health damage for patients or costs for the producer. MU has been gained value within Analytical Quality by Design (AQbD) context. Our study aims to provide deep understanding of a SIM used in quality control of primaquine (PMQ) tablets, focusing on its performance based on MU and risks of false decision to guarantee its adequate performance during entire life cycle. MU was estimated by Top-down and Bottom-up approaches. Global consumer and producer risks were calculated by Bayesian approach using Monte Carlo method. Total consumer risk was evaluated considering product stability data, shelf life and MU under varied scenarios. AQbD was applied to SIM. The Analytical Target Profile was defined as "The procedure must be able to quantify PMQ in a range from 80 to 120% in 5 mg tablets in presence of its impurities considering an allowable MU of the reportable value up to  $\pm 0,5\%$ ". Through Top-down approach, MU associated to PMQ quantification showed upper than the target (1,25%). Related to this, global consumer and producer risks were 0,8% and 5,3%. Further studies about total consumer risk showed valuable data: the risk derived from PMQ quantification was the only contributor to total risk, PMQ content at the lower specification limit leads to 70% of consumer risk and MU halved reduces risk to 0,2%. Bottom-up approach showed that sample average weight was the major source of uncertainty, which cannot be optimized to reduce MU. Thus, we decided to accept this risks. Through a heatmap four procedure parameters were elected to be investigated in a Rotate Central Composed Design.

# AQbD Approach as Support for Analytical Method Optimization in HPLC-CAD through the Study of Semi-Solid Formulation Containing Paromomycin Sulfate



## Authors

Maria Eduarda Furtado - Farmanguinhos/Fiocruz  
Mariana da Silva Gonçalves - Farmanguinhos/Fiocruz  
Monique Silva dos Santos - Farmanguinhos/Fiocruz  
Flavia Furtado de Mendonça de Sousa - Farmanguinhos/Fiocruz  
Thamara de Carvalho Mendes - Farmanguinhos/Fiocruz  
Juliana Johansson Soares Medeiros - Farmanguinhos/Fiocruz  
Alessandra Lanzillota Esteves - Farmanguinhos/Fiocruz  
Diogo Dibo do Nascimento - Farmanguinhos/Fiocruz  
Livia Deris Prado - Farmanguinhos/Fiocruz  
Camila Areias de Oliveira - Farmanguinhos/Fiocruz



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Farmanguinhos/Fiocruz



## Keywords

analytical lifecycle, measurement uncertainty, cutaneous leishmaniasis

## Abstract

Paromomycin, an aminoglycoside used for cutaneous leishmaniasis, presents challenges in quantitative analysis due to its lack of chromophore groups. Monographs often describe microbial assays that fail to meet criteria required by regulatory agencies. Thus, developing an analytical method for quantifying paromomycin is essential, and liquid chromatography with a charged aerosol detector (HPLC-CAD) is a viable option. Analytical Quality by Design (AQbD) approach, combined with measurement uncertainty (MU), ensures a reliable HPLC-CAD method, evaluating its viability for quality control. This study aims to optimize a pre-existing analytical method for paromomycin and establish its MU. The first step of this study was the definition of MU for the previous validated assay and related substances methods through its values of accuracy and precision. Results showed that MU for both methods were above established target expanded uncertainty, and precision had a greater impact on results when compared to accuracy. These divergences demonstrate the need for method optimization, thus the application of AQbD was initiated. The Analytical Target Profile (ATP) was defined after evaluation of the impact of the results in product quality and efficacy, determining targets for sensitivity, specificity, precision and accuracy. With ATP established, a risk assessment was conducted in brainstorming sessions to identify critical responses to achieve adequate method performance, and the analytical parameters that can affect them were represented by an Ishikawa diagram. These parameters were evaluated in a screening Design of Experiments (DoE) through a Plackett- Burman matrix to trial which parameters affect the analytical results. The results allowed the construction of a method operable design region that, along with evaluation of uncertainty, assisted in understanding the limitations of the analytical technology and in its better implementation in the quality control of drug products.

# Physicochemical Stability Of Pyrimethamine Compounding Formulations For The Treatment Of Congenital Toxoplasmosis



## Author

Lourena Mafra Verissimo - Universidade Federal do Rio Grande do Norte (NUPLAM/UFRN)  
Joerbson Medeiros de Paula - Universidade de Campinas (UNICAMP)  
Vitória Beatriz Silva Santana - Universidade Federal do Rio Grande do Norte (UFRN)  
Marcelo Vítor de Paiva Amorim - Universidade da Integração Internacional da Lusofonia Afro-Brasileira (UNILAB)  
Débora Araújo Othon de Aquino - Universidade Federal do Rio Grande do Norte (NUPLAM/UFRN)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

PROPESQ UFRN and NUPLAM UFRN



## Keywords

Congenital Toxoplasmosis, Stability, Compounding Formulations

## Abstract

Congenital toxoplasmosis (CT) is a global zoonosis caused by the vertical transmission of *Toxoplasma gondii*. The absence of pediatric-specific formulations restricts the availability of effective treatments for this disease in children. This study sought to assess the physicochemical stability of pyrimethamine compounding formulations for pediatric use prepared from tablets. Two formulations, utilizing different vehicles (simple syrup or 70% sorbitol) at a concentration of 2 mg/mL were evaluated based on their physicochemical properties (macroscopic aspects, pH, particle size, viscosity, and conductivity) at different temperatures ( $5^{\circ}\text{C}\pm 2$  and  $25^{\circ}\text{C}\pm 2$ ) over a period of 90 days. The formulation containing 70% sorbitol exhibited a light opaque white color, pH values approximately 7.7, particle size around 41  $\mu\text{m}$ , viscosity around 30 Cs, and conductivity around 8.4  $\mu\text{S}/\text{cm}$  at both temperatures. The suspensions prepared with simple syrup presented a light amber color, pH values around 7.0, particle size around 44  $\mu\text{m}$ , viscosity around 30 Cs, and conductivity around 7.9  $\mu\text{S}/\text{cm}$  at both temperatures. A slight change was observed between Day 0 and Day 90. However, the minor variations in the physicochemical stability study over the 90 days did not cause changes that could interfere with the use of the formulations. Both formulations can be stored at ambient and refrigerated temperatures, requiring thorough agitation for redispersion. This study highlights the potential shelf life of these compounded formulations, thereby addressing the gap in available products for the neonatal and infant population. It also improves adherence to therapy, reduces treatment costs, and avoids the need for frequent compounding over the three-months period assessed.



# Optimization of assays for quality control and assurance of Amiodarone Hydrochloride tablets commercialized in Salvador, Bahia, Brazil



## Author

Anibal de Freitas Santos Junior - Universidade Estadual da Bahia (UNEB)  
João Victor Fragoso Grima - Universidade Estadual da Bahia (UNEB)  
Keilla Santana Araújo - Universidade Estadual da Bahia (UNEB)  
Laura Beatriz Souza e Souza - Universidade Estadual da Bahia (UNEB)  
Ivana Ferreira Simões - Universidade Estadual da Bahia (UNEB)  
Luan Henrique Santos Barreto - Universidade Estadual da Bahia (UNEB)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

National Council for Scientific and Technological Development (Scholarship - Scientific initiation and master's degree)



## Keywords

quality control and assurance, Amiodarone Hydrochloride tablets, Dissolution test

## Abstract

Chronic non-communicable diseases represent around 70% of annual deaths worldwide, including cardiovascular diseases. Amiodarone hydrochloride (AC), belonging to class III of antiarrhythmic drugs, is used in patients with atrial fibrillation and other heart rhythm disorders. The Brazilian Pharmacopoeia (FB) does not have a specific methodology for AC dissolution tests, and the American Pharmacopoeia (USP) recommends the use of high volumes of solvents for this test. Therefore, there is a need to develop adequate tests for quality control for this drug, in tablets. This study aims to carry out physical and physical-chemical tests for the quality control of tablets containing AC, as well as evaluating the pharmaceutical equivalence between the specialties available for consumption in the country. The physical tests were carried out in accordance with what was recommended by FB (2019), evaluating: weight uniformity, friability and disintegration. To develop the dissolution method, a fractional experimental design was carried out as screening to generate the Pareto chart and analyze the significance of the variables studied: pH, concentration of sodium lauryl sulfate (LSS), volume of reaction medium and rotations per minutes (rpm). The Doehlert matrix response surface methodology was applied to optimize the ideal dissolution conditions: 500 mL of water with (pH = 5.5), LSS (1%) and 100 rpm. The optimized method was validated and applied to reference, generic and similar medicines containing AC. The kinetic order, dissolution efficiency (DE) and independent models (f1 and f2) were calculated. The kinetics were first order and pharmaceutical equivalence was proven. The dissolution profiles were constructed with a release percentage of at least 80% in 30 minutes of testing, with an DE between 40 and 45%, higher than that recommended by USP. Therefore, this study contributed as a significant advance in the area of pharmaceutical analysis, especially for FB.

# Determination Of The Photodegradation Kinetics Of The Drug Luliconazole



## Author

Nicolas Becker Flores - Universidade Federal do Pampa (Unipampa)  
Ariele Nunes Machado - Universidade Federal do Pampa (Unipampa)  
Jéssica Resch Erd - Universidade Federal do Pampa (Unipampa)  
Lisiane Bajerski - Universidade Federal do Pampa (Unipampa)  
Clésio Soldateli Paim - Universidade Federal do Pampa (Unipampa)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding



## Keywords

Luliconazole, photodegradation, cinética

## Abstract

Luliconazole, is an imidazole antifungal medication. As a 1% topical cream, It is indicated for the treatment of athlete's foot, jock itch, and ringworm caused by dermatophytes such as *Trichophyton rubrum*, *Microsporum gypseum*, and *Epidermophyton floccosum*. The objective of the study is to determine the chemical kinetics of degradation of the antifungal Luliconazole when subjected to the photodegradation process (UV-A radiation) at established times (5,10,15,30,60,90, 120, 240 and 360 min). The experiments were performed using high-performance liquid chromatography using the following chromatographic conditions: mobile phase consisting of a mixture of acetonitrile 90% and 0.3% (v/v) triethylamine solution (pH 3.3) (60:40 v/v) at a flow-rate of 1.1 mL/min<sup>-1</sup>, analytical column c18 (reverse phase) c18 maintained at 55°C; injection volume of 20 µL, the run time was 15 min and uv detection at 296 nm. From the results obtained, it was possible to verify that the photodegradation kinetics of luliconazole in methanolic solution obeys the second order of reaction, demonstrating that if the concentration is doubled, the reaction rate will increase by 2n. From the degradation of luliconazole under photolytic conditions, it was possible to verify the formation of a major degradation product of the drug. The results found in this study demonstrate the need to protect the drug luliconazole during the manipulation and production of its pharmaceutical forms.

# Physicochemical Stability Of Pyrimethamine Compounding Formulations For The Treatment Of Congenital Toxoplasmosis



## Author

Ariele Machado - Universidade Federal do Pampa (Unipampa)  
Jéssica Resch Erd - Universidade Federal do Pampa (Unipampa)  
Paulo Roberto Rodrigues Martini - Universidade Federal do Pampa (Unipampa)  
Nicolas Gabriel Becker Flores - Universidade Federal do Pampa (Unipampa)  
Fabiana Ernestina Barcellos da Silva - Universidade Federal do Pampa (Unipampa)  
Marcelo Donadel Malesuik - Universidade Federal do Pampa (Unipampa)  
Clésio Soldateli Paim - Universidade Federal do Pampa (Unipampa)  
Fávero Reisdorfer Paula - Universidade Federal do Pampa (Unipampa)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) e Programa de Desenvolvimento Acadêmico (PDA) - UNIPAMPA



## Keywords

Cephalosporins, forced degradation studies, in silico molecular

## Abstract

Cephalosporins, similar to penicillin, contain a  $\beta$ -lactam ring that interferes with the synthesis of the bacterial cell wall, being effective against infections caused by Gram-positive and Gram-negative bacteria. The aim of the studies is to investigate the stability and reactivity of six cephalosporins (ceftriaxone, ceftiofur, cephalothin, cefadroxil, ceftazidime and cephalixin) under conditions of the acid degradation (HCl 0.1 mol L<sup>-1</sup>) and to compare and observe differences in molecular reactivity. The quantification of drugs was carried out using pharmacopeial scientific methods by high-performance liquid chromatography and molecular modeling in silico studies. The chemical reference substances (CRS) of the medicines were purchased from the Brazilian Pharmacopoeia (Brasília-DF, Brazil). The equipment for quantitative determination was a Shimadzu Prominence® liquid chromatograph (Kyoto, Japan) with LC Solution V. 1.24 SP1 management system. Chromatographic separation was performed using an Agilent Zorbax® C-18 reversed-phase column (250 x 4.6 mm x 5  $\mu$ m ID) and the chromatographic conditions were specific for each cephalosporin. Computational analyzes were performed using Spartan 08® version for Windows (Wavefunction, Inc., USA). The results showed that the drugs ceftriaxone and cephalothin had higher delivery rates compared to ceftiofur, cefadroxil, ceftazidime and cephalixin in acidic conditions. The results demonstrated that the drugs ceftriaxone and cephalothin showed higher degradation rates compared to ceftiofur, cefadroxil, ceftazidime and cephalixin under acidic conditions. It was concluded that the specific structural characteristics of these cephalosporins can influence the degradation of the drugs. The results of these studies may be useful in understanding reactivity behavior in the cephalosporin class.

# Assessment of the Influence of the Photodegradation Process on the Stability-Indicating Test of Losartan in the Presence of Nitrosamines



## Author

Jéssica Erd - Universidade Federal do Pampa (Unipampa)  
Ariële Nunes Machado - Universidade Federal do Pampa (Unipampa)  
Paulo Roberto Rodrigues Martini - Universidade Federal do Pampa (Unipampa)  
José Luiz Ribeiro Portela - Universidade Federal do Pampa (Unipampa)  
Fávero Reisdorfer Paula - Universidade Federal do Pampa (Unipampa)  
Clésio Soldateli Paim - Universidade Federal do Pampa (Unipampa)  
Andreas Sebastian Loureiro Mendez - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) e Programa de Desenvolvimento Acadêmico (PDA) - UNIPAMPA



## Keywords

Losartan potassium, Photodegradation, Nitrosamines

## Abstract

Nitrosamines (NAs) were not included in pharmacopeial methods or guidelines by regulatory authorities until July 2018, when the European Medicines Agency (EMA) became the first to announce a recall of Angiotensin II receptor blockers (ARBs)-based products. Losartan potassium was the first in a new class of potent ARBs, well-tolerated in the treatment of hypertension. The purpose of stability testing is to investigate how the photodegradation (UVA) of the drug substance (DS) losartan changes with time under the influence of the presence and absence of the following NAs: Nitrosodimethylamine (NDMA), Nitrosodiethylamine (NDEA), Nitrosodiisopropylamine (NDIPA) and Nitrosobutylamine (NDBA). The photodegradation of losartan by direct UV photolysis was carried out using a concentration of 4 mg mL<sup>-1</sup> and exposure to a UVA lamp for 12 hours. The results were obtained through reverse phase high-performance liquid chromatography (RP-HPLC). The average residual concentration after the forced photodegradation process in the absence of NAs was 94.05% ± 2,10. The final concentration of losartan after the photodegradation process in the presence of 100 ppm (µg.mL<sup>-1</sup>) were 87.64% ± 1.35%, 88.88% ± 5.19%, 89.06% ± 1.19%, and 80.20% ± 1.52% for NDMA, NDEA, NDIPA and NDBA, respectively. According to the T-test statistical treatment, the results obtained are within the significance range (p<0.05), indicating the significance of the presence of NAs in the photodegradation process of losartan. The stability-indicating test of losartan in the presence of NAs demonstrates the importance of considering NA contamination during the stability testing of DS losartan-based products.

# Degradation study of poorly soluble drugs: the case of clofazimine.



## Authors

Maryane Ferreira - Universidade Federal de Pernambuco (UFPR)  
Julia Moraes Fernandes - Universidade Federal de Pernambuco (UFPR)  
Hilthon Alves Ramos - Universidade Federal de Pernambuco (UFPR)  
Lucas José de Alencar Danda - Universidade Federal de Pernambuco (UFPR)  
Monica Felts de La Roca Soares - Universidade Federal de Pernambuco (UFPR)  
José Lamartine Soares Sobrinho - Universidade Federal de Pernambuco (UFPR)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

FINEP (01.22.0372.00)



## Keywords

Forced Degradation, Clofazimine, HPLC-DAD

## Abstract

To achieve success in pharmacological treatment, a drug must be effective and safe. Stability is essential to maintain these characteristics, preventing the loss of therapeutic effect and exposure to toxic degradation products. Regulatory agencies worldwide advocate the development of stability-indicating methods (SIM) that are selective for the drug and allow the quantification and identification of degradation products (DP). These methods are developed through forced degradation studies, where the drug is subjected to stress conditions. There is no SIM for the drug Clofazimine (CLZ), used in the treatment of leprosy, a neglected and endemic disease in Brazil. CLZ is a drug with poorly solubility, which presents a significant challenge for degradation studies development. In this context, the focus of this work is obtaining the best degradation condition for lipophilic drug with the help of *in silico* prediction platforms and chemometric tools. The methodology comprises three parts: i. predictive degradation analysis, which includes the *in silico* prediction of DPs and degradation pathways; ii. development of an experimental design to establish the best degradation condition for the drug; iii. degradation study properly, forced degradation assays in solution, and characterization and quantification of DPs by HPLC-DAD. An SIM was developed and validated using HPLC-DAD, with a C8 column 250x4.6 mm, 5  $\mu$ m. Furthermore, the principal component analysis (PCA) could determine the best condition for DP formation at an ideal solubility level for the drug, ensuring consistency in the mass balance conducted to confirm the degradations. The drug was subjected to alkaline, acidic, and oxidative degradation, resulting in the formation of a total of 6 DPs, as confirmed by method validation. Thus, the developed SIM can be used in stability and pharmaceutical improvement studies for poorly solubility drugs, ensuring the quality of the medication distributed to the population.

# Study of the stability of nitrofurantoin in extemporaneous formulations



## Author

Priscila Sacramento - Universidade Federal da Bahia (UFBA)  
Edith Cristina Laignier Cazeday - Universidade Federal da Bahia (UFBA)



## Knowledge Area

Quality Assurance and Analytical Chemistry



## Funding

FAPESB Termo de Outorga de Bolsa N°: BOL0750/2023



## Keywords

Nitrofurantoin; Extemporaneous Solution; Physical-Chemical Quality Control.

## Abstract

Nitrofurantoin (NTF) is a widely used antibiotic for treating urinary tract infections. NTF is available in oral formulations, such as capsules, tablets, and solution. However, in Brazil, there is currently no commercial availability of oral liquid formulations, despite being listed in the National List of Essential Medicines. For patients who have difficulty swallowing solid oral formulations, especially infants and young children, hospitals and compounding pharmacies often prepare extemporaneous liquid formulations. To evaluate the stability of these oral liquid formulations containing NTF under varying conditions of temperature, pH, and light, an analytical method was developed using High-Performance Liquid Chromatography (HPLC-DAD). The method aimed to be environmentally friendly by employing solvents with lower toxicity and minimal waste generation. The mobile phase consisted of H<sub>2</sub>O (90:10), with a ZORBAX® Eclipse XDB C18 5µm 4.6 x 250 mm column, flow rate of 1.0 mL/min, and temperature set at 25°C, with an injection volume of 10 µL. The chromatographic run time was 12 minutes, with a retention time of 10.7 minutes for NTF. The performance of this method aimed to evaluate the stability of NTF by detecting potential degradation products or changes in content over time. Extemporaneous formulations provide a viable alternative but require careful preparation and monitoring to ensure safety and efficacy.

**Area**

# **Pharmaceutical and Cosmetic Technology**

# Development and evaluation of electrospun membrane of Poly(L-co-D,L lactic acid-co-trimethylene carbonate) containing vancomycin and simvastatin for treatment of osteomyelitis



## Author

Cecília de Barros - Pontifícia Universidade Católica de São Paulo (PUC-SP)  
Dario Mendes Junior - Pontifícia Universidade Católica de São Paulo (PUC-SP)  
Jessica Asami - Pontifícia Universidade Católica de São Paulo (PUC-SP)  
Bruna Quevedo - Pontifícia Universidade Católica de São Paulo (PUC-SP)  
Thais Francine Ribeiro Alves - Universidade Tiradentes (Uni)  
Eliana Aparecida de Rezende Duek - Pontifícia Universidade Católica de São Paulo (PUC-SP)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

his research was supported by PROSUP and PNPd grants from the Coordination for the Improvement of Higher Education Personnel (CAPES)



## Keywords

Osteomyelitis, Bone Regeneration, Polymer

## Abstract

Osteomyelitis, a severe bone infection, poses a significant challenge to public health, resulting in thousands of hospitalizations annually. Conventional treatments have limitations such as the need for multiple surgeries and the risk of reinfection. Thus, the development of biodegradable biomaterials emerges as a promising approach. This study developed and evaluated an electrospun membrane of Poly(L-co-D,L lactic acid-co-trimethylene carbonate) (PLDLA-co-TMC) containing vancomycin (VAN) and simvastatin (SIN) to combat infection and improve bone regeneration in osteomyelitis treatment. The PLDLA-co-TMC polymer was synthesized, and electrospun membranes containing VAN and SIN were characterized using techniques such as Fourier Transform Infrared Spectroscopy (FTIR), Thermogravimetric Analysis (TGA), and Differential Scanning Calorimetry (DSC), in addition to microbiological assays and drug release studies. The synthesis of drug-loaded membranes was successfully performed according to the established protocol. Analyses confirmed the presence of drugs in the electrospun membrane without chemical interaction. In microbiological testing, membranes containing VAN or both drugs showed inhibition against *Staphylococcus aureus* growth. Drug release was characterized by an initial rapid release phase followed by sustained release. The membranes exhibited a better fit to the Peppas-Sahlin release kinetics model, with diffusion playing a more significant role. This study suggests the potential of PLDLA-co-TMC membranes containing VAN and SIN for osteomyelitis treatment, with preliminary results indicating efficacy in bacterial inhibition. Further evaluations, including interleukin-6 (IL-6) dosage and histomorphometric analyses in Wistar rat tibia after osteomyelitis induction and treatment with the membranes, are ongoing to confirm the efficacy and safety of this biomaterial in osteomyelitis treatment.



# Preparation of microneedles containing propolis: evaluation of morphological properties



## Author

Camila Patrício Rissi - Universidade Estadual de Maringá (UEM)  
Marcos Luciano Bruschi - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).



## Keywords

propolis, polyvinyl alcohol, polyvinylpyrrolidone

## Abstract

**Introduction:** Microneedles (MN) are minimally invasive structures that pierce the stratum corneum, creating microchannels for administering drugs to blood capillaries (1). Propolis (PRP) has antibacterial, fungicidal, antioxidant, anti-inflammatory, antiviral and immunostimulating activities (2). Therefore, this work aimed to evaluate the morphology of MN composed of polyvinylpyrrolidone and polyvinyl alcohol, without poloxamer 407 (P407) for PRP delivery. **Methods:** In the production of the molds, a cartridge of DermaPen® microneedles with 36 MN, each 2 mm long, was used. The molds were prepared from polydimethylsiloxane (PDMS) by mixing part of the catalytic agent with part of the silicone base in a ratio of 1:6. Formulations were developed with varying concentrations of polymers (PVA, PVP and P407) and ethanolic propolis extract (EPRP) from a polymeric matrix. The MN were analyzed macroscopically and microscopically (optical microscopy), evaluating flexibility, integrity, homogeneity and presence of bubbles. **Results:** The molds developed were inverse replicas of the master structure, presenting white to transparent color, flexibility and ease of removal of the MN. After drying, the formulations were more easily removed from the molds than those previously prepared with P407 (2). MNs without P407 were more rigid, homogeneous and intact, with fewer bubbles, and were easier to remove from the molds compared to those containing this polymer. **Conclusion:** Molds were successfully developed from PDMS. The MN presented good appearance, solid structure, uniform composition and easy removal from the molds. The absence of P407 resulted in more rigid, homogeneous, intact MNs with fewer bubbles, indicating a direct correlation between these characteristics and the presence of P407.

**References:** (1) Bernardo AFC, Santos K, Silva DP. Rev. Saúde em Foco. 2019; 6<sup>a</sup> ed. (2) Vecchi CF, et al. Beilstein J. Nanotechnol. 2022; 13: 503-516.

# Effect Of Precoating S-Sedds Solid Carriers With Pvp On Free Fatty Acids Release



## Author

Camila Borges - Universidade Federal Fluminense (UFF)  
Jorge da Silva Pinho Junior - Universidade Federal Fluminense (UFF)  
Vanessa Naciuk Castelo-Branco - Universidade Federal Fluminense (UFF)  
Samanta Cardozo Mourão - Universidade Federal Fluminense (UFF)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPERJ; CAPES



## Keywords

Self-emulsifying systems, Linseed oil, In vitro digestion

## Abstract

Solid Self-emulsifying drug delivery systems (S-SEDDS) are anhydrous oral formulations composed of lipids, surfactants, cosolvents, cosurfactants and a solid carrier. The agitation of digestive motility forms a translucent emulsion with an extensive surface area for bioactive compounds to be released and absorbed. Flaxseed oil is a natural source of bioactive compounds and unsaturated fatty acids. Furthermore, potential health benefits, such as reducing cardiovascular diseases, have already been attributed. This study aimed to evaluate the release of free fatty acids in S-SEDDS formulations with and without polyvinylpyrrolidone (PVP) K-90 precoating. Fourteen S-SEDDS formulations (F1 to F14) containing different surfactant mix (PEG-40 and Span® 80), linseed oil, solid carrier (Neusilin® US2, Fujicalin®, 1:1 mixture of Neusilin® US2:Fujicalin®, or Aerosil® 200), and PVP K-90 ratios were evaluated by in vitro simulated digestion as described by the INFOGEST protocol, with some modifications. The assay includes the oral, gastric, and intestinal phases, and the free fatty acid levels were calculated at the end of the whole process. The S-SEDDS containing PVP K-90 presented higher release rates (28,87 to 73,76%) when compared to formulations without precoating (6,51 to 35,61%). The low results in non-precoated S-SEDDS may be due to the lipid formulations migrating deeper into the pores of the carriers. PVP K-90 may have blocked the internal regions, promoting the fast release of linseed oil from the superficial pores. Applying a PVP coating to the solid carriers significantly enhanced the release extent from S-SEDDS. The results should allow the optimization of formulations in technological and biopharmaceutical aspects, providing an improved system to release bioactive compounds.

# Study of the solubility of protoporphyrin IX in aqueous and hydroalcoholic solvent systems



## Author

Jéssica Bassi da Silva - Universidade Estadual de Maringá (UEM)  
Michelly de Sá Matsuoka - Universidade Estadual de Maringá (UEM)  
Marcos Luciano Bruschi - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq, CAPES, FINEP, Fundação Araucária.



## Keywords

Photodynamic therapy, Protoporphyrin IX, Solubility

## Abstract

Photodynamic therapy (PDT) is a non-invasive treatment that consists of the use of a photosensitizer (PS), such as Protoporphyrin IX (PpIX), a source of light and the oxygen in the tissue. PpIX is commonly used for its ability to accumulate into tumoral cells and for its phototoxicity. However, due to its physicochemical characteristics and self-aggregation property in the physiological environment, its incorporation into pharmaceutical formulations constitute a challenge. Therefore, the aim of this work was to investigate the solubility of PpIX in different solvent systems, using the shake-flask method, for further application in the development of new pharmaceutical systems containing PpIX. Ca 10 to 25 mg of PpIX, disodium salt, was placed in 25 mL of the solvent (water, 50% ethanol (v/v; EtOH50); 77% ethanol (v/v; EtOH77); absolute ethanol (EtOHabs) and polymeric systems containing 10% (w/w) poloxamer 407 (P407) in water, EtOH50 or EtOH77). The systems were stirred (100 RPM) in an orbital shaker at  $37 \pm 1$  °C. Samples were collected at specific times over 96 hours and the PpIX was determined by using a method previous validated ( $R = 0.9973$ ). All the analyzes were performed in triplicate. Although the test was performed through 96 hours, the equilibrium of dissolution was already observed after 8 hours of testing. Therefore, at this time, the amount of PpIX in solution was found to be  $0.450 \pm 0.103$  mg/mL in EtOH50;  $0.430 \pm 0.010$  mg/mL in EtOH77;  $0.138 \pm 0.003$  mg/mL in water;  $0.593 \pm 0.063$  mg/mL in aqueous solution of 10% (w/w) P407;  $0.503 \pm 0.043$  mg/mL in EtOH50 solution containing 10% (w/w) P407;  $0.507 \pm 0.104$  mg/mL in EtOH77 solution containing 10% (w/w) P407 and  $0.070 \pm 0.006$  mg/mL in EtOHabs medium. Therefore, water and absolute ethanol were inappropriate solvents for dissolving PpIX. Moreover, the system containing water and P407 demonstrated to be the most promising medium for further applications in pharmaceutical systems.

# Polymeric systems containing eprinomectin: in vitro cytotoxicity evaluation using *Artemia salina*



## Author

Thalita Schilive Faccin - Universidade Federal de Maringá (UEM)  
Alessandra Grimmes Bernardo - Universidade Federal de Maringá (UEM)  
Fernanda Belicanta Borghi Pangoni - Universidade Federal de Maringá (UEM)  
Marcos Luciano Bruschi - Universidade Federal de Maringá (UEM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPQ



## Keywords

*Artemia salina*, in vitro cytotoxicity, polymeric systems

## Abstract

**Introduction:** Eprinomectin (EPR) is a semisynthetic derivative of the avermectin group, which displays therapeutic efficiency against endo and ectoparasites. Bioadhesive polymers such as carbomers and thermoresponsive ones like poloxamers, have been used to develop controlled drug delivery systems and to enhance bioavailability. This work aimed to prepare a topical formulation and evaluate its cytotoxicity against *A. salina*. **Methods:** Two polymeric systems containing EPR (0.5%, w/w), which differ by the type of Carbopol, were prepared: F1 was composed of isopropanol (15%, w/w), poloxamer 407 (17.5%, w/w), and Carbopol 934P® (0.3%, w/w); F2 was composed of isopropanol (15%, w/w), poloxamer 407 (17.5%, w/w), and Carbopol 974P® (0.3%, w/w); These formulations were also prepared and used as blank, but without EPR (F1b and F2b). All formulations were evaluated for density and T<sub>sol/gel</sub>. To investigate the in vitro cytotoxicity, in a container with saline solution (NaCl; 0.1 mol/L), at 25 °C, cysts of the *A. salina* were added, illuminated with white lamp, in order to attract the *A. salina*, which hatched after 24 h. Afterwards, about thirty nauplius were transferred to each Petri dish containing 3.0 mL of saline solution and 1.0 mL of each formulation, separately. In the control group, the nauplius were incubated only in saline solution. After 30 and 60 min of exposure, the nauplius were evaluated for survival rate. **Results:** The negative control showed 100% nauplius survival after 30 min and 98.21 ± 2.57% after 60 min. For formulations F1 and F2, 100% of the died after 30 min of exposure, indicating a total survival rate of 0%. However, for formulations F1b and F2b, about 96.70 ± 3.70% survived after 60 min. **Conclusion:** It was possible to prepare and characterize the formulations and evaluate their in vitro activity against *A. salina*. Formulations F1 and F2 showed to be cytotoxic against the microorganisms evaluated.

# Release Kinetics Of Amphotericin B From Hydrogel Contact Lenses



## Author

Emerson Santana - Universidade Federal do Rio Grande do Norte (UFRN)  
Fabia Julliana Jorge de Souza - PPGCSa - Universidade Federal do Rio Grande do Norte (UFRN)  
Francisco Alexandrino Junior - Instituto de Tecnologia em Fármacos (Farmanguinhos/ Fiocruz)  
Lucas Gabriel da Silva Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Yasmin Ferreira da Cruz - Universidade Federal do Rio Grande do Norte (UFRN)  
Wógenes Nunes de Oliveira - LaSiD - Universidade Federal do Rio Grande do Norte (UFRN)  
Eryvaldo Sócrates Tabosa do Egito - PPGCSa - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq); Coordenação de Aperfeiçoamento de Pessoal de Nível Superior-Brasil (CAPES); FAPERN. Finance code 001



## Keywords

Fungal keratitis, Contact lenses, Hydrogel

## Abstract

Fungal keratitis (FK) is a challenging eye infection with limited treatment options, potentially leading to blindness if not managed effectively. The aim of this work was to develop a hydrogel ophthalmic lens (HOL) containing amphotericin B (AmB) as a potential alternative for FK management. The HOL was produced from a 20% (w/v) poly(vinyl alcohol) solution, incorporating 150 mg sodium trimetaphosphate (STMP) and 1,5 M sodium hydroxide. The solution was maintained at 80 °C followed by the addition of 0.5 mL of a methanolic solution of AmB (7 mg/mL). The HOL was then dried and crosslinked at  $25 \pm 2^\circ\text{C}$ . The release profile of AmB from the HOL was assessed in artificial tear fluid at  $37 \pm 2^\circ\text{C}$  over 24 hours at 100 rpm. Samples of 1 mL were periodically withdrawn and replaced with 1 mL of artificial tear fluid to maintain constant volume and sink conditions. AmB concentration was quantified by spectrophotometry using a previously validated method. The release study showed increasing AmB concentrations from 1 to 12 hours, reaching  $8.26 \pm 1.10 \mu\text{g}$  and  $34.66 \pm 5.48 \mu\text{g}$ , respectively. After 12 hours, the release remained constant at approximately  $34.66 \pm 5.48 \mu\text{g}$ , indicating that the HOL had reached a steady state, with an overall release profile of  $58.24 \pm 13.51\%$ . The release kinetics of AmB from the HOL followed a first-order process, suggesting a dissolution driven release mechanism governed by drug concentration. At 24 hours, the AmB concentration was  $30.92 \pm 5.23 \mu\text{g/mL}$ , which is promising since the minimum inhibitory concentration against *Candida albicans* (ATCC 90028), a primary strain responsible for FK, is  $0.25 \mu\text{g/mL}$ . The developed HOL demonstrated a suitable release pattern and stability, supporting its potential for further in vitro and in vivo studies to evaluate its effectiveness FK.

# Performance Evaluation Of Topical Ophthalmic Formulations Using A Cruelty-Free Polymeric Membrane



## Author

Jonad Logan Contarato - Universidade de Brasília (UnB)  
Geisa N. Barbalho - Universidade de Brasília (UnB)  
Manuel A. Falcão - Universidade de Brasília (UnB)  
Venâncio Amaral - Universidade de Brasília (UnB)  
Guilherme Gelfuso - Universidade de Brasília (UnB)  
Marcílio Cunha Filho - Universidade de Brasília (UnB)  
Taís Gratieri - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPDF - FUNDAÇÃO DE APOIO À PESQUISA DO DISTRITO FEDERAL



## Keywords

OphthalMimic, retention time, polymeric membrane.

## Abstract

Polymers are extensively used in the development of new biomaterials. In this sense, polymeric membranes containing mucin can be used to simulate the interactions between formulations and mucin biological layers. We developed a membrane to assess the residence time of formulations by considering mucoadhesiveness, viscosity, and tear flow clearance on the "OphthalMimic" device. Different compositions were evaluated to obtain the membranes with the higher resistance and sensitivity. Three membranes were developed with different proportions of Poloxamer and Mucin-type II: M1 (PLX 0.5% + MUC 0.5%); M2 (PLX 1.0% + MUC 0.5%); M3 (PLX 0.5% + MUC 1.0%). All of them also contain 2.5% gelatin, 10% polyvinyl alcohol in HEPES buffer at pH 7.4. Four formulations were tested using varying test times and tear flow with different protocols: PLX16 (Fluconazole 0.2% + Poloxamer 16%); PLX16C10 (Fluconazole 0.2% + Poloxamer 16% + Chitosan 1.0%); NEMOX (nanoemulsion containing 5% Moxifloxacin Hydrochloride and Poloxamer 5%); CONTROL (Propylene Glycol containing 5% Moxifloxacin). Flow rates were tested at 1 mL/min and 0.5 mL/min. The test was conducted with 5 min of continuous flow or with 1 min without flow followed by 4 or 9 min of continuous flow. The drainage of fluconazole over 1 mL/min for 5 minutes with PLX16 and PLX16C10 resulted in the following: M1(65%±14.0 and 27%±9.7); M2(58%±6.5 and 38%±8.8); M3(55%±6.2 and 27%±10.2). In M3, when the protocol was 1+4 min at 1 mL/min, the drainage were 54%±12.3 and 35%±11.6. When the flow was reduced to 0.5 mL/min, in M3 were 35%±7.6 and 20%±3.4. Extending the test time to a 1+9 min with 0.5 mL/min in M3, showed drainage rates of 65%±11.1 for PLX16, 38%±8.1 for PLX16C10, 76%±6 for CONTROL, and 59%±9 for NEMOX. The membrane demonstrated increased resistance to reduced flow rates, allowing for prolonged testing duration. This enhanced performance resulted in greater sensitivity in distinguishing ophthalmic formulations and improved test efficacy.

# Role of hydroxypropyl methylcellulose (HPMC) at biocompatibility and healing potential related to rheological properties



## Author

Carolina Ribeiro - Universidade Federal do Paraná (UFPR)  
Washington Luiz Esteves Magalhães - Universidade Federal do Paraná (UFPR)  
Rilton Alves de Freitas - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Fundação Araucária



## Keywords

biopolymers, viscosity, healing

## Abstract

Polymers derived from cellulose have been used in various areas as viscosity modifiers, stabilizers, thickeners, in the pharmaceutical, food and personal care products industries and others. Nowadays, the treatment of skin lesions is a challenge for the pharmaceutical industry, leading to the search for the development of new materials, such as cellulose derivatives. One of these derivatives is hydroxypropyl methylcellulose (HPMC), which is biocompatible, biodegradable and an excellent thickening agent. The present work aimed to evaluate the potential of HPMC derivative gels for biological application, with a focus on tissue healing, as well as the study of these biopolymers through biocompatibility, toxicity, physicochemical and rheological characterization tests. The biocompatibility of the selected polymers was evaluated by the agar gel diffusion test, which allows visualizing the loss of neutral red dye by non-viable cells. HPMC derivatives (KF and MF, with different modifications) were tested at a concentration of 2% (w/w) and as a negative control, the aqueous dispersion of Carbopol 940® at a concentration of 0.5% (w/w), in the L929 cell line. The polymer dispersions were characterized by oscillatory measurements to verify the viscoelastic properties of HPMC. The HPMC derivatives at 2% presented a liquid viscoelastic behavior. Using alternative methods for eye/skin irritation, the results suggest that none of the polymers showed irritation in in-vitro tests. In this way, cellulose derivatives with pharmaceutical specifications were obtained, capable of replacing commercial carbomers such as Carbopol and it seems to have high healing potential (correlated to viscosity) in accordance with biocompatibility results.

# Effect of iontophoresis on dacarbazine skin penetration for melanoma topical treatment



## Author

Paula Martins de Oliveira - Universidade de Brasília (UnB)  
Camila Oliveira Cardoso - Universidade de Brasília (UnB)  
Amandda Evelin Silva de Carvalho - Universidade de Brasília (UnB)  
Isabella De Souza Mota - Universidade de Brasília (UnB)  
Renata Fonseca Vianna Lopez - FCFRP - Universidade de São Paulo (USP)  
Marcílio Cunha Filho - Universidade de Brasília (UnB)  
Felipe Saldanha de Araujo - Universidade de Brasília (UnB)  
Taís Gratieri - Universidade de Brasília (UnB)  
Guilherme Martins Gelfuso - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPDF (Grant #00193-00000721/2021-04, Project 41/2021) and CNPq (Grant # 310291/2021-6)



## Keywords

Cell viability, Skin permeation, Iontophoresis

## Abstract

Dacarbazine (DTIC) is the drug of choice for melanoma treatment. However, its systemic administration is associated with several adverse effects. Here, DTIC topical delivery stimulated by iontophoresis is proposed to overcome such drawbacks. Hence, this work analyzed the effect of anodal iontophoresis on DTIC cutaneous delivery. The electrical stability of the drug was evaluated prior to the iontophoretic experiments and demonstrated the need to add an antioxidant to the DTIC formulation at 0.1% (w/v). DTIC cutaneous permeation was evaluated in vitro for 6 h using three current densities (0.10, 0.25, and 0.50 mA/cm<sup>2</sup>). In addition, the effect of DTIC against skin cancer cells (MeWo and WM164) was investigated for 72 hours of exposure to the drug. Anodal iontophoresis stimulated skin drug permeation compared to the passive control. However, the antioxidant presence reduced DTIC permeation under lower currents of 0.10 and 0.25 mA/cm<sup>2</sup>, which was compensated by increasing the current density to 0.50 mA/cm<sup>2</sup>. At 0.50 mA/cm<sup>2</sup>, iontophoresis enhanced cutaneous drug penetration by 7-fold ( $p < 0.05$ ) compared to the passive control. DTIC showed a concentration-dependent antiproliferative effect on melanoma cell lines. Thus, iontophoresis intensifies DTIC skin penetration in concentrations that can reduce cell viability and induce cell death. In conclusion, DTIC cutaneous delivery mediated by iontophoresis is a promising approach for treating melanomas and other skin tumors.



# Exploring Lignosulfonate as an Emerging Biosurfactant



## Author

Natália Mello da Silva - Universidade Federal do Paraná (UFPR)

Joslaine Jacumazo - Universidade Federal do Paraná (UFPR)

Rilton Alves de Freitas - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq/Fundação Araucária (202360297)



## Keywords

Cell viability, Skin permeation, Iontophoresis

## Abstract

Lignosulfonates are derivatives of lignin obtained in the sulfite pulping process, especially in the cellulose industry. About one million tons of lignosulfonate are produced annually, most of it used for energy production through burning. Despite this, lignosulfonates possess notable qualities including good water solubility, antioxidant and promising surfactant capabilities. At the same time, synthetic surfactants are widely used to stabilize formulations and exhibit high toxicity and poor degradability, posing concerns due to their harmful effects on the human body and environment. The goal is to increase the value of this plentiful and cost-effective byproduct by employing it in high-value applications. This approach aims to gradually substitute synthetic molecules with an ecological use of the product, promoting the circular economy and aligned with UN Sustainable Development Goals. Thus, this study aimed to carry out a characterization of the physicochemical properties of lignosulfonate to use it as a surfactant and test it for stabilizing emulsions. Surface tension measurements were conducted to assess its micellization properties, while confocal microscopy and macroscopic analysis were employed to understand the behavior of micelles/nanoaggregates and oil-in-water emulsion. The critical micellar concentration was determined to be 16 mg/mL, with a surface excess of 1.7  $\mu\text{mol}/\text{m}^2$ , a surface area of 99.5  $\text{\AA}^2/\text{molecule}$  and a surface pressure of 25.2 mN/m. Micro and macroscopic analysis revealed a formation of a hydrophobic environment and a successful stabilization of oil-in-water emulsions. These findings suggest the formation of nanoaggregates resembling micellar structures, resulting in reduced surface tension, which is indicative of surfactant behavior. Ongoing investigations involve tests regarding biological activity, aiming to further elucidate the potential applications of lignosulfonate nanoaggregates/micelles.

# Quality by Design approach to obtain solid pediatric-friendly formulations: A scoping review



## Author

Carla Gurski - Universidade Federal do Paraná (UFPR)  
Raul Edison Luna Lazo - Universidade Federal do Paraná (UFPR)  
Laiene Antunes Alves - Universidade Federal do Paraná (UFPR)  
Milena Schastai Sovinsk - Universidade Federal do Paraná (UFPR)  
Marcel Henrique Marcondes Sari - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)  
Luana Mota - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Não



## Keywords

Pediatric formulations, Solid oral forms, Quality by Design

## Abstract

Evidence demonstrates a lack of suitable medicines for children due to strict regulations and the complexity of clinical trials. The Quality by Design (QbD) approach is essential in developing medicines for children as it helps manufacturers address issues of safety, efficacy, and palatability. Given this, the aim of this study was to address the gap in scientific information in solid pediatric-friendly formulations by compiling and understanding relevant studies using QbD tools. The eligibility criteria were based on the PCC (Population, Concept, and Context) acronym, where the population consists of pediatric patients, the concept element was based on the application of QbD tools, and the context considered the QbD tool in predicting the influence excipients and process parameters on the final product. The databases used were PubMed, Scopus, and Web of Science. A total of 86 studies were identified, and 37 articles were included in the review. This analysis discloses the most common material attributes, process parameters, quality attributes, and other variables that are critical for the quality, efficacy, and safety of solid pediatric-friendly formulations. Orally dispersible tablets were the most common formulation in this study, accounting for 70.3% of the cases, with antibiotics being the most frequently used therapeutic class, representing 25% of the studies. The main risk assessment tool used was the Ishikawa diagram (7.7%), and the factorial was the most design of experiments (DoE) methodology cited (43.6%). Pediatric solid formulations offer significant advantages over liquid forms, including improved dosing accuracy, ease of administration, and better storage stability. This systematic framework will have a definite contribution to facilitating pharmaceutical development and increase the number of pediatric medications reaching the market soon with higher acceptability.

# Enhancing Solubility of Furosemide through Solid Dispersions



## Author

Stéfany Scalco - Universidade Federal do Paraná (UFPR)  
Beatriz Funes de Oliveira - Universidade Federal do Paraná (UFPR)  
Cassiano Pires - Universidade Federal do Paraná (UFPR)  
Raul Edison Luna Lazo - Universidade Federal do Paraná (UFPR)  
Fábio Seigi Murakami - Universidade Federal do Paraná (UFPR)  
Jaqueline Carneiro - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Federal University of Paraná



## Keywords

Furosemide, Spray dryer, Solid dispersion

## Abstract

Solubility plays a critical role in the absorption and effectiveness of drugs. Poorly soluble drugs struggle with achieving adequate dissolution rates in the gastrointestinal tract, which can lead to suboptimal therapeutic outcomes. Furosemide, a loop diuretic used for treating edematous conditions associated with heart, kidney, and liver failure, as well as hypertension, faces challenges due to its low oral bioavailability. This limitation is mainly attributed to its poor water solubility and permeability (Class IV - Biopharmaceutical Classification System). Solid dispersion technology offers a promising approach to enhancing drug solubility. It involves dispersing a poorly soluble drug within a hydrophilic polymer matrix. This process not only disperses the drug but also induces amorphization, transforming its crystalline structure—characterized by strong intermolecular bonds—into an amorphous form lacking long-range order. This transformation significantly increases dissolution rates, thereby improving bioavailability. This study aimed to enhance the solubility of furosemide by preparing polymeric solid dispersions using Polyvinylpyrrolidone K30 (PVP K30) and Hydroxypropyl methylcellulose (HPMC) at concentrations ranging from 0.1% to 1.0%. Various drug-to-polymer ratios (1:0.25, 1:0.5, and 1:1) were tested. The solid dispersions were produced using a spray dryer (LabMaq MSD 1.0) under specific conditions: an inlet temperature of 160°C, a pump feed rate of 0.30 L/h, and an air flow rate of 30 L/min. Scanning electron microscopy (SEM) analysis demonstrated that the solid dispersions resulted in small particle sizes (10-100  $\mu\text{m}$ ) with a spherical morphology. The transformation of the drug's solid morphology positively influenced its solubility by reducing particle size, enhancing surface area, and modifying crystal morphology into microspheres. These findings underscore the potential of solid dispersions as a strategy to enhance the bioavailability of furosemide.

# Development and evaluation of textural mechanical properties of polymeric systems containing T. catigua for nasal administration

## Solubility of Furosemide through Solid Dispersions



### Author

Maria Vitoria Gouveia Botan - Universidade Estadual de Maringá (UEM)  
João Carlos Palazzo de Mello - Universidade Estadual de Maringá (UEM)  
Humberto Milani - Universidade Estadual de Maringá (UEM)  
Marcos Luciano Bruschi - Universidade Estadual de Maringá (UEM)



### Knowledge Area

Pharmaceutical and Cosmetic Technology



### Funding

CAPES, Fundação Araucária and FINEP



### Keywords

Texture profile analysis, neurological diseases, nose to brain

### Abstract

Due to the numerous challenges of neurological treatments, such as low drug bioavailability and crossing the blood-brain barrier, new strategies for development of drug delivery systems are being studied, along with new active agents (1). *Trichilia catigua*, popularly known in Brazil as *catuaba*, is widely used in folk medicine, and studies have shown the presence of compounds with anti-inflammatory and neuroprotective activity against ischemia (2). Therefore, the aim of this study was to develop and evaluate the texture profile of formulations containing the ethyl acetate fraction of *T. catigua* for nasal administration, aiming at brain delivery. Systems were prepared containing 15 or 17.5% (w/w) poloxamer 407 (P407), 0.1 or 0.4% (w/w) hydroxypropyl methylcellulose (HPMC), and 1.5 or 7% (w/w) ethyl acetate fraction of *T. catigua*. Texture profile analysis was performed in triplicate at 25 °C and 37 °C using a TA-XT plus instrument, where an analytical probe was compressed twice into each sample to generate force versus distance and force versus time graphs used to calculate hardness, compressibility, adhesiveness, elasticity, and cohesiveness of the systems using Exponent 3.2 software. All analyses were statistically compared using analysis of variance (ANOVA) with Statistica 10 software. Temperature increase significantly affected ( $p < 0.05$ ) all parameters except elasticity. P407 and HPMC had a statistically significant positive effect ( $p < 0.05$ ) on the systems in terms of hardness, compressibility, and adhesiveness, while the presence of *T. catigua* had a negative influence. The active agent also significantly influenced ( $p < 0.05$ ) the cohesiveness parameter, whereas elasticity was significantly affected ( $p < 0.05$ ) by HPMC. Based on texture profile analysis, it can be concluded that the polymeric systems exhibited satisfactory mechanical characteristics considering their objective, especially at 37 °C.

# Stabilization of Vitamin C using Biopolymers



## Author

Heloísa Fernanda Kuchenbecker - Universidade Federal do Paraná (UFPR)

Patrícia Rodon Gallina - Universidade Federal do Paraná (UFPR)

Joyce Emanuelle de Oliveira Luis Augusto - Universidade Federal do Paraná (UFPR)

Laura Batsef Souza - Universidade Federal do Paraná (UFPR)

Rilton Alves de Freitas - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES, CNPq e Fundação Araucária



## Keywords

Ascorbic acid, Biopolymer, Chemical stability

## Abstract

Ascorbic acid (AA), also known as vitamin C, is an anti-aging molecule and a potent antioxidant that can neutralize oxidative stress triggered by various factors, in addition to playing a fundamental role in collagen biosynthesis. However, vitamin C is easily degraded in aqueous medium in the presence of oxygen, making its stability the biggest challenge in the utilization of this compound. This adds difficulty in including it in cosmetic formulations without suffering any degradation. The aim of the work was the development of a system capable of guaranteeing the stability of ascorbic acid through its interaction with biopolymers. The biopolymer obtained was evaluated for its interaction with ascorbic acid, while the formation of complexes was analyzed through titration associated with zeta potential measurements. In this manner, the samples of the biopolymer, ascorbic acid and the complex formed were subjected to size exclusion chromatography, dynamic light scattering, FTIR and NMR techniques for their characterization. The results obtained confirmed the complex formation. In stability studies, the complex demonstrated greater stability against oxidation when compared to the ascorbic acid control in the same conditions. Demonstrating the potential use of vitamin C in cosmetic formulations while ensuring the maintenance of its chemical stability, making its use viable in topical applications.

# Development Of Nanoemulsions Based Avocado Oil: Effect Of Surfactant



## Author

Samanta Cardozo Mourão - Universidade Federal Fluminense (UFF)  
Beatrice Faria de Almeida Barboza Brasil - Universidade Federal Fluminense (UFF)  
Camila Melo Borges - Universidade Federal Fluminense (UFF)  
alter Teixeira dos Santos Filho - Universidade Federal Fluminense (UFF)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPERJ; CAPES



## Keywords

nanoemulsion; avocado oil; low energy method

## Abstract

Nanoemulsions are dispersions of two immiscible liquids stabilized using an appropriate surfactant. In general, they have a droplet size of 20 to 200 nm and improved kinetic stability compared to classic emulsions. Furthermore, they have low viscosity, a large interface area, a bluish reflection, and applications in various fields. Nanoemulsions can be obtained by different methods, including the low-energy approach. In this process, the surfactants, as well as the oil, surfactant, and water ratio, must be appropriately adjusted. Considering the antioxidant potential of avocado oil, the objective of this work was to study the conditions for obtaining nanoemulsions using the low-energy method. The nanoemulsions were prepared using the phase inversion composition method. In this process, the surfactants and oil were weighed and mixed, and increasing amounts of water were added under constant stirring. Initially, three hydrophilic surfactants were tested. PEG-40 Hydrogenated Castor Oil was chosen, and from this result, nanoemulsions were prepared with different HLBs, using different proportions of sorbitan monoleate. The prepared formulations were initially evaluated by their visual appearance. The formulation was considered adequate when it presented a fluid, homogeneous, translucent system with a bluish reflection after 24 hours. Using 1.5% of the oil, formulations with HLB values of 12.9 (B1) and 11.8 (B2) were selected. At a concentration of 2.5% of the oil, it was possible to obtain nanoemulsions with HLB values of 12.9 (B3), 11.8 (B4), 10.7 (B5), and 9.7 (B6). Additionally, a dynamic light scattering analysis was carried out. The best formulations were B1 (diameter = 24.58 nm) and B6 (diameter = 37.49 nm). The results indicated the best proportion between the components of avocado oil nanoemulsions. This work combines a simple and quick technique to obtain a system with promising antioxidant activity for future cosmetic or pharmaceutical applications

# Chlorhexidine-loaded Contact Lenses: Development and evaluation for Acanthamoeba keratitis treatment



## Author

Vitória Luísa Lopes de Souza - Universidade Federal de Minas Gerais (UFMG)  
Armando da Silva Cunha Junior - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq



## Keywords

Acanthamoeba keratitis, Chlorhexidine, Contact lenses

## Abstract

Acanthamoeba is a genus of free-living amoebae known to cause severe corneal inflammation. Acanthamoeba keratitis (AK) manifests with symptoms including intense pain, photophobia, ring-shaped stromal infiltrates, and epithelial defects, potentially resulting in vision loss or even enucleation if inadequately treated. Predisposition to AK is often associated with excessive or improper use of contact lenses, which can create ocular surface wounds facilitating direct protozoan inoculation. Current treatment involves frequent application of 0.02% to 0.05% Chlorhexidine Digluconate (CD) eye drops every 30 minutes during the acute phase, causing significant patient discomfort and sleep disturbance due to the high frequency of administration. In this context, this research aimed to develop therapeutic contact lenses containing CD in safe dosages to enhance patient comfort during treatment. To the drug-loading, “breathing in” technique was utilized, by soaking hydrogel-Hioxifilcon A contact lenses in 20 ml of ultra-purified water for 4 hours at room temperature on a shaker to remove salts, followed by drying in an oven at 60 °C for 1 hour to eliminate moisture. Subsequently, the dried lenses were immersed in 10 ml of 0.5% CD solution for 24 hours to achieve normal hydration and drug absorption. This was followed by a 24-hour immersion in 5 ml of absolute ethanol to complete drug release, and UV spectrometry was performed to quantify drug deposition which was approximately 348 µg per lens. In the next stages of this research, the drug in vitro release profile will be carried out under controlled conditions, and the in vitro efficiency of inhibiting parasite multiplication will be accomplished utilizing Acanthamoeba culture in contact with the lens environment. Additionally, the in vivo safety and toxicity of this new drug delivery system will be fulfilled.

# Preparation And Characterization Of Inclusion Complex Of $\beta$ -Cyclodextrin And Triterpenic Derivative With Antitrypanosomal Activity



## Author

Odoiza Naftaly Magalhães da Silva Lins - Universidade Federal do Amazonas (UFAM)  
Victoria Nunes Figueiredo - Universidade Federal do Amazonas (UFAM)  
Aryane Maia de Castro - FCFRP - Universidade de São Paulo (USP)  
Fernanda Guilhon-Simplicio - Universidade Federal do Amazonas (UFAM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq



## Keywords

Cyclodextrins, Inclusion Complexes, Amyrins

## Abstract

Cyclodextrins are cyclic oligosaccharides composed of D-glucopyranose units linked by  $\alpha$ -1,4 glycosidic bonds. The specific arrangement of glucopyranose units and bonds forms their conical structure. Hydroxyl groups from the monomer units are positioned on the outer surface, while hydrophobic rings are oriented towards the interior. Consequently, cyclodextrins possess a structure and characteristics that facilitate the formation of inclusion complexes with lipophilic substances, thereby improving their physicochemical and pharmacological properties. In this context, the objective of this study was to enhance the complexation conditions of  $\beta$ -cyclodextrin ( $\beta$ CD) with a proven trypanosomatid activity triterpenic derivative (FGS-10), which is insoluble in water (Guilhon-Simplicio, 2022), focusing on complexation time and solvent mixing. The substance and  $\beta$ CD were mixed in a 1:1 molar ratio and solubilized in solvent mixtures (THF, ethanol, and water) at various proportions, with continuous agitation for either 48 or 96 hours. Solvent evaporation in a forced air circulation oven led to environment supersaturation, promoting complex precipitation. Samples were characterized using Fourier-transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM). The FTIR spectrum of sample ET14D (ethanol and THF 1:1, 96 hours) shows prominent bands characteristic of  $\beta$ CD, while bands typical of semi-synthetic structure are absent or diminished. SEM images of samples ET14D and ET24D (ethanol 2:1, 96 hours) reveal overall structural changes in cyclodextrin as conglomerates, deformation of the initial crystalline structure of cyclodextrin, and absence of amyirin crystals. Under these analysis conditions, the optimal solvent for FGS-10 and  $\beta$ CD complexation was a 1:1 mixture of ethanol and THF. Complexation time did not significantly affect the outcomes. These findings will facilitate future investigations into the pharmacological properties of this promising molecule.



# Development of Polymeric Micelles for Curcumin Skin Delivery



## Author

Nara Juliana Teles Santos - Universidade de Brasília (UnB)  
Breno N. Matos - Universidade de Brasília (UnB)  
Seila Tolentino - Universidade de Brasília (UnB)  
Marcilio Cunha-Filho - Universidade de Brasília (UnB)  
Tais Gratieri - Universidade de Brasília (UnB)  
Guilherme M. Gelfuso - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPDF (Grant #00193-00000721/2021-04, Project 41/2021) and CNPq (Grant # 310291/2021-6)



## Keywords

Skin cancer, Topical Delivery, Poloxamer

## Abstract

Curcumin is a natural polyphenol that exhibits action against various tumors such as melanoma, breast, head and neck, prostate, and ovarian cancers. However, its poor solubility in water and chemical instability at physiological pH pose significant challenges to its use. This work aimed to develop polymeric micelles to increase curcumin solubility and enhance its penetration into the deeper layers of the skin, focusing on a topical delivery. Curcumin (24 mg), 240 mg Poloxamer, and 240 mg polyethylene glycol were solubilized in ethanol, which was further extracted using a rotary evaporator. The resulting film was hydrated (5 ml water) and left under stirring for 30 min. The curcumin solubility in water and the formed micelles was assessed using a previously validated HPLC method. The micelles were characterized by evaluating average hydrodynamic diameter, size distribution (Pdl), zeta potential, pH, and morphological characteristics. The skin penetration of curcumin from the micellar solution was evaluated in vitro over 48 h in Franz diffusion cells. The micelles increased curcumin aqueous solubility from 0.006 to  $1,215.9 \pm 0.6$  g/l. The polymeric micelles exhibited an average size of  $36.9 \pm 0.2$  nm, Pdl of  $0.27 \pm 0.01$ , and zeta potential of  $-0.6 \pm 0.1$  mV. The pH value of the micellar solution ( $6.0 \pm 0.1$ ) is compatible with human physiological skin pH. Transmission Electronic Microscopy (TEM) analysis confirmed the average size of the micelles. Skin permeation studies established that the micellar formulation could considerably promote skin permeation since  $72.2 \pm 18.6$   $\mu\text{g}/\text{cm}^2$  of curcumin was retained in the stratum corneum and  $382.9 \pm 115.6$   $\mu\text{g}/\text{cm}^2$  in the viable skin. Thus, the micellar system successfully improved the solubilization of curcumin and effectively facilitated the penetration of the substance into the deeper layers of the skin, enabling its topical use.

# Development of Dutasteride-loaded Liposomes for Androgenic Alopecia Treatment



## Author

Jayanaraian Martins Andrade - Universidade de Brasília (UnB)  
Rafael Vieira Rocho - Universidade de Brasília (UnB)  
Marcílio Cunha-Filho - Universidade de Brasília (UnB)  
Guilherme Martins Gelfuso - Universidade de Brasília (UnB)  
Tais Gratieri - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

DPG Edital nº 005/2024



## Keywords

Dutasteride, Liposomes, Hair Follicles.

## Abstract

Androgenic Alopecia (AGA) is the most prevalent among non-cicatricial alopecia and comes with a great psychological burden but lacks an effective and safe treatment. Dutasteride (DUT) has gained interest for showing promising results in hair regrowth. However, oral DUT causes serious sexual adverse events. Therefore, a local treatment is of great interest. Here, we aim to obtain and characterize DUT-loaded liposomes with different compositions and assess their hair follicle (HF) targeting factor (TF). Liposomes were obtained by lipid film hydration and were fully characterized. For penetration tests, porcine skin discs were mounted in a Hanson diffusion cell assembly (area=1.77 cm<sup>2</sup>). 0.5 mL of DUT-loaded liposomes (0.025%) was placed in the donor compartment, and 0.5% Tween® 80 aqueous solution filled the receptor compartment. Control was a mineral oil DUT solution (0.025%). After 12h, differential tape-stripping technique was performed for HPLC DUT quantification. All data were expressed as mean ± standard deviation (n=6). Statistical significance of the data was evaluated by ANOVA two-way with Tukey's post hoc test ( $\alpha = 0.05$ ) in GraphPad Prism 9.0. Three liposomes were obtained. Liposome A contained only phosphatidylcholine and DUT; Liposome B – phosphatidylcholine, cholesterol, and DUT, while Liposome C had phosphatidylcholine, Tween®80, and DUT. Skin penetration tests showed Liposome C was more efficient in targeting HFs ( $p < 0.0001$ ), with a TF of 0.32, compared to A and B (0.14 and 0.15, respectively); and slightly superior to control (TF: 0,31) ( $p > 0.05$ ). No DUT was quantified in the receptor compartment. Liposomes had sizes from 220 to 460 nm, Pdl ranged from 0.24 to 0.34, zeta potential around zero (pH 5.5), and encapsulation efficiency around 80.5%. In conclusion, DUT-loaded liposome with Tween®80 in its composition is a promising drug delivery system to effectively and safely deliver DUT to HFs, enhancing AGA treatment.

# Development Of Polymeric Nanoparticles Loaded With Azithromycin For Topical Treatment Of Follicular Infections



## Author

Mikaella Costa de Sousa - Universidade de Brasília (UnB)  
José Lenart Lucena Alcântara - Universidade de Brasília (UnB)  
Marcilio Cunha-Filho - Universidade de Brasília (UnB)  
Tais Gratieri - Universidade de Brasília (UnB)  
Breno Noronha Matos - Universidade de Brasília (UnB)  
Guilherme Martins Gelfuso - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPDF (Grant n. 00193-00002389/2023-76).



## Keywords

Dutasteride, Liposomes, Hair Follicles.

## Abstract

When applied topically, solid nanoparticles tend to deposit into hair follicle casts. Thus, this study aimed to develop polycaprolactone nanoparticles loading azithromycin and evaluate drug follicular deposition upon topical application. To prepare the nanoparticles, an organic phase composed of 0.5% (w/v) azithromycin and 75% (w/v) polycaprolactone was poured onto an aqueous phase containing 0.5% (w/v) Tween 80 under stirring until evaporation of the organic phase. The nanoparticles' diameter, Pdl, zeta potential, morphology, and entrapment efficiency were then determined. In vitro drug release from the nanoparticles was evaluated for 12 h. Drug penetration from the nanoparticles was accessed for 6 and 12 h in porcine skin mounted on diffusion cells coupled to a Phoenix® device. The nanoparticles were spherical, with a diameter of  $158.3 \pm 0.4$  nm (Pdl =  $0.09 \pm 0.02$ ), zeta potential of  $-22.8 \pm 0.5$  mV, and entrapped  $92.5\% \pm 0.1\%$  of azithromycin. The nanoparticles reduced drug release by 2.8 times compared to free-azithromycin diffusion. Within 6 h, nanoparticles doubled the azithromycin penetration in the hair follicles compared to the control ( $16.2 \pm 8.1$   $\mu\text{g}/\text{cm}^2$  versus  $8.2 \pm 2.7$   $\mu\text{g}/\text{cm}^2$ ,  $p < 0.05$ ). At 12 h, this concentration of azithromycin in the hair follicles was maintained for nanoparticles and decreased 5.2-fold ( $p < 0.05$ ) with the application of the control drug solution. Such a nanoparticulate system, therefore, effectively targets the hair follicles and prolonged drug release, being a promising alternative for the skin treatment of infections that affect hair follicles, such as acne.

# Rheological Analysis Of Thermoresponsives Systems Containing Ketamine For Oral Administration In Small Animals



## Author

Sabrina Barbosa de Souza Ferreira - Universidade Estadual de Maringá (UEM)  
Carolina Parcerio Hernandez - Universidade Estadual de Maringá (UEM)  
Michael Cavalheiro Jorge - Universidade Estadual de Maringá (UEM)  
Samara Bossa Aleixo - Universidade Estadual de Maringá (UEM)  
Marilda Onghero Taffarel - Universidade Estadual de Maringá (UEM)  
Marcos Luciano Bruschi - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq and Finep



## Keywords

Rheology, Ketamine, Small animals

## Abstract

Ketamine is a dissociative anesthetic that blocks NMDA receptors. Its effectiveness varies depending on the concentration: at low levels, it exhibits analgesic properties, while higher concentrations result in anesthetic effects. Used in Veterinary Medicine, especially in small animals, ketamine is commonly administered by direct infusion. Recently, there is interest in its administration via the oral cavity to achieve systemic effect, using poloxamers, thermoresponsive copolymers that allow prolonged release of the drug. The objective of this study was to prepare and evaluate the rheological properties of formulations containing ketamine for oral administration in cats, using rheology. The gels were composed of 17.5% or 20% (w/w) poloxamer 407 (P407) and 5% or 8% (w/w) ketamine, prepared according to the "cold method". Flow and oscillatory rheological analyses were conducted using a MARS II rheometer with cone and plate geometry under controlled shear stress. Each sample was tested with a minimum of three repetitions in all analyses. Consistency index (K) values significantly increased ( $p < 0.05$ ) with higher temperatures. At 5 °C, K varied with the increase of concentration of P407 and ketamine. At 25 °C, formulations containing 20% P407 displayed lower K than 17.5%, even with ketamine added; 20% ketamine formulations also showed lower K than 17.5% P407. At 37 °C, 20% P407 showed higher K, indicating a greater viscosity than 17.5%. Flow behavior varied: Newtonian at 5 °C and for 17.5% and 20% P407 with 5% ketamine, at 25 °C; pseudoplastic or plastic at 37 °C and for 17.5% with ketamine at 25 °C. The oscillatory rheology evidenced viscoelastic behavior at 5 °C and 25 °C, while elastoviscous behavior was observed at 37 °C. Therefore, formulations containing higher concentrations of P407 and ketamine were the most promising aiming the application in the oral cavity of small animals.

# Influence of temperature on collagen extracted from tilapia skin using Raman spectroscopy



## Author

Denise Tiemi Uchida - Universidade Estadual de Maringá (UEM)  
Adriane Nascimento Volnistem - Universidade Estadual de Maringá (UEM)  
Michael Thomas Cook - University College London  
Marcos Luciano Bruschi - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES - Financing code n°. 001; CNPq process n°. 404163-2021/1



## Keywords

Fish Collagen, *Oreochromis niloticus*, protein denaturation

## Abstract

Collagen extracted from tilapia skin has garnered significant attention due to its potential applications in various fields and its unique properties. In the context, Raman spectroscopy plays a fundamental role in understanding the effects of environmental conditions, such as temperature, on the structure and stability of this essential protein. Thus, the aim of the work is to investigate possible conformational changes resulting from heating. Raman spectroscopy measurements were carried out as a function of temperature (24 °C, 34 °C, 40 °C, 50 °C and 60 °C) on both samples, EA5 (acid extraction, using acetic acid) and EAp6 (acid extraction with pepsin). For temperature-related measurements, a temperature control system compatible with a confocal Raman microscope, composed of gas and humidity sensors, was used. The temperature range measured was between 24°C and 60°C at a rate of 3°C/min. For collagen EA5, it is possible to verify the presence of an evident band centered at 1244 cm<sup>-1</sup> in the amide III region. However, at a temperature of 34 °C, the formation of a band centered at 1258 cm<sup>-1</sup> was observed, which remained up to 40 °C. For the amide I region, a peak centered at 1640 cm<sup>-1</sup> was observed at a temperature of 24 °C, which disappears after 34 °C. Bands centered at 930 cm<sup>-1</sup> and 945 cm<sup>-1</sup>, clearly present at a temperature of 24 °C, ceased to exist after 34 °C. For the EAp6 sample, in relation to the temperature function, no significant changes were observed in the analyzed spectral regions compared to the EA5 sample. The observed conformational changes may indicate the possibility of denaturation or reversible unfolding of collagen, especially around 34 °C. In summary, the results indicate that the extraction methods adopted and the heat treatment employed affect the structure and conformation of collagen, with the acid extraction method with pepsin providing greater thermal stability and a more preserved structure.

# Bigels: case studies of an innovative topical dosage form



## Author

Paulo Cunha - Gattefossé  
Kelly Bueno - Gattefossé  
Delphine Pelisson - Gattefossé Saint-Priest  
Manon Rossano - Gattefossé - Saint-Priest  
Philippe Caisse - Gattefossé - Saint-Priest  
Elise Dauphin-Chanard - Gattefossé - Saint-Priest



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Gattefossé SAS



## Keywords

bigel, characterization, topical formulations

## Abstract

Topical treatments are often considered time-consuming and unpleasant when compared to oral ones, and depend on the formulation characteristics, such as sensory properties, impacting treatment compliance and potentially resulting in suboptimal outcomes. Bigels, an emerging and innovative topical dosage form, combine an oily gel and a hydrogel, offering an alternative dosage form for dermal therapies, possibly leading to increased therapeutic adherence. Bigel formulations (F1, F2 and F3) were developed using Emulfree® Duo as oil stabilizer and different vehicles, gelling and thickening agents through either cold or hot processes. The formulations were evaluated for appearance, consistency, microscopical structure, pH, viscosity, flow measurement, yield stress and thixotropy. Stability tests were conducted for up to 12 months at 25 and 40°C. Additionally, a panel of sensory experts analyzed their sensory profiles, including spreadability, greasiness and afterfeel. Depending on the combination of excipients, the formulations exhibited different viscosity and other rheological properties, achieving distinct bigel textures: F1 presented the viscosity suitable for a lotion, and F3, the most viscous, showed to be appropriate for the development of a thick cream. F2 presented intermediate viscosities, functioning as a traditional cream. During stability tests, all formulations performed well up to 6 months, highlighting their potential for the development of stable bigels for pharmaceutical applications. Regarding the sensory analysis, illustrated in a spider diagram, the formulations differ on spreadability and afterfeel properties, though all of them provided a cooling effect after administration. In conclusion, bigels are an innovative type of topical formulation that, with the possibility of obtaining various sensory profiles, their tolerance and stability, may be used for the development of dosage forms that may increase adherence of patients to topical treatments.

# Development and Characterization of Biodegradable Intraocular Implants containing Metoprolol for the treatment of Retinal Hemangioblastoma



## Author

Ana Luiza Silvério - Universidade Federal de Minas Gerais (UFMG)  
Armando da Silva Cunha Junior - Universidade Federal de Minas Gerais (UFMG)  
Thomas Toshio Inoue - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq



## Keywords

Metoprolol, Biodegradable implants, Retinal hemangioblastoma

## Abstract

The management of vascular tumors, such as retinal hemangioblastoma, includes invasive therapies like laser photocoagulation, cryotherapy, and radiotherapy for larger tumors. Recently, alternative pathways to inhibit disease progression have been studied with the aim of preserving patients' vision. The clinical intravitreal use of  $\beta$ -blockers has been proposed, and the safety of intravitreal Metoprolol administration were evaluated by the group, suggesting a mechanism to reduce angiogenesis and capillary growth. However, intravitreal injection may be associated with some adverse effects. In this context, drug delivery alternatives, such as biodegradable intraocular implants, provide sustained drug release with less invasive treatment administration for the patient. The aim of this work is to develop and characterize these ocular delivery systems. The biodegradable implants were developed using PLGA 75:25 as the polymeric matrix and Metoprolol as the drug at 25% w/w. The polymer and drug were dissolved in an appropriate organic solvent/water mixture (4:1), and the resulting solution was lyophilized to obtain a homogeneous cake. The previously prepared homogeneous cake was molded into rods by hot extrusion technique at 90°C to 105°C. To evaluate the stability of Metoprolol and the thermoplastic polymer, the possibility of interactions between the drug and PLGA, and to assess the final implants, differential scanning calorimetry (DSC) and thermogravimetry were performed. The next steps of this study are to monitor the in vitro degradation of the implants and analyze the in vitro drug release profile. Furthermore, in vivo studies would evaluate the safety and toxicity of using the developed implants as a long-term intraocular delivery system to treat posterior eye disease.

# Oral simvastatin emulsion for the paediatric patient



## Author

Cristiane dos Santos Giuberti - Universidade Federal do Espírito Santo (UFES)  
Gabriel Poltronieri do Nascimento - Universidade Federal do Espírito Santo (UFES)  
Larissa Moreira Coelho - Universidade Federal do Espírito Santo (UFES)  
Fernanda Leite Pereira Martins - Associação Vitoriana de Ensino Superior (FAVI)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

This research was funded by FAPES project number 207/2024



## Keywords

Dyslipidemias. Pharmaceutical compounding. Nonsterile preparations.

## Abstract

Dyslipidemias are a leading global cause of morbidity and mortality, contributing to the development of cardiovascular diseases. Due to various sociodemographic, dietary, and lifestyle changes, dyslipidemia is becoming increasingly prevalent among children. Statins, a class of drugs used to lower lipid levels, are considered one of the primary treatment options for paediatric patients. However, these medications are currently only available in solid form, which presents challenges for paediatric patients, potentially affecting treatment adherence and therapeutic outcomes. In response to this issue, our study aimed to develop a liquid oral emulsion of simvastatin and assess its physicochemical stability. The simvastatin emulsions were prepared and stored in amber glass bottles at room temperature, protected from light, for 28 days. Analysis was conducted on organoleptic characteristics, density, pH, zeta potential, particle size, and polydispersity index (PDI). The research resulted in the development of an oral nanoemulsion of simvastatin, with a concentration of 5 mg/mL, characterized as an oil-in-water type, with a particle size of  $145.57 \pm 16.07$  nm, homogeneity (PDI  $11.73 \pm 5.54$ ), and zeta potential of  $-37.77 \pm 1.65$  mV. This formulation was stable for 28 days, although the pH values decreased during the storage period ( $p < 0.05$ ). Given the lack of commercially available liquid simvastatin formulations, this study aims to address the growing need within the paediatric population. Additionally, the information provided is intended to support the determination of the beyond-use date of the formulation, offering technical and scientific support for the pharmaceutical compounding sector. Ultimately, this oral formulation of simvastatin has the potential for application in pharmaceutical compounding.



# Novel blend microcapsules for vaginal delivery of *Lactobacillus* spp



## Author

Ligia Carine Wess - Universidade Federal de Santa Maria (UFSM)  
Gabriela Wink Stringhini - Universidade Federal de Santa Maria (UFSM)  
Tielle M. de Almeida - Universidade Federal de Santa Maria (UFSM)  
Quellen M. Ribeiro - Universidade Federal de Santa Maria (UFSM)  
Iasmin Caroline de Almeida Veeck - Universidade Federal de Santa Maria (UFSM)  
Cristiano R. Menezes - Universidade Federal de Santa Maria (UFSM)  
Cristiane de B. da Silva - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq and Finep



## Keywords

PROBIC/FAPERGS, CAPES/Brazil, CNPq/Brazil, and COANA.

## Abstract

Lígia Wess<sup>1</sup>; Gabriela W. Stringhini<sup>2</sup>; Tielle M. de Almeida<sup>1</sup>, T.; Quellen M. Ribeiro<sup>3</sup>; Iasmin Caroline de Almeida Veeck<sup>3</sup>; Cristiano R. Menezes; Cristiane de B. da Silva<sup>1</sup>

<sup>1</sup>Programa de Pós-Graduação em Ciências Farmacêuticas, UFSM; <sup>2</sup>Curso de Farmácia, UFSM; <sup>3</sup>Programa de Pós-Graduação em Ciência e Tecnologia dos Alimentos, UFSM

*Lactobacillus* spp. play a crucial role in the vaginal microbiota, maintaining an acidic environment and inhibiting the growth of pathogens. However, they are vulnerable to various adverse conditions, complicating the development of pharmaceutical products that keep them viable and effective. Microencapsulation is a strategy to protect them against physicochemical instabilities, improving stability, viability, and efficacy. This study aims to preparation of a novel microparticulate formulation containing *Lactobacillus rhamnosus* and *L. acidophilus* based on LBG/trehalose/maltodextrin blend by spray-drying process. The dispersion containing lactobacillus (n=3) was atomized using a spray dryer with a 1 mm atomizer nozzle, at an inlet temperature of 120 °C and an outlet temperature of 85 °C ± 5 °C. The feed dispersions, kept under agitation, were introduced into the drying system through a peristaltic pump with a flow rate of 0.31 L/h, a drying air flow rate of 30 L/min, and an air pressure of 0.6 MPa. The granulometric profile of the microcapsules was analyzed by laser diffraction and the viability was assessed by the plate count method. The microcapsules achieved a yield of 26%, with a granulometric distribution in the micrometric range (31 ± 2 µm; Span values around 4.0). The microcapsules exhibited colony counts of 8 log CFU/g. Based on the results, it was possible to optimize the dispersion and spray-drying parameters, allowing microcapsules containing lactobacillus to be obtained for subsequent use in the development of pharmaceutical forms for vaginal use.

# Validation of analytical methodology for RU determination, preparation, complexation, and evaluation of the solubility of the RU/ $\beta$ -CD complex



## Author

Fernanda Belincanta Borghi Pangoni - Universidade Estadual de Maringá (UEM)  
Arthur Henrique Pereira Lobato - Universidade Estadual de Maringá (UEM)  
Deborath de Lima Salamonczyk - Universidade Estadual de Maringá (UEM)  
V́ctor Nery Lippa - Universidade Estadual de Maringá (UEM)  
Andrea - Universidade Estadual de Maringá (UEM)  
Graciette Matioli - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Universidade Estadual de Maringá



## Keywords

Rutin, Beta-cyclodextrin, Solubility

## Abstract

Rutin (RU) is a flavonoid with low solubility. Beta-cyclodextrin ( $\beta$ -CD) improves solubility. Therefore, the aim of this study was to validate the analytical methodology for RU determination using UV-Vis spectrophotometry (at 360 nm) and to determine the solubility of the RU: $\beta$ -CD complex. For linearity assessment, a calibration curve was constructed with seven RU concentrations (2.0, 4.0, 6.0, 8.0, 10, 14, 20  $\mu\text{g}/\text{mL}$ ) in ethanol (P.A), evaluating coefficient of variation (CV%), correlation coefficient, regression analysis, lack of fit, homoscedasticity, and adequacy. Precision was evaluated at three RU concentrations (3, 7, 9  $\mu\text{g}/\text{mL}$ ) for repeatability and intermediate precision. Robustness and accuracy were determined at concentrations of 3, 7, 9, and 15  $\mu\text{g}/\text{mL}$ . Two mixtures of the RU: $\beta$ -CD complex were prepared using the physical mixing method in ratios of 1:1 and 1:2, and their solubilities were analyzed via shake-flask technique over 24 hours at 37°C in five media: FaSSIF, FaSSGF, HCl (pH 1.2 and water), phosphate buffer (PB) (pH 6.8) and water. The linear regression equation obtained was  $y = 0.0315x + 0.0219$  with  $R^2 = 0.9982$ . The model showed no lack of fit, and the regression was significant, with a detection limit of 0.590  $\mu\text{g}/\text{mL}$  and quantification limit of 0.590  $\mu\text{g}/\text{mL}$ . Precision and robustness were adequate, and accuracy showed recovery within acceptable limits. The 1:1 complex exhibited similar solubility across all tested media (FaSSIF =  $13.59 \pm 0.55$   $\mu\text{g}/\text{mL}$ , FaSSGF =  $15.07 \pm 0.18$   $\mu\text{g}/\text{mL}$ , HCl pH 1.2 =  $13.59 \pm 0.32$   $\mu\text{g}/\text{mL}$ , PB =  $14.65 \pm 0.97$   $\mu\text{g}/\text{mL}$ , and water =  $14.86 \pm 1.38$   $\mu\text{g}/\text{mL}$ ). Meanwhile, the 1:2 complex showed slight improvement in solubility in the tested media (FaSSIF =  $19.15 \pm 0.67$   $\mu\text{g}/\text{mL}$ , FaSSGF =  $20.58 \pm 1.93$   $\mu\text{g}/\text{mL}$ , HCl pH 1.2 =  $20.26 \pm 1.34$   $\mu\text{g}/\text{mL}$ , PB =  $22.91 \pm 0.48$   $\mu\text{g}/\text{mL}$ , and water =  $23.33 \pm 1.11$   $\mu\text{g}/\text{mL}$ ). In conclusion, the method was validated. The solubility assay revealed that the 1:2 complex exhibited better solubility than the 1:1 complex in different media.

# Development of a natural emulsion with guanandi seed oil (*Calophyllum brasiliense*)



## Author

Maurília de Oliveira Souza - Universidade Federal do Espírito Santo (UFES)  
Thalita de Sousa Ferreira - Universidade Federal do Espírito Santo (UFES)  
Raissa de Souza Vassoler - Universidade Federal do Espírito Santo (UFES)  
Rodrigo Rezende Kitagawa - Universidade Federal do Espírito Santo (UFES)  
Janaina Cecília Oliveira Villanova - Universidade Federal do Espírito Santo (UFES)  
Cristiane dos Santos Giuberti - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

This research was funded by FAPES grant number 109/2024



## Keywords

Vegetable oils, upcycling, stability

## Abstract

Vegetable oils are rich in fatty acids, endowing them with a high capacity for tissue hydration and repair, making them potential emollient raw materials for cosmetic product formulations. Guanandi (*Calophyllum brasiliense*) is a species known for its exceptional potential in sustainable cosmetics due to the presence of linoleic, oleic, palmitoleic, and stearic acids in its seed oil obtained through cold pressing. Guanandi seed oil (GSS) is adaptable and offers a pleasing sensory experience, making it suitable to be used in emulsified cosmetic formulations. This study aimed to develop and characterize a natural emulsion containing guanandi seed oil for topical use. Formulations with different concentrations of GSS were created and underwent centrifugation and thermal stress tests to select the most physically stable option. The chosen formulation underwent a preliminary stability test over 35 days, analyzing its macroscopic and microscopic aspects, pH, electrical conductivity, spreadability, and texture. The emulsion, prepared using natural raw materials, formed an oil-in-water (O/A) emulsion due to the emulsifiers used. The emulsion with 10% oil exhibited stability, maintaining its physical properties. Macroscopic analysis revealed a cream with a shiny and uniform appearance, while light microscopy indicated well-distributed droplets without signs of phase separation. The pH remained around 5, similar to that of the skin, and the electrical conductivity remained constant, indicating stability. Spreadability tests and texture analysis confirmed a smooth and pleasant application to the skin. The natural emulsion with 10% guanandi seed oil has proven to be feasible and stable, making it a sustainable alternative for the cosmetic industry and adding value to plant waste. Future research can further explore the potential benefits of guanandi oil in various cosmetic applications.

# Development Of Melatonin Analytical Hplc Method For Quantifying Topical Formulations On The Skin



## Author

Giovanna Adrielle Franco Barcelos - Universidade de Brasília (UnB)  
Geisa Nascimento Barbalho - Universidade de Brasília (UnB)  
Guilherme Martins Gelfuso - Universidade de Brasília (UnB)  
Marcilio Sérgio Soares da Cunha Filho - Universidade de Brasília (UnB)  
Tais Gratieri - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPDF, CAPES, PPGCF



## Keywords

Melatonin, HPLC UV method, Topical application

## Abstract

**INTRODUCTION:** Melatonin is a natural hormone mostly secreted by the pineal gland during the circadian cycle and demonstrates remarkable potential as a topical intervention. It has high lipophilicity with a Log P = 1.65, solubility (25°C) in water of 0.1 mg/mL and in ethanol of 50 mg/mL, allowing it to easily penetrate the blood-brain barrier and cells, accelerating acute healing in chemical and UV wounds, reducing skin oedema, and suppressing inflammatory genes by neutralizing oxidative stress. This product presents powerful properties that promote anti-ageing, anti-wrinkle, and anti-inflammatory effects in skin care products. **OBJECTIVES:** Develop and validate a simple, precise, and specific HPLC-UV method for quantifying melatonin in the skin. **METHODS:** The melatonin was analyzed using HPLC-UV with a mobile phase consisting of methanol and water (50/50, v/v). The flow rate was 0.5 mL/min, the injection volume was 20 µL, and detection was performed at a wavelength of 278 nm. A Luna C18 reverse phase column (250 × 4.60 mm, 5 µm, 100 Å, Phenomenex® - Torrance, USA) was used with an oven temperature of 45°C. **RESULTS:** The validated method showed good linearity between 0.5 and 50.0 µg/mL ( $y = 54474x - 41600$  and  $r^2 = 0.998$ , inter- and intraday variability lower than 2 %, accuracy between 100 % and 104 %, and detection and quantification limits of 1.9 µg/mL and 5.5 µg/mL, respectively. The recovery test was carried out for 24 hours static for the stratum corneum, hair follicle and viable skin and melatonin recovery was between 91.5% and 117%. **CONCLUSIONS:** The method has been proven to be simple, linear and precise for quantifying melatonin in different skin layers, demonstrating the potential for quantifying topical cosmetic formulations containing melatonin with a controlled delivery in the skin.

# Development And Perception Of Hair Conditioner Formulation



## Author

Giulia Sarah Mendes - Universidade Federal de São João Del-Rei (UFSJ)  
Carolina Soares Teixeira - Universidade Federal de São João Del-Rei (UFSJ)  
Beatriz Rocha Lobo Parreira - Universidade Federal de São João Del-Rei (UFSJ)  
Luna Cunha Metzker - Universidade Federal de São João Del-Rei (UFSJ)  
Carlos Eduardo de Matos Jensen - Universidade Federal de São João Del-Rei (UFSJ)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPEMIG/MG (project number: 27275)



## Keywords

Cosmetics, Hair Preparations, Perception

## Abstract

The hair cortex is the region most affected by hair preparations, such as hair dyeing or shampooing, causing disorganization of the cuticle scales and leaving the fibers vulnerable to external aggressions. Therefore, it is important to use hair conditioners (HCD) that can minimize these damages, as hair care, color, and style play a significant role in people's physical appearance and self-perception. The aim of this study was the development and evaluation of HCD, with or without citric acid as a conditioning agent. Two HCD formulations were developed: [HCD-A] containing cetrimonium chloride (2.0%) and [HCD-B] containing citric acid (2.0%). The pH of the HCD formulations was 5.0 and 2.7, respectively. After preliminary stability tests at 4°C, 25°C, and 45°C, the developed HCD showed normal organoleptic characteristics without any changes. Additionally, pH and viscosity remained stable throughout the study period. In the first stage of the human research protocol, approved by the Human Research Ethics Committee (CEPCO/UFSJ), the Preference Test was conducted according to ASTM E2263-12 (2018). HCD-B was significantly more preferred by participants. In the second stage, preference was assessed between HCD-B and a commercial HCD-C with a pH of 2.7. No significant difference in preference was observed between HCD-B and HCD-C. In the third stage of the research protocol, the Difference Test was conducted according to ASTM E2139-05 (2018) for products HCD-B and HCD-C. According to the results obtained using the Chi-Square test, these conditioners are sensorially similar ( $p < 0.001$ ). Our results suggest that the HCD containing citric acid is stable at different temperatures. In perception studies, HCD-B was preferred by volunteers, and in the Difference Test, it was found to be sensorially equivalent to a commercial product.

# Modeling supersaturation and recrystallization of amorphous pharmaceuticals: a case study with indomethacin using free-to-use MATLAB Online



## Author

Lucas Danda - Universidade Federal de Pernambuco (UFPE)  
Azael Francisco Silva Neto - Universidade Federal de Pernambuco (UFPE)  
Alane Rafaela de Carvalho Amaral - Universidade Federal de Pernambuco (UFPE)  
José Lamartine Soares-Sobrinho - Universidade Federal de Pernambuco (UFPE)  
Monica Felts de La Roca Soares - Universidade Federal de Pernambuco (UFPE)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE), Brazil, IBPG-0579-4.03/18



## Keywords

supersaturation, modeling

## Abstract

Poor drug solubility poses a significant challenge in pharmaceuticals. In response to this problem, supersaturable formulations, such as amorphous solid dispersions, have been increasingly approved by the FDA as an effective strategy to address poorly soluble drugs and enhance bioavailability. Supersaturation and recrystallization phenomena are critical in these drug delivery systems, affecting bioavailability performance. Predicting these dynamics can be decisive in early development stages, such as for selecting appropriate polymer carriers. This study applies a modeling for these processes using free-to-use MATLAB Online, with indomethacin as a case study. Our method builds on previous studies using the multiphysics simulation software COMSOL® and is based on a mass balance approach to account for concentration increase during constant-rate supersaturation generation and consequent decrease due to precipitation. A set of ordinary differential equations rooted in classical nucleation theory and crystal growth were simultaneously solved for the precipitation rate, allowing for the construction of a kinetic-solubility profile. To compare with the simulated results, an *in vitro* experiment was performed by infusing a concentrated indomethacin solution (1000 µg/mL in ethanol) at 0.333 mL/min, achieving 20 mg dissolved in 15 min in a dissolution vessel with 250 mL of pH 3.0 buffer, agitated at 150 RPM using a USP 2 paddle apparatus. Samples were collected up to 8h, centrifuged at 14000 RCF for 5 min, and the supernatant was read by UV-Vis to obtain experimental kinetic-solubility profiles. A great correlation was achieved ( $R \approx 0.96$ ) between the mathematical and experimental data. This result indicates that the method can be safely used on the MATLAB platform to predict the kinetic solubility profiles of pure amorphous drugs. Further experimental studies are needed to determine the necessary constants for other drugs to benefit from this model.

# Development of oral anesthetic films with physical and functional adaptations: application in pediatric dentistry



## Author

Ana Clara Wada de Carvalho - FCFRP - Universidade de São Paulo (USP)  
Isabella Miguel Villa - FCFRP - Universidade de São Paulo (USP)  
Guilherme Prado Corrêa - FCFRP - Universidade de São Paulo (USP)  
Maira Peres Ferreira Duarte - FCFRP - Universidade de São Paulo (USP)  
Gisele Inácio - FORP - Universidade de São Paulo (USP)  
Alexandra Mussolino de Queiroz FORP - Universidade de São Paulo (USP)  
Oswaldo de Freitas - FCFRP - Universidade de São Paulo (USP)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES PROEX 88887.508680/2020-00



## Keywords

Films, Release Profile, Mucoadhesion

## Abstract

Even with advances in the use of infiltrative local anesthetics in dentistry, many patients still experience anxiety due to fear of needles, which can result in postponement and avoidance of treatment. Several anesthetic systems for dental procedures have been developed to provide greater patient comfort during anesthesia, however, despite the good acceptance of these systems, their effectiveness in general dentistry is limited. The administration of conventional local anesthesia in children is even more difficult due to anxiety and fear, the reduced size of the jaw and the adequacy of the dose, which must be carefully calculated to avoid possible side/adverse effects. Currently, there are no anesthetic systems capable of meeting all the needs of pediatric dental clinics, therefore, the project aims to develop mucoadhesive films, which contain lidocaine and prilocaine in their base forms, seeking to partially or completely replace injectable local anesthesia during dental treatment. . The proposed film-forming system is a trilaminated system composed of an occlusive layer, an adhesive layer and an anesthetic layer. Nine compositions with different proportions of cellulose and chitosan were subjected to *in vitro* release tests, with a rapid release profile being observed within the first two hours of release, suitable for the proposed application, and reaching a release plateau after 6 hours of experiment. Mechanical and mucoadhesive properties tests were carried out using texture analyzer equipment. The systems showed low rupture strain and low elongation due to the crystallization of the drugs after 48h of storage. The detachment force and mucoadhesion work of the anesthetic compositions presented lower values than the adhesive layer developed for the trilaminated system, which emphasizes the need for the development of the complete system.

# Ex Vivo Whole Eye Models For Evaluation Of Performance And Efficacy Of Ophthalmic Products



## Author

Geisa Barbalho - Universidade de Brasília (UnB)  
Stefan Brugger - University of Auckland  
Priyanka Agarwal - University of Auckland  
Rupenthal, Ilva - University of Auckland  
Cornelia M. Keck - Universität Marburg  
Guilherme Gelfuso - Universidade de Brasília (UnB)  
Marcílio Cunha-Filho - - Universidade de Brasília (UnB)  
Tais Gratieri - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES, CNPQ, FAPDF, PPGCF



## Keywords

Ex vivo models; Ophthalmic products; Dynamic tear flow.

## Abstract

The efficacy of ophthalmic products is influenced by formulation attributes, tear flow and drainage. Conventional ex vivo models inadequately replicate the physiological conditions. This can impact drug interaction with the eye surface and affect delivery. Thus, there is an urgent requirement for innovative ex vivo methods to accurately evaluate the performance and efficacy of ophthalmic products. This study was to compare two models: (i) the static whole-eye model and (ii) the dynamic model with tear flow. The system was tested with two different formulations containing curcumin-oily solution (MCT-CUR) and liposomes (LP-CUR). Both formulations were added to the donor compartments (300  $\mu$ L) for 15 min. Fluorescence microscopy (475 nm) was used to analyse the penetration of curcumin into the porcine corneal layers, conjunctiva, and eyelid. The porcine eye were placed on support with two different types of donor media - one without flow and the other designed to mimic tear flow (flow rate of 48  $\mu$ L/min for the first 2 min followed by 33  $\mu$ L/min). The models were able to differentiate the formulations in terms of their ability to deliver a lipophilic drug in different tissues. The LP-CUR formulation showed greater curcumin penetration in static and dynamic models compared to the MCT-CUR oily formulation in different tissues. In the static model, it is evident that the formulation creates a film on the cornea's external layer, reproducing the eye dry disease. In contrast, the dynamic model showed that tear flow influenced the distribution of the two formulations on the surface of the cornea, simulating a healthy eye. Ex vivo models offer a robust and cost-effective method for accurately evaluating drug penetration after topical ophthalmic administration. By simulating real-life conditions, penetration tests precisely reflect ophthalmic formulation performance, enabling the development of safer and more effective medications with confidence.



# Pre-Moisturizing Effect On The Cutaneous Drug Penetration



## Author

Daiane Luiza Rost - Universidade de Brasília (UnB)  
Geisa N. Barbalho - Universidade de Brasília (UnB)  
Tais Gratieri - Universidade de Brasília (UnB)  
Guilherme Martins Gelfuso - Universidade de Brasília (UnB)  
Marcílio Cunha Filho - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPDF, CAPES, PPGCF



## Keywords

CUTANEOUS DRUG PENETRATION, betamethasone dipropionate, PRE-MOISTURIZING EFFECT

## Abstract

**Introduction:** The sequential application of moisturizers and medications is a common practice, usually starting with the most fluid and ending with the densest product. However, there is no evidence that this protocol can affect drug penetration. Therefore, this study examined how this application sequence affects the cutaneous permeation.

**Objective:** to evaluate drug penetration in different orders of application and types of moisturizers, aiming to differentiate the effects according to the variables tested.

**Methodology:** Two commercial samples (cream and ointment) containing betamethasone dipropionate were used. The drug was quantified by High-Performance Liquid Chromatography (HPLC). Ex-vivo skin penetration tests were performed using pig skin in a modified Franz cell system for 12 hours. The drug was extracted from the stratum corneal and remaining skin layers and quantified to evaluate the penetration depth. In vitro permeation studies protocols included (i) commercial formulations applied for 6h; (ii) commercial formulations applied for 12h; and (iii) moisturizers applied on the skin 20 minutes before the commercial formulations, left for 12 h.

**Results and Discussion:** Higher betamethasone dipropionate was achieved from cream ( $9.8 \pm 5.3 \text{ mg/cm}^2$ ) formulations compared to ointment ( $1.2 \pm 1.0 \text{ mg/cm}^2$ ). When the moisturizer was previously applied, drug permeation maintained the amount in the stratum corneum layer for the cream ( $9.3 \pm 5.1 \text{ mg/cm}^2$ ), but the ointment's quantity could not be determined. **Conclusions:** These findings highlight the importance of product formulation and the order of application of cosmetics and medications in skin permeation, directly influencing the effectiveness of drug therapy and drug absorption through the skin.

# Mechanical analysis of pharmaceutical films composed of Soluplus® and copaiba oil-resin



## Author

Luana Yumi Nagai Miyakubo - Universidade Estadual de Maringá (UEM)  
Marcos Luciano Bruschi - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq, Finep and Araucaria Foundation.



## Keywords

Soluplus®, Copaiba oil-resin, Drug delivery systems

## Abstract

Introduction: Soluplus® (SOL) has been studied in the development of nanocarriers for intravenous cancer therapy, for topical administration system, as well as film-forming systems (1). Copaiba oil-resin (CO) from *Copaifera reticulata* Ducke has been utilized as anti-inflammatory, antitumor and mainly for skin and mucosal infections (2). Therefore, the development of technology to obtain pharmaceutical films with Soluplus® can be a good strategy (3). Objective: The aim of this work was to prepare and evaluate the mechanical properties of films composed of SOL and CO. Material and Methods: Three pharmaceutical films were prepared using ethanol (E) as solvent: FA: 15% SOL, 25% CO and 60% E, FB: 15% SOL, 20% CO and 65% E and FE: 20% SOL, 20% CO and 60% E. The characterization of them was carried out in relation to tension and elongation, and bending resistance. Results: There was excess oil, which can be explained by the micelle formation process, in which there was no sufficient entrapment. FA broke at 291 folds, FB at 180 and FE at 73. FA displayed the tension of 2.707 N, FB: 1.080 N, and FE: 0.907 N. Moreover, FA displayed the elongation of 55.051 mm<sup>2</sup>%, FB: 92.283 mm<sup>2</sup>%, and FE: 0.994 mm<sup>2</sup>%. Conclusion: It was possible to obtain films composed of SOL and CO using ethanol. Their mechanical properties were dependent on SOL:CO ratio.

Acknowledgements: CNPq, Finep and Araucaria Foundation.

# Enhanced Bioavailability of Quercetin through Solid Dispersion Tablets: Development and Characterization



## Author

Lara Lopes - Universidade do Vale do Itajaí (UNIVALI)  
Ruth Meri Lucinda da Silva - Universidade do Vale do Itajaí (UNIVALI)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

UNIEDU GOV.SC and CNPq.



## Keywords

Quercetin; Solid Dispersions; Bioavailability

## Abstract

Flavonoids, such as quercetin, are molecules with therapeutic potential against various pathologies, such as inflammatory diseases, but they have limited bioavailability due to low solubility. Technological strategies, such as incorporation into solid dispersions (SD), can be employed to overcome these limitations. The objective was to develop and characterize tablets containing SD of quercetin in PVP to obtain an oral drug with improved bioavailability. Quercetin SD with different flavonoid concentrations (5%, 10%, and 15%) were produced by kneading and solvent evaporation methods. These were characterized in terms of morphology, size, content, rheology, solubility, and in vitro dissolution. Tablets were prepared by the direct compression process with quercetin SD and pure quercetin in a dosage of 10 mg quercetin, in the proportion of 2.5%. These were characterized in terms of physical properties and quercetin release profile. The solubility found for quercetin was 18.92 µg/mL. A considerable increase in solubility was observed in relation to SD when compared to the drug alone. The in vitro dissolution profile showed that the samples MA5% and MA10% had 77.09% and 70.49% dissolution, and these were chosen for the production of the tablets. The tablets presented physical properties according to the specifications described by the Brazilian Pharmacopoeia (2019). The final percentage of the dissolved drug was 27.93%, 76.65%, and 71.54% for CPQUER, CPMA5%, and CPMA10%, respectively. The proportion of quercetin dissolved from the tablets containing the solid dispersions CPMA5% and CPMA10% was about three times higher compared to tablets containing pure quercetin. Therefore, CPMA5% and CPMA10% showed promising in vitro dissolution profiles, with possible improvements in flavonoid bioavailability, and are candidates for a new drug of national production with high therapeutic potential.

# Development and characterization of emulsified suspension loaded with itraconazole for the treatment of sporotrichosis



## Author

Letícia Rocha de Moura - Universidade Federal de Minas Gerais (UFMG)  
Marie Gabriele Santiago - Universidade Federal de Minas Gerais (UFMG)  
Bianca Moreira de Souza - Universidade Federal de Minas Gerais (UFMG)  
Yamara Viana Sousa - Universidade Federal de Minas Gerais (UFMG)  
Caroline Dohanik da Silva - Universidade Federal de Minas Gerais (UFMG)  
Camila Stefanie Fonseca de Oliveira - Universidade Federal de Minas Gerais (UFMG)  
Raquel Virgínia Rocha Vilela - Universidade Federal de Minas Gerais (UFMG)  
Lucas Antônio Miranda Ferreira - Universidade Federal de Minas Gerais (UFMG)  
Gisele Assis Castro Goulart



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPEMIG (Fundação de Amparo à Pesquisa do Estado de Minas Gerais, Brazil); project number APQ-01982-21



## Keywords

Sporotrichosis, Itraconazole, Emulsified suspension

## Abstract

Sporotrichosis is an endemic fungal infection in Brazil, with cats being the main vector of transmission to humans<sup>1,2,3</sup>. Itraconazole (ITZ), an antifungal with low water solubility<sup>4</sup>, is the drug of first choice in the treatment of sporotrichosis. However, on the national market, ITZ is only available for oral administration<sup>1</sup>. Therefore, we developed an emulsified suspension with ITZ (4% w/v) for subcutaneous administration to be used in the treatment of feline sporotrichosis. The formulation was developed with excipients approved for subcutaneous administration, sterilized by gamma irradiation and characterized in terms of appearance, ITZ content, Zeta potential (PZ), pH and osmolarity. The developed formulation presented a homogeneous appearance, white and opaque color and easy resuspension. The rheological behavior was typical of non-Newtonian dilatant systems, the osmolarity was  $0.89 \pm 0.06$  Osm/Kg, PZ of  $-12.1 \pm 0.72$ , pH of  $5.1 \pm 0.04$ , 107.85 % ITZ and total impurities of 0.64% after irradiation sterilization process. Therefore, in this work we verified that it was possible to develop a sterile preparation loaded with 4% ITZ and with characteristics suitable for subcutaneous administration in animals contaminated with sporotrichosis.

1 - BARROS, M. B. D. L., et al. Doi: 10.1093/cid/cir245

2 - GREMIÃO, I. D. F., et al. Doi: 10.3201/eid2603.190803

3 - SILVA, M. B. T. D., et al. Doi: 10.1590/S0102-311X2012001000006

4-KELLER, KA. Doi:10.1053/j.jepm.2011.02.012

# Cell viability, cytotoxicity and migration of fibroblasts cells treated with niobium nanoparticles as a model of scarring process.



## Author

Paula Lopes Armond Carvalho - Universidade Federal de Minas Gerais (UFMG)  
Larissa Camila Ribeiro de Souza - Universidade Federal de Minas Gerais (UFMG)  
Carlos Alberto Tagliati - Universidade Federal de Minas Gerais (UFMG)  
Diego dos Santos Ferreira - Universidade Federal de Minas Gerais (UFMG)  
Luiz Carlos Alves de Oliveira - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPEMIG



## Keywords

niobium, cytotoxicity, healing

## Abstract

Nb nanoparticles (Nb-NP) have been used mostly for industrial applications such as sensors and catalysts. Recently, Nb is being studied for biomedical purposes due to its antiviral and antibacterial activities [1][2]. Previous studies showed that Nb used as implant coating material led to improvement in the biocompatibility of the material with increased biological activity and significant increase in fibroblast cell proliferation [3]. In this work we intend to select, from a series of Nb-NP, the most promising to be incorporated into a biofilm for wound healing. Methodology: Mixtures composed of four different Nb-NP (Nb1OX, NbPCO, NbPG and Nd2OX), collagen and hyaluronic acid (HA) were used. Cell viability in human fibroblasts cell lines (MRC-5) was determined by the SRB and MTT assays after 24h. Cytotoxicity was assessed by the Neutral Red test in 3T3 murine cells after 24h. Cell migration and proliferation was performed using the scratch method. Results: Cell viability was performed using suspensions of Nb-NP at 2000 ppm to 3.9 ppm. NbPCO and Nb1OX samples were chosen because they presented better results in cell viability compared to the other samples, these two samples were then added with collagen (5% v/v) and HA (2% v/v) and the denomination of those became NbPCOA5 and Oxy-cola5 respectively, MTT viability assay was performed and both samples did not show cytotoxic activity. NbPCOA5 was classified as Category 3 (50-300mg/kg) and Oxy-cola5 was classified as Category 4 (300-2000 mg/kg) by the GHS in Neutral Red test. In the migration assay NbPCOA5 and Oxi-cola5 presented superior migration percentage when compared to control. Conclusion The substances tested did not show cytotoxic effect and have a promising effect for the use in healing formulations.

## References

- [1] C.G.O. Bruziquesi, et.al. doi:10.21577/0100-4042.20170442.
- [2] A. Lokesh Kumar, et.al. DOI:10.1016/j.surfcoat.2021.127161.
- [3] M.S. Safavi, et.al. DOI:10.1021/acsomega.2c00440.

# Development of hydrophilic semi-solid formulations containing microagglomerates of metal oxide coated with polymeric nanospheres and lipid core nanocapsules



## Author

Priscilla de Bastos Souza - Universidade Federal do Rio Grande do Sul (UFRGS)  
Danieli Rosane Dallemole - Universidade Federal do Rio Grande do Sul (UFRGS)  
Karina Paese - Universidade Federal do Rio Grande do Sul (UFRGS)  
Sílvia Stanisçuaski Guterres - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Capes



## Keywords

polymeric nanoparticles, spray drying, titanium dioxide (TiO<sub>2</sub>)

## Abstract

Zinc oxide and titanium dioxide (TiO<sub>2</sub>) are the most commonly used inorganic filters for reflection and absorption of ultraviolet (UV) light that reaches the skin. Their application is limited to hydrophobic formulations. In this study, a new methodology was proposed for the production of TiO<sub>2</sub> microagglomerates coated with lipid core nanocapsules or nanospheres, produced with the polymer poli(ε)caprolactone, for subsequent dispersion in hydrogels. The microagglomerates obtained with the incorporation of 3% (w/v) of Eusolex T- AVO® in the nanocarrier suspensions, and subsequently dried by spray-drying, presented a powdery appearance and low moisture content. Scanning Electron Microscopy analysis revealed improved morphological characteristics compared to the raw adjuvant. These particles were then incorporated into Carbopol® Ultrez 10 (0.3%, w/v) or Lecigel® (0.8%, w/v) hydrogels at a final concentration of 1% (w/v). Control formulations, containing dispersed Eusolex T-AVO® in both hydrogels, were also produced. The nanoparticle formulations enabled the dispersion of TiO<sub>2</sub> in an aqueous semi-solid base. In contrast, topical application of the control formulation resulted in the deposition of white agglomerates on the skin surface. The rheological evaluation of the hydrogels containing Eusolex T-AVO® 1% (w/v) was unworkable due to the presence of coarse agglomerates that interfered with the shear sensor of the viscometer. In contrast, the semi-solid formulations containing microagglomerates coated with nanocarriers exhibited adequate macroscopic and rheological characteristics. These formulations were evaluated for skin permeation on pig skin, and no detectable titanium was found in the receptor medium (Phosphate buffer, pH 7,4), as expected from a potential inorganic sunscreen. The coating of titanium dioxide with polymeric nanocarriers was effective in hydrophilizing the surface of the metal oxide, enabling its incorporation into hydrophilic semi-solid formulations.

# Avocado oil-based gel-cream with healing potential: characterization and in vitro evaluation



## Author

Giovanna Araujo de Moraes Trindade - Universidade Federal do Paraná (UFPR)  
Laiene Antunes Alves - Universidade Federal do Paraná (UFPR)  
Raul Edson Luna Lazo - Universidade Federal do Paraná (UFPR)  
Karine Campos Nunes - Universidade Estadual de Maringá (UEM)  
Francielle Pelegrin Garcia - Universidade Estadual de Maringá (UEM)  
Celso Vataru Nakamura - Universidade Estadual de Maringá (UEM)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)  
Luana Mota Ferreira - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPEMIG



## Keywords

Avocado oil, gel-cream, Wounds

## Abstract

Wounds are changes in the skin integrity resulting from trauma. Treatments can be limited by discomfort to the patient and concerns about active ingredient application. Natural ingredients with healing properties, like avocado oil, known for its nutrients and antimicrobial effects, can be promising. In addition, polysaccharides as gelling agents enhance bioadhesion in the wound site. Given this, this study aimed to prepare gel-creams of avocado oil using kappa-carrageenan as a gelling agent. Formulations were obtained by the emulsification method and characterized in terms of pH, spreadability, rheology, physical stability, in vitro cytotoxicity, and in vitro wound healing potential. The pH was determined from a 1% dispersion of the formulation in water, achieving values of  $4.74 \pm 0.12$ . Using the parallel plate method to measure spreadability, it was found that the spread area increased as more weight was added, resulting in a spreading factor of  $8.46 \pm 2.40 \text{ mm}^2/\text{g}$ . This result was corroborated by the rheological analysis, performed with a rheometer, which showed pseudoplastic behavior, meaning that the viscosity decreased as more force was applied. Physical stability was determined by subjecting the formulation to a 15-minute centrifugation test at 3.500 rpm, and no instability was observed upon visual evaluation. To evaluate the viability of fibroblasts in the presence of the tested samples (7.81 – 1000  $\mu\text{g}/\text{mL}$ ), the L-929 cell line was used, and an  $\text{IC}_{50}$  value of  $390.03 \pm 8.06 \mu\text{g}/\text{mL}$  was obtained. For in vitro wound healing evaluations, cells were plated and then a wound was created in the cell monolayer. The formulation was used at a concentration of 7.8125  $\mu\text{g}/\text{mL}$ . At time zero, the open wound area was 100%. After six hours, the damage decreased by about 25.24%. Avocado oil-based gel-cream demonstrated satisfactory physicochemical properties, showing promise for healing potential.

# Optimizing clofazimine bioavailability through self-emulsifying drug delivery systems (SEDDS): a comprehensive review



## Author

Azael Francisco Silva Neto - Universidade Federal de Pernambuco (UFPE)  
Alane Rafaela de Carvalho Amaral - Universidade Federal de Pernambuco (UFPE)  
Lucas José de Alencar Danda - Universidade Federal de Pernambuco (UFPE)  
Monica Felts de La Roca Soares - Universidade Federal de Pernambuco (UFPE)  
José Lamartine Soares Sobrinho - Universidade Federal de Pernambuco (UFPE)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPEMIG



## Keywords

Clofazimine, Bioavailability, Self-emulsifying

## Abstract

Clofazimine is a drug used in multi-drug therapy for leprosy that has low water solubility (0.3 µg/mL) and high lipophilicity (log P>7), resulting in poor and variable bioavailability (45-62%). One strategy to improve the solubility of such drugs is through self-emulsifying drug delivery systems (SEDDS), which are an isotropic mixture of drug, oil phase, surfactant, and cosurfactant, forming a fine oil-in-water emulsion upon mild agitation in gastrointestinal fluid. However, relationships between clofazimine, lipids, and excipients that can potentially optimize the system are diverse and remain unclear. This review delves into the existing literature to elucidate how different excipients influence clofazimine's absorption and solubility within SEDDS and critically evaluates their impact. Full research articles published to date (Jun 2024) were searched on Scopus, PUBMED, and Web of Science. Exclusion criteria were studies not addressing the topic, duplicates, and conference proceedings. Twenty-four articles were found, of which seven were chosen after the eligibility criteria. The research showed that the potential of SEDDS is deeply influenced by the appropriate combination of excipients. Emulsion formation works well with medium-chain triglycerides (MCTs), such as Capmul MCM. In under 60 minutes, SEDDS optimized with Capmul MCM, Tween-20, and Labrasol released almost 85% of the daily dose of clofazimine in water. On the other hand, long-chain triglycerides (LCTs) in castor oil and non-ionic surfactants such as polysorbate 80 improve self-emulsification and lymphatic absorption, which directly raises bioavailability by promoting peristalsis and water secretion in the intestinal lumen. The solubility and absorption of clofazimine can be enhanced by the combination of MCTs and LCTs, indicating that SEDDS can optimize leprosy therapy by improving the therapeutic efficacy and permitting dose modifications in formulations.



# Mechanical textural properties of thermoresponsive and bioadhesive systems containing partially methylated mannogalactan



## Author

Gabrielli Furlan - PCF - Universidade Estadual de Maringá (UEM)  
Fernanda Fogagnoli Simas - PCF - Universidade Estadual de Maringá (UEM)  
Marcos Luciano Bruschi - PCF - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES– Financing code n°.001, CNPq process n°. 404163-2021/1 and Finep



## Keywords

Polymeric systems, Technology, Polysaccharides

## Abstract

The use of polysaccharides extracted from edible mushrooms has been shown to be effective for the treatment of tumors. Partially methylated mannogalactan (MG-Pe), extracted from the species *Pleurotus eryngii*, has demonstrated promising antimelanoma activity in vitro and in vivo studies. Considering the topical administration of this compound in the tumor region, polymeric platforms for drug delivery, which depend on the body temperature range, allow the prolonged and/or controlled release of the drug they carry. Hydrogels as semisolid pharmaceutical forms most are ideal for topical application and attractive to improve therapeutic efficacy. Therefore, the aim of this study was to perform the texture profile analysis (TPA) of thermoresponsive bioadhesive systems containing MG-Pe. The systems were prepared using 17.5% (w/w) P407 and 0.3% (w/w) cellulose derivative (sodium carboxymethylcellulose or hydroxypropyl methylcellulose), loaded with 0.01% or 0.1% (w/w) Mg-Pe. The analyses were performed using a TA-XTplus texture analyzer in TPA mode, at 25 and 34 °C, the probe was compressed twice inside the sample, to calculate parameters: hardness, compressibility, adhesiveness, elasticity and cohesiveness. The temperature significantly influenced ( $p > 0.05$ ) all parameters except the elasticity, with a significant increase mainly at 34 °C. There is also a difference in the type of cellulose derivative used, and the increase in parameters was significant ( $p > 0.05$ ) mainly for HPMC systems. The presence of the active ingredient was significant ( $p > 0.05$ ) for both types of formulation, except for cohesiveness, where no significant increase was observed in relation to the Mg-Pe concentration. The results obtained are compatible with those in the literature, and these formulations are promising. However, additional tests are necessary to evaluate their topical performance.

# Development of mucoadhesive films for application of formulations on the oral mucosa



## Author

Isabela Miguel Villa - FCFRP - Universidade de São Paulo (USP)  
Ana Clara Wada de Carvalho - FCFRP - Universidade de São Paulo (USP)  
Oswaldo de Freitas - FCFRP - Universidade de São Paulo (USP)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

PUB 3358/2023



## Keywords

films, mucoadhesion, solvent casting

## Abstract

Films are flexible solid dosage forms that can be developed for different forms of release. Mucoadhesive films allow controlled release of drugs and may have several layers to direct the drug to the application site or to ensure prolonged release. It is important to ensure that the physical and physical-chemical properties of the films are adequate to avoid displacement of the pharmaceutical form and for the formulation to be comfortable and easy to apply. This study aims to develop mucoadhesive films to aid in the adhesion of systems containing drugs for dental application. Four films (AL1, AL2, AL3, AL4) were developed with different combinations of gums and cellulose polymers, prepared by the solvent casting method in a climatic chamber with controlled temperature and humidity. The formulations were subjected to experiments to determine moisture content and water absorption. The AL1 film transformed into a gel within 5 minutes, making it impossible to determine the amount of water incorporated into the system, while AL3 and AL4 remained intact after 30 minutes in the buffer solution, demonstrating suitability for oral application. Tests were also conducted to determine the water content of the systems, and from these results, it was possible to infer that the ideal relative humidity for storage would be 50%. The thickness of the films was determined, which should be homogeneous for better patient comfort. The AL4 film showed the least variation in thickness. The mucoadhesion tests demonstrated that AL3 had the highest force and total energy required to separate the film from the mucosal surface and the greatest resistance during the initial displacement until complete separation from the mucosa. Analyzing the rheology results, it is possible to infer that AL3 has the highest shear stress and AL4 has the highest viscosity. The formulation AL2 was not included in many tests because it was heterogeneous.

# Development of an Injectable Hydrogel Platform for Controlled Release of Angiotensin 1-7



## Author

Letícia Fujii - Universidade Federal de Minas Gerais (UFMG)  
Gabriel Henrique da Silva - Universidade Federal de Minas Gerais (UFMG)  
Marco Túllio Rodrigues Alves - Universidade Federal de Minas Gerais (UFMG)  
Pedro Pires Golart Guimarães - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPEMIG (APQ-00826-21;APQ-02402-23;RED-00202-22 Rede de Pesquisa em Imunobiológicos e Biofármacos para terapias avançadas e inovadoras)



## Keywords

Angiotensin-(1-7), injectable hydrogel, controlled release

## Abstract

Angiotensin-(1-7) (Ang-(1-7)) is a peptide derived from the renin-angiotensin system with significant physiological relevance. However, its therapeutic use is limited due to its rapid degradation. To address this, this study aims to incorporate the peptide into an injectable GelMa hydrogel, enabling controlled release of Ang-(1-7). The hydrogel consists of GelMa (10% w/v) dispersed in water. Then, 1% of the polymerization agent was added along with 100  $\mu$ L of an Ang-(1-7) water solution at 1 mg/mL. To observe controlled release, the hydrogels were placed in dialysis membranes (50 kDa cut-off) and cross-linked using UV light for 3 minutes. The dialysis process was conducted under stirring for up to 5 days, and aliquots of the dialysate were withdrawn to quantify Ang-(1-7) release using a fluorimeter. The total amount released was determined by comparing the area under the emission curve (AUC) of the samples with the AUC of a standardized Ang-(1-7) solution at a specific concentration. No Ang-(1-7) was detected in the 5-day sample, likely due to degradation. At the initial time points, we suspect a small amount of the released peptide did not reach the detection limit of the equipment. The detection method for Ang-(1-7) was successful, as it allowed comparison of the sample results with the standardized solution for quantification. However, the release was only detectable at the 24-hour dialysis time point, suggesting a significant amount of the peptide was present only at this time. Improving the dialysis method by reducing the dialysate volume and conducting the process at 37°C may enhance our study's outcomes.

# Enhancing Clofazimine Efficacy in Leprosy Treatment through Amorphous Solid Dispersions: A Systematic Review



## Author

Alane Rafaela de Carvalho Amaral - Universidade Federal de Pernambuco (UFPE)  
Heloísa Casé Rigonatto - Universidade Federal de Pernambuco (UFPE)  
Azael Francisco Silva Neto - Universidade Federal de Pernambuco (UFPE)  
Lucas José de Alencar Danda - Universidade Federal de Pernambuco (UFPE)  
Mônica Felts de La Roca Soares - Universidade Federal de Pernambuco (UFPE)  
José Lamartine Soares-Sobrinho - Universidade Federal de Pernambuco (UFPE)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Editais FINEP Doenças Negligenciadas 02/2021



## Keywords

Amorphous Solid Dispersion, Clofazimine, Leprosy

## Abstract

Leprosy predominantly affects less developed countries, with Brazil leading in cases in the Americas and ranking second globally. Clofazimine, a key therapeutic component, suffers from low aqueous solubility, resulting in poor bioavailability (20%). Amorphous solid dispersions (ASDs) are formulation strategies that enhance the kinetic solubility of poorly soluble drugs such as clofazimine. However, maintaining the amorphous state in ASDs presents challenges, particularly in preventing crystallization due to insufficient interactions. Understanding these interaction types and functional groups in amorphous materials remains a critical hurdle for developing effective systems, and this systematic review aims to elucidate these less-understood aspects. A search was performed in the PubMed, Web of Science, and Scopus databases using the terms "Clofazimine" and ("Amorphous Solid Dispersion" or "Solid Dispersion" or "Amorphous"). Out of the initial 71 articles retrieved, 36 duplicates and 26 irrelevant articles were excluded. One review article and one article unavailable online were also excluded. Ultimately, 7 articles were included, focusing on the development, characterization, and performance of clofazimine ASDs. These studies demonstrated that formulations containing specific polymers significantly enhanced drug loading capacity, achieving levels of up to 70%. The stability and effectiveness of these systems relied on precise molecular interactions between clofazimine and the polymers. Characterization techniques, including high-resolution NMR spectroscopy and computational calculations, facilitated a thorough analysis of these interactions and binding patterns within clofazimine ASDs, offering crucial insights for developing more robust and efficient systems. Moreover, the studies underscored the potential for innovative formulations that ensure stability under tropical storage conditions and facilitate faster drug dissolution compared to its crystalline form.

# Mechanical Properties Of Thermoresponsive Systems Containing Ketamine For Buccal Administration In Small Animals



## Author

Carolina Parcero Hernandez - Universidade Estadual de Maringá (UEM)  
Michael Cavalheiro Jorge - Universidade Estadual de Maringá (UEM)  
Samara Bossa Aleixo - Universidade Estadual de Maringá (UEM)  
Marilda Onghero Taffa - Universidade Estadual de Maringá (UEM)  
Marcos Luciano Bruschi - Universidade Estadual de Maringá (UEM)  
Sabrina Barbosa de Souza Ferreira



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq, finep



## Keywords

TPA, KETAMINE, Poloxamer

## Abstract

Poloxamers are copolymers displaying thermoresponsive properties. Ketamine is a dissociative anesthetic drug that acts by physically blocking N-Methyl-D-Aspartate (NMDA) receptors to prevent acute or chronic pain and the sensitization of neurons in the dorsal horn region. This drug has mainly been used in small animals by direct infusion. The buccal route of administration for systemic effects can promote increased convenience and bioavailability. The aim of this work was obtain the mechanical characteristics of formulations containing ketamine for buccal administration in cats. Gels were composed of 17.5% or 20% (w/w) poloxamer 407 and 5% or 8% (w/w) ketamine. Texture Profile Analysis (TPA), mucoadhesion, and syringeability analyses were performed. TPA was performed at temperatures of 5, 25, and 37°C, and the hardness, compressibility, adhesiveness, elasticity, and cohesiveness were obtained from force-time and force-distance graphs. In vitro mucoadhesiveness was carried in tension mode, at 37°C, by measuring the force required to detach a formulation from a mucin disc. Through TPA analysis, it was possible to demonstrate a significant increase ( $p < 0.05$ ) in the analyzed parameters as the temperature increased. The effect of the presence of ketamine led to an increase in hardness and compressibility values. For the mucoadhesive analysis, the formulations containing ketamine showed significantly higher values compared to the formulation containing only poloxamer. Syringeability decreased with the presence of ketamine. Formulations containing ketamine showed promising characteristics for application in the oral cavity of small animals.

# Development and comparison of electrospinning anesthetic films with different polymers



## Author

Guilherme Corrêa - Universidade de São Paulo (USP)  
Ana Clara Wada de Carvalho - Universidade de São Paulo (USP)  
Osvaldo de Freitas - Universidade de São Paulo (USP)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPESP - 2024/00701-3



## Keywords

Anesthetics, nanofibers, polymers

## Abstract

The use of anesthesia in medical and dental procedures was essential to increase and maintain patients' adherence to treatments, which are often painful and uncomfortable, thus promoting significant improvements in people's health and quality of life. These drugs act on the central nervous system, inhibiting the perception of pain and providing greater comfort during surgeries and other procedures. However, many patients are still scared by traditional infiltrative anesthesia, carried out by injections, so less invasive methods, such as the administration of anesthetics through topical formulations, for example films, have proven to be a promising alternative. The monoaxial electrospinning method is capable of forming polymeric fibers when the dispersion, subjected to pressure and voltage, passes through the eye of a needle towards a metallic collector, also electrically charged, making it possible to produce film systems through this method. This method was designed in this project in order to form nanofibers with a large contact surface and porosity, which allows for a potential rapid release of the drug. Different dispersions containing a combination of amide-type local anesthetics and HPMC associated with chitosan or zein were tested, varying the proportions between the polymers. For the formulations with HPMC and chitosan, the formation of fibers was observed, however, due to the low proportion of polymers in the formulation, necessary for the adequate viscosity used in the method, the fibers produced were insufficient to remove the metal collector, remaining adhered. The crystallization of the drugs was also observed in scanning electron microscopy, due to their high content in relation to the total solid content of the dispersions. Different proportions of HPMC and zein are being tested in order to increase the percentage of polymers without significantly increasing viscosity, which can be a limitation for the use of the electrospinning method.

# Development of buccal films containing sesamol with potential application in treating oral mucosa diseases.



## Author

Cassiana Schowantz Reichert - Universidade Federal de Santa Maria (UFSM)  
Júlia Carine Blume - Universidade Federal de Santa Maria (UFSM)  
Camila Parcianello Saccol - Universidade Federal de Santa Maria (UFSM)  
Lucas Saldanha da Rosa - Universidade Federal de Santa Maria (UFSM)  
Ticiane da Rosa Pinheiro - Universidade Federal de Santa Maria (UFSM)  
Roberto Christ Vianna Santos - Universidade Federal de Santa Maria (UFSM)  
Letícia Cruz - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

INCT\_3D-Saúde, funded by CNPq, Brazil (Grant #406436/2022-3) and Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS - 21/2551-0002062-8)



## Keywords

Buccal films, Sesamol, Oral diseases.

## Abstract

Sesamol (3,4-methylenedioxyphenol) is a phenolic compound obtained from sesame with numerous therapeutic properties, including antioxidant and antimicrobial activities, which have yet to be fully explored, making it a promising substance for oral disease therapy. Therefore, this study aimed to develop a buccal film for topical delivery of sesamol to the oral mucosa. The films were prepared using the solvent evaporation method, hydroxypropyl methylcellulose K100 and polyethylene glycol 400, to achieve suitable characteristics for the intended purpose. The films were defined as thin ( $23.7 \pm 1.15 \mu\text{m}$ ), homogeneous in content ( $94.89 \pm 2.26\%$ ), combining flexibility (bending resistance  $> 300$ ) and strength ( $24.36 \pm 10.70 \text{ MPa}$ ). Furthermore, they exhibited mucoadhesive properties ( $9997.66 \pm 140.73 \text{ dyne/cm}^2$ ), hydrophilicity ( $\theta 35.63 \pm 2.36$ ), rapid swelling ( $785.68 \pm 19.73\%$ ), and sesamol release ( $81.87 \pm 9.07\%$  in 45 min). Despite low sesamol retention in porcine mucosa ( $11.83 \pm 3.3\%$ ), it remains suitable for topical use. Sesamol inhibited the growth of *Candida albicans* and non-*albicans* strains, and the film showed antioxidant activity in ABTS+ assays ( $99.88 \pm 0.50$ ) and DPPH assays ( $88.72 \pm 0.61\%$ ). Additionally, the film was biocompatible in hemolysis assays and non-irritating in the HET-CAM test, suggesting its safety. Thus, the buccal sesamol film demonstrates itself as a promising pharmaceutical form for topical application in patients with conditions affecting the oral mucosa.

# Association of Nucleation-inhibiting Polymers with Lamotrigine Cocrystals as an Alternative to Improve Bioavailability in Anticonvulsant Therapy.



## Author

Diana Lopes - Universidade Estadual do Centro Oeste - Campus Santa Cruz (Unicentro)  
Isabela Fanelli Barreto Biscaia - Universidade Estadual do Centro Oeste - Campus Santa Cruz (Unicentro)  
Gustavo Rocha Siqueira - Universidade Estadual do Centro Oeste - Campus Santa Cruz (Unicentro)  
Rafaela Cristina Brancalione - Universidade Estadual do Centro Oeste - Campus Santa Cruz (Unicentro) -  
Universidade Estadual do Centro Oeste - Campus Santa Cruz (Unicentro)  
Larissa Sakis Bernardi - Universidade Estadual do Centro Oeste - Campus Santa Cruz (Unicentro)  
Paulo Renato Oliveira - Universidade Estadual do Centro Oeste - Campus Santa Cruz (Unicentro)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

This research was funded by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brasil (CAPES) - Foment Code 001; Fundação Araucária de Apoio ao Desenvolvimento Científico e Tecnológico do Estado do Paraná (FA) and Conselho Nacional de Desenvolvm



## Keywords

dissolution, solubility, pharmaceutical technology

## Abstract

Poorly water-soluble drugs often face reduced bioavailability. Cocrystals, composed of different molecules in a single crystalline network held by non-ionic and non-covalent bonds, can enhance bioavailability by maintaining supersaturation. However, drug precipitation can occur due to the thermodynamic instability of supersaturated systems. To prolong this state, nucleation-inhibiting polymers can be used to delay recrystallization. This study evaluated the poorly soluble antiepileptic drug Lamotrigine (LAM) associated with five coformers: Nicotinamide (NIC), Mandelic Acid (MA), Glycolic Acid (GA), Succinic Acid (SA), and Citric Acid (CA), and the use of polymeric additives, aiming to maintain the supersaturated state. The cocrystals were formed from the association of LAM with the coformers by the reaction crystallization method. Excess concentrations of the physical mixture of cocrystals and polymers were added to water at 25°C, 100 rpm in an orbital shaking incubator. Aliquots were sampled over time for HPLC analysis, using two polymers: HPMC E6 (Hydroxypropylmethylcellulose) and PVP (Polyvinylpyrrolidone). Results showed that LAM-CA and LAM-MA cocrystals enhanced solubility, though polymer use was not significant. The LAM-SA cocrystal, however, showed notable solubility improvement with polymers, especially within the first 50 minutes. The LAM-GA cocrystal stood out as the most promising result of this study, showing a 30-fold solubility increase compared to pure LAM, and polymer addition boosted this to 40-fold with PVP and 50-fold with HPMC E6. The LAM-NIC cocrystal also benefited from polymer association, especially with E6, leading to a five-fold solubility increase. Overall, the study indicates that polymers can effectively inhibit LAM cocrystal precipitation, enhancing solubility and maintaining supersaturation. HPMC E6 was the most effective polymer, with the LAM-GA cocrystal showing the greatest solubility improvement when combined with polymers.



# Cocrystals for improved dissolution and antifungal activity of ketoconazole



## Author

Ellen Chade - Universidade Estadual do Centro Oeste (Unicentro)  
Ana Karolina Goes Silva - Universidade Estadual do Centro Oeste (Unicentro)  
Diana Schon Lopes - Universidade Estadual do Centro Oeste (Unicentro)  
Sarah Jauregui Zela - Universidade Estadual do Centro Oeste (Unicentro)  
Larissa Sakis Bernardi - Universidade Estadual do Centro Oeste (Unicentro)  
Gabriela Lechuk Dos Santos - Universidade Estadual do Centro Oeste (Unicentro)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

This research was funded by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—B (CAPES) - Foment Code 001 and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).



## Keywords

Solubility, Dissolution, Pharmaceutical Technology.

## Abstract

The therapeutic efficacy of drugs is highly dependent on their solubility. Ketoconazole (KTZ), an antifungal agent, has low solubility despite high permeability. The use of cocrystal has been a critical approach to increasing the solubility of poorly water drugs. This study developed a KTZ cocrystal using succinic acid (SAC) and evaluated its biopharmaceutical and antifungal properties. The cocrystals of KTZ with SAC were prepared by reaction crystallization and were characterized using FT-IR, XRD, SEM, and DSC techniques. Solubility was assessed in water and simulated fasting intestinal fluid (FaSSIF) under non-sink conditions. Dissolution rates were evaluated as per USP guidelines in hydrochloric acid (HCl) pH 1.2, acetate buffer pH 4.5, and simulated intestinal fluid (FIS) pH 6.8. Antifungal activity was determined by measuring the minimum inhibitory concentration (MIC) against *Candida albicans* (ATCC 10231) using a colorimetric method. The study tested KTZ-SAC cocrystals, KTZ, SAC (control), and a KTZ-SAC physical mixture, all at 500 µg/mL. In the kinetic study, the cocrystal showed 240 times higher solubility than KTZ in water at 90 minutes (min) and 110 times higher in FaSSIF at 40 min. In dissolution study, in HCl medium, the cocrystal dissolved 98% in 20 min, versus 57% for KTZ. In acetate buffer, the cocrystal had an 84% dissolution rate in 120 min, compared to 29% for KTZ. In FIS, the cocrystal's dissolution rate was 20%, compared to 7% for KTZ over 120 min. Antifungal activity indicated that the MIC for KTZ and the physical mixture was 62.5 µg/mL, while the KTZ-SAC cocrystal's MIC was 31.2 µg/mL. The cocrystal also exhibited lower IC<sub>50</sub>% and IC<sub>90</sub>% values than KTZ. Cocrystallization with succinic acid significantly enhances the solubility and dissolution rates of ketoconazole, along with its antifungal properties. These results suggest the potential for further in vivo studies to explore the therapeutic benefits of KTZ cocrystals.

# Chia Mucilage: Cost-Effective Alternative for Modified Release Matrix Tablets



## Author

Karina França - Universidade Federal Fluminense (UFF)  
Samanta Cardozo Mourão - Universidade Federal Fluminense (UFF)  
Patrícia de Castro Moreira Dias - Universidade Federal Fluminense (UFF)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPERJ



## Keywords

chia mucilage, matrix systems, hydrophilic biopolymers

## Abstract

Matrix tablets are a simple and low-cost alternative for obtaining modified release systems aimed at optimizing therapy. They can be produced through conventional processes using a retardant material, such as hydrophilic polymers. Chia mucilage (*Salvia hispanica*) demonstrates excellent retention capacity, gel and film formation, being highly soluble in water and generating viscous solutions even at low concentrations. Therefore, chia mucilage is a promising material for obtaining matrix tablets as well as other pharmaceutical systems. In this work, studies were carried out to standardize the separation between mucilage and seeds in the chia mucilage extraction process. The extraction was done in water for 60 minutes at 50°C under constant stirring, using a 1:30 ratio (seed:solvent). The separation methods tested included vacuum filtration, microfiber cloth filtration, and ultrasonication, and the drying methods tested included oven drying and lyophilization. The highest yield obtained with the separation was through ultrasonication (4.36%), while the lowest yield was with microfiber cloth filtration (0.057%). Regarding swelling, there was no difference between the separation methods. Lyophilization was chosen due to its greater reproducibility. Based on this standardization, further studies will be conducted to optimize the extraction, where the independent variables will be pH, agitation time, concentration (w/v), and temperature. Additionally, it aims to offer an alternative functional excipient for pharmaceutical products, adding value to sustainable crops and making production more economical and accessible.

# Development and Characterization of dissolving microneedles for transdermal delivery of beta-caryophyllene



## Author

Ketly Nunes - Universidade Federal do Rio Grande do Sul (UFRGS)  
Patrícia Weimer - Universidade Federal do Rio Grande do Sul (UFRGS)  
Leticia Scherer Koester - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq 317458/2021-3, CAPES 001



## Keywords

polymeric microneedles, nanoemulsified system, beta-caryophyllene

## Abstract

Beta-caryophyllene (CAR) is a multitargeted terpenic compound which acts on type 2 endocannabinoid receptors (CB2) and modulates inflammatory mediators. CAR presents reduced bioavailability by oral route. In this context, this study proposed the incorporation of CAR in polymeric microneedles to ensure stratum corneum rupture and release of this compound close to the inflammatory site, aiming a transdermal delivery. The dissolving microneedles (MN) were obtained using the micromolding technique. The first step involved the fabrication of polydimethylsiloxane female molds, where different master molds with distinct geometries and materials were tested (i. Dermastamp®; ii. Comercial Cosmetic Microneedles and iii. Microneedles obtained by 3D stereolithography printing). In a next step, the need of nanometric carrier was tested to promote the stability of CAR and its uniformity in the polymer matrix of the microneedle. The choice of polymers forming the MN matrix and the best ratio of polymer relative to CAR content was supported by analyses of viscosity, morphology (Digital and Scanning Electron Microscopy), mechanical properties, insertion capacity, and stability of CAR during the micromolding process. It was concluded that the female molds made from MNs obtained by 3D printing showed better results than commercial MNs due to the higher reproductivity and lower bubble entrapment. A combination of polyvinylpyrrolidone and polyvinyl alcohol, making up a solid content of 40 % (w/w), was chosen due to the good mechanical and dissolution properties. The incorporation of nanoemulsified CAR at 9 % (w/w) relative to total solid content showed good stability and lower tendency to phase separation. In addition, the combination resulted in greater tip failure force (> 50N/array) than the average manual application force (11 N). In summary, our findings demonstrate the feasibility of incorporating the volatile/lipophilic CAR in a transdermal dissolving microarray patch.

# 3D printed thermo-responsive bioadhesive films containing Fludroxycortide and Pterostilbene for topical administration in the treatment of scars



## Author

Rafaela Cristina Brancalione - Universidade Estadual do Centro Oeste (Unicentro)  
Andressa Panegalli Hosni - Universidade Estadual do Centro Oeste (Unicentro)  
Diana Schon Lopes - Universidade Estadual do Centro Oeste (Unicentro)  
Larissa Sakis Bernardi - Universidade Estadual do Centro Oeste (Unicentro)  
Paulo Renato de Oliveira - Universidade Estadual do Centro Oeste (Unicentro)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPESP - 2024/00701-3



## Keywords

3D printing, Bioadhesives, Healing

## Abstract

**Introduction:** Trauma, ischemia, pressure and surgery can lead to the formation of hypertrophic scars or keloids, the result of an abnormal healing process. Fludroxycortide (FLX), an anti-inflammatory drug already used to treat these scars, can have its therapeutic activity optimized by the addition of Pterostilbene (PTE), a bioactive compound with antioxidant and anti-inflammatory properties. 3D printing (3DP) allows the creation of personalized and controlled-release pharmaceutical forms, offering advantages for the development of new drug delivery systems. **Objective:** To develop and evaluate thermoresponsive bioadhesives based on FLX and PTE for the treatment of hypertrophic scars and keloids, using the 3D printing technique. **Methodology:** Thermoresponsive bioadhesives were obtained by 3DP, incorporating FLX and PTE in different concentrations and number of layers. The morphology of the films was evaluated by optical microscopy and the quantification of the drugs by High Performance Liquid Chromatography (HPLC). **Results:** Analysis by optical microscopy revealed the presence of crystals in the films with a higher concentration of FLX, while the films containing PTE and FLX in reduced concentrations showed homogeneity. The FLX and PTE content in the films ranged from 4.19 to 6.66 ug/mg and from 1.77 to 3.61 ug/mg of adhesive, respectively, depending on the number of layers printed. **Conclusion:** The thermoresponsive bioadhesives developed by 3DP showed potential for the treatment of hypertrophic scars and keloids. However, future studies are needed to optimize the formulation and evaluate the efficacy in vitro or in vivo.

# Rheological behavior of thermosensitive hydrogels containing hydrolyzed extract from Nile tilapia skin (*Oreochromis niloticus*)



## Author

Priscileila Colerato Ferrari - Universidade Estadual de Ponta Grossa (UEPG)  
Rodrigo Tozetto - Universidade Estadual de Ponta Grossa (UEPG)  
Fábio Henrique Breda Filho - Universidade Estadual de Ponta Grossa (UEPG)  
Évelin Lemos de Oliveira - Universidade Estadual de Maringá (UEM)  
Eduardo César Meurer - Universidade Federal do Paraná (UFPR)  
Benjamim de Melo Carvalho - Universidade Estadual de Ponta Grossa (UEPG)  
Flávio Luís Beltrame - Universidade Estadual de Ponta Grossa (UEPG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Fundação Araucária (PBA2022011000208)



## Keywords

wound healing, dressing, collagen peptides

## Abstract

Nile tilapia (*Oreochromis niloticus*) skin demonstrates potential application as a biological dressing with high biocompatibility due to its histomorphological structure similar to human skin. Through enzymatic hydrolysis of Nile tilapia skin, collagen peptides were obtained, which showed a wound-healing effect related to inflammatory and antioxidant processes. Afterward, the peptides extracted from the skin of Nile Tilapia were incorporated into thermosensitive hydrogels for wound dressing. This work aimed to evaluate the rheological behavior of the hydrogel composed of chitosan and Poloxamers. Parallel plate geometry (40 mm diameter) using Discovery HR-2 (TA, USA) at a frequency of 1HZ and a strain of 0.1% was used, and samples were equilibrated at 25 °C before tests. The rheological behavior was measured at the heating rate of 5 °C/ min, and the temperature ranged from 4 °C to 50 °C. The storage modulus  $G'$  (Pa) and loss modulus  $G''$  (Pa) were recorded as a function of temperature to evaluate the gelation temperature of samples. At low temperatures,  $G' < G''$  shows a viscous behavior predominance, and when  $G' = G''$  was the critical point of the sol-gel transition. The faster storage modulus increases resulted in the  $G' > G''$  after the transition point and indicated that the network structures with higher elasticity were developed during continuous gelation. The sol-gel transition occurred until 50 seconds, and the intersection of  $G'$  and  $G''$  curves was the sol-gel transition point, which varied from about 25.7 to 26.8 °C. Both moduli remained stable with the increased temperature until 50 °C, suggesting a steady hydrogel structure. These results show a promising application of hydrogels for treating both chronic and acute wounds since the temperature of the wound is lower than that of healthy skin, allowing the fast in situ sol-gel transition for good applicability over the wounds.

# Investigating polymers and surfactants for the formulation of solid dispersion



## Author

Isadora Calone Bitencourt - Universidade Federal do Pampa (Unipampa)  
Andrieli Rodrigues - Universidade Federal do Pampa (Unipampa)  
Taiane Medeiro Ciocheta - Universidade Federal do Pampa (Unipampa)  
Flávia Elizabete Guerra Teixeira - Universidade Federal do Pampa (Unipampa)  
Sandra Elisa Haas - Universidade Federal do Pampa (Unipampa)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

LABFAR, FAPERGS, grant 19/2551-0001970-0, CNPq (no. 309401/2020-8), CAPES (no. 88881.506652/2020-01), and UNIPAMPA



## Keywords

Solubility, Screening, Nimesulide

## Abstract

Nimesulide (NIM), a non-steroidal anti-inflammatory drug, acts as a selective competitive inhibitor of COX-2. Among its therapeutic indications are the treatment of acute pain, and osteoarthritis. NIM has low aqueous solubility, limiting its dissolution and oral bioavailability. Besides that, its hepatotoxicity limits its use. Therefore, development of solid dispersions becomes an interesting and scalable option, as it allows the use of different adjuvants that help increase aqueous solubility, dissolution rate and promote controlled release. The purpose of this study is to evaluate different polymers and surfactants aiming to improve NIM solubility for the development of solid dispersions. A screening test was carried out with the following constituents polyvinylpyrrolidone (PVP), Poloxamer, PEG, Compritol, Sodium Lauryl Sulfate (SLS), Polysorbate 80 (P80) and Polysorbate 20 (P20). For this test, an excessive amount of NIM was placed into an aqueous solution 1% polymer or surfactant and remained under magnetic stirring at a controlled temperature for 24 hours. Then the samples were centrifuged, the supernatant diluted in acetonitrile, and filtered for evaluation by HPLC using a previously validated method. The experiment was carried out in triplicate. The statistical evaluation was carried out in GraphPrism 8. As a result solubility of NIM in water was  $10.61 \pm 1.91$  mg, which is lower than Compritol and PVP, being  $13.76 \pm 1.42$  mg and  $18.07 \pm 0.68$  mg, respectively. For the surfactant, all values were high, being  $248.84 \pm 37.56$  mg,  $37.56 \pm 4.99$  mg and  $21.63 \pm 2.60$  mg for LSS, P80 and P20, respectively, and a significant difference was obtained with the PVP and LSS. Finally, it can be observed that the using drug-polymer-surfactant it will be possible to increase the solubility of NIM solid dispersions.

# Enhanced photoprotection in Pickering emulsions by incorporating karanja oil and cork extract



## Author

Marina Gomes - Universidade Federal de Santa Catarina (UFSC)  
Luís Gouveia - Research Institute for Medicine (iMed.U LISboa), Faculty of Pharmacy, University of Lisbon  
Helena Margarida Ribeiro - Research Institute for Medicine (iMed.U LISboa), Faculty of Pharmacy, University of Lisbon  
Joana Marto - Research Institute for Medicine (iMed.U LISboa), Faculty of Pharmacy, University of Lisbon  
Bianca Ramos Pezzini - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES/MEC (Ministry of Education, Brazil) and Fundação para a Ciência e Tecnologia, Portugal (UIDB/04138/2020 and UIDP/04138/2020 to iMed.U LISboa and CEECINST/00145/2018 to J. Marto).



## Keywords

Pickering emulsion, photoprotection, plant ingredients

## Abstract

Pickering emulsions are surfactant-free systems stabilized by solid particles, offering resistance to coalescence, reduced toxicity, and a sustainable preparation process. In a previous study, we optimized a photoprotective water-in-oil Pickering emulsion (formulation 1) using Central Composite Design, resulting in 13% trihydroxystearin, 20% zinc oxide, 22% purified water, and 45% squalane. This formulation exhibited *in vitro* sun protection factor (SPF) and UVA protection factor (UVAPF) results of 2.94 and 2.95, respectively, using a Labsphere® UV-2000 Ultraviolet Transmittance Analyzer. In this study, we evaluated the impact of adding karanja oil or cork hydroglycolic extract, known for their photoprotective and antioxidant properties, on the photoprotective efficacy of the formulations. Initially, the antioxidant capacity of karanja oil (previously extracted with methanol) and cork extract was assessed using ferric-reducing antioxidant power and oxygen radical absorbance capacity assays. Their spectrophotometric SPF<sub>s</sub> were determined using the Mansur method with modifications. The cork extract exhibited higher antioxidant properties (98.54±2.79 mM Fe<sup>2+</sup> equivalents and 926.37±16.12 μM TE/mL) compared to the karanja extract (5.78±0.53 mM Fe<sup>2+</sup> equivalents and 357.42±15.43 μM TE/mL). On the other hand, karanja oil showed a higher spectrophotometric SPF (4.68±0.15) than cork extract (0.28±0.09). Formulations 2 and 3 were derived from formulation 1 by substituting 5% of the oil phase with karanja oil and replacing all the water in the formulation with 22% cork extract, respectively. Photoprotective efficacy was higher for formulations 2 (*in vitro* SPF=5.49 and UVAPF=5.57) and 3 (*in vitro* SPF=3.65 and UVAPF=3.75) compared to formulation 1, demonstrating the positive impact of incorporating these plant ingredients. Our next investigation will combine both these ingredients in the same formulation, aiming at increasing even more the photoprotective efficacy.

# Stability of microencapsulated *Cymbopogon flexuosus* (DC.) essential oil and its performance as an antioxidant in cosmetic formulation



## Author

Giovana Carolina Bazzo - Universidade Federal de Santa Catarina (UFSC)  
Hellen Karine Stulzer Koerich - Universidade Federal de Santa Catarina (UFSC)  
Bianca Ramos Pezzini - Universidade Federal de Santa Catarina (UFSC)  
Giovana Carolina Bazzo - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

None.



## Keywords

lemongrass essential oil; microencapsulation; antioxidant activity

## Abstract

Lemongrass (*Cymbopogon flexuosus*) essential oil has several properties, including antioxidant action. However, due its instability, microencapsulation is being investigated in order to make it more stable. This study aimed to evaluate the antioxidant activity of microparticles containing lemongrass essential oil and its performance as antioxidant in a formulation for cosmetic application. Microparticles were prepared using arabic gum via the spray drying technique and exhibited an encapsulation efficiency of 51%. The antioxidant activity was assessed using the DPPH (2,2-diphenyl-1-picrylhydrazyl) assay after storage at ambient temperature and 40°C during 60 days. No statistically significant differences were observed in the antioxidant activity values (AA%) between pure (76.1±5.6%) and microencapsulated oil (69.9±4.9%), at the concentration of 3500 µg/mL, indicating that the microencapsulation process did not compromise its antioxidant efficacy. Furthermore, the microparticles demonstrated enhanced stability when stored at elevated temperatures. Although both samples showed a decline in antioxidant activity after 60 days, the non-microencapsulated oil exhibited a greater decrease in AA% values (from 76.1±5.6% to 20±3.1%). Additionally, incorporation of both pure oil and microparticles into a water-in-oil emulsion was performed. Parameters such as pH, viscosity, centrifugation test and macroscopic characteristics were evaluated after 60 days of storage at room temperature and 40°C. The pH remained in the range of 6.8, the viscosity around 70,000 cP and no color changes were observed during storage, suggesting the ability of microencapsulated oil to prevent oxidation. In conclusion, microencapsulation significantly enhanced the stability of lemongrass essential oil while preserving its antioxidant properties. Furthermore, the microencapsulated oil can be considered as a promising antioxidant agent, of natural origin, for use in cosmetic formulations.



# Recombinant production of a highly efficient photolyase from *Thermus thermophilus*



## Author

Carla Castelo Branco Martins - Faculdade de Ciências Farmacêuticas-Universidade de São Paulo (USP)  
Karin Torres-Obreque - Faculdade de Ciências Farmacêuticas-Universidade de São Paulo (USP);  
Department of Civil, Chemical and Environmental Engineering, University of Genoa  
Felipe Gobbi Gonçalves - Faculdade de Ciências Farmacêuticas-Universidade de São Paulo (USP)  
Rafael Bertelli Ferraro - Faculdade de Ciências Farmacêuticas-Universidade de São Paulo (USP)  
Tales Alexandre Costa-Silva - Faculdade de Ciências Farmacêuticas-Universidade de São Paulo (USP)  
Gisele Monteiro - Faculdade de Ciências Farmacêuticas-Universidade de São Paulo (USP)  
Patrizia Perego - Department of Civil, Chemical and Environmental Engineering, University of Genoa  
Carlota de Oliveira Rangel-Yagui - Faculdade de Ciências Farmacêuticas-Universidade de São Paulo (USP)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPESP-Brazil (2020/08129-6, 2022/01138-5, 2018/15104-0, 2022/02456-0); CNPq-Brazil (309953/2020-0, 306060/2022-1); CAPES-Brazil (Process number: 001); ANID Becas/Doctorado en el Extranjero (2020-722104)



## Keywords

dermatological enzyme, photoprotection, bioprocess

## Abstract

The skin is the body's first protective barrier and therefore is exposed to aggressions including solar radiation that have the potential to cause damage at different levels of this tissue. Overexposure to UV radiation in turn is associated with skin damage such as erythema or "sunburn", premature skin aging and skin cancer. Usually, topical photoprotection involves molecules that absorb or reflect UV radiation. However, this passive strategy does not completely prevent the effects of continuous exposure to UV radiation. In this sense, topical application of enzymes such as photolyase, which can repair DNA and more specifically CPD lesions, could serve as a preventive strategy increasing protection against UV radiation to reduce aging and photocarcinogenesis. Here we produced a recombinant photolyase expressed in *Escherichia coli* BL21 (DE3) strain containing the pET15b vector (histidine-tagged N-terminal fusion protein) with the *Thermus thermophilus* photolyase gene, and demonstrated the enzyme activity on CPD-DNA through ELISA test. Both batch and fed-batch processes were investigated in a bioreactor and the later resulted in 5.6 increase in final biomass produced compared to shaker conditions, reaching 20.2 g/L, and an increase of 3.6 in productivity ( $P_x = 1.84$  g/L.h). While 15.6 mg of pure photolyase was produced per liter in shaker cultivation, 170 mg/L was produced in batch bioreactor and 480 mg/L in fed-batch bioreactor. Photolyase activity was confirmed by CPD-DNA Elisa test and even low enzyme concentrations such as 15  $\mu$ g/mL recovered 90% of CPD photodamage; a concentration of 150  $\mu$ g/mL resulted in 98% recovery. With these results we demonstrated an efficient production of recombinant *T. thermophilus* photolyase and proved the enzyme high activity in repairing CPD damage. The photolyase produced is a potential active ingredient to be incorporated in dermatological products to prevent skin aging and photocarcinogenesis.

# Evaluation of the composition of ultraviolet filters in aerosol sunscreens



## Author

Sofia Lins Dias

Pedro Ferreira de Oliveira - Universidade Federal de São João Del-Rei (UFSJ)

Renê Oliveira do Couto - Universidade Federal de São João Del-Rei (UFSJ)

Ana Julia Pereira Santinho Gomes - Universidade Federal De São João Del-Rei (UFSJ)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Any



## Keywords

cosmetics security, UV rays, adverse effects

## Abstract

Aerosol sunscreens are a practical and innovative option. However, they may present risks associated with the inhalation of nanoparticles present in it, in addition to the absorption of the components through the skin. The aim of this work was to qualitatively evaluate the composition of ultraviolet (UV) filters in aerosol sunscreens available in Brazil, highlighting the most prevalent active substances and those that may present adverse events. Among the 29 products found SPF 15 (6.9% = 2/29), SPF 30 (34.5% = 10/29), SPF 40 (3.4% = 1/29), SPF 50 (41.4 % = 12/29), SPF 60 (10.3% = 3/29), and SPF 80 (3.4% = 1/29). The most frequent UV filters were ethylhexyl salicylate ~93%, octocrylene (OCR) and butyl methoxydibenzoylmethane (BMDBM), both ~83%. Considering filters with reported adverse events, OCR, BMBDM, homosalate 31%, benzophenone-3 (BP3) ~28%, ethylhexyl methoxycinnamate ~24%, 4-methylbenzylidene camphor (MBC) ~7% and titanium dioxide (TiO<sub>2</sub>) ~3% were observed. Nevertheless, BP3 and MBC can induce more serious adverse events, due to the potential for bioaccumulation. TiO<sub>2</sub> is present in a product for kids, a worrying fact as it can lead to respiratory problems, which is why it was banned from sunscreen aerosols in the United States of America and even from food in France due to its bioaccumulative and carcinogenic effect. Finally, aerosol sunscreens require more care in terms of use and require more detailed and enlightening studies on adverse events and potential risks for humans.

# Dry microparticles of fluconazole for the treatment of breast candidiasis



## Author

Venâncio Alves Amaral - Universidade de Brasília (UnB)  
Rayssa Hellen Ferreira Costa - Universidade de Brasília (UnB)  
Marcílio Cunha-Filho - Universidade de Brasília (UnB)  
Guilherme Martins Gelfuso - Universidade de Brasília (UnB)  
Tais Gratieri - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), n. 88887.691377/2022-0



## Keywords

Microparticles, Spray-drying, Fluconazole

## Abstract

Breast infection by *Candida* spp. during the postpartum period is common, causing discomfort and potential breastfeeding interruption. Topical treatments are often ineffective due to low penetration and moisture retention, leading to recurrences. Microparticles obtained by spray-drying provide an easily obtainable formulation that offers an alternative for targeted drug delivery, while maintaining the treatment area dry. To develop and characterize dry fluconazole mucoadhesive microparticles obtained via spray-drying, intended for topical application in treating breast candidiasis. Dry mucoadhesive fluconazole microparticles were prepared by spray drying using different proportions of lactose and starch (50:50, 75:25, 25:75, w/w). The microparticles were characterized for process yield, fluconazole content, moisture content, swelling, Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), and formulation irritation potential study (HET-CAM). The powder yield was  $45.83 \pm 0.92\%$  for F1,  $49.35 \pm 3.10\%$  for F2, and  $40.08 \pm 7.84\%$  for F3, with a significant difference ( $p < 0.05$ ) between F1 and F3. The analysis of fluconazole content in the microparticles showed content uniformity, ranging from 93.68% to 110.12%. Moisture content averaged 4.57%, 5.14%, and 5.28% for F1, F2, and F3, respectively. Initial swelling was higher for F3 at 10 minutes, indicating rapid water absorption, underscoring starch's exudate absorption potential. Morphological analysis showed spherical particles with smoother surfaces in F2 due to higher lactose content. FTIR data demonstrated the chemical stability and a high degree of interaction between the drug, lactose, and starch. All microparticles had a mean diameter of approximately 10  $\mu\text{m}$ . HET-CAM assays confirmed no skin irritant potential. In conclusion, the fluconazole microparticles are promising systems for drug delivery, presenting high potential as an alternative option in the treatment of breast candidiasis.

# Preliminary Analysis of Oils and Alkaline Aqueous Extracts of *Bixa orellana* L. as Synergistic Agents in Sunscreens



## Author

Ister Mariotini - Universidade Federal do Espírito Santo (UFES)  
Mariana Santos Pinheiro - Universidade Federal do Espírito Santo (UFES)  
Fabiana Vieira Lima Solino Pessoa - Universidade Federal do Espírito Santo (UFES)  
Aliny Rodrigues de Jesus da Conceição - Universidade Federal do Espírito Santo (UFES)  
Rodrigo Rezende Kitagawa - Universidade Federal do Espírito Santo (UFES)  
André Rolim Baby - Universidade Federal do Espírito Santo (UFES)  
Claudinéia Aparecida Sales de Oliveira Pinto - Universidade de São Paulo (USP)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Fapes.



## Keywords

*Bixa orellana* L.; sun protection factor; antioxidant activity

## Abstract

In Brazil, the estimated number of new cases of non-melanoma skin cancer for each year from 2023 to 2025 is 220,490. In search of new ways to protect against this type of cancer, the use of antioxidants in sunscreens has been investigated. Antioxidants protect cells against free radicals, and studies have shown that some topical antioxidants in formulations with sunscreens reduce erythema and immunosuppression. *Bixa orellana* L., known as urucum and native to Brazil, was chosen for its flavonoids, carotenoids, gallic and alfitolic acids, among others. Carotenoids, especially bixin and norbixin, are of interest for their antioxidant effects. The objective was to evaluate whether a native Brazilian plant with proven antioxidant activity could generate a synergistic effect with known sunscreens. Preliminary phytochemical tests, in vitro antioxidant effect assay with ABTS<sup>•+</sup>, and in vitro SPF determination using a sphere ultraviolet transmittance analyzer were conducted. The results of ABTS<sup>•+</sup> and in vitro SPF were statistically analyzed using Minitab Statistical Software, with one-way ANOVA and Dunnett's method at a 95% confidence interval. Four samples were prepared: alkaline aqueous extracts with whole (EAA1) and ground (EAA2) urucum seeds, extracted oil (OE), and commercial oil (OC). The phytochemical analysis showed no discrepancies for EAA1, EAA2, and OE, but OC differed, showing only the presence of coumarins. The in vitro antioxidant assay revealed that Trolox had better action than the samples, but EAA1, EAA2, and OE showed close and good results, with means below 50. OC showed no antioxidant activity even at the highest concentration used (100 µg/mL). For the in vitro SPF determination, a base cream with 5% avobenzone, 10% ethylhexyl methoxycinnamate, and 5% of each sample was used. Formulations with EAA1 (86,7) and EAA2 (86,33) showed significantly higher in vitro SPF values than the control (23,33), indicating greater efficacy as synergistic agents in sunscreens.

# Ulcerations Caused By Sickle Cell Disease: Proposal For An Accessible Biodressing



## Author

Vanessa Nascimento do Carmo - Universidade Federal da Bahia (UFBA)  
Vitória Ellen Batista de Moraes Nascimento - Universidade Federal da Bahia (UFBA)  
Thiago Moreira Trindade - PDME(Programa Municipal de Medicamentos Excepcionais) de Camaçari  
Neila de Paula Pereira - Universidade Federal da Bahia (UFBA)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior).



## Keywords

Bioinput, Chronic wounds, Healing

## Abstract

Sickle cell disease is a genetic disorder that affects the shape and function of red blood cells, leading to a series of complications. Ulcers on the lower limbs (LL) are chronic recurrent wounds that are difficult to heal, requiring significant treatment costs and having a negative impact on patients' quality of life. This study aims to formulate a stable blend composed of ethanolic extract of red propolis from Alagoas and oleoresin from *Copaiba officinalis*, to be incorporated into an emulgel designed as a biodressing agent, potentially useful in the treatment of ulcers on the lower limbs caused by sickle cell anemia. To develop the formulation, a 3:7 blend of red propolis extract from Alagoas and *Copaiba* oil was made, then an active pharmaceutical ingredient plant (API) stabilized with equal parts of cetiol V®, emulgin® and vitamin F®. The API in question was incorporated into an emulsified system based on acrylic acid copolymers. The formulation was subjected to preliminary, accelerated and shelf-life physical and chemical stability tests, as well as an in vitro spreadability profile check. The formulation showed stability with no signs of alteration in its physicochemical and organoleptic characteristics. In addition, a prospective bibliographic and patent study showed promising results in the treatment with propolis-based biodressing in the healing process. Furthermore, the mapping of patents using the Orbit Questel intelligent® tool showed that in the last decade there have been patents filed in Brazil for biodressing for different types of wounds, but without any mention of ulcerations caused by sickle cell disease. Therefore, the formulation conceived can be seen as a new pharmaceutical bioproduct containing a natural API with potential for use on sickle cell disease wounds, with the cost-benefit ratio needed by sickle cell patients.

# Characterization and Stability of Lipid Nanoparticles for Dry Eye Therapy



## Author

Leticia Braghini Lima - Universidade de São Paulo (USP)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CNPq



## Keywords

nanoparticles, hyaluronic acid, dry eye disease

## Abstract

Dry Eye Disease (DED) is an ocular condition that results in discomfort, damage to the eye surface, inflammation, and vision problems due to inadequate tear production or excessive tear evaporation. This project aims to develop nanoparticles that can effectively alleviate these symptoms, enhance patient adherence to treatment, and minimize side effects. We prepared and characterized two types of lipid nanoparticles: solid lipid nanoparticles (SLNs), containing lipids present in the tear film, and nanostructured lipid carriers (NLCs), composed of liquid lipids with potential anti-inflammatory activity. The most promising nanoparticles were enriched with hyaluronic acid (HA), a natural polymer found on the ocular surface that can interact with specific receptors of the corneal epithelium, forming hybrid nanoparticles (HA-NP) aimed at providing more efficient therapy. The SLNs exhibited an average diameter greater than 100 nm and a high polydispersity index (PDI), while the NLCs showed sizes between 50 and 60 nm, with a PDI of less than 0.3 and a neutral zeta potential. The nanoparticles were stable for up to 14 days. The selected formulations were enriched with HA, resulting in HA-NPs with physical-chemical characteristics similar to the original NPs and an infrared spectrum confirming HA incorporation. Initial results indicate that HA-NPs have significant potential to improve adherence to DED treatment due to their physical-chemical properties. Future studies will focus on modeling these nanoparticles into elliptical shapes to study the influence of shape on ocular bioadhesion.

# Evaluation of Decellularization Methods for ECM-Based Hydrogel Preparation from Human Skin



## Author

Oluwapelumi Oloyede Oyeniyi - Universidade de São Paulo (USP)  
Profa. Dra. Renata Fonseca Vianna Lopez - Universidade de São Paulo (USP)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES-PROEX 88887.911395/2023-00



## Keywords

Hydrogel, Decellularization method, Dermal decellularized matrix

## Abstract

Hydrogels are three-dimensional polymer networks with high water content widely used in biomedical applications. Recently, natural polymers derived from native extracellular matrix (ECM) proteins have shown promise for full-thickness wound dressings. These biocompatible and biodegradable ECM-based hydrogels offer superior biological properties, fostering a supportive regenerative microenvironment for wound repair. This study systematically assessed various strategies for decellularizing human skin ECM to facilitate the development of future wound-healing hydrogels. Abdominal skin samples obtained from plastic surgery (CAAE: 11726919.0.0000.5403) were subjected to chemical methods involving surfactants and saline solutions, physical methods including ultrasound and freeze-thaw cycles, and enzymatic methods employed alone or in combination. The decellularized skin was evaluated against native skin through macroscopic analysis, histology, and immunohistochemistry. The most promising method involved pretreating the skin with dispase enzyme, followed by immersion in a solution of 2% Triton X-100, 2% sodium dodecyl sulfate, and DNase-I enzyme for 36 hours, based on macroscopic characteristics. Histological examination confirmed the effective removal of cells and nuclear material while preserving ultrastructural components in the decellularized skin tissue. Collagen quantification demonstrated preserving at least 75% of native skin collagen, and DNA quantification indicated 70% removal of nuclear material. Picrosirius red staining further validated the preservation of collagen types I and III. Immunohistochemistry revealed the retention of key proteins, including collagen I, collagen III, elastin, laminin, and fibronectin in the decellularized dermal matrix. Further investigations are warranted to evaluate the gelling properties of these dermal matrices and the impact of different treatment combinations on hydrogel formulation and 3D printing of constructs.

# Evaluation of Decellularization Methods for ECM-Based Hydrogel Preparation from Human Skin



## Author

Maria Luiza R. Azevedo de Oliveira - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Thalita Martins da Silva - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Juliana Johansson Soares Medeiros - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Alessandra Lazillotta Esteves - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Camila Areias Nascimento- Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Diogo Dibo Nascimento - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Livia Deris Prado - Instituto de Tecnologia em Fármacos - Farmanguinhos, Fiocruz  
Z



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)



## Keywords

biopredictive dissolution method, AqBd, safe space

## Abstract

In order to develop a suitable dissolution method, it is necessary to consider its intended use in drug product lifecycle. Analytical Quality by Design (AQbD) has been adopted for the development of analytical methods, however, the application of AQbD to dissolution methods is scarce in the literature. To develop a dissolution method, ideally a link must be established between in vitro and in vivo release. This leads to the definition of a safe space to justify clinically relevant specification. Innovatively, this work aims to integrate AQbD with Physiologically Based Biopharmaceutics Modelling (PBBM) for development of a dissolution method for benzimidazole (BZN) 100 mg tablets, in order to guarantee the discriminative power while ensuring the clinical relevance. The PBBM model was established and refined using the GastroPlus software based on clinical observations. For dissolution method development, solubility test was carried out and it was observed that BZN does not exhibit pH-dependent solubility, and the sink condition is maintained in media with pH 1.2, 4.5, and 6.8. The Analytical Target Profile was established and risk assessment was carried out to define critical method parameters. A fractional factorial design was used to study the critical parameters and DDDPlus software was used for modelling in silico dissolution profiles. Apparatus type and the rotation speed had an impact on the dissolution percentage. Method conditions were defined: 900 mL of HCl and paddle apparatus. Rotation speed was investigated to provide the method operable design region (MODR). With the MODR conditions, PBBM was used to determine the biopredictive method. With virtual bioequivalence, safe space was determined. The integrated approaches of AQbD and PBBM allowed ensuring an adequate dissolution method for the product lifecycle that provides quality and clinically relevant results.



# Clinical Evaluation Of An Emulsified Suspension Loaded With Itraconazole In The Treatment Of Sporotrichosis



## Author

Caroline Dohanik da Silva - Universidade Federal de Minas Gerais (UFMG)  
Leticia Rocha de Moura - Universidade Federal de Minas Gerais (UFMG)  
Bianca Moreira de Souza - Universidade Federal de Minas Gerais (UFMG)  
Yamara Viana Sousa - Universidade Federal de Minas Gerais (UFMG)  
Marie Gabrielle Santiago - Universidade Federal de Minas Gerais (UFMG)  
Camila Stefanie Fonseca de Oliveira - Universidade Federal de Minas Gerais (UFMG)  
Lucas Antônio Miranda Ferreira - Universidade Federal de Minas Gerais (UFMG)  
Raquel Virgínia Rocha Vilela - Universidade Federal de Minas Gerais (UFMG)  
Gisele Assis Castro Goulart - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)



## Keywords

sporotrichosis, itraconazole, emulsified suspension

## Abstract

Sporotrichosis is a subcutaneous mycosis caused by fungi from the *Sporothrix* complex that affects humans and animals. Among animals, cats are the most affected and the main vector of zoonotic transmission. The first-choice treatment is oral Itraconazole (ITZ), often associated with long regimens and adverse effects. Aiming at solutions for managing the infection, we developed an emulsified suspension with 4% ITZ (GTL) sterilized by gamma radiation, which was evaluated in 11 cats and 01 dog diagnosed with sporotrichosis (CEUA 24/2020). Treatment was carried out with weekly subcutaneous administration of GTL and, depending on the animal's clinical condition, oral treatment (potassium iodide-PI and/or ITZ) was associated. Throughout the study, three male cats died after 21, 28, and 77 days of treatment due to bacterial infection, systemic sporotrichosis, and multiple lesions on the body. Five cats (3 females and 2 males) did not progress to cure, even after replacing GLT treatment with oral ITZ (associated or not with IP), being followed up for around 150 days (they are still undergoing treatment). Three cats (2 males and 1 female) and 1 dog (male) were cured with GLT treatment after 42, 49, 140, and 112 days of treatment, respectively. In the cat treated for 140 days, from 112 days onwards, treatment with GTL was replaced by ITZ + oral PI. During the study, laboratory tests were carried out to check liver function, and no changes were found in any animal. These results show how challenging the treatment of sporotrichosis is, especially when animals arrive for treatment in poor health, rescued from abandoned conditions, as was the case with the animals included in the study.

# Podcasts as an open educational resource tool in teaching pharmaceutical sciences: Challenges in drug design



## Author

Marcia Pietroluongo - Fundação Oswaldo Cruz (FIOCRUZ)  
Thiago Frances Guimarães - Fundação Oswaldo Cruz (FIOCRUZ)  
Renata Ribeiro de Castro - Fundação Oswaldo Cruz (FIOCRUZ)  
Rafael Dias Mesquita - Universidade Federal do Rio de Janeiro (UFRJ)  
Rodrigo fonseca da Silva Ramos - Fundação Oswaldo Cruz (FIOCRUZ)  
Flavia Furtado de Mendonça de Sousa - Fundação Oswaldo Cruz (FIOCRUZ)  
Alessandra Leda Valverde - Universidade Federal Fluminense (UFF)  
Eduardo Gomes Rodrigues de Sousa - Fundação Oswaldo Cruz (FIOCRUZ)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Fundação Oswaldo Cruz - FIOCRUZ



## Keywords

Pharmaceutical industry, Open educational resource, teaching

## Abstract

Accessing pharmaceutical facilities is often difficult due to confidentiality issues and the scarcity of openly available teaching materials, especially during professional training. Considering these challenges, it is essential to explore new tools that can bring innovation to education and make learning more accessible and engaging. With the Covid-19 pandemic, new educational challenges emerged that required the redefinition of teaching methods. There has been an increased demand for online teaching tools, and podcasts have emerged as a valuable resource. The success of podcasts is due to their flexible use, allowing teaching and learning without temporal or physical restrictions; mobile access through portable devices, increasing accessibility; simplicity of production and rapid distribution. The objective of the work was to produce five audio episodes, lasting 10 to 15 minutes, on the themes of pharmaceutical technology, analytical development, analytical validation, medication stability, and medication registration, following the interview profile with professionals who live the daily routine of the topics covered. The proposal's innovation consists of offering an educational resource that can be used beyond the physical classroom. As a result, five episodes were recorded and uploaded to Educare, a Fiocruz open educational resources repository, which will serve as a valuable complement to traditional teaching methods, enhancing technical-professional development in the pharmaceutical industry in an innovative and inclusive manner. With these podcasts, students can access information at any time and from any location, removing geographical barriers and ensuring inclusivity.

# Development of 3D printing hydrogel containing paromomycin for the cutaneous leishmaniasis treatment



## Author

Beatriz Hecht Ortiz - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Beatriz Andrade da Silva - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Ana Paula dos Santos Matos - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz  
Alessandra Lifschitz Viçosa - Instituto de Tecnologia em Fármacos- Farmanguinhos, Fiocruz



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

Farmanguinhos; Proep; CNPq; CAPES Fellowship



## Keywords

Cutaneous leishmaniasis, Paromomycin, 3D printing hydrogels

## Abstract

Leishmaniasis is a neglected disease, endemic in 99 countries, with approximately 12 million infected, caused by protozoa of the genus *Leishmania*. Cutaneous leishmaniasis (CL) is the most common clinical form and is characterized by the appearance of skin lesions (PAHO, 2024). The current treatment presents several side effects and poor patient adherence. Paromomycin (PM), an aminoglycoside antibiotic, has been studied and used for CL and is administered intramuscularly and intravenously. PM is a drug, which belongs to a class III of Biopharmaceutical Classification System (Matos et al., 2020). Based on this, studies to improve PM permeability to be used in topical formulations are under developing in the literature. 3D printing technology is an innovation in a pharmaceutical area and shows several advantages aiming customized medicines (Seoane-Viaño et al., 2021). 3D semi-solid extrusion model (SSE) promotes to develop customized topical formulations, which represents an interesting option to produce dressings to wound treatments, including CL treatment. The objective of this study was to develop alginate, carboxymethylcellulose and 10% PM hydrogel, by 3D printing, for topical treatment of CL. The formulations with and without PM were printed by a M3DIMAKER™ pharmaceutical 3D printer using SSE model, with the following printing parameters: 100% rectilinear filling pattern, disc shape (3.0 cm height x 3.0 cm width x 3.0 cm length) and 20 mm/s printing speed. The hydrogels after impression were crosslinked with 2 mol/L CaCl<sub>2</sub> solution (Moreira-Filho et al., 2020). The samples were characterized by visual appearance, pH and viscosity. The samples showed a light-yellow color, pH of 6.79 ± 0.04 and 5.73 ± 0.01 and viscosity of 386,400 cP and 382,800 cP, respectively. The hydrogels demonstrated promising results for use as a dressing for CL. However, more studies are under developing to characterize the 3D hydrogels.

# Polymeric nanofiber device crosslinked with an antifibrotic agent for preventing capsular opacification after cataract surgery



## Author

Thomas Toshio Inoue - Universidade Federal de Minas Gerais (UFMG)  
Armando da Silva Cunha Júnior - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding



## Keywords

capsular opacification, intraocular lens, polymeric nanofiber

## Abstract

Cataract surgery, the most common ophthalmic surgery globally, can be followed by early postoperative issues such as inflammation and pain. Additionally, long-term complications such as capsular opacification can occur, leading to secondary cataracts and requiring further YAG laser capsulotomy intervention, with the potential for retinal damage and increased intraocular pressure. Pharmacological interventions targeting capsular opacification, including antifibrotic, steroidal and non-steroidal anti-inflammatory, and antiproliferative drugs, are being explored. To address this challenge, the present work proposes to develop a polymeric nanofiber device coupled to the intraocular lens and crosslinked with a potent antifibrotic agent peptide (PAAP). This device aims to reduce secondary cataracts and, consequently, the need for additional laser procedures, improving patient outcomes. To obtain the polymeric nanofibers, polyurethane was synthesized using a one-pot acetone method with polycaprolactone diol as the polyol and 1,4-butanediol as the chain extender. Following purification and drying, the polymer was dissolved in a chloroform-dimethylformamide solution and subjected to electrospinning. To understand the physicochemical properties of the polymer and polymeric nanostructure, characterization techniques such as nuclear magnetic resonance spectroscopy, infrared spectroscopy, and thermal analysis were employed. Scanning and transmission electron microscopy were applied to access morphological and structural information. The synthesis yielded a translucent polymer, and electrospinning produced a nanofibrous membrane with fibers in the nanoscale range. Physicochemical characterization confirmed the successful formation of polyurethane and demonstrated the thermal stability of both the bulk polymer and the nanofibers. Future work includes crosslinking PAAP with the polyurethane nanofibers and in vitro and in vivo safety and activity evaluation.

# Evaluation of Antioxidant Activity, Toxicity and Irritant Potential of Nanoemulgel Containing Gallic Acid and Ellagic Acid with Potential Application in Melasma Treatment



## Author

Camila Fortes Castelo Branco Magalhães - Universidade Federal do Piauí (UFPI)  
André Luiz Pinheiro de Moura - Universidade Federal do Piauí (UFPI)  
Matheus Oliveira do Nascimento - Universidade Federal do Piauí (UFPI)  
Bianca Soriano dos anjos - Universidade Federal do Piauí (UFPI)  
Paulline Paiva Mendes de Souza Leal - Universidade Federal do Piauí (UFPI)  
Michel Muálem de Moraes Alves - Universidade Federal do Piauí (UFPI)  
Fernanda Sousa Reinaldo - Universidade Federal do Piauí (UFPI)  
Sidney Gonçalo de Lima - Universidade Federal do Piauí (UFPI)  
André Luis Menezes Carvalho - Universidade Federal do Piauí (UFPI)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

No



## Keywords

Pentaclethara macroloba, Nanostructured System, Tannins

## Abstract

Melasma is a chronic hyperpigmentation condition that primarily affects the skin in sun-exposed areas. Effective treatment for melasma remains a challenge due to the limitations of conventional therapies. Gallic acid (GA) and ellagic acid (EA) are well-documented in the literature and are highlighted for their antimelanogenic activity. Similarly, pracaxi oil is also a notable product with potential depigmenting activity. In this study, a nanoemulgel containing gallic acid and ellagic acid (Nanogel-GA-EA) delivered in pracaxi oil was evaluated for its antioxidant activity, toxicity, and irritant potential to determine the feasibility of the formulation for future applications in melasma treatment. The previously developed and optimized formulation was subjected to an *in vitro* test to assess its antioxidant activity using the DPPH radical scavenging method. Additionally, toxicity tests were conducted using an alternative method with *Zophorbas morio* larvae through melanin quantification. The irritant potential was evaluated using the hen's egg chorioallantoic membrane test (HET-CAM). The formulation containing the combination of GA and EA exhibited good antioxidant activity when compared to gallic acid in a 1% solution. Regarding toxicity, it was observed that the group treated with Nanogel-GA-EA demonstrated a decrease in melanin concentration compared to the positive control (DMSO). The nanogel also showed low irritant potential, especially when compared to a commercial depigmenting formulation. In light of these positive results, the developed formulation demonstrated great potential for future applications and testing, with low irritant potential, and presents itself as a cosmetic formulation with low toxicity, good stability, and suitability for topical administration.

# Evaluation of the Safety of an Active Ingredient Delivery System for Skin Treatment Based on Bacterial Cellulose



## Author

Thais Oliveira - Universidade de Sorocaba (UNISO)  
Ana Carolina Souza Chacon - Universidade de Sorocaba (UNISO)  
Gabriel Pereira Machado - Universidade de Sorocaba (UNISO)  
Erika Leão Ajala Caetano - Universidade de Sorocaba (UNISO)  
Larissa Oliveira Simões - Universidade de Sorocaba (UNISO)  
Denise Grotto - Universidade de Sorocaba (UNISO)  
Angela Faustino Jozala - Universidade de Sorocaba (UNISO)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), n. 88887.691377/2022-0



## Keywords

Acne, Skin disease, Clean Beauty

## Abstract

Among skin diseases, acne is a highly common condition, estimated to affect 94% of the global population at some point in their lives. Today, there is a growing demand for environmentally conscious products that treat skin diseases without harming the environment, known as Clean Beauty. To meet this concept, two natural-origin actives with cosmetic properties were chosen. Mandelic acid (MA) is an AHA group acid extracted from almonds that has antibacterial activity and is also used for mild peels according to the literature. Nisin (NI), on the other hand, is produced through the fermentation of lactic bacteria and is widely used in the food industry as a preservative. The objective was to develop a delivery system based on bacterial cellulose loaded with natural actives NI and MA for the treatment of acne-related skin disease. The system utilized bacterial cellulose from the fermentation of *Komagataeibacter xylinus*, and was tested for antibacterial activity against *Staphylococcus aureus*, antioxidant activity, active release through Franz cells, and scanning electron microscopy of the system with and without the actives. Finally, the product's stability at room temperature was evaluated for 180 days, considering that no chemical preservatives were added, since Nisin itself also has properties of a natural preservative. The results indicate antibacterial activity against the tested strain and high antioxidant activity. The release of actives from bacterial cellulose showed that both actives were able to permeate the skin in different concentrations. Scanning Electron Microscopy showed that both actives remained trapped in the bacterial cellulose meshes after incorporation. This highlights the natural and petroleum-free dermocosmetic properties of bacterial cellulose, aligned with Clean Beauty.

# Domiphen Bromide stimulates the transcription of antimicrobial and regenerative genes in gingival fibroblasts



## Author

Felipe Saldanha-Araujo - Universidade de Brasília (UNB)  
Leticia Rodrigues de Brito - Universidade de Brasília (UNB)  
Elizabete Cristina Iseke Bispo - Universidade de Brasília (UNB)  
Tais Gratieri - Universidade de Brasília (UNB)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

FAPDF, CAPES, and CNPQ



## Keywords

Chlorhexidine gluconate, Domiphen bromide, gingival fibroblasts

## Abstract

Chlorhexidine gluconate (GC) is a disinfectant with antiplaque activity used in mouthwashes. Currently, GC-based mouthwashes are the main products used to control the growth of *S mutans* and oral biofilm. More recently, Domiphen bromide (DB) has been investigated in the field of dentistry, due to its antibacterial and antiplaque properties. Here, using MTT assay we evaluated the impact of GC and BD on the viability of fibroblasts isolated from human gingiva. Then, we investigated by Real-Time PCR the effect of the isolated and combined use of GC and BD on the expression of anti-inflammatory, antimicrobial, and regenerative genes in gingival fibroblasts. Interestingly, the MTT assay revealed that after 24 hours of cell culture, both GC and BD only showed toxicity to gingival fibroblasts when used at a concentration  $\geq 1$   $\mu\text{g/ml}$ . Using GC and BD alone or in combination, at a non-toxic concentrations of 0.5  $\mu\text{g/ml}$ , we identified that the isolated use of BD induces an increase in the expression of COL1A, ANGPT2, and LCN2 in gingival fibroblasts. Furthermore, compared to untreated cells, the treatment with BD induced a 2-fold increase in HAMP expression and a 4-fold increase in CXCR4 expression, although these differences were not statistically significant. Despite preliminary, our results indicate that treatment with BD can induce greater antimicrobial and regenerative potential in gingival fibroblasts, compared to treatment with GC.

# Dexamethasone-loaded hydrogel implants for inflammation management post ocular surgery



## Author

Raine-Clênia Castro - Universidade Federal de Goiás (UFG)  
Bianca Bueno Fontanezi - Universidade Federal de Goiás (UFG)  
Jader Pires - Universidade Federal de Goiás (UFG)  
Ailton Antônio Sousa-Junior - Universidade Federal de Goiás (UFG)  
Eliana Martins Lima - Universidade Federal de Goiás (UFG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

No



## Keywords

Ocular implants, Sodium alginate, Dexamethasone

## Abstract

Controlled release formulations, such as implants, are important alternatives to address the shortcomings of conventional ophthalmic formulations, such as low bioavailability of the drugs as a result of protective biological barriers, the need for multiple administrations and the lack of patient adherence to the treatment. These issues can be even more relevant during treatment or prevention of inflammatory processes associated with ocular surgeries. Biofabrication and hydrogel cross-linking techniques allow the preparation of implants from polymers such as sodium alginate (ALGS), with tunable properties. The aim of this study was to develop and characterize ALGS implants for the controlled release of dexamethasone for application in the anterior chamber of the eye after cataract surgery. ALGS implants containing micronized dexamethasone were prepared by extruding ALGS hydrogels at 2 and 4 % over a calcium chloride (CaCl<sub>2</sub>) crosslinking solution at concentrations ranging from 25 mM to 100 mM. In order to improve the drug loading content of the implants, 0.01 % Pluronic® F-68 or 1% soy phosphatidylcholine was added. Dexamethasone content was measured by HPLC-DAD and the drug release profile was evaluated in simulated aqueous humor (SAH). Implants composed of 4% ALGS, 1% soy phosphatidylcholine, cross-linked in 100 mM CaCl<sub>2</sub> solution showed a spherical shape, an average weight of  $7.78 \pm 0.73$  mg (n = 10), with a dexamethasone content of  $123.47 \pm 5.02$  µg per implant. Dexamethasone release analysis from the implants in SAH showed a burst release of the drug during the first 24 hours of the assay, suggesting that further optimization of the implant matrix is required to achieve a slower and more controlled release profile. These implants represent potential alternatives for anti-inflammatory therapy following cataract surgery. Adjustments are needed to prolong the drug release kinetics at therapeutic doses in the anterior chamber of the eye.



# Citronellol in vitro skin permeation from supramolecular gels prepared by hot-melt extrusion



## Author

Ricardo Marreto - Universidade Federal de Goiás (UFG)  
Daniela Borges Marquez Barbosa - Universidade Federal de Goiás (UFG)  
Stela Alves Rodrigues Pereira de Oliveira - Universidade Federal de Goiás (UFG)  
Stephania Fleury Taveira - Universidade Federal de Goiás (UFG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

None



## Keywords

solid dispersion, hot-melt extrusion, supramolecular gel

## Abstract

Supramolecular gels based on interactions between polymers and cyclodextrins show potential for topical or transdermal drug delivery. This study investigated whether thermal treatment by hot-melt extrusion (HME) could alter the properties of gels containing drug, cyclodextrin, and polymer, including its in vitro drug skin permeation. The mixtures consisted of an amphiphilic polymer (Soluplus®), alpha-cyclodextrin, plasticizing agent (PEG 400), colloidal silicon dioxide, and citronellol (10, 15, or 20% w/w), a terpene with analgesic and anti-inflammatory activities. HPLC, DSC, and XRD were used to characterize the extrudates. The HME gels and those prepared by the physical mixing of constituents (MF gels) were analyzed by HPLC, dynamic light scattering (DLS), in vitro release, and in vitro skin permeation of citronellol. HME processing resulted in minimal citronellol loss. HME gels exhibited a faster release of citronellol than MF gels, indicating the potential of HME gels as superior citronellol delivery systems for topical application. Additionally, HME gel with higher citronellol concentration (20%, m/m) showed the highest drug skin permeation. The results highlighted that hot-melt extrusion processing could effectively alter supramolecular gels' properties and show that in vitro skin permeation depended on citronellol concentration.

# Development and characterization of biomaterial derived from extracellular matrix (ECM) of porcine placenta for application in regenerative medicine



## Author

Maria Claudia Passos - Universidade Federal de Goiás (UFG)  
Marize Campos Valadares - Universidade Federal de Goiás (UFG)  
Artur Christian Garcia da Silva - Universidade Federal de Goiás (UFG)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

None



## Keywords

Porcine placentas, extracellular matrix (ECM), lesion recovery

## Abstract

Biomaterials derived from extracellular matrix (ECM) have been desirable materials for regenerative medicine, as they provide sufficient biological signals for cell migration, proliferation, and differentiation. The placenta, due to its role in the development and maintenance of the fetus, has an ECM rich in bioactive molecules capable of accelerating tissue regeneration processes with low immunogenicity. Therefore, the aim of this study was to obtain and characterize a biomaterial derived from porcine placental ECM. To achieve this, porcine placentas were collected immediately after delivery, subjected to freezing and thawing cycles, and immersed in a detergent solution with mechanical agitation for tissue decellularization, confirmed by histology, Hoechst staining, and DNA quantification. For biomaterial preparation, the decellularized ECM was lyophilized and digested with a solution of acetic acid and 0.5 M pepsin. Biomaterial characterization included colorimetric assays to quantify total proteins, collagen, glycosaminoglycans (GAGs), and growth factors. The results demonstrate that the decellularization methods employed effectively removed immunogenic components from the animal tissue while preserving key ECM components, such as collagen, GAGs, and growth factors involved in tissue regeneration processes. This indicates that the biomaterial derived from porcine placenta can serve as a biological scaffold capable of providing a favorable environment for injury recovery.

# Effect of Vehicle Composition on the Preparation of Different Types of Dapsone Crystals for Topical Drug Delivery



## Author

Bianca da Costa Bernardo Port - Universidade Federal de Santa Catarina (UFSC)  
Gabriela Schneider-Rauber - Universidade Federal de Santa Catarina (UFSC)  
Débora Argenta - Universidade Federal de Santa Catarina (UFSC)  
Thiago Caon - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

CAPES



## Keywords

Gel formulation, Crystal forms, Topical Drug Delivery

## Abstract

Topical formulations composed of API-pure crystals have been increasingly studied, especially in regards to the impact of particle size in penetration efficiency. Less attention, however, has been devoted to the solid-state properties of drugs delivered to the skin. In this study, we address the effect of formulation composition on the crystal form existing in topical products. Dapsone (DAP) gel formulations were prepared by mixing an organic solution containing DAP with an aqueous solution containing polymers and preservatives. The organic solvent was chosen as ethoxydiglycol (DEGEE), polyethylene glycol (PEG), or 1-methyl-2-pyrrolidone (MPR) to assess the impact of composition on DAP crystal form. Such solvent variations resulted in different particulate matter. In terms of crystalline nature, the presence of DEGEE in formulations induced the crystallization of DAP hydrate, while PEG cocrystal and a mixture of hydrate and MPR solvate crystallized from the same amounts of PEG and MPR, respectively. Microscopic analysis of the gels showed heterogeneous particles with different characteristics. The behavior of gels after application to the skin was also tested. Interestingly, the different formulations seemed to accumulate in different regions of the skin. This could be the result of the effect of vehicle composition/excipients on the characteristics of the skin, such as hydration. The site-specific accumulation, however, was more pronounced in crystal-loaded gels as opposed to blank formulations. These results indicate that future studies should consider the effect of formulation composition on the API crystal form landscape as part of the strategies used to successfully target drug delivery to the skin.

# Human Reconstructed Epidermis (Skinethic™): A New Approach For Evaluating Equivalence Of Topical Products



## Author

Leila Bastos Leal - NUDFAC - Universidade Federal de Pernambuco (UFPE)  
Juliana Kishishita - NUDFAC - Universidade Federal de Pernambuco (UFPE)  
Danilo Cesar Galindo Bedor - NUDFAC - Universidade Federal de Pernambuco (UFPE)  
Vanja Dakic - NUDFAC - Universidade Federal de Pernambuco (UFPE)  
Davi Pereira de Santana - NUDFAC - Universidade Federal de Pernambuco (UFPE)



## Knowledge Area

Pharmaceutical and Cosmetic Technology



## Funding

None



## Keywords

In vitro alternatives. Human Reconstructed Epidermis. Topical products.

## Abstract

Generic drugs must be bioequivalent and pharmaceutically equivalent to innovative products. Depending on the country, the evaluation of bioequivalence for topical products follows different requirements and regulations. For this purpose, the use of in vitro permeation tests (IVPT) using human skin has been important in assessing the quality and equivalence of topical medications. Human Reconstructed Epidermis (RhE) models are validated for irritation and dermal corrosion testing, and despite being more permeable than human skin, they are currently considered suitable alternatives for assessing dermal absorption and screening the bioavailability of topical products, mainly due to their similarity to human skin and allowing greater lot-to-lot reproducibility. Therefore, this study aimed to conduct IVPT using Human Reconstructed Epidermis (SkinEthic™/Episkin®) as the membrane to assess the equivalence of creams containing 1% terbinafine hydrochloride, marketed in the Brazilian market. For the IVPT test, RhE inserts were placed in a 12-well plate containing 2 mL of receptor fluid (PBS + 0.8% Tween 80) and maintained in an incubator at  $37 \pm 1^\circ\text{C}$ , 5%  $\text{CO}_2$ , and  $\geq 90\%$  relative humidity, with agitation (250 rpm) for 48 hours. Approximately 10 mg of each product was applied to the membrane (0.5 cm<sup>2</sup> area), and at different time intervals, 500  $\mu\text{L}$  of receptor fluid was sampled and quantified by validated HPLC-UV methods. Although the results show that the products have similar pH, content, spreadability, and viscosity, the IVPT results showed significant differences (Student's t-test,  $p < 0.05$ ), approximately twofold, in the amount of permeated drug, flux, permeability coefficient, and retention in RhE among the evaluated products. Finally, despite RhE models being more permeable than human skin, these results may support their acceptance as suitable biological membranes for IVPT, in bioavailability screening and assessments of dermal absorption of topical products.

**Area**

# **Nanotecnologia**

# Nanostructured Lipid Carriers Enhance Wound Healing Efficacy of *Piper cernnum* Leaf Extract: In Vivo Assessment in Swiss Mice



## Author

Jenny Sumara Sozo - Universidade do Vale do Itajaí (UNIVALI)  
Ruth Meri Lucinda da Silva - Universidade do Vale do Itajaí (UNIVALI)  
Angela Malheiros - Universidade do Vale do Itajaí (UNIVALI)  
Carlos Rafael Vaz - Universidade do Vale do Itajaí (UNIVALI)  
Márcia Maria de Souza - Universidade do Vale do Itajaí (UNIVALI)



## Knowledge Area

Nanotechnology



## Funding

Capes, Cnpq and Fapescc



## Keywords

*Piper cernnum*;; Nanostructured lipid carriers, Skin regeneration;

## Abstract

**Background:** Plants of the *Piper* genus are rich in lignans, characteristic secondary metabolites known for their diverse bioactivities, including antimicrobial, anti-inflammatory and cytotoxic properties. With this in mind, we aimed to explore the wound healing effects of *Piper cernnum* leaf extract on skin lesions. Given the low solubility of plant-derived actives, we developed nanostructured lipid carriers (NLC) to encapsulate these hydrophobic extract. **Objectives:** To assess the in vivo wound healing potential of animals treated with crude *P. cernnum* leaf extract and encapsulated ones comparing them with control groups. **Methods:** Nanostructured lipid carriers containing *P. cernnum* leaf extract ( $29.13 \pm 0.31$  nm; PDI  $0.179 \pm 0.10$ ;  $pZ -12.7 \pm 0.31$ ) were developed using Compritol®888ATO. Swiss mice (20–30g) from the Central Animal House of UNIVALI were used in accordance with ethical guidelines. Animals were housed in controlled conditions with ad libitum access to food and water. The cutaneous wound model described by Yadav et al. (2014) was employed. Four groups ( $n=10$ ) were treated with NLC-blank, NLC-CLE, CLE and Nebacetin daily until wound closure. Wound contraction was measured using the scoring system by Sultana et al. (2009). **Results:** Skin regeneration scores were categorized as good (16–19), fair (12–15), or poor (8–11). The scores obtained were: Naive:11; NLC-blank:10; CLE:11; NLC-CLE:16; Nebacetin:8. Significant differences in wound remission over time were observed in the Naive, NLC-CLE and Nebacetin groups. NLC-CLE group showed more significant wound recession compared to others. No statistical difference was found between the Naive, NLC-blank, and CLE. **Conclusions:** Nanostructured lipid carriers interacted with the skin's lipid barrier, facilitating drug penetration through superficial layers. Their lipid nature allowed them to merge with cell membranes, aiding drug internalization. Additionally, their small particle size favored cutaneous absorption.

# Enhanced Efficacy of Tacrolimus-Loaded Lipid Core Nanocapsules in Modulating Immune Responses in Autoimmune Disease



## Author

Graziela Gomes - Universidade Federal do Rio Grande do Sul (UFRGS)  
Silvia Guterres - Universidade Federal da Bahia (UFBA)  
Adriana Pohlmann - Universidade Federal do Rio Grande do Sul (UFRGS)  
Maria Serena - Harvard Medical School  
Luiza Frank - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

CNPq; FAPERGS, CAPES



## Keywords

Lipid-core nanocapsules; autoimmune hepatitis; tacrolimus

## Abstract

This study evaluates the efficacy of tacrolimus-loaded nanocapsules (NCTac) in modulating immune responses, specifically those mediated by T-regulatory (Treg) and T-effector (Teff) cells, both in vitro and in vivo, using an experimental model of acute liver injury. Total CD4<sup>+</sup> cells, Tregs, and Teff were isolated from the peripheral blood of patients with autoimmune hepatitis (AIH) and healthy controls (HC), and cultured in the presence of 20nM NCTac, NC, or TAC for 24 hours. Levels of FOXP3 and ROR $\gamma$ T were measured by flow cytometry. Additionally, cell proliferation and Treg suppressive abilities were evaluated, and the therapeutic efficacy of NCTac was further investigated in a Concanavalin-A-induced liver injury model in NOD/scid/gamma immunodeficient mice, reconstituted with human CD4 T-cells. In AIH samples, treatment of total CD4<sup>+</sup> cells with NCTac led to increased levels of FOXP3 and decreased expression of ROR $\gamma$ T compared to untreated or TAC-treated cells. Furthermore, NCTac addition inhibited the proliferation of both HC and AIH-derived CD4<sup>+</sup> cells and enhanced Treg suppression in AIH samples. Notably, both NC and NCTac significantly inhibited the activation of Teff, highlighting the nonspecific immunosuppressive capacity of the nanocapsules delivery system. In vivo, NCTac administration resulted in a significant reduction in ALT levels and a decrease in lymphocytic infiltration compared to non-encapsulated TAC, confirming its efficacy in reducing hepatic inflammation and potentially mitigating liver damage. Overall, these findings demonstrate that NCTac exhibits superior immunomodulatory effects compared to non-encapsulated TAC, by enhancing Treg suppression while concurrently reducing inflammation both in vitro and in vivo. The development of NCTac signifies a promising advancement in the treatment of autoimmune disorders such as AIH, offering a more effective and targeted approach to deliver immunosuppression and therefore improve disease outcomes.

# Preformulation Of Nanoemulsions Targeted To Nose-To-Brain Administration Of Antifungals: An Initial Step



## Author

Éverton Alencar - Universidade Federal de Mato Grosso do Sul (UFMS)  
Maria Beatriz Chelotti de Moraes - Universidade Federal de Mato Grosso do Sul (UFMS)  
Luiz Fernando Polizelli - Universidade Federal de Mato Grosso do Sul (UFMS)  
Júlio Abreu Miranda - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Nanotechnology



## Funding

CNPq



## Keywords

nose-to-brain; nanoemulsion; fungal infection

## Abstract

The increase in fungal infections in the central nervous system, especially in immunosuppressed patients, has driven the search for more effective therapies. Nanoemulsions for nose-to-brain drug delivery have become a promising alternative to improve the local bioavailability of anti-infective agents. Accordingly, this work aimed to preformulate a nanoemulsion intended for the nose-to-brain delivery of antifungals. For this, a pseudoternary phase diagram (PTPD) was created using the water titration method to provide the composition necessary for forming a nanoemulsion (NE). Next, 3 NEs from the PTPD with the highest oil content and Tyndall effect were reproduced. A NE was chosen based on droplet size and polydispersity index (Pdl) and further assessed for conductivity and stability. For the latter study, the NE was stored in triplicate over 30 days at 4, 25, and 50°C and analyzed periodically for their droplet size, Pdl, and zeta potential. The selected NE had the following proportions: oil (6%), Tween 80 (8.82%), Span 80 (5.18%), and water (80%). It presented a droplet size of  $\approx 42$  nm, Pdl of  $\approx 0.165$ , and zeta potential of  $\approx -24$ . The conductivity curve displayed regions of oil-in-water (O/W), bicontinuous, and water-in-oil dispersions, wherein the NE presented conductivity ( $171,7 \mu\text{S}/\text{cm}$ ) compatible with the O/W region. The stability study evidenced that the greatest parameter variations were present in the formulations kept at 50 °C (stressed condition), while no significant variations occurred at further conditions over 30 days. From the results, it is concluded that an oil-in-water (O/W) NE was obtained. It displayed adequate stability for room temperature storage at a preformulation level. This NE displays encouraging possibilities for nose-to-brain optimization and nasal administration.



# Multi-loaded liquid crystalline nanoparticles with piperine, siRNA IFN $\gamma$ and siRNA HSP70: a potential therapy for vitiligo



## Author

Ana Vitória Pupo Silvestrin - FCFRP- Universidade de São Paulo (USP)  
Maria Vitória Lopes Badra - FCFRP- Universidade de São Paulo (USP)



## Knowledge Area

Nanotechnology



## Funding

Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, grant #2022/01969-4, #2014/50928-2 and #2019/08568-2) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, grant #465687/2014-8).



## Keywords

liquid-crystalline nanoparticles, vitiligo, gene therapy

## Abstract

Vitiligo is a chronic, immune-mediated and multifactorial disease, characterized by macules and hypopigmented patches on the skin and mucous membranes, which occur secondary to the destruction of melanocytes. The therapeutic clinical scenario faces major challenges in achieving effective and effective long-term treatment. In this study, we propose the development of liquid crystalline nanoparticles (LCN) multi-loaded with piperine (Pip) and small interfering RNA targeting interferon gamma (IFN $\gamma$ ) and 70 kDa heat shock protein (HSP70). siRNAs will act by reducing the production of these markers that stimulate the immune response, and Pip, an alkaloid present in *Piper nigrum*, will contribute to the reduction of pro-oxidant and inflammatory mediators, and restoration of melanocytic homeostasis. LCNs showed unimodal size distribution curves with an average hydrodynamic size between 157 and 206 nm, low polydispersity (<0.25), positive zeta potential, high Pip encapsulation efficiency (>86%) and high siRNA binding efficiency and protection against RNase A. The reverse hexagonal mesophase of the LCN was confirmed by small-angle X-ray scattering and cryogenic electron microscopy. LCN promoted greater in vitro cutaneous penetration and retention of Pip and siRNA compared to drug solutions. In different cell lines the LCN promoted rapid internalization of siRNA, significantly increasing its bioavailability. Finally, in healthy melanocytes or induced by oxidative stress, the multi-loaded LCN (Pip, siIFN $\gamma$  and siHSP70) increased melanin content and tyrosinase activity by more than 2-folds, as well as restoring viability and reduced levels of reactive oxygen species. Taken together, these results demonstrate that LCN are capable of overcoming extra- and intracellular barriers and delivering Pip and siRNA. In addition, the triple combination of therapeutic agents can control the harmful effects of oxidative stress on melanocytes, supporting future in animal model investigations.

# An antifungal nanocrystal suspension as a promising treatment for dermatomycosis



## Author

Francielli Lima dos Santos - Universidade Federal Do Rio Grande Do Sul (UFRGS)  
Júlia Capp Zilles - Universidade Federal Do Rio Grande Do Sul (UFRGS)  
Simone Jacobus Berlitz - Universidade Federal Do Rio Grande Do Sul (UFRGS)  
Bárbara Souza Da Costa - Universidade Federal Do Rio Grande Do Sul (UFRGS)  
Alexandre Meneghello - Universidade Federal Do Rio Grande Do Sul (UFRGS)  
Irene Clemes Kulkamp - Universidade Federal Do Rio Grande Do Sul (UFRGS)  
Renata Vidor Contri - Universidade Federal Do Rio Grande Sul(UFRGS)



## Knowledge Area

Nanotechnology



## Funding

Financial support from CNPq (project 423066/2018–8), FAPERGS (23/2551-0000953-6) and CAPE: (F.L.S master´s scholarship)



## Keywords

DERMATOMYCOSIS, RECALCITRANT, NANOSUSPENSION

## Abstract

Dermatophytic fungi, non-dermatophytic fungi and yeasts can cause dermatomycoses, which are fungal infections of the skin. Several strategies are being studied to improve the topical antifungal treatment, including the use of nanotechnology. Nanocrystals are composed of 100% active substance and stabilizing agent, with a particle size smaller than 1000 nm. The aim of this study was to develop and characterize clioquinol nanocrystals, to evaluate its in vitro skin penetration and its in vitro antifungal efficacy against recalcitrant fungal strains. Initially, the nanocrystals were obtained using different techniques (wet bead milling and probe sonication), also varying the drug concentration (1% and 0.1%) while maintaining the surfactant concentration at 1%. Subsequently, the impact of changing the surfactant from poloxamer 407 to polysorbate 80 was evaluated, as well as the impact of reducing the Ytria-stabilized zirconium oxide beads size from 0.8 to 0.3mm. The most suitable formulation presented a cloudy yellowish appearance, a particle size of  $307 \pm 2.5$  nm, and a PDI of  $0.254 \pm 0.02$  (dynamic light scattering). A zeta potential of  $-7.6 \pm 2$  mV (electrophoretic mobility), pH of  $5.4 \pm 0.3$ , drug content of  $97.3 \pm 6.4\%$  of the theoretical concentration, and nanocrystalization efficiency of  $96.1 \pm 1.2\%$  (UV spectrophotometry) were also obtained. The nanocrystals demonstrated a more sustained in vitro skin penetration and a greater in vitro antifungal efficacy (with a reduction in MIC values that ranged from 3 to 52 times) compared to the drug solution. The nanocrystals performance regarding skin penetration and antifungal efficacy can be attributed to the nanometric size and the increase in saturation solubility. Therefore, the developed clioquinol nanocrystals can be considered a promising treatment against recalcitrant fungal infections of the skin.

# Miltefosine loaded-alginate nanoparticles have antifungal activity on *Sporothrix brasiliensis*



## Author

Andriéli Bacega - Universidade de São Paulo (USP)  
Luciana Biagini Lopes - Universidade de São Paulo (USP)  
Kelly Ishida -Universidade de São Paulo (USP)



## Knowledge Area

Nanotechnology



## Funding

FAPESP (grant 2023/12190-0 and scholarship 2023/12443-6), CAPES (finance code 001) and CNPq (306041/2022-7)



## Keywords

Sporotrichosis; Feline; Sustained release.

## Abstract

Sporotrichosis is a neglected mycosis caused by *Sporothrix* ssp. and the species *Sporothrix brasiliensis* is associated to zoonotic transmission, mainly by felines. Cases of sporotrichosis are reported in Brazilian states, with the southeast region considered the epidemiological center. *S. brasiliensis* is the predominant species in reported cases in South America and is also the most virulent species and less susceptible to antifungals. The first line of treatment is itraconazole (ITC), although terbinafine (TRB) and potassium iodide are used as alternative treatments. In recurrent or severe cases of the sporotrichosis, Amphotericin B (AMB) may be employed. Drug shortages, fungal resistance, and toxicity require the search for new treatment strategies for controlling sporotrichosis. Previous studies showed antifungal activity of miltefosine (MFS) on several *Sporothrix* isolates; however, it presents several side effects. Then, we standardized the miltefosine loaded-alginate nanoparticles (MFS-AN-P80) to reduce the MFS toxicity due to its release in a sustained manner. The aim of this study is to evaluate the inhibition effect of standard antifungals (ITC and TRB), free MFS and MFS-loaded alginate nanoparticles. For that, the microdilution broth assay was performed to determine the minimum inhibitory concentrations (MIC) and minimum fungicidal concentration (MFC) values against three *S. brasiliensis*. ITC and TRB, respectively, showed fungistatic effects presenting MIC values of 0,5 - 4 µg/mL and 0,125 - 0,5 µg/mL. AMB inhibited at 0,5 - 2 µg/mL. Free MFS inhibited at 1 - 2 µg/mL and it was fungicide (MFC = 1 µg/mL); however, MFS-AN-P80 showed higher MIC and fungistatic effect (MIC = 50 - 400 µg/mL) because the nanoparticle promoted a slow and sustained release of MFS. Together, MFS-AN-P80 may be a potential therapy option against human and feline sporotrichosis.

# Development, characterization and cellular evaluation of the antitumoral activity of nanoemulsions O/W containing Andiroba oil and doxorubicin



## Author

Ana Luisa Magalhães - Universidade de Minas Gerais (UFMG)  
Nayara Santana Peixoto Mourana - Universidade de Minas Gerais (UFMG)  
Janaina de Alcântara Lemos - Universidade de Minas Gerais (UFMG)  
Bruna Beatriz Politi Gimenes - Universidade de Minas Gerais (UFMG)  
Eduardo Aguiar Ferreira de Paula - Universidade de Minas Gerais (UFMG)  
Juliana de Oliveira Silva - Universidade de Minas Gerais (UFMG)  
Lucas Antônio Miranda Ferreira - Universidade de Minas Gerais (UFMG)  
Sued Eustáquio Mendes Miranda - Centro de Desenvolvimento da Tecnologia Nuclear  
Marina Bicalho (Centro de Desenvolvimento da Tecnologia Nuclear)  
Anna Eliza Maciel de Faria Mota - Universidade Federal do Amapá (UNIFAP)  
André Luís Branco de Barros - Universidade de Minas Gerais (UFMG)



## Knowledge Area

Nanotechnology



## Funding

CAPES, FAPEMIG (APQ-01553-23), CNPq (404586/2021-0; 403054/2023-0)



## Keywords

Andiroba oil, Breast cancer, Nanoemulsion

## Abstract

Triple-negative breast cancer is a health world problem, with high incidence and mortality rate. Doxorubicin (DOX) is a relevant drug widely used in breast cancer therapy. However, this drug has considerable toxicity. Nanotechnology has been used to produce efficient drug delivery systems. Nanoemulsions are systems that are easy to produce and can incorporate natural products, contributing to disease treatment. Andiroba oil, a Brazilian naturally derived product, is largely known for its anti-inflammatory effects. Therefore, an Andiroba oil-based nanoemulsion loading DOX might be an effective strategy to achieve tumor growth suppression. In this scenario, a nanoemulsion O/W from Andiroba oil was produced by the high-energy emulsification method and characterized according to hydrodynamic diameter, polydispersity index, and zeta potential utilizing the Dynamic Light Scattering (DLS). Furthermore, the DOX encapsulation content was evaluated using UV-VIS Spectroscopy, and the DOX release profile was verified by High-Performance Liquid Chromatography (HPLC). The IC<sub>50</sub> was defined by cellular viability, which was acquired using 4T1 cellular lines. The nanoemulsion size was  $102.73 \pm 1.90$  nm, the polydispersity index was  $0.198 \pm 0.016$  and the zeta potential was  $-41.1 \pm 4.53$  mV. The doxorubicin encapsulation content was  $99.48 \pm 0.20$  % (w/w). The doxorubicin release in pH 7.4 was nearly 5% while in pH 5.0 reached about 50% after 24 hours. The IC<sub>50</sub> for the nanoemulsion was  $0.21 \pm 0.04$   $\mu$ M which was similar to the free drug. Therefore, the nanoemulsion prepared in this study showed a suitable size and encapsulation rate for biological assays. Additionally, the nanosystem presented a pH-responsive drug release which may enhance to the action of DOX in the tumor environment. The IC<sub>50</sub> in 4T1 cells demonstrated that DOX remains effective in killing tumor cells even after encapsulation, highlighting the system's capability to maintain doxorubicin's cytotoxic action.

# Preparation, characterization and cytotoxicity studies of Copaiba oil-based nanoemulsion loading doxorubicin



## Author

Nayara Moura - Universidade Federal de Minas Gerais(UFMG)  
Ana Luisa Pinto - Universidade Federal de Minas Gerais (UFMG)  
Janaina de Alcântara Lemos - Universidade Federal de Minas Gerais (UFMG)  
Eduardo Burgarelli Lages - Universidade Federal de Minas Gerais(UFMG)  
Juliana de Oliveira Silva - Universidade Federal de Minas Gerais(UFMG)  
Lucas Antônio Miranda - Universidade Federal de Minas Gerais (UFMG)  
Anna Eliza Maciel de Faria Mota Oliveira Universidade Federal do Amapá (UNIFAP)  
André Luis Branco de Barros - Universidade Federal de Minas Gerais(UFMG)



## Knowledge Area

Nanotechnology



## Funding

CAPES, FAPEMIG (APQ-01553-23), CNPq (404586/2021-0; 403054/2023-0)



## Keywords

doxorubicin, nanoemulsion, copaiba oil

## Abstract

Doxorubicin (DOX) is commonly used to treat breast cancer but is limited by severe cardiotoxicity. To reduce these side effects, research is exploring targeted drug delivery via nanosystems and the combination of DOX with anti-inflammatory natural compounds such as copaiba oil. These strategies aim to reduce toxicity to healthy tissues and enhance anticancer effectiveness, potentially improving the safety and efficacy of DOX therapy. As part of this approach, the development and characterization of copaiba oil-based nanoemulsions (NE) loaded with DOX are being pursued, along with the evaluation of their cytotoxicity against 4T1 tumor breast cells. NE were prepared using the hot homogenization method and characterized for average diameter, polydispersity index (PDI) and zeta potential. Encapsulation efficiency and in vitro drug release were determined by HPLC. Additionally, in vitro studies were conducted against 4T1 breast tumor cell lines. NE showed mean diameter of  $162 \pm 2,7$  nm, PDI of  $0,247 \pm 0,023$ , zeta potential of  $- 41 \pm 4$  mV, DOX encapsulation efficiency  $98,3 \pm 0,15$  %, and pH  $7,3 \pm 0,13$ . The NE exhibited pH-sensitive characteristics, showing a higher drug release at pH 5 compared to that obtained at pH 7.4. In vitro studies with NE showed low IC<sub>50</sub> (comparable to the free DOX) against 4T1 breast tumor cells ( $0,155 \pm 0,07$   $\mu$ M and  $0,198 \pm 0,07$   $\mu$ M, respectively). The developed copaiba oil-based NE demonstrated favorable characteristics for targeted drug delivery, including optimized size, low PDI, favorable zeta potential, high DOX encapsulation efficiency, and pH sensitivity. The NE showed promising pH-sensitive release profiles, with high drug release at tumor-like pH and minimal release at blood pH. In addition, low IC<sub>50</sub> obtained for NE indicate that the encapsulation of DOX does not compromise its effectiveness against breast tumor cells, supporting further studies on their potential to enhance the safety and efficacy of doxorubicin therapy for breast cancer.

# Cationic liposomes as carriers of the CRISPR/Cas system and in vivo assay in neonatal mice



## Author

Vinícius Monteagudo de Barros - Universidade Federal do Rio Grande do Sul (UFRGS)  
Melaine Maiara da Silva Lopes - Universidade Federal do Rio Grande do Sul (UFRGS)  
Eduarda Peres Couto - Universidade Federal do Rio Grande do Sul (UFRGS)  
Bruna Brazeiro Brum - Universidade Federal do Rio Grande do Sul (UFRGS)  
Edina Poletto - Universidade de Stanford  
Nathalya Tesch Brazil - Universidade Federal do Rio Grande do Sul (UFRGS)  
Bruna Medeiros-Neves - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ana Helena Paz - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ursula Matteu - Universidade Federal do Rio Grande do Sul (UFRGS)  
Flávia Nathiely Silveira Fachel - Universidade Federal do Rio Grande do Sul (UFRGS)  
Roberto Giugliani - Universidade Federal do Rio Grande do Sul (UFRGS)  
Helder Teixeira - Universidade Federal do Rio Grande do Sul (UFRGS)  
Guilherme Baldo - Universidade Federal do Rio Grande do Sul (UFRGS)  
Roselena Silvestri Schuh - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

National Council for Scientific and Technological Development (CNPq) (grant numbers 470888/2014-8 and 141742/2014-3) and FIPE/HCPA (grant number #20160482)



## Keywords

CRISPR/Cas; Genome editing; Liposomes

## Abstract

**Objective:** Investigate if the hydrodynamic administration of the CRISPR/Cas9 system complexed in cationic liposomes (CL) in neonatal mice results in off-target sites and/or induces tumor formation. **Methods:** The formulation was prepared from the CRISPR-Cas9 system plasmid and the IDUA donor gene, which transcribes the deficient enzyme of Mucopolysaccharidosis type 1 (MPSI). The CL was obtained through the film formation method, followed by hydration and microfluidization. The plasmids were incorporated into the formulation through adsorption, considering the negative charge of the phosphate groups of the DNA. The liposomes were characterized by the average droplet size (ADS) and zeta potential. Twelve C57BL/6 mice with MPSI were divided into two groups: 6 received the formulation hydrodynamically in the superficial temporal vein of the CL complex in one application, 6 received saline as control group. After 21 months, euthanasia was performed, and the lungs and liver were selected, removed, and subjected to molecular analysis. This analysis was conducted by qPCR, targeting the murine ROSA26 locus, using primers for each potential off-target region indicated in a silico test through the COSMID software, selecting chromosomes 2, 5, 11, 17, and X. The amplicons were sequenced using the Sanger method, and the sequences were subsequently submitted to the ICE tool for indels scoring and knockout possibilities. **Results:** The CL exhibited an ADS of approximately 133 nm and a zeta potential of around +43 mV. The lungs and liver were predominantly marked by the biodistribution of the CL complex, with no significant increase in tumor induction frequency (20%) compared to the control (33%). Molecular analyses showed 0% off-target sites for all proposed locations. **Conclusion:** The experiments provide a perspective on the safety of the CRISPR/Cas9 genome editing approach.

# Co-Nanoencapsulation Of An Innovative Organoselenium Compound And Paclitaxel Showed A Synergistic Antitumor Effect And Overcame Resistance Of Mdr Spheroids



## Author

Bruna Fracari do Nascimento - Universidade Federal de Santa Maria (UFSM)  
Daniela Mathes - Universidade Federal de Santa Maria (UFSM)  
Bianca Costa Maia - Universidade Federal de Santa Maria (UFSM)  
Luísa Fantoni Zano - Universidade Federal de Santa Maria (UFSM)  
Julliano Guerin Leal - Universidade Federal de Santa Maria (UFSM)  
Oscar Endrigo Dorneles Rodrigues - Universidade Federal de Santa Maria (UFSM)  
Clarice Madalena Bueno Rolim - Universidade Federal de Santa Maria (UFSM)  
Daniele Rubert Nogueira-Librelotto - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Nanotechnology



## Funding

CAPES and FAPERGS (Project 21/2551-0002067-9)



## Keywords

in vitro assays, tumor cells, bioactive compounds

## Abstract

**Background:** New approaches to increase the efficacy of antitumor therapy and strategies for overcoming multidrug resistance (MDR) are necessary. Given that, using nanotechnology-based drug delivery systems presents themselves as promising alternatives. **Objectives:** To evaluate the synergism of an innovative organoselenium, 5'-Seleno-(phenyl)-3'-(ferulic-amido)-thymidine (AFAT-Se), and the antitumor drug paclitaxel (PTX) co-encapsulated in poly( $\epsilon$ -caprolactone) (PCL) nanoparticles (NPs) against a resistant/MDR tumor cell line, using monolayer/two-dimensional (2D) and spheroid/three dimensional (3D) assays. **Methods:** The 2D and 3D assays were used to evaluate the in vitro antiproliferative and synergistic antitumor effect of NPs in NCI/ADR-RES cells (human ovarian cancer). In the 2D assay, the cells were seeded in 96-well plates and treated for 72 h. The results were expressed as percentage of cell viability. In the 3D assay, spheroids were obtained using the hanging drop method. The treatment lasted 12 days, and their size was measured and compared to the control. **Results:** The antiproliferative activity of the free compounds, their association in the free form, the co-loaded NPs, as well as the corresponding NPs without the co-loading, was initially verified by the 2D assay. It was found that the association of free compounds showed greater cytotoxicity than non-associated compounds. Also, the synergism was more prominently observed for the co-loaded nanoformulation. In the 3D assay, the co-delivery of AFAT-Se and PTX by the NPs showed the ability to inhibit 57.4% of spheroid growth, at the highest concentration. In comparison, the association of free bioagents reduced the size only by 38.7%. **Conclusions:** The co-delivery of the compounds by the PCL NPs showed an antiproliferative effect with synergistic results against MDR cancer cells. These findings evidence a promising nanoformulation with antitumor potential and as an alternative for overcoming the MDR effect.

# Stability evaluation of ferritin-based nanoparticle for EGFRvIII peptide delivery



## Author

Camila Machado França de Almeida Universidade de São Paulo (USP)  
Maria Vitória de Oliveira Couto(Universidade de São Paulo (USP)  
Fabiana Testa Moura de Carvalho Vicentini (Universidade de São Paulo (USP)



## Knowledge Area

Nanotechnology



## Funding

This work was supported by the CNPq #403588/2021-0. MVOC is recipient of PIBIC/CNPq fellows #123549/2023-0. CMFA was recipiente of FAPESP fellowship #2021/05482-0.



## Keywords

Stability study, Apoferritin nanoparticle, Peptide vaccine

## Abstract

Ferritin is a biologic nanoparticle with potential for drug delivery due to its natural nanocage structure which contributes to the function of molecular delivery [1]. The variant III of epidermal growth factor receptor (EGFRvIII) peptide was chosen to be encapsulated on a ferritin-based system. The peptide antigen is characterized by its cell proliferation and inhibition of apoptosis, being associated with tumorigenicity in several types of cancer [2,3]. In this study it was developed an apoferritin vaccine using the EGFRvIII peptide as antigen and it was evaluated the stability of this system, considering the peptide behavior by itself and associated with apoferritin. The peptide (with and without the apoferritin) was exposed to different temperatures (-20, 4 and 25 °C) during 21 days (with and without light) and cycles of freezing were evaluated and quantified with high pressure liquid chromatography. Besides, the vaccine formulation was characterized by dynamic light scattering, polyacrylamide gel electrophoresis and the protein quantified by Bradford assay. The result for the EGFRvIII peptide showed that its integrity is maintained for 4 days on 25 °C, 7 days on 4 °C and 21 days on -20 °C, with a maximum of 4 cycles of freezing without changing the initial concentration. The vaccine formulation stability, unlike peptide by itself, might endure more time in freezing conditions without alterations of the nanostructure. Finally, this study showed that the apoferritin vaccine was stable in the various established environments and offered more protection to EGFRvIII peptide.

HE, J.; FAN, K.; YAN, X. *Journal of Controlled Release*, v. 311, p. 288–300, 2019.

HUMPHREY, P. A. et al. *Proc. Nati. Acad. Sci.*, v. 87, p. 4207–4211, 1990.

CHEN, Y. et al. *Biomaterials Science*, v. 6, n. 5, p. 1120–1128, 2018.



# Polymeric nanocapsules for the cutaneous delivery of tacrolimus: A targeted approach for the treatment of psoriasis



## Author

Eduarda Cristina Jacobus Ferreira - Universidade Federal do Rio Grande do Sul (UFRGS)  
Graziela Scheuer Gomes - Universidade Federal do Rio Grande do Sul (UFRGS)  
Tainara Benin - Universidade Federal do Rio Grande do Sul (UFRGS)  
Victor de Mello Palma (Universidade Federal do Rio Grande do Sul (UFRGS)  
Aline de Cristo Soares Alves - Universidade Federal do Rio Grande do Sul (UFRGS)  
Fernanda Visioli - Universidade Federal do Rio Grande do Sul (UFRGS)  
Maria Serena Longhim - Harvard University  
Adriana Raffin Pohlmann - Universidade Federal do Rio Grande do Sul (UFRGS)  
Sílvia Stanisçuaski Guterres - Universidade Federal do Rio Grande do Sul (UFRGS)  
Luiza Abrahão Frank - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

CNPq (Grant # n°405865/2023-6, CAPES, FAPERGS. This research was carried out in the framework of the National Institute of Science and Technology in pharmaceutical Nanotechnology: a transdisciplinary approach INCT-NANOFARMA, which is supported by São Paulo



## Keywords

Nanotechnology, Tacrolimus, Pectin-based hydrogel

## Abstract

A novel nanotechnological pectin-based hydrogel (PEC-Nctac) containing tacrolimus-loaded nanocapsules (Nctac) has been developed for psoriasis treatment. The study evaluated physicochemical characteristics, safety profile (in vitro), effects on immune cells (in vitro), adhesiveness, permeation, and penetration (in vitro using porcine skin), irritation, and anti-inflammatory activity (ex vivo) in the HET-CAM model. In vitro, Nctac demonstrated nearly 100% cell viability (HaCat) at concentrations from 0.95 to 9.95 nmol.L<sup>-1</sup>. Additionally, Nctac treatment significantly reduced pro-inflammatory cytokine (IL-17A), indicating effective immune modulation. The reduction of IL-17A in CD4<sup>+</sup> T cells suggests that Nctac can more precisely and effectively disrupt the inflammatory pathways in psoriasis. Laser diffraction and scanning electron microscopy confirmed the presence of NC in the hydrogel. PEC-Nctac showed strong adhesion on healthy (73 mN.mm) and lesioned skin (251 mN.mm) and increased TAC penetration into the epidermis of lesioned skin (40.2%). PEC-Nctac exhibited a non-irritating profile in the HET-CAM/CAM-TBS test. Additionally, in the modified HET-CAM assay, PEC-Nctac demonstrated superior anti-inflammatory effects compared to free TAC (75.0% vs. 58%). This assay, bridging in vitro and in vivo testing, revealed that PEC-Nctac effectively normalized inflammation induced by SDS, aligning with histological analyses. The ex vivo results align with the in vitro CD4<sup>+</sup> cells evaluation. The enhanced anti-inflammatory effect observed with Nctac underscores the benefit of nanoencapsulation, which improves TAC delivery and efficacy. In conclusion, PEC-Nctac shows promising potential for psoriasis treatment due to its strong adhesion, drug penetration, safety profile, and enhanced anti-inflammatory activity.

# In vitro evaluation of nanotechnological formulations carrying the CRISPR-Cas9 system for the treatment of joint symptoms of mucopolysaccharidosis type I



## Author

Willian da Silva Carniel - Universidade Federal do Rio Grande do Sul (UFRGS)  
Leticia Jesus Hipólito De Souza - Universidade Federal do Rio Grande do Sul (UFRGS)  
Gabriela Fusinato de Oliveira - Universidade Federal do Rio Grande do Sul (UFRGS)  
Larissa Cristina Barbosa Flores - Universidade Federal do Rio Grande do Sul (UFRGS)  
Luísa Degrandi Sehn - Universidade Federal do Rio Grande do Sul (UFRGS)  
Patrícia Bencke Grudzinski - Hospital de Clínicas de Porto Alegre  
Melaine Maiara da Silva Lopes - Universidade Federal do Rio Grande do Sul (UFRGS)  
Guilherme Baldogbaldo - Hospital de Clínicas de Porto Alegre (UFRGS)  
Helder Teixeir - Universidade Federal do Rio Grande do Sul (UFRGS)  
Flávia Nathiely Silveira Fachel - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ursula Mattematte - Hospital das Clínicas de Porto Alegre  
Roselena Silvestri Schuh - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

CNPq/MCTI/FNDCT N. 18/2021 - Faixa A - Grupos Emergentes/ Processo n°: 403587/2021-2



## Keywords

nanoemulsion, mucopolysaccharidosis, CRISPR-Cas9

## Abstract

This study aims to evaluate the safety and transfection efficiency of nanoemulsions thickened with poloxamer 407 as co-carriers of dexamethasone, the CRISPR-Cas9 system plasmid and the IDUA gene sequence donor plasmid in fibroblast-like synoviocytes (FLS) of MPS I model mice. To evaluate the complexation of the plasmid to the nanostructure, electrophoresis was performed; visualization of the internalization of the formulations with fluorescence optical microscopy; evaluation of cell viability by MTT; evaluation of the irritant potential of the formulations by HET-CAM assay and evaluation of the transfection capacity determined by IDUA enzymatic activity. In view of the studies, efficient complexation of the plasmids to the formulations was observed because there was no migration of nucleic acids from the point of application of the nanoemulsion. The internalization of the formulations into the cells was evaluated at two moments, observing greater visualization of complexes after 4 hours of contact with the FLS than after 2 hours. MTT revealed high cell viability, above 75%, after 72 hours in contact with increasing concentrations of the formulation. The enzymatic activity of IDUA in FLS cultures in contact with nanoemulsion/pCas9/pIDUA complexes showed greater enzymatic activity (with poloxamer  $7.5\% \pm 2.5$  and without poloxamer  $5.6\% \pm 4.2$ ) than the groups of cells in contact with the free plasmids pIDUA or pIDUA/pCas9, respectively  $2.8\% \pm 0.6$  and  $4.0\% \pm 1.2$ . The HET-CAM safety trial indicated high tolerability and low irritant potential of the formulations, with the formulations without poloxamer 407 being non-irritating, the nanoemulsion with polymer being slightly irritating and the nanoemulsion with polymer associated with dexamethasone being moderately irritating. It is concluded that the nanoemulsions have a profile compatible with the route of administration and are shown to be safe and effective in in vitro tests, demonstrating their potential for use in vivo.

# Preformulation Of Nanoemulsions Targeted To Nose-To-Brain Administration Of Antifungals: An Initial Step



## Author

Larissa Eduarda Steil - Universidade Federal de Santa Maria (UFSM)  
Taís Baldissera Pietatais - Universidade Federal de Santa Maria(UFSM)  
Letícia Bueno Macedo - Universidade Federal de Santa Maria(UFSM)  
Clarice Madelena Bueno Rolim - Universidade Federal de Santa Maria (UFSM)  
Daniele Rubert Nogueira - Universidade Federal de Santa Maria(UFSM)



## Knowledge Area

Nanotechnology



## Funding

CNPq-PIBIC and FAPERGS (Project 21/2551-0002067-9)



## Keywords

in vitro assays, polymeric nanoparticles, berberis

## Abstract

**Background:** Glioblastoma multiform is the main cancer that affects brain tissue, classified as a grade IV tumor. Due to the poor prognosis, there is a need for new treatments for this disease. In this sense, natural compounds with antitumor properties, such as berberine, are being explored as an alternative for the treatment of glioblastoma. This compound has some properties such as cell protection, induction of apoptosis and autophagy, and suppression of angiogenesis and metastasis. However, it presents certain limitations due to its pharmacokinetic characteristics, requiring new strategies to overcome this problem, being the nanotechnology-based drug delivery systems a promising approach. **Objectives:** To develop nanoparticles (NPs) containing berberine and evaluate its in vitro antitumor activity using a glioblastoma cell line. **Methods:** The NPs were obtained by the nanoprecipitation method, using the polymer poly- $\epsilon$ -caprolactone (PCL) and, after the formulation optimization, it was characterized regarding their physicochemical properties. The human glioblastoma cell line U281 was used for the in vitro assays, and the cell viability was detected by the MTT endpoint. The biological safety of the NPs was estimated by the hemolysis assay. **Results:** The NPs showed suitable mean hydrodynamic size, polydispersity index (PDI), zeta potential and pH. Regarding the in vitro evaluations, it was observed that berberine nanoencapsulation increased its antitumor activity in a concentration-dependent manner, showing significant results at the highest tested concentration. Moreover, the NPs proved to be non-hemolytic, with hemolysis rates lower than 2%. **Conclusions:** The NPs proposed were successfully prepared, presenting adequate physicochemical parameters. In addition, the results showed that the berberine-loaded NPs have improved antitumor activity, indicating that encapsulating berberine in polymeric nanoparticles may be an alternative to enhance its antitumor potential.

# Incorporation of pDNA expressing the epidermal growth factor EGFRVIII into apoferritin/chitosan complexes as a melanoma treatment strategy



## Author

Natália Floriano Paiva - FMRP - Universidade de Sao Paulo (USP)  
Wendy Martin Rios - RBI-FMRP - Universidade de Sao Paulo (USP)  
Fabiana Testa Moura de Carvalho Vicentini - FMRP - Universidade de Sao Paulo (USP)



## Knowledge Area

Nanotechnology



## Funding

FAPESP (#2022/13379-7) and CAPES (#88887.713617/2022-00)



## Keywords

DNA plasmid, apoferritin/chitosan complex, melanoma treatment

## Abstract

Strategies based on nucleic acids combined with immunotherapy are promising alternatives to improve the therapeutic outcome of various tumors, even those at an advanced stage. DNA vaccines aim to use the host cell machinery to produce encoded protein antigens, stimulating humoral and cell-mediated immunity. The use of nanoparticles as delivery systems for nucleic acid vaccines is advantageous because it allows the protection of the nucleic acid against degradation, overcomes the barriers of cellular internalization, increases stability and there is also the possibility of delivery of several vaccine nucleic acids to the same target cell to improve the immune response activation. In this context, the present work aimed to evaluate the best condition for incorporating the DNA construction that expresses the variant III of the epidermal growth factor receptor (EGFRvIII) into apoferritin/chitosan complexes obtained by the Maillard reaction. For this, the following conditions were tested: (1) pDNA addition before the complex formation through disorganization of the apoferritin structure at acidic pH (close to 2.0) and subsequent return to neutral pH (between 6.5 and 8.0); (2) pDNA addition in the apoferritin solution; (3) pDNA addition before the dialysis step of the apoferritin/chitosan complex and (4) pDNA addition in the solution containing the already formed apoferritin/chitosan complex. The initial results demonstrated that for condition (1) there was a considerable increase in the particle size compared to the Apo/Ch complex alone. However, there was no significant change for the other conditions, with particle sizes in the 400 to 600 nm range. About the particle's surface charge, it showed positive values for all the conditions. So, the next steps include the pDNA quantification in a nano spectrophotometer and the evaluation of maintenance of the pDNA structure in agarose gel electrophoresis to select the best condition.

# Antifungal effect of terbinafine-loaded polymeric nanoparticles in the treatment of dermatophytosis



## Author

Sabrina Barros Cavalcante - Universidade de São Paulo (USP)  
Luciana B. Lopes - Universidade de São Paulo (USP)  
Kelly Ishida - Universidade de São Paulo (USP)



## Knowledge Area

Nanotechnology



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, finance code 001) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, 306041/2022-7), FAPESP (2018/13877-1)



## Keywords

Antifungal, mycosis, nanoparticle

## Abstract

Skin diseases affect at least one third of the world's population. Dermatophytes are highly infectious fungi that affect the skin, hair and nails and are commonly treated with oral or topical antifungals. However, the increasing fungal infections and high rates of therapeutic failure are growing concerns. In this study, we developed polymeric nanoparticles (NP) to cutaneous availability and reduce the frequency of administration of terbinafine in the treatment of dermatophytosis. The polycaprolactone polymeric nanoparticles (PCL) were obtained by the nanoprecipitation for the encapsulation of terbinafine (TRB). The average diameter, polydispersity, and zeta potential of empty (PCL) and TRB-loaded nanoparticles (PCL-TRB) were determined by dynamic light-scattering and encapsulation efficiency using High-performance liquid chromatography. The antifungal activity of NPs (PCL and PCL-TRB) and free TRB were tested by the broth microdilution method against *Trichophyton mentagrophytes* ATCC 9533. Toxicity was evaluated using a *Galleria mellonella* larval model. PCL-TRB showed nanometric size ( $199.2 \pm 0.6$ ), negative zeta potential ( $-17.4 \pm 1.4$  mV), low polydispersity ( $0.28 \pm 0.15$ ), high encapsulation efficiency ( $>98\%$ ), and stability for 60 days. Unloaded and PCL-TRB nanoparticles were considered safe due to the high health index rates and no deaths of *G. mellonella* larvae. TRB in PCL nanoparticles showed inhibitory activity and fungicidal effect on *T. mentagrophytes* at  $0.03 \mu\text{g/mL}$ . The drug in solution presented similar results, indicating that encapsulation did not impair the antifungal effect of TRB. These results demonstrate a promising nanocarrier system for the treatment of dermatophytosis, highlighting the possibility of a local and less invasive treatment. Terbinafine encapsulation in the polymeric nanocarrier can contribute to efficacy and lower frequency of administration.

# Development and application of multimodular nanoparticles for RNAi therapy of melanoma



## Author

Frederico Pittella Silva - Universidade Federal de Juiz de Fora (UFJF)  
Estael Luzia Coelho da Cruz-Cazarime - Universidade Federal de Juiz de Fora (UFJF)  
Kézia Cristine Barbosa Ferreira - Universidade Federal de Juiz de Fora (UFJF)  
Davi Trombini Aleixo - Universidade Federal de Juiz de Fora (UFJF)  
Ana Beatriz Caribé dos Santos Valle - Universidade Federal de Juiz de Fora (UFJF)  
Ilza Tenório Cavalcante Santos - Universidade Federal de Juiz de Fora (UFJF)  
Maurilio de Souza Cazarim - Universidade Federal de Juiz de Fora (UFJF)  
Virgílio de Carvalho dos Anjos - Universidade Federal de Juiz de Fora (UFJF)  
Maria José Valenzuela Bell - Universidade Federal de Juiz de Fora (UFJF)



## Knowledge Area

Nanotechnology



## Funding

Fundação de Amparo à Pesquisa do Estado de Minas Gerais, grant number RED-00053-21.



## Keywords

Melanoma; siRNA; VEGF.

## Abstract

Skin cancer is one of the most prevalent diseases in the world. Melanoma is the most serious due to its high potential to cause metastasis which has been attributed to the overexpression of vascular endothelial growth factor (VEGF). One of the main strategies for new therapeutic approaches involves the use of short interfering RNA (siRNA). However, it is necessary to protect and deliver such molecules into the target cells. Several studies have demonstrated that controlled delivery into the cytoplasm is possible through the use of transfection agents in vitro. In this context, the objective of this work was to develop, prepare, and apply nanocarriers containing siRNA for the topical treatment of melanoma. The target gene used for the design of the siRNA was VEGF-A (ID 22339), while multimodular nanoparticles (MN) were developed as carriers for this genetic material. The designed VEGF-A siRNA showed 100% complementarity to six variants of VEGF-A and an E value of 0.007. Further, the MN incorporating VEGF-A siRNA exhibited an average hydrodynamic diameter ( $146.32 \pm 4.14$  nm), Pdl ( $0.192 \pm 0.02$ ), Zeta potential ( $-12.68 \pm 1.11$  mV), and encapsulation efficiency ( $95.37 \pm 4.62$ %) suitable for topical application on the skin. During stability analysis ( $4^\circ\text{C}$ ), the system was stable (28 days) in terms of size and Pdl. The FT-IR spectrum demonstrated a high presence of water ( $\sim 3327$  and  $\sim 1636$   $\text{cm}^{-1}$ ), indicating the need for lyophilization of the sample for further analysis. The Raman spectrum showed expected and characteristic vibrations of the system with prominent peaks at  $\sim 1060$   $\text{cm}^{-1}$  ( $\text{CaCO}_3$ ),  $\sim 1296$   $\text{cm}^{-1}$  (lipid), and  $\sim 1439$   $\text{cm}^{-1}$  (Pluronic® F127). In cell viability assays using MTT (24 and 48 hours), MN-Blank, scrambled siRNA, and free siRNA did not exhibit cytotoxicity for either of the two cell lines investigated (B16F10 and L-929). The developed system has characteristics suitable for topical application on the skin and demonstrates potential for further study.

# Thermosensitive hydrogel for nasal delivery of paclitaxel to treat brain tumor



## Author

Anna Carolina da Silva Sousa - Universidade Federal de Minas Gerais (UFMG)  
Caroline Mari Ramos Oda - Universidade Federal de Minas Gerais (UFMG)  
André Luís Branco de Barros - Universidade Federal de Minas Gerais (UFMG)  
Elaine Amaral Leite - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Nanotechnology



## Funding

FAPEMIG (APQ-02203-23), CNPq e CAPES



## Keywords

glioblastoma multiforme, hybrid nanoparticle, thermosensitive hydrogel

## Abstract

Brain tumors pose significant challenges due to their location and the blood-brain barrier (BBB), which limits drug delivery. Traditional treatments struggle to reach therapeutic levels in the brain, leading to suboptimal outcomes. Intranasal administration is a non-invasive route capable of bypassing the BBB for drug delivery to the brain and eliminating systemic side effects. This study aimed to prepare a paclitaxel-loaded hybrid nanoparticle (PHN) and incorporate it in thermosensitive hydrogel with suitable characteristics for nose-to-brain delivery. In order to define optimized conditions for the production of PHN, different lipid and polymer ratios and surfactant concentrations were used. The PHN was developed using the nanoprecipitation method followed by solvent evaporation. Results showed that the PHN average diameter was below 200 nm (varying from 140 to 180 nm), narrow particle size distribution (PDI < 0.3), negative zeta potential (varying from -30.0 to -20.0 mV) and pH around 6.0. The average encapsulation efficiency obtained for the most promising formulation was 60%. Besides, thermosensitive hydrogel formulations composed of different polymers and concentrations were evaluated using the cold solubilization method. The formulation with a gelation time lower than 5 minutes was selected for PHN incorporation. After incorporation, the formulations showed rapid gelation (130-148 s) at 34 °C and (35-41 s) at 37 °C, within the human nasal cavity temperature spectrum. Droplet size distribution profiles led to Dv50 value compatible with nasal spray products. The results from this study are promising, suggesting that the developed formulation can potentially carrier paclitaxel to intranasal applications focusing on brain tumor treatment.

# Incorporation of neomycin into polymeric nanoparticles for topical administration: a new method for aminoglycoside delivery.



## Author

Josué Guilherme Lisboa Moura - Universidade Federal do Rio Grande do Sul (UFRGS)  
Flávia Pires Peña Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA)  
Diego Fontana de Andrade - Universidade Federal do Rio Grande do Sul (UFRGS)  
Tanira Alessandra S. Aguirre - Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA)  
Karina Paese - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ); Processo: 407233/2021-0



## Keywords

Nanoantibiotics, pH-dependent, methacrylate

## Abstract

Aminoglycosides are highly potent antibacterials effective against both Gram-positive and Gram-negative bacteria. However, their high water solubility and near insolubility in organic solvents present challenges for the development of advanced pharmaceutical forms such as nanotechnology. The aim of this study was develop and characterize polymeric nanoparticles using neomycin sulfate (NEO) as a model aminoglycoside. Polymeric nanoparticles were prepared using the pH jump method in 3 phases: (1) babassu oil, sorbitan monooleate, and ethanol; (2) Eudragit® L30-D55 in pH 7.0 phosphate buffer with NEO; (3) polysorbate 80 in pH 1.4 phosphate buffer. The resulting suspension was concentrated to 0.5 mg/mL (NanoNeo) and control formulations without drug (NBlank) using a rotary evaporator. Particle size was characterized by laser diffraction (LD) and photon correlation spectroscopy (PCS), while zeta potential was measured by electrophoretic mobility. Drug quantification was performed by LC-MS/MS. Encapsulation efficiency was determined by centrifugation-ultrafiltration (10 kDa cutoff). The volume-weighted mean diameter ( $D[4,3]$ ) determined using LD was  $129 \pm 2$  nm (Span  $0.832 \pm 0.04$ ) for NBlank and  $129 \pm 4$  nm (Span  $0.899 \pm 0.01$ ) for NanoNeo. The z-average size determined by PCS was  $125 \pm 16$  nm for NanoNeo and  $129 \pm 2$  nm for NBlank. The zeta potential for NanoNeo was  $-2.67 \pm 0.62$  mV, while for NBlank, it measured  $-1.67 \pm 0.12$  mV, in pH  $2.3 \pm 0.03$ . Drug content was determined to be  $0.545 \pm 0.080$  mg/mL, with  $42.0 \pm 3.6\%$  of the drug associated with the nanoparticles. We have developed nanoparticles used significantly less organic solvent than usual methods and incorporated an oil from Brazilian biodiversity (babassu oil), which not only contributes to its antioxidant activity but also served as a structuring material for the system. This study demonstrated that it is possible to obtain polymeric nanoparticles containing aminoglycosides, aimed at human and veterinary topical use.



# Fipronil-Loaded Nanocapsules: Preparation And Physicochemical Characterization



## Author

Izabel Quevedo Cunha Koehler (Universidade Federal de Santa Maria (UFSM))  
Tielle Moraes de Almeida (Universidade Federal de Santa Maria (UFSM))  
Kathiane Baumann Kudrna (Universidade Federal de Santa Maria (UFSM))  
Igor Roesch Felix - Universidade Federal de Santa Maria (UFSM)  
Yara Peluso Cid - Universidade Federal do Rio de Janeiro (UFRJ)  
Diego Fontana de Andrade - Universidade Federal do Rio de Janeiro (UFRJ)  
Cristiane de Bona da Silva (Universidade Federal de Santa Maria (UFSM))



## Knowledge Area

Nanotechnology



## Funding

The researchers thank INCT 3D-Saúde, CNPq and CAPES.



## Keywords

Fipronil, Veterinary, Nanotechnology

## Abstract

Fipronil (FIP) is used as a veterinary drug for treating ectoparasites. Typically administered topically, this route presents issues due to exposure of humans to residual FIP. Consequently, oral dosages are safer for owners, offering greater stability and efficiency. The pharmacokinetic properties of FIP can be enhanced by association with nanocarriers, providing photoprotection and controlled release, thus permitting the use of smaller, spaced dosages. The aim of this work was to produce fipronil-loaded nanocapsules (NC-F), using polycaprolactone (PCL), for future combination with oral pharmaceutical dosage forms for the veterinary treatment of ectoparasites. NC-F (3 mg/mL) were prepared by nanoprecipitation method, along with blank NC (NC-B) for comparative purposes. Both types of nanocapsules were characterized by measuring droplet size, zeta potential, pH, FIP content, and encapsulation efficiency. The nanocarriers demonstrated physical-chemical characteristics suitable for colloidal systems, with content close to the theoretical 100%. NC-F exhibited a size of 183 nm, while NC-B measured 181 nm, both with a polydispersity index <0.1. The zeta potential was -5.2 mV for NC-F and -10.7 mV for NC-B. Additionally, NC-F showed a FIP content percentage of  $100.9 \pm 1.2\%$ , within a pH range of  $4.8 \pm 0.2$ , whereas NC-B maintained a pH range of  $5.7 \pm 0.3$ . The encapsulation efficiency was  $99 \pm 0.6\%$ . The results confirm the viability of obtaining NC-F, which demonstrated satisfactory physical-chemical characteristics and indicated their potential applicability in future oral pharmaceutical formulations for the treatment of ectoparasites in animals.

# Evaluation of the Required Hydrophilic-Lipophilic Balance of Moringa oil using Design of Experiments



## Author

Mariana Maressa Ferreira de Medeiros - Universidade Federal do Rio Grande do Norte (UFRN)  
Wallacy Silva de Lima - Universidade Federal do Rio Grande do Norte (UFRN)  
Hericles Afonso de Carvalho Couto - Universidade Federal do Rio Grande do Norte(UFRGS)  
Daniel Torres Pereira - Universidade Federal do Rio Grande do Norte (UFRN)  
Sabrina Ribeiro Roque - Universidade Federal do Rio Grande do Norte (UFRN)  
Emerson José de Jesus Santana - Universidade Federal do Rio Grande do Norte (UFRN)  
Wógenes Nunes de Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Eryvaldo Sócrates Tabosa do Egito(Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Nanotechnology



## Funding

This research was funded by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível superior - Brasil (CAPES) - Finance code 001



## Keywords

Moringa oilifera oil, Emulsion, Hydrophilic-Lipophilic Balance

## Abstract

Moringa oleífera seed oil (MO) contains fatty acids with remarkable anti-inflammatory properties. However, its direct use is hindered by undesirable features. Emulsified (EM) systems, composed of water, oil and surfactants, can overcome these limitations. For effective EM production, the required Hydrophilic-Lipophilic Balance (rHLB) of the oil must match the HLB of the surfactants. The aim of this study was to determine the rHLB of MO using a Design of Experiments (DoE) approach. Design Expert® software facilitated the creation of a mixture design to produce 21 EMs with HLB values ranging from 4.3 to 16.7. Briefly, the oil phase (MO + mix of Tween® 20 and Span® 80) and the water phase (purified water) were separately homogenized and heated to 50 °C. The water phase was added dropwise to the oil phase, and the mixture was homogenized for 10 min. After 24 hours, the EMs were centrifuged for 5 min at 1452 RCF for evaluate the cream rate (Cr). The transmittance (TE) was also analyzed by spectrophotometry. The Cr varied from 5 % ± 0.009 to 67 % ± 0.015 and TE between 0 and 3.5 ± 0.346. ANOVA confirmed the significance of Cr and TE in determining rHLB. The R<sup>2</sup> values of 0.95 for Cr and 0.79 for TE, along with p-values ≤ 0.05, indicated that both models significantly contributed to the rHLB evaluation. The EMs with the lowest Cr and TE values were identified as matching the rHLB for MO. The EM containing 34.6% Span® 80, 65.4% Tween® 20, 5% MO with an rHLB of 12.41 and desirability of 83.0%, was selected due to its low predicted Cr (9% ± 3) and TE (0.3 % ± 0.4). A triplicate of this EM was produced and characterized to compare experimental values to those predicted by the DoE. The observed Cr of 5% ± 0.009 and 0% TE confirmed that the experimental values aligned with the theoretical ones. Therefore, the DoE approach was suitable for determining the rHLB of MO (12.41) and for the subsequent production of EMs for MO delivery.

# Development and characterization of propranolol-loaded Eudragit RL® nanocapsules with wound healing purposes



## Author

Naomi Gerzvolff - Universidade Federal do Paraná (UFPR)  
Soraia de Oliveira Simiao - Universidade Federal do Paraná (UFPR)  
Raul Edson Luna Lazo - Universidade Federal do Paraná (UFPR)  
Luana Mota Ferreira - Universidade Federal do Paraná (UFPR)  
Jéssica Brandão Reolon - Universidade Estadual do Centro Oeste (UNICENTRO)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Nanotechnology



## Funding



## Keywords

propranolol, nanocapsules, Development and characterization

## Abstract

Anti-hypertensive drugs such as propranolol have been studied for their healing properties in skin wounds. Propranolol is a nonselective  $\beta$ -adrenergic blocker, mainly used in the management of hypertension. Its oral absorption is rapid and complete, presenting a short half-life time, in which nearly 25% of the drug reaches systemic circulation due to high first-pass metabolism and crosses the blood-brain barrier. The incorporation of propranolol into nanosized systems protects the drug from degradation, increases the half-life, prolongs the release, and enhances bioavailability. Aiming to utilize propranolol as a drug-repurposing option for treating skin wounds, incorporating it into nanocapsules can enhance the permeation of the drug into the skin, thereby increasing its effectiveness. Given the above, this study aims to incorporate propranolol in nanocapsules and characterize the suspensions regarding particle size, polydispersity index (PDI), zeta potential, pH, and drug content. The nanocapsules were prepared using the interfacial deposition of the preformed polymer technique, using Eudragit RL® as the polymer and avocado oil as the oily core. The mean particle size and PDI were evaluated using the dynamic light scattering technique, and the values obtained were  $158 \pm 4$  nm and  $0.158 \pm 0.020$ , respectively. The zeta potential, obtained by the electrophoretic mobility, was positive ( $43.5 \pm 2.4$  mV), due to the cationic characteristic of the polymer. The pH was determined directly in the nanocapsule suspensions, where acid values were observed  $4.2 \pm 0.1$ . For drug content, High-Performance Liquid Chromatography with a Diode Array Detector (HPLC-DAD) was used. The content of propranolol in nanocapsules was  $80.88 \pm 0.12\%$ , which could be indicative of losses or degradation. In conclusion, despite the preliminary results, the formulation demonstrates the feasibility of allowing future experiments in its applications and effects on skin wounds.

# Association With Nanoparticles Protects Caffeic And Ferulic Acids From Photoisomerization



## Author

Igor Roesch Felix - Universidade Federal de Santa Maria (UFSM)  
Gabriela Wink Stringhini - Universidade Federal de Santa Maria (UFSM)  
Eduarda Biasuz - Universidade Federal de Santa Maria (UFSM)  
Beatriz Miguel Giovane - Universidade Federal de Santa Maria (UFSM)  
Clarissa Piccinin Frizzo - Universidade Federal de Santa Maria (UFSM)  
Alisson Vasques Pazalisson - Universidade Federal de Santa Maria (UFSM)  
Scheila Rezende Schaffazick - Universidade Federal de Santa Maria (UFSM)  
Cristiane de Bona da Silva - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Nanotechnology



## Funding

CAPES (Finance Code 001) and CNPq



## Keywords

Photoisomerization, Phenolic compounds, Nanoparticles

## Abstract

Background: Phenolic compounds like ferulic (FA) and caffeic (CA) acids are renowned for their pharmacological activities, including anti-inflammatory and antioxidant effects. However, their stability and therapeutic efficacy are impacted by physicochemical characteristics. Incorporating these compounds into nanostructured systems offers a potential solution. Objectives: The aim of this study was to evaluate the handling of phenolic bioactives coencapsulated in Eudragit® RL100 nanospheres against UVA radiation. Methods: A photostability test used a UVA lamp in a mirror chamber. A 0.5 mg/mL aliquot of nanospheres (NsCF) and their respective solution (SolCF) were exposed to light at intervals to assess CA and FA degradation. Light-protected controls were used for comparison. An HPLC validated method to quantify simultaneously the active ingredients was used. The atomic mass of the degradation products was analyzed by LC-MS/MS, in negative ion mode. Results: Exposure to radiation generated two chromatographic peaks, the absorption spectra in the UV range of both products were obtained with the HPLC diode array detector and were analogous to those described for cis-CA and cis-FA. The mass values obtained in LC-MS-MS analysis, confirmed that the reaction that occurred was photoisomerization. The half times calculated for CA and FA respectively were 1.81h and 1.17h in NsCF and 0.70h and 0.94h in SolCF. The degradation constant (k) was also evaluated, and the reactions follows a second order kinetic. Conclusions: Photostability tests show phenolic compounds benefit from nanospheres because the coencapsulation improves stability. UV protection is important to these phenolic compounds because isomerization reduces their activity.

Acknowledgement: The researchers thank CNPq and CAPES

# The Effects of PEGylation on the Development and In Vitro Transfection Efficiency of Ionizable Lipid Nanoparticles for pDNA Delivery



## Author

Gabriel Vieira Azevedo - Universidade Federal de Minas Gerais (UFMG)  
Pedro Henrique Dias Moura Prazeres - Universidade Federal de Minas Gerais (UFMG)  
Marco Túllio Rodrigues Alves - Universidade Federal de Minas Gerais (UFMG)  
Sérgio Ricardo Aluotto Scalzo Júnior - Universidade Federal de Minas Gerais (UFMG)  
Pedro Pires Goulart Guimarães - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Nanotechnology



## Funding

Ministério da Ciência, Tecnologia e Inovação (MCTI) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq)



## Keywords

Lipid nanoparticles, pDNA delivery, PEG-lipid

## Abstract

Ionizable lipid nanoparticles (LNPs) have emerged as a versatile tool for nucleic acid delivery. Traditionally, LNPs consist of four lipids: an ionizable lipid, a helper lipid, cholesterol and a polyethylene glycol (PEG)-lipid conjugate. Together, they encapsulate the nucleic acid, protecting it from degradation and promoting delivery into cells. However, even with the great success of messenger RNA (mRNA) vaccines, the impact of different LNP compositions on physicochemical parameters and transfection efficacy can still be further explored. In this study we focus on how PEG impacts these characteristics of LNPs encapsulating plasmid DNA (pDNA). LNPs were synthesized by microfluidic mixing, combining an aqueous phase containing pDNA encoding for green fluorescent protein and an ethanolic phase containing the lipid mix. Variations in molar ratios and PEG type were explored. Hydrodynamic size, zeta potential, and polydispersity index of the LNPs were measured by dynamic light scattering technique. Apparent pKa was determined using the TNS assay and encapsulation efficiency (EE) was evaluated using Qubit. To assess in vitro transfection and cytotoxicity of the LNPs, L929 cells were plated in a 96-well plate (5.000 cells/well) and treated with 0.2  $\mu\text{g}$  of pDNA. After 72 hours, fluorescence images were captured and cell viability was assessed using alamarBlue. Fluorescence intensity of images was quantified using a Python script. The hydrodynamic size of the LNPs varied between 89.3 and 216.5 nm, demonstrating that higher PEG ratios yield in smaller LNPs. Apparent pKa ranged from 6.5 to 7.2, suggesting strong ionizability at endosomal pH for all formulations, while lower PEG ratio increased EE. In vitro, C14PEG2000 containing LNPs showed higher transfection. Our data demonstrate that PEG can modulate physicochemical properties of LNPs and affect their transfection capacity. Future experiments will explore these effects on mRNA delivery both in vitro and in vivo.

# Initial stability studies of formulations containing apoferritin and the apoferritin/chitosan complex regarding the physicochemical characteristics of particle size and zeta potential.



## Author

Isabela Pimenta Domingos - FCFRP - Universidade de São Paulo (USP)

Natália Floriano Paiva - FCFRP - Universidade de São Paulo (USP)

Fabiana Testa Moura de Carvalho Vicentini - FCFRP - Universidade de São Paulo (USP)



## Knowledge Area

Nanotechnology



## Funding

This work was supported by grant from Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2022/13379-7). I.P.D. is recipient of FAPESP (FAPESP #2024/00575- 8).



## Keywords

Apoferitin/Chitosan complex, Stability study, Maillard reaction

## Abstract

Apoferitin is an abundant protein in the human body, capable of encapsulating and carrying other molecules. Thus, its application in gene vaccine delivery presents as an attractive proposal in the field of vaccinology, as it promises greater formulation stability compared to conventional methods. However, despite its potential as a delivery system, the process of cell transfection is a challenge since these nanoparticles have a negative surface charge. To overcome this limitation, our studies propose to bind this protein to positively charged polysaccharides, such as chitosan, through the Maillard reaction. Thereby, the binding of cationic groups of this molecule with anionic groups of apoferritin allows the formation of complexes with favorable physicochemical and functional properties for encapsulation, emerging as a promising alternative to produce gene vaccine carrier systems. In this context, it is known that stability studies are essential in pharmaceutical formulations development, so this work aimed to evaluate the stability of apoferritin/chitosan complexes at a 1:6 ratio as an essential study step to the application of this formulation. So far, the initial stability studies were conducted by evaluating apoferritin solution at 0.23 mg/mL in Tris-HCl buffer and Apo/Ch complex by Dynamic Light Scattering (DLS) for the determination of particle size and zeta potential, up to 15 days after their preparation. Initial results indicated that formulations containing the Apo/Ch complex are more stable in size compared to solutions containing apoferritin and apoferritin/chitosan without the Maillard reaction. The Apo/Ch complex showed a size of approximately 450 nm and a zeta potential of -0.205 mV, with no significant variations over 15 days. Therefore, there are indications that obtaining the complex may be a promising alternative to achieve desirable reproducible pharmaceutical characteristics.

# 3D printed skin delivery films: permeation/penetration behavior of two nanoencapsulated polyphenols



## Author

Thayse Viana de Oliveira - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ana Paula Farias Leão - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ruy C. R. Beck - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

FAPERGS/Brazil, CAPES/Brazil (Finance Code 001) and CNPq/Brazil. This study is part of the INCT \_3D-Saúde, funded by CNPq, Brazil (Grant #406436/2022-3).



## Keywords

3D printing, nanotechnology, polyphenols

## Abstract

**Introduction:** Semisolid extrusion (SSE) is a 3D printing technique used to produce personalized medicines. In this work, polymeric films containing different nanoencapsulated polyphenols were produced by SSE to evaluate the effect of nanoencapsulation and the type of polyphenol on their skin permeation/penetration behavior. **Methods:** Curcumin or resveratrol-loaded nanocapsules (C-NC and R-NC, respectively) were produced, characterized, and subsequently used to produce 3D printed films for skin delivery (n=3). Four films were produced using a polymeric blend composed of carbopol and pectin (65:35 w/w) as printing ink: containing C-NC (F-C-NC), R-NC (F-R-NC), non-encapsulated curcumin (F-C-S), or non-encapsulated resveratrol (F-R-S). Physical and physicochemical characterization of the films was carried out, followed by in vitro permeation/penetration studies using intact or injured porcine skin models. **Results:** C-NC and R-NC had mean diameters of  $217.56 \pm 5.32$  nm and  $244.00 \pm 3.46$  nm, respectively, with nearly 100% encapsulation efficiency. The mean polyphenol content of the 3D printed films ranged between 290 and 400  $\mu\text{g}/\text{film}$ . Curcumin penetrated the skin layers in both skin conditions, regardless of the film formulation. However, resveratrol behaved differently, reaching higher amounts in the intact skin layers from F-R-S than F-R-NC ( $p \leq 0.05$ ). The opposite was found in tests carried out on injured skin ( $p \leq 0.05$ ). Curcumin did not permeate across the skin, regardless of the skin conditions and film content. After 24 hours, F-R-S reached different amounts in the receptor compartment:  $3.37 \pm 0.01$   $\mu\text{g}$  (injured skin) and  $6.86 \pm 0.92$   $\mu\text{g}$  (intact skin) ( $p \leq 0.05$ ). **Conclusion:** 3D printed films containing nanoencapsulated polyphenols were produced by semisolid extrusion, showing that nanoencapsulation promotes the skin penetration of resveratrol in injured skin and reduces the chance of systemic absorption.

# Development and characterization of polymeric nanocapsules containing natural butter as lipid core.



## Author

Scheila Lopes dos Santos - Universidade Federal do Rio Grande do Sul (UFRGS)  
Daniela Lana Schmitt - Universidade Federal do Rio Grande do Sul (UFRGS)  
Karina Paese - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

CNPQ



## Keywords

Lipid polymeric nanocapsules, natural butter, Eudragit® RS100

## Abstract

Lipid polymeric nanocapsules (LNPs) are nanostructures with a lipid core surrounded by a polymeric shell that can be administered through various routes, including topical application, which gained popularity in recent years for the treatment of skin diseases and skincare. Synthetic or natural lipids can be used, where natural lipids can serve both structural and functional purposes. Natural butters, such as mango, avocado, murumuru, bacuri, and cupuaçu are known for their beneficial properties in skin health maintenance due to the presence of fatty acids that play a crucial role in maintaining skin barrier function, reducing transepidermal water loss, and exerting anti-inflammatory effects. The aim of this study was to prepare and characterize LNPs containing natural butters as lipid core and evaluate the influence of two different polymers. Polymeric nanocapsules suspensions were prepared by interfacial deposition of preformed polymer. The organic phase was composed of Eudragit® RS100 or poli(caprolactone) (PCL) 14k and natural butter dissolved in acetone, while the aqueous phase was composed of polysorbate 80 and water. The formulations showed homogeneous aspect. The D[4,3] and Span values ranged from  $131\pm 2$  to  $180\pm 19$  nm and  $1.19\pm 0.06$  to  $2.09\pm 0.06$  for Eudragit® RS100, and from  $135\pm 2$  to  $568\pm 162$  nm and  $0.85\pm 0.03$  to  $2.05\pm 0.00$  for PCL 14k. The zeta potential was positive for Eudragit® RS100, approximately  $+4.42$  mV, and negative for PCL 14k, around  $-6.82$ . The pH was similar with both polymers, ranging between 4.3 and 5.8. Both polymers are suitable for topical application, with Eudragit® RS100 showing superior performance due to its smaller diameter and positive zeta potential, making it more suitable for topical use. Therefore, the results demonstrate the promising use of natural butters as lipid core in the preparation of LNPs for topical application.



# Optimization Of Cinnamon Essential Oil Nanoemulsion Using Box-Behnken Design



## Author

Juliana Mesadri - Universidade Federal de Santa Maria (UFSM)  
Laísa Pes Nascimento - Universidade Federal de Santa Maria (UFSM)  
Pedro Pause de Jesus (Universidade Federal de Santa Maria (UFSM)  
Roger Wagne - Universidade Federal de Santa Maria (UFSM)  
Vítoria Hagemann Cauduro - Universidade Federal de Santa Maria (UFSM)  
Érico Marlon de Moraes Flores - Universidade Federal de Santa Maria (UFSM)  
Cristiane de Bona da Silva - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Nanotechnology



## Funding

CAPES/Brazil and CNPq/Brazil.



## Keywords

Nanoemulsion, Response Surface Methodology, Ultrasonication

## Abstract

Cinnamon essential oil is known for its pharmacological properties, such as antimicrobial, antioxidant, anti-inflammatory and healing. However, its use in pharmaceutical formulations is limited by low solubility, reduced stability and vulnerability to oxidative degradation. Encapsulating these oils in nanoemulsions is an efficient solution to enhance their stability and biological activity. To prevent destabilization, such as Ostwald ripening, insoluble oils can be added to the organic phase. In this study, the response surface methodology (RSM) of Box-Behnken design (BBD) was used to optimize three independent factors in the production of nanoemulsions, aiming for appropriate droplet size and monodisperse distribution. The aqueous phase consisted of ultrapure water and Tween 80, while the organic phase included microalgae oil (2%), cinnamon essential oil (0.5%), and Span 80. The nanoemulsions were produced by high-speed homogenization followed by sonication using a probe at 20 kHz and nominal power of 750 W (13 mm tip and length of 254 mm, Sonics and Material Inc, USA). The influence of sonication time (1-5 min), ultrasound amplitude (20-70%), and surfactant concentration (9:1) (1.2-2%) were investigated. The BBD matrix included fifteen points, with three central points, showing various combinations of the independent factors. The average droplet size ranged from 80 to 170 nm, and the PDI ranged from 0.1 to 0.4. Variance analysis indicated that all variables and interactions were statistically significant (quadratic model  $p < 0.05$  and  $r > 0.99$ ). RSM analysis identified the optimal condition: sonication time of 3 min, probe amplitude of 45%, and surfactant concentration of 1.6%, producing an optimal nanoemulsion with a droplet size of 88.9 nm and a  $PDI < 0.2$ . This formulation results in a uniform particle size distribution and reduced sizes and optimizes energy consumption by reducing sonication time and amplitude.

# In Vitro Skin Permeation/Penetration Evaluation Of A Hydrogel Containing Tioconazole Nanocapsules Under Different Dosage Regimens



## Author

Euarda Biasuz - Universidade Federal de Santa Maria (UFSM)  
Igor Roesch Félix - Universidade Federal de Santa Maria (UFSM)  
Tielle Moraes de Almeida - Universidade Federal de Santa Maria (UFSM)  
Juliana Mesadri - Universidade Federal de Santa Maria (UFSM)  
Euarda Oliveira Wagner - Universidade Federal de Santa Maria (UFSM)  
Cristiane de Bona da Silva - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Nanotechnology



## Funding

Acknowledgement: The authors thank CAPES/Brazil, CNPq/Brazil and São Bento slaughterhouse (Lajeado, Brazil).



## Keywords

Permeation, infinite dosage, finite dosage

## Abstract

The skin is the largest organ in the human body, which is divided into three layers: epidermis, dermis and hypodermis. Permeation/penetration studies aim to assess the ability of an active ingredient to reach these layers. Penetration, usually with finite dosage, provides data on the total amount of active ingredient in the skin; permeation, usually with infinite dosage, leads to data on pharmacokinetic parameters. and permeation, usually with infinite dosage, leads to data on pharmacokinetic parameters. Analyses of both configurations are important to verify the possibility of correlation and obtain information on the data mentioned above. Therefore, the aim of this study was to evaluate the in vitro permeation/penetration of tioconazole (TIO)-loaded nanocapsules incorporated into a Aristoflex® AVC hydrogel, using a finite and infinite dose regime. Nanocapsules (1.0 mg/mL) were prepared by interfacial deposition of the pre-formed polymer. To obtain the semisolid formulations, the polymer was added to the dispersion, followed by moderate stirring (HG-TIO-NC). A hydrogel containing free TIO (non-encapsulated) was also prepared (HG-TIO). The in vitro study was carried out using Franz diffusion cells and porcine skin. The infinite dose was set at 0.5 g and the finite dose at 0.0283 g based on the diffusion area. After 8 h, the excess of formulation was removed with cotton, the skin was separated into layers, aliquots of the receptor medium were collected and the amount of TIO of the samples was quantified by HPLC-UV-DAD. The results showed a greater amount of TIO in the stratum corneum both at the finite dose (48.3  $\mu\text{g}/\text{cm}^2$  and 77.1  $\mu\text{g}/\text{cm}^2$  for HG-TIO-NC and HG-TIO, respectively) and at the infinite dose (7.0  $\mu\text{g}/\text{cm}^2$  and 18.0  $\mu\text{g}/\text{cm}^2$  for HG-TIO-NC and HG-TIO, respectively). These data may indicate that the application of excessive doses of the formulation can lead to saturation of the drug at the site, making it difficult for the drug to diffuse through the skin.

# Development and Characterization of an Ivermectin Microemulsion for Enhanced Delivery in Dogs



## Author

Sabrina Ribeiro Roque - Universidade Federal do Rio grande do Norte (UFRN)  
Ícaro Chaves Girão - Universidade Federal do Rio Grande do Norte (UFRN)  
Hericles Afonso de Carvalho Couto - Universidade Federal do Rio Grande do Norte (UFRN)  
Yasmin Ferreira da Cruz - Universidade Federal do Rio Grande do Norte (UFRN)  
Mariana Maressa Ferreira de Medeiros - Universidade Federal do Rio Grande do Norte (UFRN)  
Júlio Abreu Miranda - Universidade federal dop Rio Grande do Norte (UFRN)  
Wógenes Nunes de Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Eryvaldo Sócrates Tabosa do Egito - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Nanotechnology



## Funding

This research was funded by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível superior—Brazil (CAPES)—Finance code 001.



## Keywords

Ivermectin, microemulsion, linseed oil.

## Abstract

Ivermectin (IVM) is a widely used antiparasitic drug, valued for its broad-spectrum efficacy and low cost. However, current IVM dosage forms present challenges, such as difficulties in administration in animals and limited skin permeation. The aim of this study was to develop a microemulsion system (IVM-MeLO) for the delivery of IVM to treat parasitic infections in dogs. The IVM-MeLO was prepared by homogenizing the organic phase (linseed oil, Kolliphor® RH40, Span® 80, and IVM) and the aqueous phase (purified water), separately, by magnetic stirring at 1000 rpm and 40 °C for 10 minutes. The aqueous phase was then added dropwise to the organic phase, followed by ultrasonication for 1.5 minutes and ultrasound bath for 2 minutes. Characterization of the IVM-MeLO included measurement of hydrodynamic diameter, polydispersity index (Pdl), pH and conductivity. Entrapment efficiency (EE %) of IVM was determined using a UV-Vis method, with quantification before and after centrifugation at 9000 RCF for 10 minutes, based on calibration curve previously constructed. Results indicated a hydrodynamic diameter of  $21.7 \pm 0.2$  nm, Pdl of  $0.10 \pm 0.01$ , pH value of  $5.3 \pm 0.05$ , conductivity of  $318 \pm 2.00$   $\mu\text{S}\cdot\text{cm}^{-1}$  and EE of  $93.92 \pm 3.76\%$  (final concentration of 19.5 mg/mL). These characteristics are typical of microemulsified systems. Stability assessment in a climatic chamber ( $30 \text{ }^\circ\text{C} \pm 2 \text{ }^\circ\text{C}$ ,  $75 \pm 2\%$  humidity) over 30 days revealed no significant changes in hydrodynamic diameter, Pdl, pH, and conductivity, indicating suitable stability. The IVM concentration remained close to 100% over the study period. These findings suggest that IVM-MeLO is a stable formulation, warranting further studies to evaluate its in vivo and in vitro efficacy for the treatment of parasitic infections in dogs.

# Silva Morawski    A new approach in the treatment of ulcerative colitis using bilirubin-loaded polymeric nanocapsules



## Author

Andrey Silva Morawska - Universidade Federal do Rio Grande do Sul (UFRGS)  
Eduarda Fardo Filippi Chiella - Universidade Federal do Rio Grande do Sul (UFRGS)  
Graziela Scheuer Gomes - Universidade Federal do Rio Grande do Sul (UFRGS)  
Maria Serena Longhim - Harvard Medical School  
Fernanda Visiolife - Universidade Federal do Rio Grande do Sul (UFRGS)  
Luiza Abrahão Frank - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

CNPq (Grant # n°405865/2023-6, CAPES, FAPERGS). INCT-NANOFARMA (FAPESP, Brazil) Grant #2014/50928-2, and CNPq Grant #465687/2014-8.



## Keywords

Ulcerative Colitis, Bilirubin, Nanotechnology

## Abstract

Ulcerative colitis is the most common inflammatory bowel disease, and its treatment is often hampered by severe adverse effects reducing patients' quality of life. Bilirubin has shown promise in restoring immune homeostasis in ulcerative colitis, but its therapeutic potential is limited by its physicochemical properties. One possible solution is its incorporation into polymeric nanocapsules (NCs). This study aimed to develop an innovative and effective therapy for treating ulcerative colitis. NCs containing bilirubin (NCs-BIL) were prepared using the nanoprecipitation method and evaluated for particle size, surface charge, encapsulation efficiency, and content. These parameters were monitored over 30 days to assess stability. NCs-BIL were exposed to UVC light to test the photostability of encapsulated bilirubin. Additionally, the in vitro effect of treatment on CD4<sup>+</sup> T lymphocytes was evaluated. Finally, preclinical studies of this new formulation are being conducted in C57BL/6 mice using a DSS-induced colitis model. NCs-BIL were successfully developed, characterized by nanometric size, negative zeta potential, high encapsulation efficiency, and content, and has been stable over 30 days. Photostability studies showed over 50% degradation of the free drug under UVC light for 8 hours, whereas less than 10% degradation was observed when the drug was associated with NCs. In vitro studies did not show any changes in cell viability when treated with NCs-BIL, but an increase in IL-10 expression and maintenance of FOXP3 and ROR $\gamma$ T were observed. In conclusion, the NCs-BIL exhibited suitable physicochemical properties and system stability for at least 30 days, protecting bilirubin from degradation under UVC light exposure. The proposed treatment suggests anti-inflammatory and immunomodulatory effects, promoting immune cell homeostasis. Thus, presenting the possibility of an innovative formulation for treating ulcerative colitis.

# Development of Chitosan Coating Aminophylline-Loaded PCL Nanocapsules



## Author

Hericles Afonso de Carvalho Couto - Universidade Federal Rio Grande Norte (UFRN)  
Sabrina Ribeiro Roque - Universidade Federal Rio Grande Norte (UFRN)  
Mariana Maressa Ferreira de Medeiros - Universidade Federal Rio Grande Norte (UFRN)  
Wallacy Silva de Lima - Universidade Federal Rio Grande Norte (UFRN)  
Daniel Torres Pereira - Universidade Federal Rio Grande Norte (UFRN)  
Wógenes Nunes de Oliveira - Universidade Federal Rio Grande Norte (UFRN)  
Eryvaldo Sócrates Tabosa do Egito - Universidade Federal Rio Grande Norte (UFRN)



## Knowledge Area

Nanotechnology



## Funding

This research was funded by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível superior—Brazil (CAPES)—Finance code 001.



## Keywords

Aminophylline, chitosan, polymeric nanocapsules.

## Abstract

Aminophylline (Am) is a drug used for pulmonary diseases due to its bronchodilation and anti-inflammatory properties. However, its side effects compromise efficacy and patient compliance. To address this, polymeric nanocapsules (Nc) can enhance drug's biopharmaceutical properties. This study developed and characterized chitosan-coated Am nanocapsules (AmNc-Chi) with mucoadhesive properties. AmNc were produced using a double emulsion-solvent evaporation method. An organic phase containing Span® 80, dichloromethane and polycaprolactone (PCL) was homogenized by magnetic stirring at 300 rpm. Am (20 mg/mL) aqueous solution was added to the organic phase and ultrasonicated to obtain a W1/O emulsion, which was then added to a polyvinyl alcohol solution in purified water and ultrasonicated, forming a W1/O/W2 emulsion. Solvent evaporation occurred over 8 hours at 300 rpm. A chitosan coating assay was performed adding chitosan solution ranging from 0.06 mg to 0.36 mg to obtain the AmNc-Chi. Both AmNc and AmNc-Chi were characterized by hydrodynamic diameter, polydispersity index (Pdl) and zeta potential (Zp) over 30 days. Results showed that AmNc had a particle size of  $231.4 \pm 13.6$  d.nm, a Pdl of  $0.28 \pm 0.06$  and a Zp of  $-22.1 \pm 1.4$  mV. As expected, the addition of chitosan resulted in an increase on Zp accordingly to the chitosan concentration, with a Zp of  $-1.64 \pm 5.87$  mV for 0.06 mg and  $+24 \pm 5.1$  mV for 0.36 mg. Therefore, the AmNc-Chi was produced containing 0.3 mg of chitosan/1.2 mg of PCL. The AmNc-Chi exhibited a particle size of  $289.8 \pm 36.0$  nm, a Pdl of  $0.23 \pm 0.06$  and a Zp of  $+29.5 \pm 5.6$  mV. The increase in particle size and change in Zp suggest suitable chitosan coating due to chitosan positive charge from amine groups. Both formulations remained stable over 30 days, with no changes in physicochemical properties. These results indicate successful AmNc-Chi production, warranting further biological safety evaluations through in vitro and in vivo studies.

# Ferulic Acid-Loaded Chitosan Nanoparticles



## Author

Kathiane Baumann Kudrna Universidade Federal de Santa Maria (UFSM)  
Silvia Leticia Baldis Universidade Federal de Santa Maria (UFSM)  
Igor Roesch Felix - Universidade Federal de Santa Maria (UFSM)  
Tielle Moraes de Almeida - Universidade Federal de Santa Maria (UFSM)  
Scheila Rezende Schaffazick - Universidade Federal de Santa Maria (UFSM)  
Cristiane de Bona da Silva - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Nanotechnology



## Funding

FIT-BIT/UFSM; PIBIT/CNPq; CAPES/Brazil; CNPq/Brazil



## Keywords

nanoparticles, phenolic compound, stability

## Abstract

Ferulic acid (FA), a phenolic bioactive compound, is used topically because of its substantial properties, including antioxidant, anti-inflammatory and wound healing effects. Despite these benefits, ferulic acid's tendency to oxidize and its low water solubility make it difficult to include in water-based pharmaceutical preparations. To overcome these limitations, the development of nanocarriers for bioactive molecules has gained considerable interest. Chitosan, a polymer known for its low toxicity, biodegradability, and biocompatibility, exhibits properties such as wound healing, antimicrobial activity, and mucoadhesion, making it an ideal candidate for nanoparticle formation. This study aimed to prepare FA-loaded chitosan-TPP nanoparticles by ionotropic gelation process, using Poloxamer 407 as a surfactant. The nanoparticles ( $n=3$ ) were characterized by mean particles size, zeta potential, pH, FA content, and encapsulation efficiency. The results demonstrated that the nanoparticles possessed a positive zeta potential, a polydispersity index below 0.2, an average particle size of  $155 \pm 3$  nm; FA content close to 100%, and an encapsulation efficiency of approximately 50%. The nanoparticles maintained a pH suitable for cutaneous application and remained stable for 15 days under refrigeration. Photostability tests revealed that the nanoparticles effectively protected ferulic acid from UVA light. These findings indicate promising potential for the future use of the developed nanoparticles in pharmaceutical dosage forms for topical application. Moving forward, this study aims to investigate the *in vitro* release of FA from nanoparticles and evaluate toxicity and biological activity to provide clearer insights and results.

# Electro-conductive scaffold containing gold nanoparticles and graphene oxide as a promising solution in cardiac tissue engineering.



## Author

Thais Francine Ribeiro Alves de Almeida - Universidade Tiradentes (UNIT)  
Wanessa Santana Mota - Universidade Tiradentes (UNIT)  
Cecília Torqueti de Barros - Pontifícia Universidade Católica de São Paulo (PUC-SP)  
Kessi Marie de Moura Crescencio (Universidade de Sorocaba)  
Marco Vinicius Chaud - Universidade de Sorocaba (UNISO)  
Patrícia Severino - Universidade Tiradentes (UNIT)



## Knowledge Area

Nanotechnology



## Funding

CNPq 408377/2022-4



## Keywords

Cardiac scaffold. Gold nanoparticle. Graphene Oxide.

## Abstract

Acute myocardial infarction and its complications are significant contributors to mortality. The limited regenerative capacity of adult cardiac tissue suggests investigating tissue engineering as a promising solution for restoring the mechanical structure and functionality of the heart following myocardial injury. In this effort, an electro-conductive device comprising a dense lamellar scaffold is being developed and evaluated. The electro-conductive scaffolds consisted of collagen, fibroin solution, chitosan, hyaluronic acid, proanthocyanidin, and gold nanoparticles (AuNPs) or graphene oxide (GO), produced using plastic compression and lyophilization methods. The devices were evaluated for their biomechanical and adhesive properties, conductivity, SEM, and cell viability by MTT assay. The AuNP-scaffold exhibited a puncture resistance of  $0.41 \pm 0.05$  N and elasticity of  $290,87 \pm 0.029$  Pa, while the GO-scaffold exhibited a puncture resistance of  $0.40 \pm 0.028$  N and elasticity of  $816,48 \pm 115,10$  Pa. The detachment force of the electro-conductive scaffold from the mucin disk was  $0.69 \pm 0.06$  N, while for GO-scaffold was  $0.42 \pm 0.114$  N. Conductivity was measured at  $1.62 \times 10^{-5}$  S/cm<sup>2</sup>, and  $3.67 \times 10^{-6}$  S/cm<sup>2</sup> for GO-scaffold. Pores were open and uniform, with an average pore size of 100  $\mu$ m. The cell viability for AuNP-scaffolds and GO-scaffolds was 76.05% and 77.02%, respectively, compared to the control group not subjected to any treatment (did not show a significant reduction in cell viability). Thus, both electro-conductive scaffolds, AuNP-scaffold and GO-scaffold, showed promising and innovative characteristics for use in regenerative medicine, promoting the functional recovery of cardiac tissue.

# Pickering emulsions stabilized with lignosulfonate nanoparticles



## Author

Leonardo Poletto Igarashi (Universidade Federal do Paraná)  
Rilton Alves de Freitas (Universidade Federal do Paraná)



## Knowledge Area

Nanotechnology



## Funding

CNPq (305768/2021-2). CAPES (Finance Code 001). CAPES/PrInt 41/2017 (88887.311748/2018-00).  
Fundação Araucária Notice N. 006/2022 (23075.012009/2023-90).



## Keywords

Emulsion. Biopolymer. Lignosulfonate.

## Abstract

As of today, synthetic surfactants are still being applied across many areas. This is a huge concern considering its potentially intrinsic toxicity towards humans and the environmental impact. Thus, a more sustainable approach in consonance with the 2030 Agenda for Sustainable Development and its 17 Sustainable Development Goals (SDGs) is needed. Tens of millions of tons of lignin are generated each year. However, most of it is discarded or used as an energy source through burning. Therefore, this abundant natural resource should be better explored. Lignosulfonate is a lignin-based biopolymer whose chemical structure makes it soluble in water, turning it into a greener option to work with. Pickering emulsions stabilized with lignosulfonate nanoparticles may be an environment-friendly approach. The nanoparticle fabrication followed a deep characterization of the material physico-chemically and structure-wise. The chosen method was nanoprecipitation. Lignosulfonate was dispersed in purified water and added at a controlled rate on a certain amount of ethanol, the antisolvent, under magnetic stirring. Then, the resulting nanoparticle static contact angle was measured through the sessile drop technique. At last, the emulsions were prepared with 30% oil phase and 70% aqueous phase varying the nanoparticle concentration range from 0.01% to 0.1%. The nanoparticles were hydrophobic with a contact angle slightly above 90°. The emulsion fraction undergoes noticeable creaming within a day due to gravitational forces; nonetheless, the metastability of the system was confirmed even at nanoparticle concentrations as low as 0.025% and lasts for over 60 days. Lignosulfonate nanoparticles work on different systems. Thanks to its versatility, they are able to stabilize both conventional and unconventional emulsions. Furthermore, its low cost, inherent biocompatibility and biodegradability makes it a good candidate as an alternative stabilizer for pharmaceuticals and cosmetics.



# Nanostructured hydrogel as a strategy for effective hormone modulation



## Author

Andressa Zago (Unicentro)  
Samila Horst Peczek(Unicentro)  
Tatiane Patrícia Babinski (Universidade Estadual do Centro-Oeste)  
Rubiana Mara Mainardes (Unicentro)



## Knowledge Area

Nanotechnology



## Funding

Not applicable



## Keywords

Nanoparticles, Polymers, Progesterone

## Abstract

Progesterone (PGT) is a progestogen hormone with diverse physiological roles, but its exogenous vaginal administration faces limitations due to its short retention time. Thermosensitive hydrogels, which gel in situ in response to temperature, offer a promising solution for this route of administration. To improve water solubility and bioavailability of PGT, this study developed and characterized zein nanoparticles containing PGT, incorporated into a thermosensitive hydrogel for vaginal application. Nanoparticles were obtained by the liquid-liquid dispersion method and incorporated into a thermosensitive hydrogel formulated with 20% w/w poloxamer 407. The nanoparticles had an average diameter of 256 nm, a polydispersity index of 0.132, a zeta potential of -26.7 mV, and an encapsulation efficiency of 53%. The hydrogel maintained structural integrity and reproducibility. These results suggest that the developed technology can increase the residence time on the vaginal mucosa, avoiding hormone losses and providing an improved therapeutic response.

# Development of hybrid lipid-polymeric nanoparticles for topical co-delivery of coenzyme Q10 and siRNA TNF $\alpha$



## Author

Milena Finazzi Moraes (USP Ribeirão Preto)  
Ana Vitória Pupo Silvestrini (USP Ribeirão Preto)  
Thatiani Figueiredo dos Santos (USP Ribeirão Preto)  
Maria Vitória Lopes Badra Bentley (USP Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP, n° 2014/50928-2 and 2018/08253-9); Conselho Nacional de Desenvolvimento Científico e Desenvolvimento Tecnológico (CNPq, Brasil, bolsa n° 465687/2014-8)



## Keywords

nanostructured lipid carriers, gene therapy, topical delivery

## Abstract

The skin as a route of drug administration stands out due to its practicality and safety. However, because of its primary function as a barrier, its complex and selective structure limits the type and quantity of drugs administered through it. To enable the delivery of molecules with characteristics limiting cutaneous penetration, nanostructured lipid carriers (NLC) have been explored due to their structural similarity to lipids in the stratum corneum and permeability through the skin. Therefore, this study aims to develop NLC using a cationic polymer to enable the topical co-delivery of two therapeutic agents: coenzyme Q10 (CoQ10), a high lipophilic molecule with antioxidant and anti-inflammatory properties, and small interfering RNA (siRNA), a polyanionic macromolecule that silences gene expression, targeting TNF- $\alpha$ , a cytokine highly expressed in cutaneous inflammations. The NLC were able to complex with siRNA and fully release it in electrophoretic assays, with an average hydrodynamic size of  $248.9 \pm 4.1$  nm, Pdl of  $0.12 \pm 0.03$ , zeta potential of  $21.7 \pm 1.6$  mV, and entrapment efficiency >90%. Franz cell diffusion assays using synthetic membranes exhibited a release profile of CoQ10 according to Higuchi kinetics over 48 hours. In assays with biological membranes, the NLC showed increased penetration of CoQ10 and siRNA into the stratum corneum, epidermis, and dermis compared to drug solutions. Cell studies demonstrated that NLC significantly increased the internalization of siRNA in macrophages and keratinocytes. In macrophages induced by LPS, NLC-mediated co-delivery significantly reduced TNF- $\alpha$  levels compared to therapeutic agent solutions. Thus, this study developed hybrid lipid-polymeric nanoparticles containing CoQ10 and siRNA, enabling efficient delivery of both therapeutic agents to the skin and cells, indicating a reduction in the inflammatory response in macrophages by decreasing the levels of exacerbated TNF- $\alpha$ , providing support for future in vivo assays.

# Development and Characterisation of Cationic Nanocapsules Containing Nitrofurazone for Cutaneous Application



## Author

Maria Gabriela Borges Hermes (Universidade Federal do Rio Grande do Sul)  
Daniela Vasconcelos Lopes (Universidade Federal do Rio Grande do Sul)  
Josué Guilherme Lisboa Moura (Universidade Federal do Rio Grande do Sul)  
Karina Paese (Universidade Federal do Rio Grande do Sul)



## Knowledge Area

Nanotechnology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Processo 407233/2021-C



## Keywords

nanotechnology; methacrylate; nitrofurazone.

## Abstract

Nitrofurazone (NTZ) is a potent topical antimicrobial, however, its lipophilicity complicates its therapeutic use in chronic wounds and skin grafts. Our objective was to develop and characterize lipid-core nanocapsules (LNC) loaded with NTZ and incorporate them into a hyaluronic acid (HA) gel. LNC were prepared using the interfacial deposition method of the preformed polymer, with differentiation of the continuous phase by the presence or absence of polysorbate 80 (P80). The organic phase consists of Eudragit® RS100, licuri oil, and NTZ at concentration of 1 mg.mL<sup>-1</sup>. The formulations were incorporated into the gel with 1% (w/v) HA. The suspensions and gels were characterized for diameter, zeta potential, pH, content, and encapsulation efficiency (EE%). Dynamic light scattering indicates that the z-average and PDI of LNC without P80 were 132 ± 6 nm and 0.14 ± 0, respectively, and with P80 were 127 ± 8 nm and 0.15 ± 0. Laser diffraction analysis provided D[4,3] values were 134 ± 2 nm for LNC without P80, and 135 ± 4 nm for LNC with P80. The Span value was 0.89 ± 0 and 0.95 ± 0 for LNC without and with P80, respectively. The z-average of the gel containing LNC were 581 ± 36 nm without P80, and 213 ± 53 nm with P80, indicating the preservation of LNC even without P80. This highlights that the P80 amphiphile facilitates the dispersion of the LNC in the HA gel. The zeta potential of the LNCs was +38 ± 3 without P80 and +39 ± 1 with P80, while the gel had a zeta potential of -53 ± 27 without P80 and -39 ± 5 with P80. The pH of the LNCs ranged from 4.6 to 5.3, while the gel had a pH of approximately 7.0. The NTZ content evaluated by HPLC-UV was 0.44 ± 0 mg/mL with P80 and 0.57 ± 0 mg/mL without P80. The EE% was 75 ± 3% for LNCs without P80 and 55 ± 0% with P80, suggesting the influence of the P80 on the nanoparticles structure. In conclusion, it is feasible to produce LNCs containing NTZ and incorporate them into HA gel, thereby creating a potential nanoantibiotic.

# Development and Physicochemical Characterization of Prednisone-Loaded Polymeric Nanocapsules for Veterinary Use



## Author

Camila Duarte Rosa da Cunha (Universidade Federal do Rio Grande do Sul)  
Rovena Sangineto Botoni (Universidade Federal do Rio Grande do Sul)  
Diego Fontana de Andrade (Universidade Federal do Rio Grande do Sul)



## Knowledge Area

Nanotechnology



## Funding

FAPESP, Brazil (National Institute of Science and Technology in Pharmaceutical Nanotechnology)  
Grant #2014/50928-2; FAPERGS, Brazil Grant #23/2551-0000893-9



## Keywords

Veterinary Medicines, Polymeric nanocapsules, Prednisone

## Abstract

Pharmaceutical nanotechnology shows significant promise for masking the taste of bitter drugs, making it valuable for developing innovative medicines for special populations, such as veterinary patients. Prednisone, a widely used glucocorticoid in veterinary therapy, faces challenges in medication acceptance due to its poor palatability, emphasizing the need for novel formulations. In this scenario, this study aimed to encapsulate prednisone in polymeric nanocapsules to enhance its acceptance by veterinary patients. Various combinations of polymers (Polycaprolactone (PCL), Eudragit® RS, and Eudragit® RL) and oils (castor oil, medium-chain triglycerides, oleic acid, and sesame oil), with or without sorbitan monostearate, were evaluated to determine the best combination. This involved assessing polymer-oil compatibility and the drug's saturation concentration in the oils. Using the optimal combinations of polymers, oil, and surfactants, nanocapsules were produced by interfacial deposition of preformed polymer, containing prednisone in concentrations of 0.25 mg/mL and 0.50 mg/mL. Their physicochemical properties were assessed by measuring average particle diameter, polydispersity index, zeta potential, drug content, and encapsulation efficiency. The results showed that the combination of PCL and castor oil, with surfactants sorbitan monostearate, yielded formulations with desirable nanotechnological characteristics, such as unimodal particle size distribution on the nanometer scale ( $251.6 \pm 9.90$  nm), low polydispersity index ( $< 0.2$ ), negative zeta potential ( $-13.5 \pm 0.28$  mV), and drug content close to theoretical values. The formulation with 0.25 mg/mL prednisone exhibited higher encapsulation efficiency ( $53.46 \pm 4.33\%$ ) compared to the 0.50 mg/mL formulation ( $34.74 \pm 16.40\%$ ). Therefore, the 0.25 mg/mL formulation is preferred for use as an intermediate product in producing medicinal premixes for veterinary use, representing the next step of this project.

# Development of a nanostructured system for LMM6 delivery aiming the treatment of systemic fungal infections



## Author

Larissa Meireles Navarro Miranda - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Nanotechnology



## Funding

FINEP



## Keywords

nanotechnology, polymeric micelles, P407

## Abstract

**INTRODUCTION:** LMM6 is a compound that exhibits antifungal activity against various *Candida* species and efficacy in the treatment of systemic fungal infections [1]. Nanotechnology, through nanostructured systems, enhances the potency, efficacy, and release control of drugs, and polymeric micelles are an example of these systems. P407 is an amphiphilic triblock copolymer that forms micelles useful in the solubilization and delivery of drugs [2]. Therefore, this work aims to develop and characterize nanostructured micellar systems with P407 and LMM6 for parenteral administration in the treatment of systemic fungal infections. **METHODS:** The base formulations (BF) were prepared with water or PBS and P407 at concentrations of 0.5; 1; 1.25; 2; 3; 4; 5; 6 and 7% by the direct dissolution method. The temperature and micellar concentrations of the BF were evaluated using light scattering with a particle size analyzer (DLS). 1.0 mL of each sample was inserted into the equipment, with a scattering angle of 90°, for readings at 25, 27, 29, 31, 33, 35, and 37°C. The analyses determined the hydrodynamic size of the particles (DH) and the polydispersity index (PDI). **RESULTS:** The results showed that the dispersions presented nanoscale sizes and became more homogeneous with increasing temperature, suggesting the formation of a single population of micelles. In both solutions, the micellar system was more efficient at higher temperatures, indicating a positive influence of temperature on the stability and formation of the micelles. This behavior may be relevant for intravenous applications, as P407 presented suitable DH and low PDI from 29°C onwards, indicating greater efficiency and uniformity in micelle formation. **CONCLUSION:** The results highlight the efficacy of P407 in forming homogeneous micelles in both media, suggesting its potential in drug delivery systems.

REFERENCES: [1] Faria D. R, et al. *Pathogens*. 2021. [2] Aulton, M. E, et al. 4th Ed. Elsevier, 2016.

# Obtention and Characterization of Dutasteride-loaded Ethosomes for Hair Follicle Targeting



## Author

Rafael Vieira Rocho - Universidade de Brasília (UnB)  
Jayanaraian F. Martins de Andrade - Universidade de Brasília (UnB)  
Marcílio Cunha-Filho - Universidade de Brasília (UnB)  
Guilherme Martins Gelfuso - Universidade de Brasília (UnB)  
Tais Gratieri - Universidade de Brasília (UnB)



## Knowledge Area

Nanotechnology



## Funding

HairDAO



## Keywords

Ethosomes, Dutasteride, Androgenic Alopecia

## Abstract

Androgenetic alopecia is a condition which treatment options are very limited. Dutasteride (DUT) is a potent inhibitor of 5-alpha-reductase, allowing spaced applications, but oral DUT can cause serious sexual adverse effects. Thus, a topical application to avoid DUT's systemic absorption emerges as a promising alternative treatment. Here, we aim to develop and characterize DUT-loaded ethosomes for hair follicle targeting to treat androgenic alopecia. The ethosomes were obtained by dropping water into an ethanolic solution of soybean phosphatidylcholine (200 mM) and DUT (0.02 mM) [1]. DUT amount was fixed at 0.035%, while ethanol concentration varied from 10 to 45%. The ethosomes obtained were fully characterized. Targeting potential was assessed by in vitro skin penetration tests in Hanson diffusion cell assembly (area=1.77 cm<sup>2</sup>), using pig ear skin from a local as a skin model. Ethosomes with ethanolic concentrations from 10% to 25% showed multiple-size populations reflected in the higher Pdl and were excluded, while ethanol amounts superior to 35% resulted in ethosomes of smaller sizes and were also excluded. Thereby, the ethosomes with 30% ethanol were selected to conduct the skin penetration tests due to a more suitable size for hair follicle targeting [2], indeed, this system promoted more DUT accumulation in hair follicles than in stratum corneum ( $p > 0.05$ ), showing a targeting factor of 0.52, statistically superior to control. No DUT was quantified in viable skin and the receptor compartment. Ethosomes with 30% ethanol had a mean size of 369.5 nm, Pdl = 0.149, a zeta potential of  $2.2 \pm 0.24$  mV, pH 5.5, and EE of  $\approx 52\%$ . In conclusion, ethosomes with 30% ethanolic content showed promising results in promoting a target delivery of DUT to hair follicles.

# Sustainable nanostructured lipid carriers containing beeswax and passion fruit oil



## Author

Maria Eduarda Lima Dan - Universidade Estadual de Maringá (UEM)  
Hélen Cassia Rosseto - Universidade Federal do Mato Grosso do Sul (UFMS)  
Maddalena Sguizzato - Università degli Studi di Ferrara  
Francesca Ferrara - Università degli Studi di Ferrara  
Rita Cortesicr - Università degli Studi di Ferrara  
Marcos Luciano Bruschi - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Nanotechnology



## Funding

Fundação Araucária



## Keywords

beeswax, passion fruit oil, nanostructured lipid carriers

## Abstract

**Introduction:** Nanostructured lipid carriers (NLCs) can effectively encapsulate hydrophobic drugs, targeting challenging sites like tumours [1]. Natural compositions provide benefits such as biocompatibility and sustainability. However, their complex nature can be a challenge for solubility, bioavailability, and stability. The aim of this work was to optimize the best combination of beeswax (BW), passion fruit oil (PFO) and soy lecithin (LEC) by monitoring the particle size and polydispersity index (PDI) over time. **Methods:** Following a 32-factorial design, NLCs were prepared by microemulsion technique, varying the LEC in water concentration (1.5, 2.0, and 2.5%, w/w) and the lipid concentration in the formulation (1.0, 1.5, and 2.0% w/w). The lipid phase was composed of 70% (w/w) BW and 30% (w/w) PFO. The prepared systems were characterized by dynamic light scattering (DLS) using a Zetasizer Nano S90 (Malvern) at 1st day, 1st week, and 15th days post-preparation. **Results and discussion:** Particle sizes ranged from 197 to 285 nm at 1st day after preparation, 201-287 nm at 1st week, and 203-287 nm at 15th days. The highest LEC concentration combined with increased lipid content, led to larger particle sizes. After 15 days, larger particles formed small agglomerates and showed slight adhesion to the bottle wall. Lower LEC concentrations (1.5% and 2.0%, w/w) resulted in smaller, and more stable particles. PDIs were 0.17-0.24 at 1st day after preparation, 0.19-0.25 at 1st week, and 0.20-0.25 at 15th days, indicating uniformity and successful preparation. The higher lipid content formulations showed greater influence of time on the particle size and PDI. **Conclusion:** Since significant variations in particle size and PDI over time can compromise the drug delivery, the 1.5 % (w/w) LEC concentration and 1.0% (w/w) lipid content were considered the optimal combination for obtaining stable and homogeneous NLCs.

[1] Wong HL et al. Nanotechnology for Cancer Therapy. (1) 2006 36p.

# In vivo studies of protein-polymeric hybrid nanoparticles containing insulin for oral administration



## Author

Rubiana Mara Mainardes - Unicentro Guarapuava  
Jeferson Ziebarth - Unicentro Pitanga



## Knowledge Area

Nanotechnology



## Funding

Brazilian National Council for Scientific and Technological Development (CNPq) (processes numbers 141136/2021-9 and 429728/2018-2)



## Keywords

Oral administration; Insulin; Diabetes mellitus

## Abstract

Being one of the diseases that most affect the world's population, diabetes mellitus affects around 537 million people worldwide. The disease can be classified into three forms: type 1 diabetes (T1D), type 2 diabetes (T2D), and gestational diabetes, accounting for 90% of cases, T2D is the most common type. Several medications are used to treat diabetes, including regular insulin. Due to degradation in the gastrointestinal tract, due to enzymes or low pH, it is not possible to administer this drug orally, with the subcutaneous route being used for administration. This work aimed to develop hybrid protein-polymeric nanoparticles (Nps) to encapsulate regular insulin, aiming at oral administration. After several physicochemical analyses and in vitro tests to evaluate the Nps produced, pre-clinical studies were carried out in vivo, such as pharmacokinetics (PK), biodistribution, and diabetes induction study in rats, with assessment of blood glucose and body weight of the animals. PK showed that Nps were able to protect and promote great bioavailability of drugs after oral administration, where the insulin released from Nps presented a pharmacokinetic curve very similar to the curve obtained for subcutaneous insulin, reaching the same maximum concentration (C<sub>max</sub>) as the drug and AUC without significant differences ( $p > 0.05$ ). In the diabetes induction trial, during the treatment period, it was possible to obtain a reduction of approximately 61% in the glycemic levels of rats treated with Nps containing insulin, where at the beginning of treatment the glycemia of these animals was approximately 350 mg/dL, reaching the end with a blood glucose level of 132 mg/dL. The reduction in glycemia promoted by Nps was similar to that of insulin administered subcutaneously. These results are very interesting, demonstrating that insulin-containing Nps are a promising system for the treatment of diabetes by oral administration. UNESP CEUA/FCF/CAR n°10/2022, approved on 4 August 2022.



# Oil-in-Water Emulsions Stabilized with Lignin Nanoparticles



## Author

Joslaine Jacumazo - Universidade Federal do Paraná (UFPR)  
Larissa Souza - Universidade Federal do Paraná (UFPR)  
Bruno Iles - Universidade de Brasília (UnB)  
Jaqueline Carneiro - Universidade Federal do Paraná (UFPR)  
Rilton Alves de Freitas - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Nanotechnology



## Funding

Fundação Araucária Edital nº 006/2022 (23075.012009/2023-90); CNPq nº 305768/2021-2



## Keywords

Oil-in-water emulsions, Pickering stabilization, Lignin nanoparticles

## Abstract

Pickering emulsions are emulsions that use solid or colloidal particles as emulsifiers. Instead of surfactants, these particles adhere to the droplet interface, stabilizing the emulsion. A variety of solid or colloidal particles can be used in this type of emulsion, including lignin nanoparticles. Lignin is the most abundant aromatic biopolymer present in nature, with global production around 70-80 million tons/year. It is an attractive biopolymer due to its excellent properties, including low toxicity, numerous functional groups, reduced cost, high yield, and renewable origin, in addition to possessing photoprotective, antioxidant, and antimicrobial properties. However, it has limited solubility in water. When in nanoparticle form, it improves emulsification capacity and can be used to stabilize Pickering emulsions. Considering the above, the objective of this study was to produce lignin-based nanoparticles (LNPs) using lignin dispersions fractionated by different solvents and employ them as stabilizers for oil-in-water emulsions. To this end, LNPs were developed through a simple route using solvents such as acetone (L1NPs) and ethanol (L2NPs). The sizes, zeta potential, and three-phase contact angle of both LNPs formulations were investigated. Subsequently, oil-in-water emulsions were prepared with different concentrations of LNPs, using a 30% oil phase. At this stage, the droplet size, morphology, and stability of the emulsions during storage were evaluated. Our results demonstrated that the LNPs produced have an average size and zeta potential of 159 nm and zeta potential of -40 mV for L1NPs, and 223 nm with a zeta potential of -39 mV for L2NPs. Regarding the emulsions, LNPs effectively stabilized the oil-water interface at low concentrations and maintained stable for over 30 days. Therefore, this study reveals a promising approach preparing lignin-based nanoparticles, with potential applications in oil-in-water emulsions for the cosmetic industry.

# Synthesis and Characterization of Lignin Nanoparticles via Nanoprecipitation



## Author

Bruno Iles - Universidade de Brasília (UnB)  
Vera Fernandes - Universidade Federal do Paraná (UFPR)  
Larissa Souza - Universidade Federal do Paraná (UFPR)  
Jaqueline Carneiro - Universidade Federal do Paraná (UFPR)  
Joslaine Jacumazo - Universidade Federal do Paraná (UFPR)  
Rilton Alves de Freitasrilton - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Nanotechnology



## Funding

CNPq n° 305768/2021-2. Fundação Araucária Edital n°006/2022 (23075.012009/2023-90)



## Keywords

Emulsion. Biopolymer. Lignosulfonate.

## Abstract

Lignin is the second most abundant renewable natural biopolymer on the planet. Despite its abundance, lignin is predominantly used to produce energy through burning, thus underutilizing its potential. In the context of the transition to a more sustainable economy, it is essential to explore new applications for lignin, such as the preparation of lignin nanoparticles (LNPs). LNPs exhibit greater reactivity due to their high surface-to-volume ratio, offering advantages such as mechanical reinforcement in polymer matrices, UV-blocking additives, antibacterial and antioxidant agents, and controlled drug delivery systems. Lignin nanoformulation represents an innovative approach to valorize this biopolymer, promoting advanced technological solutions and contributing to more sustainable industrial development. The lignin used in this study was donated by a private partner company. It was initially fractionated and then centrifuged. The pellet was discarded and the supernatant was stored. Lignin was characterized by gravimetric and infrared analyses. The nanoparticles were obtained via nanoprecipitation using varying volumes of lignin in acetone and water. The nanoparticles were characterized using dynamic light scattering analysis, zeta potential, atomic force microscopy and contact angle assessment. Gravimetric analyzes showed that 1.5 mg mL<sup>-1</sup> of lignin was recovered and infrared spectra showed no differences between the supernatant and the pellet. The particles ranged from 545 nm to 980 nm in size, with zeta potential between -50.8 mV and -53.2 mV when the aqueous phase was poured onto the organic phase. When the organic phase was poured into the aqueous phase, the sizes ranged from 160 nm to 203 nm with zeta potential between -40 mV and -42 mV. The particles exhibited spherical morphology with a contact angle of 160°, indicating high hydrophobicity. In this way, the development and characterization of LNPs was achieved through a simple and versatile route.

# Preliminary evaluation of the stability of PLGA nanospheres formulated with 2 types of Poloxamers.



## Author

Yanka Machado de Paula Santos - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Kauã Henriquy Mendonça Souza - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Vitória Santos Fogaça - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Henrique Pascoa - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Eliana Martins Lima - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Luís Antônio Dantas Silva - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Danielle Guimarães Almeida Diniz - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)



## Knowledge Area

Nanotechnology



## Funding

CNPq (305768/2021-2), CAPES (Finance Code 001), CAPES/PrInt 41/2017 (88887.311748/2018-00),  
Fundação Araucária Notice N. 006/2022 (23075.012009/2023-90).



## Keywords

nanospheres, PLGA, poloxamers

## Abstract

Herpetic stromal keratitis is an ocular infection of the cornea caused by the herpes simplex virus and is considered the leading cause of visual disorders worldwide. Acyclovir is the selective antiviral for the virus, however, the drug has low absorption and bioavailability and is only available as an ophthalmic ointment, requiring frequent applications and potentially causing irritability and blurred vision. Considering the difficulties of administering medications for the ocular topical route, such as nasolacrimal drainage, tight junctions between epithelial cells, blinking, tear flow, and the composition of the corneal epithelium itself, nanostructured formulations have been reported as a potential approach for drug delivery through this route. The objective of this work is to present a preliminary study of the development of polymeric nanoparticle formulations of Poly-(D,L-lactic-co-glycolic acid) (PLGA 50:50 and 85:15) stabilized with poloxamers (poloxamer 188 or poloxamer 407) for acyclovir delivery, as well as to evaluate the preliminary stability of the system by reflected light intensity technique (TurbScan® Lab). Nanoparticles were produced using the nanoprecipitation method adapted from Fessi et al. (1989). Particle size, polydispersion index (PDI) and Zeta Potential were determined by Dynamic Light Scattering, and the measurements were made soon after obtaining the particles and after 72 hours. Preliminary stability was evaluated with scans performed every 1 hour for 3 days. The samples with equal proportions of polymer and surfactant obtained Backscattering variations between 0.1% and 0.6%, indicating lower sedimentation or flocculation profiles. In addition, the formulations containing poloxamer 407 showed smaller particle sizes after 72 hours and a higher flocculation profile for samples with PLGA 85:15, suggesting the differing influence of the polyethylene oxide and polypropylene oxide chains.

# Anticancer potential in vitro against DU-145 cells of curcumin-encapsulated in polymeric nanoparticles containing D- $\alpha$ -tocopheryl-polyethylene glycol 1000 succinate (TPGS)



## Author

Jennifer Thayanne Cavalcante de Araujo - (UNESP-Araraquara)  
Aline Martins dos Santos (UNESP-Araraquara)  
Barbara Bassan (IRCCS Multimedica)  
Maria Tereza Palanomia (IRCCS Multimedica)  
Lorenzo Mortara (University of Insubria)  
Antonino Bruno (IRCCS Multimedica)  
Marlus Chorilli (UNESP-Araraquara)



## Knowledge Area

Nanotechnology



## Funding

São Paulo Research Foundation (FAPESP) – Process nº 2020/06212-3 and 2023/02591-8. Ricerca Corrente, IRCCS Multimedica. Italian Association for Cancer Research (AIRC-MFAG, ID 22818)



## Keywords

Curcuma longa L., Prostate cancer, polymeric nanoparticles

## Abstract

Curcumin (CUR) is a polyphenol obtained from *Curcuma longa* L. and has shown antitumor properties against prostate cancer cells. To overcome its limitations of use, CUR was encapsulated in polymeric nanoparticles containing the surfactant D- $\alpha$ -tocopheryl-polyethylene glycol 1000 succinate (TPGS). The size, distribution, and zeta potential of CUR nanoparticles (CUR-NP) and empty nanoparticles (NP) were evaluated by dynamic light scattering. The cytotoxicity in vitro against DU-145 cells was evaluated up to 72 h and in vitro functional analysis of cell adhesion on fibronectin, migration, and invasion (Boyden chamber) was also performed at the lowest concentration of cytotoxicity. The CUR-NP and NP have sizes of 176.7 and 186.4 nm, a distribution below 0.3, and zeta potential of -30.1 and -26.1 mV. CUR demonstrated cytotoxic activity only after 48 h and maintained it up to 72 h. CUR-NP and NP showed a reduction in cell viability of 19 and 29%, respectively, in 24 h at 13.57  $\mu$ M, gradually reducing to 72 h. CUR, CUR-NP, and NP demonstrated a reduction in cell adhesion to the fibronectin layer of 84.6, 81.5 and 69.8%, respectively. In the cell migration assay, CUR-NP showed better performance with a reduction of 53.1%, the CUR reduced by 35.2% and NP demonstrated low migration inhibitory activity with only 6%. In the cell invasion assay, CUR and CUR-NP showed around 40% reduction and NP showed no activity. These results demonstrated that CUR has cytotoxic activity against DU-145 and that the nanoencapsulation process improves this activity, depending on the time and concentration. At a concentration of 0.27  $\mu$ M, it was observed that despite the significant inhibitory activity on cytotoxicity and cell adhesion of NP, there was no activity in the migration and invasion assays, demonstrating that curcumin is essential for the inhibition of simulated metastasis in vitro.

# Construction of a pseudoternary phase diagram for the development of a microemulsion formulation with medium-chain triglycerides.



## Author

Anna Julia Rodrigues Borges - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Yanka Machado de Paula Santos - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Henrique Pascoa - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Eliana Martins Lima - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Luís Antônio Dantas Silva FARMATEC/FF/ - Universidade Federal de Goiás (UFG)  
Danielle Guimarães Almeida Diniz - FARMATEC/FF/ - Universidade Federal de Goiás (UFG)



## Knowledge Area

Nanotechnology



## Funding

No funding



## Keywords

Phases diagram, microemulsion, ocular delivery

## Abstract

Topical ophthalmic drug absorption faces significant challenges due to the physical and biochemical barriers of ocular structure. The composition of the corneal epithelium acts as a barrier for hydrophobic and hydrophilic drugs and the tear drainage, tight junctions between epithelial cells, and blinking further contribute to decreased drug absorption, requiring frequent administration. Herpes simplex infections can lead to corneal ulcerations, considered the leading cause of visual disorders worldwide. It presents significant limitations in topical ocular application, which can reduce patient adherence to treatment, therefore. Different strategies have been reported as an approach with the potential to act on the release of drugs by this route, nanostructured formulations such as microemulsions, can modify the solubility profile of drugs, generating a larger contact surface favoring their permeability in the eye. Thus, the objective of this work is to determine the rate of lipid, surfactant and co-surfactant in formulation, by constructing a pseudoternary phase diagram, for the development of topical microemulsions for ocular delivery of the acyclovir. The method used was adapted from Mahboobian et al (2020), using the water titration technique, with the construction of three diagrams with different ratios of surfactant and co-surfactant (1:1, 1:2 and 2:1), using Poloxamer 188 as surfactant, Span 80 as co-surfactant and Miglyol 812 as oil phase. The formation of a microemulsion region was accompanied by the measurement of droplet size and polydispersion index by Dynamic Light Diffusion. The results showed that the concentration of surfactant 1:1 presented a larger formation area for microemulsion, and that it can be exploited for optimization of the future formulation, with adjustments in the concentration of each component, as well as the application of shear energy to obtain droplets with better size distribution.

# Evaluating Cryoprotectants for Effective Lyophilization of Simvastatin-Encapsulated Hybrid Nanoparticles



## Author

Dara Grundmann - Universidade Federal der Santa Catarina (UFSC)  
Carolina Lourenço - Universidade Federal der Santa Catarina (UFSC)  
Hellen Stulzer - Universidade Federal der Santa Catarina (UFSC)



## Knowledge Area

Nanotechnology



## Funding

CNPq (305768/2021-2). CAPES (Finance Code 001). CAPES/PrInt 41/2017 (88887.311748/2018-00).  
Fundação Araucária Notice N. 006/2022 (23075.012009/2023-90).



## Keywords

Lyophilization, Cryoprotectants, Hybrid nanoparticles

## Abstract

A low solubility of drugs poses a challenge in pharmaceutical formulation development. Simvastatin (SIM), used to treat hypercholesterolemia, is classified as Class II in the Biopharmaceutical Classification System due to its low aqueous solubility, necessitating improvements in this property. Hybrid nanoparticles (NH) emerge as a promising strategy to enhance the oral bioavailability of SIM. However, NH suspensions often face issues of physical and chemical instability, such as aggregation and microbiological contamination. Lyophilization emerges as an effective technique to stabilize NH. However, due to the rigorous conditions of this process, cryoprotectants (CP) such as mannitol (MA) and trehalose (TRE) are used to prevent nanoparticle aggregation, improve the redispersibility of the dried product, and ensure stability over time. The aim of this study was to evaluate the physicochemical properties of lyophilized NH containing SIM, using MA and TRE as CP. NH were lyophilized using an E-C MicroModul lyophilizer (Thermo Fisher Scientific, USA) under 0.2 mbar pressure. Analyses were conducted using X-ray diffraction (XRD), differential scanning calorimetry (DSC), and Fourier-transform infrared spectroscopy (FTIR) at the beginning and after 30 days to assess stability. XRD diffractograms showed characteristic peaks only for MA and TRE at both time points analyzed. Similarly, FTIR and DSC analyses indicated that NH exhibited characteristics of amorphous materials, confirming the amorphization of SIM due to the loss of its crystalline form. Evaluation of NH stability with TRE by DSC was limited due to overlap of endothermic events associated with TRE and SIM melting. These observations suggest that there were no changes in the chemical composition of NH during the storage period, reinforcing their stability. Furthermore, maintaining the amorphous form of NH over time is advantageous as it contributes to improving the solubility of SIM

# Enhanced delivery of resveratrol and curcumin via Mesoporous Silica in a mice colitis model



## Author

Renan Stein - Universidade Federal do Rio Grande do Sul (UFRGS)  
Miquel Martine - Universitat de València  
Antonio Guillot - Universitat de València  
Ana Melero Zaera - Universitat de València  
Monique Deon - Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA)  
Ruy Carlos Ruver Beck Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA)



## Knowledge Area

Nanotechnology



## Funding

CAPES, INCT 3D-Saúde, PPGCG UFRGS



## Keywords

mesoporous silica, polyphenols, ulcerative colitis

## Abstract

Unfortunately, there is no current treatment to cure this condition. Consequently, it is crucial to explore alternative treatment approaches. Polyphenols like resveratrol (RSV) and curcumin (CUR) could be good candidates, due their pharmacological properties, such as strong antioxidants and anti-inflammatory agents. Despite their benefits, these compounds suffer from low solubility and permeability, resulting in their limited use in current therapies. In order to overcome the physical-chemical issue surround RSV and CUR, this work aims to encapsulate them in mesoporous silica particles (MS) as a strategy to improve their properties in the colitis treatment, using a mice model. The particles were synthesized through the sol-gel method, using tetraethyl orthosilicate (TEOS). Therefore, RSV and CUR were nanoencapsulated separately into MS particles (drug loading 19%). Mice were induced to ulcerative colitis using 3% dextran sodium sulfate (DSS) added to the animal's water. The animals were divided into 8 groups, including healthy and DSS controls, sulfasalazine (100 mg/kg), free polyphenols (40 mg/kg), MS-CUR and MS-RSV (200 mg/kg) and blank particles (200 mg/kg), during 7 days. At the end of the treatments, after sacrifice, the colons were measured and their homogenates submitted to cytokines evaluation and histological analysis. The encapsulated polyphenols maintained the colon length/weight ratio in the animals, unlike free polyphenols ( $p < 0,05$ ). In the same way, they were able to reduce the interleukins IL-1 $\beta$  and IL-6 ( $p < 0,05$ ). Characterization tests showed partial amorphization of polyphenols, which contributed to an increase in their solubility. These findings corroborate by the results from the colitis model, indicating that MS particles loaded with RSV and CUR are suitable for treating ulcerative colitis by reducing the local inflammation.

# Preparation, Physicochemical, Morphological And Viability Evaluations Of Nanotechnological Polymeric Films Containing Tacrolimus For The Treatment Of Topical Autoimmune Diseases



## Author

Jordano Cichelero Facchin - Universidade Federal do Rio Grande do Sul (UFRGS)  
Gabriela da Costa Lemos - Universidade Federal do Rio Grande do Sul(UFRGS)  
Maria Ismenia Z. Lionzo - Universidade Federal de Ciências da Saúde de Porto Alegre(UFCSPA)  
Luiza Abrahão Frank - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

ACKNOWLEDGMENTS: CNPq (Grant # n°405865/2023-6, Grant # n° 465687/2014-8), CAPES, FAPERGS; INCT-NANOFARMA supported by FAPESP, Grant #2014/50928-2.



## Keywords

Cutaneous lupus erythematosus, Polymeric films, Nanoparticles

## Abstract

Cutaneous administration of drugs for disease treatment represents an alternative to oral administration therapy, especially when aimed local action, such as in skin diseases treatment. Cutaneous lupus erythematosus (CLE) is an autoimmune disease that causes skin lesions in patients. This study aimed to produce polymeric films composed of chitosan-collagen blends (CH-COL) associated with polymeric nanocapsules (NCF) or liposomes (LIPF) containing tacrolimus (NCTF and LIPTF) and evaluate their physicochemical characteristics through Dynamic Mechanical Analysis (DMA), Small Angle X-ray Scattering (SAXS), and Atomic Force Microscopy (AFM), as well as the drug release profile from the nanostructures and films. Additionally, we aimed to evaluate the safety profile in cell cultures of keratinocytes, fibroblasts and T cells and the adhesiveness of the films on porcine skin. The mechanical results from DMA demonstrated high flexibility of the CH-COL films and an increase of resistance in LIPF and LIPTF, NCF and NCTF. SAXS diffraction profiles demonstrated the presence of nanometric structures in the films, and AFM showed surface differences, with an increase in roughness between the CH-COL films and LIPF, LIPTF, NCF, and NCTF. The release profiles of the particles demonstrated controlled release, with nanocapsules releasing around 99% of the drug and liposomes 71% over 24 hours. The LIPTF films released 75% and NCTF around 20% of the drug over 72 hours. Cell assays showed high viability of the CH-COL, LIPF, LIPTF, NCF, and NCTF in keratinocytes and fibroblasts. The T cell culture showed a decrease in cell number in LIPTF and NCTF, justified by the presence of the immunosuppressant in the system. LIPF demonstrated higher adhesiveness on the skin than FNC and CH-COL, possibly due to the increased surface charge of the liposomes. Furthermore, a permeation and penetration assay on porcine skin will be conducted to evaluate the presence of the drug in each skin layer.



# Machine learning used to support the development of polymeric nanoparticles



## Author

Alice de Oliveira Paiva e Souza - Universidade de Brasília (UnB)



## Knowledge Area

Nanotechnology



## Funding

It does not have



## Keywords

nanoparticles, systems, model

## Abstract

Drug-loaded nanosystems have remarkable therapeutic potential. Polymeric nanoparticles, in particular, are stable and have great potential for loading and targeting drugs. Machine learning can be a powerful tool to build reliable predictive models for systems with complex relationships among production variables. This work aimed to explore the use of machine learning for producing polymeric nanoparticles using the model drug acetaminophen. Polymeric nanoparticles loading acetaminophen were prepared using the nanoprecipitation method. Different concentrations of the surfactants PVA 40-88 and Tween 80 were used, together with the cationic polymer Eudragit L100 and the anionic Eudragit E100. The influence of the organic and aqueous phases, temperature, and mixing technique was also evaluated, totaling 49 experiments. The nanoparticles were characterized by particle size, polydispersity, zeta potential, and encapsulation efficiency. Different models were developed and trained, with the same input layer but different output and hidden layers. The first model considers the nanostructuring or not of the systems as the output, while the second model considers the colloidal properties of the systems. From the colloidal systems obtained, a wide range of results could be achieved: particle size from 49.4 to 530.7 nm, zeta potential from -79.2 to 48.5 mV, polydispersity index from 0.002 to 0.577, and the encapsulation efficiency ranged from 0 to 45.3%. All mathematical models tested resulted in high accuracies (above 75%). The validation of these models showed better performance for Random Forest and Neural Networks with an accuracy of approximately 80%. The amount of solid surfactant and polymer and the ratio of aqueous/organic phases had a higher impact. On the other hand, the temperature and mixing method subtly influenced the nanoparticle's synthesis. So far, there are encouraging prospects for increasing the accuracy of using neural networks with more future experiments.

# Dexamethasone-loaded chitosan-decorated PLGA nanoparticles: a step forward in attenuating the COVID-19 cytokine storm?



## Author

Mirsiane Pascoal Costa - Universidade Federal de Juiz de Fora (UFJF)  
João Octavio Carneiro Abdu - Universidade Federal de Juiz de Fora (UFJF)  
Maria Clara Machado Resende Guedes - Universidade Federal de Juiz de Fora (UFJF)  
Michelle Alvares Sarcinelli (FIOCRUZ- Rio de Janeiro)  
Fernanda Maria Pinto Vilela - Universidade Federal de Juiz de Fora (UFJF)  
Frederico Pittella Silva- Universidade Federal de Juiz de Fora (UFJF)  
Gilson Costa Macedo - Universidade Federal de Juiz de Fora (UFJF)  
Helvécio Vinícius Antunes Rocha (FIOCRUZ- Rio de Janeiro)  
Guilherme Diniz Tavares - Universidade Federal de Juiz de Fora (UFJF)



## Knowledge Area

Nanotechnology



## Funding

CNPq projeto nº 404202/2021-7



## Keywords

SARS; PLGA; chitosan

## Abstract

Severe Acute Respiratory Syndrome (SARS), triggered by an exaggerated immune response to pathogens like SARS-CoV-2, can cause a "cytokine storm," damaging the respiratory system and leading to death. Dexamethasone (DEX) is effective for SARS treatment but may cause adverse effects with prolonged use. Nanostructuring corticosteroids target phagocytic cells involved in inflammation, especially in the lungs, enhancing control of inflammation and reducing toxic effects by lowering doses. Chitosan (CS) has documented anti-inflammatory properties, and combining it with DEX could improve outcomes. This study aims to develop and characterize PLGA nanoparticles decorated CS for the encapsulation of dexamethasone (DEX) (NP-DEX-CS), targeting improved efficacy in treating SARS associated with COVID-19. The nanoparticles were systematically characterized for size, zeta potential (ZP), morphology, encapsulation efficiency, and in vitro drug release. The incorporation of CS resulted in significant modifications in the nanoparticles' physical properties, notably an increase in size and a shift in ZP to positive values. The NP-DEX-CS achieved high encapsulation efficiency (~84%). Moreover, the nanoparticles demonstrated a reduced DEX release rate after CS coating. Microscopy analyses revealed a smoother surface on the CS-decorated nanoparticles. FTIR and XRD analyses confirmed successful chitosan coating and DEX encapsulation. The CS coating enhanced the tolerability of J774.A1 cells to the nanoparticles. Importantly, the NP-DEX-CS significantly reduced nitric oxide levels and inflammatory cytokines (IL-1, IL-6, IL-12, and TNF- $\alpha$ ). These findings suggest that CS-decorated PLGA nanoparticles hold promise as an effective dexamethasone delivery system for treating SARS related to COVID-19. The CS coating not only improved the physical properties and drug release profile of the nanoparticles but also enhanced their anti-inflammatory efficacy and biocompatibility.

# Development and analysis of the integrity, homogeneity, and structure of polymeric nanotechnological films containing tacrolimus aimed at treating Cutaneous Lupus Erythematosus



## Author

Gabriela da Costa Lemos - Universidade Federal do Rio Grande do Sul (UFRGS)  
Jordano Cichelero Facchini - Universidade Federal do Rio Grande do Sul (UFRGS)  
Luiza Abrahão Frank - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

CKNOWLEDGMENTS: CNPq (Grant # n°405865/2023-6, Grant # n° 465687/2014-8), CAPES, FAPESP INCT-NANOFARMA supported by FAPESP, Grant #2014/50928-2.



## Keywords

Cutaneous Lupus Erythematosus; Liposomes; polymeric nanocapsules.

## Abstract

Cutaneous Lupus Erythematosus (CLE) is an autoimmune disease associated with the activation of self-reactive immune cells, causing variable skin lesions in severity and appearance, resulting in pain and discomfort. Currently, there are no approved treatments for CLE, but some medications are used off-label. It is crucial to develop specific therapies for CLE that are safe, effective, accessible, and protect the affected skin. Biodegradable and biocompatible polymers chitosan (CH) and collagen (COL), combined with nanotechnology, represent an innovative approach for CLE treatment. This study aimed to produce nanotechnological polymeric films with CH-COL, incorporating tacrolimus-loaded liposomes (LIPTF) or polymeric nanocapsules-loaded tacrolimus (NCTF). The films were prepared by combining CH-COL with liposome dispersions (LIP-TAC) produced by reverse evaporation or with polymeric nanocapsules (NC-TAC) produced by nanoprecipitation, followed by drying by casting method. Both nanostructures showed nanometric size and negative zeta potential. The encapsulation efficiency (EE%) and drug content of NC-TAC were  $99.89 \pm 0.025\%$  and  $95.2 \pm 1.95\%$ , respectively. For LIP-TAC were  $97.65 \pm 2.11\%$  and  $99.66 \pm 0.42\%$ , respectively. Thermal analysis showed that the films maintained the integrity of CH-COL transitions, LIPTF showed chemical interactions between liposomes and tacrolimus, while the NCTF exhibited a characteristic endothermic peak of crystalline polymer, indicating material integrity within nanocapsules wall. Film morphology was evaluated by Scanning Electron Microscopy (SEM), revealing characteristic microphases in the CH-COL film, increased roughness in LIPTF, and spherical structures in NCTF. Both films showed integrity, homogeneity, and absence of drug crystals, suggesting viability for future safety and efficacy assessments in dermal applications.

# Evaluating Cryoprotectants for Long-Term Stability of pDNA-Loaded Lipid Nanoparticles



## Author

Heloisa Athaydes Seabra Ferreira - Universidade Federal de Minas Gerais (UFMG)  
Sérgio Ricardo Aluotto Scalzo Júnior - Universidade Federal de Minas Gerais (UFMG)  
Kevin Kelton Santos de Fariak - Universidade Federal de Minas Gerais (UFMG)  
Gabriel Henrique Costa Silva - Universidade Federal de Minas Gerais (UFMG)  
Marco Túllio Rodrigues Alves - Universidade Federal de Minas Gerais (UFMG)  
Anderson Oliveira Lobo - Universidade Federal de Piauí (UFPI)  
Pedro Pires Goulart Guimarães - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Nanotechnology



## Funding

CAPES (88887.506690/2020-00), FAPEMIG (APQ-00826-21; RED-00202-22 Rede de Pesquisa em Imunobiológicos e Biofármacos para terapias avançadas e inovadoras), CNPq (442731/2020-5; 305932/2022-5)



## Keywords

Lipid nanoparticles, Cryoprotectants, Freeze-drying

## Abstract

Long-term stability is key challenge in the development and clinical translation of nanomedicines. While most conventional vaccines can be stored at 2-8°C for at least 6 months, mRNA-lipid nanoparticles (LNP) vaccines need to be stored frozen, presenting a considerable obstacle. Freezing-drying (FD) is commonly used in the pharmaceutical industry to increase the stability and shelf life of various products by removing the water from drug formulations. Most of the studies focusing nanoparticles FD showed the importance of use cryoprotectant. Here, we give insight into the variables that play a role during LNPs FD by evaluating the impact of cryoprotectants and storage on properties such as size, polydispersity index (PDI), and in vitro transfection efficiency. These LNPs were formulated by microfluidic mixing which C12-200, DOPE, cholesterol and C14-PEG 2000 encompassed lipid phase and pDNA and citrate buffer was aqueous phase. The final formulation was denominated Fresh. Cryoprotectants solutions of sucrose, trehalose, and sorbitol (10%, 15%, and 20%) were added (1:1) to Fresh. One group were stored moist at -20°C and 2-8°C for 28 days and were denominated middle and low stress, respectively. Another group were freeze-dried and followed stored at -20°C, 2-8°C, and room temperature and were denominated high stress. Sorbitol samples showed inefficient protective effect even in low stress conditions. This observation can be explained because sorbitol is a monosaccharide with osmoprotective action. Sucrose and trehalose, disaccharides widely used in LNP FD, showed a well capacity to protect the samples after all stressed conditions during short-term storage. However, after 24 months, only trehalose samples avoided increases in size and PDI. Among all conditions, 20% trehalose maintained 60% of biological activity compared to Fresh samples. Our studies highlight the optimal cryoprotectant concentration to preserve LNP stability after FD and extended storage.

# The effect of nanostructured lipid carriers' composition on the controlled Ibrutinib skin deposition for melanoma treatment



## Author

Mateus Torquato Silva - Universidade de Brasília (UnB)  
Lucas F. F. Albuquerque - Universidade de Brasília (UnB)  
Guilherme M. Gelfuso - Universidade de Brasília (UnB)



## Knowledge Area

Nanotechnology



## Funding

FAPDF (Grant n. 00193-00000721/2021-04, Project n. 41/2021).



## Keywords

Melanoma, Topical delivery, nanostructured lipid carriers

## Abstract

Melanoma is responsible for more than 80% of deaths related to skin diseases. Ibrutinib, a Bruton's tyrosine kinase inhibitor, has been proposed to treat this type of tumor. However, its low solubility, extensive first-pass effect, and severe adverse reactions with systemic administration affect therapeutic success. This study proposes developing and comparing the performance of two compositions of nanostructured lipid carriers (NLCs) to load ibrutinib for the topical management of melanomas in their early stages. Preformulation tests were then conducted to characterize the physical compatibility between the drug and the selected components used in NLCs preparation. Sequentially, two lipid compositions were used to develop the NLCs and formulations were then characterized and subjected to permeation tests on porcine skin. The NLCs containing oleic acid effectively controlled ibrutinib release over 24 h compared to the NLCs composed of pomegranate seed oil. Furthermore, the nanoparticles acted as permeation enhancers, increasing the fluidity of the lipids in the stratum corneum, as determined by EPR spectroscopy, which stimulated the ibrutinib penetration more profoundly into the skin. However, the NLCs composition also influenced the permeation promotion factor. Thus, these findings emphasize the importance of the composition of NLCs in controlling and increasing the skin penetration of ibrutinib and pave the way for future advances in melanoma therapy.

# Arginine-based surfactants nanoparticles as a strategy for prevention and treatment of infected wounds



## Author

Francisco Fábio Oliveira de Sousa - Universidade Federal do Amapá (UNIFAp)  
Aurora Pinazo - Universitat de Barcelona -IQAC-CSIC)  
Zakaria Hafidi - Universitat de Barcelona -IQAC-CSIC)  
María Teresa García - Universitat de Barcelona -IQAC-CSIC)  
Elena Bautista - Universitat de Barcelona -IQAC-CSIC)  
Maria del Carmen Moran - Universitat de Barcelona -IQAC-CSIC)



## Knowledge Area

Nanotechnology



## Funding

Grant PID2022-136354-NBI00: MCIN/AEI/10.13039/501100011033 , “ERDF A way of making Europe”.  
Grant PTA2020-018511-I: MCIN/AEI/10.13039/501100 011033. FAPEAP and CNPq (PRONEM grant #95/20218), CNPq (DT) and FAPEAP (Programa Doutor Empreendedor)



## Keywords

gemini; arginine; surfactants; antimicrobial; biofilm; enzymatic; cytotoxicity

## Abstract

Bacterial infection is the most common complication in chronic wounds, delaying the cure in surficial lesions and becoming potentially dangerous in deeper wounds. The management of infected wounds is yet limited, due to the lack of materials capable of treating the infections and simultaneously promote the healing process. Although cationic surfactants have a remarkable antimicrobial activity, they present an intrinsic toxicity that discourages their usage. The antimicrobial and antibiofilm properties of gemini arginine-based surfactants have been evaluated. The inhibitory activities of the surfactants over key enzymes enrolled in the skin repairing processes (collagenase, elastase and hyaluronidase) were evaluated. In order to reduce their inherent cytotoxicity, novel zein nanoparticles loaded with arginine-based surfactants are also presented. Their cytotoxicity over keratinocytes was also investigated. These gemini surfactants exhibited good activity against a wide range of bacteria, including some problematic resistant microorganisms, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*. These two biological properties depend on both the alkyl chain length and the spacer chain nature. Moreover, surfactants with a C10 alkyl chain and C3 spacer inhibited the (MRSA) and *Pseudomonas aeruginosa* biofilm formation at concentrations as low as 8 µg/ml and were capable to eradicate established biofilms of these two bacteria at 32 µg/ml. They exhibited moderate anti-collagenase activity while the activity of hyaluronidase was boosted by the presence of these surfactants. The nanoencapsulation reduced the cytotoxicity of these molecules. These findings make these surfactants as promising candidates for wound care applications. This approach opens new possibilities for using cationic surfactants and their extraordinary antimicrobial responses for prevention and treatment of infected wounds.

# Apoferitin as a drug delivery platform: Comparison between uses of pH and the principle of passive diffusion for the association of molecules



## Author

Isabella Kriunas Demonari - FCFRP, Universidade de São Paulo (USP)  
Camila Machado França Almeida- FCFRP, Universidade de São Paulo (USP)  
Natália Floriano Paiva - FCFRP, Universidade de São Paulo (USP)  
Fabiana Vicentini - FCFRP, Universidade de São Paulo (USP)



## Knowledge Area

Nanotechnology



## Funding

This work was supported by the São Paulo Research Foundation (FAPESP) [grant number 2022/13379-7] and Conselho Nacional de Desenvolvimento Científico e Tecnológico [grant number 403588/2021-9]. IKD is recipient of CNPq, process [grant number 140091/2024-6]



## Keywords

Apoferitin, Association Process, Drug-Delivery

## Abstract

Apoferitin, a biological macromolecule, is increasingly studied for its potential as a drug delivery platform. Previous research has focused on a method involving pH-modulated destabilization of its spherical cage structure to associate drugs. However, other approaches exist for binding molecules to apoferitin, such as biomineralization, passive diffusion, high hydrostatic pressure, and thermal modification. While biomineralization and passive diffusion align with biological iron homeostasis principles, methods like high pressure and pH alterations can induce reversible structural instability and subunit disorganization. This study evaluates two apoferitin formulations, incorporated with peptide or pDNA, using distinct preparation methods. One method disorganize/reorganizes structure via pH adjustment, while the other relies on the passive diffusion through molecular mixing. Formulations underwent analysis via circular dichroism, electrophoresis, and dynamic light scattering. Results showed that the pH-adjusted formulations had lower stability with precipitation and sizes exceeding 1000 nm in DLS. Conversely, mixed formulations exhibited nanometric sizes without precipitation. Electrophoresis indicated similar bands, with pH-adjusted formulations showing trailing. Circular dichroism revealed reduced regular  $\alpha$ -helices and increased distorted  $\alpha$ -helices for DNA formulations and left-twisted antiparallel  $\beta$ -sheets for mixed formulations. System incorporated with peptide, pH adjustment reduced  $\alpha$ -helices by 31.1% and increased right-twisted antiparallel  $\beta$ -sheets and parallel  $\beta$ -sheets; mixed formulations showed more significant  $\alpha$ -helix reduction and increased right-twisted antiparallel  $\beta$ -sheets. These findings underscore the impact of preparation methods on the apoferitin stability and structure. Future studies should explore the efficiency in binding molecules to apoferitin, determining whether pH adjustment is optimal.

# Flavonoids loaded Nanostructured Lipid Carrier (NLC) and their antiviral activity for dengue virus.



## Author

Poliana Gomes da Silva - Instituto Oswaldo Cruz - Fiocruz Pernambuco  
Luíse Lopes Chaves - Instituto Oswaldo Cruz - Fiocruz Pernambuco  
Douglas Dourado Oliveira - Instituto Oswaldo Cruz - Fiocruz Pernambuco  
Lindomar José Penal - Instituto Oswaldo Cruz - Fiocruz Pernambuco  
Fábio Rocha Formiga - Instituto Oswaldo Cruz - Fiocruz Pernambuco



## Knowledge Area

Nanotechnology



## Funding

FACEPE - APQ-0116-7.08/18



## Keywords

dengue, antivirals, nanoparticles

## Abstract

Naringenin (NRG) and Sakuranetin (SAK) are flavonoids found in citrus fruits. Recently, our group identified the antiviral activity of these molecules against the dengue virus, serotype 2. However, they presented limitations such as low aqueous solubility that compromise their bioavailability. In this context, nanoparticles such as the nanostructured lipid carrier (NLC) have been used as a molecule delivery platform to ensure better delivery to a specific target as well as improve the activity of therapeutic compounds such as NRG and SAK. Thus, the objective was to evaluate the physicochemical and antiviral properties of NLC with NGR and SAK. Empty-NLC, Naringenin (NLC-NRG) and Sakuranetin (NLC-SAK) were synthesized by hot emulsification. Particle size distribution and zeta potential were evaluated by Zetasizer Nano ZS90, and their encapsulation efficiencies (EE) by the previously developed HPLC method (0.1 phosphoric acid % on distilled water (A): methanol (B) – flow rate of 1.0 mL/min). Empty-NLC, NLC-NRG and NLC-SAK showed particle size of  $79.6 \pm 0.6$ ;  $90.8 \pm 0.5$  and  $61.6 \pm 0.1$  nm and polydispersity index of  $0.368 \pm 0.008$ ;  $0.177 \pm 0.2$  and  $0.419 \pm 0.003$  respectively and negative charge for all nanoparticles (NPs). Furthermore, NLCs showed EE of 47.2% for NLC-NRG; and 89.9% for NLC-SAK. Following the NPs characterization; cytotoxicity analyses were performed on Vero CCL-81 cells, presenting Cytotoxic Concentration – CC50 of 114.8 for NLC-NRG and CC50 of 134.2 for NLC-SAK. Finally, we evaluated the antiviral activity of each formulation against dengue serotype 2 in a post-treatment assay. NLC's presented satisfactory results by demonstrating significant antiviral activity with Inhibitory Concentration - IC50 of 36.35 and Selective Index (SI) of 3.1 for NLC-NRG; IC50 of 59.09 and SI of 2.27 for NLC-SAK. Consequently, flavonoid-loaded NLC revealed promising antiviral formulations against dengue virus.



# Nanotechnological Delivery of N,N-Dimethyltryptamine: Production and Characterization of an Oral Microemulsion



## Author

Lucas Gabriel da Silva Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Emerson José de Jesus Santana - Universidade Federal do Rio Grande do Norte (UFRN)  
Fabia Julliana Jorge de Souza - Universidade Federal do Rio Grande do Norte (UFRN)  
Lourena Mafra Veríssimo - Universidade Federal do Rio Grande do Norte (UFRN)  
Wógenes Nunes de Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Eryvaldo Sócrates Tabosa do Egito - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Nanotechnology



## Funding

This research was funded by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq); Coordenação de Aperfeiçoamento de Pessoal de Nível superior—Brasil (CAPES)—Financ code 001



## Keywords

Microemulsion, Dimethyltryptamine, Ayahuasca tea

## Abstract

N,N-Dimethyltryptamine (DMT), a psychoactive compound found in the inner bark of *Mimosa tenuiflora* and Ayahuasca tea, has been highlighted as a potential alternative treatment for mental disorders as anxiety, depression and major depressive disorder. However, DMT presents several biopharmaceutical limitations due to its high lipophilicity, low bioavailability and susceptibility to metabolism by the enzyme monoamine oxidase (MAO). Therefore, the aim of this study was to develop a microemulsion (ME-B) containing DMT to overcome these biopharmaceutical drawbacks for its potential oral administration. The ME formulation was composed of Lipoid® S100 (6.3%), Tween® 80 (14.7%), Miglyol 812N (11%) and purified water (68%). All components were homogenized using magnetic stirring followed by sonication an ultrasound probe. Then, 100 mg of the DMT was incorporated into the ME-B using the direct incorporation method, under continuous stirring, overnight, producing the DMT-ME. Both ME-B and DMT-ME were evaluated for (i) droplet size (nm), (ii) polydispersity index (Pdl), and (iii) pH. The drug content of DMT-ME was evaluated using spectrophotometry at 281 nm. The results showed values of  $25.44 \pm 0.34$  nm for droplet size, a Pdl of  $0.221 \pm 0.005$ , and a pH of  $6.1 \pm 0.07$  for ME-B. These parameters indicate the successful production of ME-B with characteristic size and physicochemical properties of a microemulsion. Following DMT incorporation, DMT-ME presented values of  $21.98 \pm 0.67$  nm for droplet size, a Pdl of  $0.374 \pm 0.006$ , and a pH of  $9.6 \pm 0.03$ , in addition to a drug content of  $9.79 \pm 0.13$  mg/mL. These data suggest that DMT incorporation did not significantly affect the physicochemical properties of ME-B and that ME-B was able to incorporate a substantial amount of DMT. Based on this, the DMT-ME was successfully produced and characterized, indicating its potential use as an alternative approach for N,N-dimethyltryptamine delivery.

# Development, optimization and characterization of a 2-amino-thiophene (6CN10) nanocrystals



## Author

Carlos Alberto Arcelly Santos Bezerra - Universidade Federal da Paraíba (UFPB)  
Rodrigo Santos Aquino de Araújo - Universidade federal da Paraíba (UFPB)  
Ricardo Dias de Castro - Universidade federal da Paraíba (UFPB)  
Francisco Jaime Bezerra Mendonça Junior - Universidade federal da Paraíba (UFPB)  
Elquio Eleamen Oliveira - Universidade federal da Paraíba(UFPB)



## Knowledge Area

Nanotechnology



## Funding

FACEPE - APQ-0116-7.08/18



## Keywords

nanocrystal, drug delivery system, thiophene derivative

## Abstract

The 2-aminothiophene derivative 2-[(4-nitrobenzylidene)amino]-4,5,6,7-tetrahydro-4H-benzo[b]thiophene-3-carbonitrile, named 6CN10, shows antifungal activity against strains of *Cryptococcus neoformans* and *Candida albicans*, however, its low solubility in water limits its potential as a drug candidate. The goal of this work was to develop, optimize and characterize 6CN10 nanocrystals aiming to increase the water solubility of the drug candidate. The nanocrystals were obtained using the anti-solvent nanoprecipitation technique followed by lyophilization. An experimental design using the Design Expert software was building and the variables solvent volume, percentage and type of stabilizer were investigated using average diameter and polydispersity index (PDI) as response variables. The nanocrystals were characterized by dynamic light scattering (DLS) and electrophoretic light scattering (ELS). The optimized nanocrystal formulation before lyophilization presented an average diameter of  $242 \pm 12.31$  nm and PDI of  $0.04 \pm 0.03$  with a negative zeta potential of  $-7.93 \pm 0.63$  mV. The lyophilized nanocrystals presented a mean size of  $256 \pm 10.23$  nm with a PDI of  $0.17 \pm 0.07$  in D<sub>0</sub> and a mean size of  $250.5 \pm 6.8$  nm and PDI of  $0.04 \pm 0.01$  after 90 days. The nanocrystals improve the solubility of 6CN10 in water by 5 times. Although the study is still under development to complete the evaluation of the biological activity of the nanocrystals, the early results reveal that the nanocrystallization is an effective and low-cost platform to increase the water solubility of 6CN10.

# Enhancing the Stability of Cannabidiol in Microemulsions through Lyophilization



## Author

Lucas Gabriel da Silva Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Emerson José de Jesus Santana - Universidade Federal do Rio Grande do Norte (UFRN)  
Fabia Julliana Jorge de Souza - Universidade Federal do Rio Grande do Norte (UFRN)  
Lourena Mafra Veríssimo - Universidade Federal do Rio Grande do Norte (UFRN)  
Wógenes Nunes de Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Eryvaldo Sócrates Tabosa do Egito - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Nanotechnology



## Funding

UFRN - PROPESQ - Rede Científica; UFRN - PPG; CNPq; Capes - Finance code 001; FAPERN; UFR NUPLAM



## Keywords

Cannabidiol; Nanotechnological; Microemulsion.

## Abstract

Microemulsions (ME) stands out as a suitable nanotechnological approach to address the biopharmaceutical drawbacks of cannabidiol (CBD). However, their high water content compromises stability, leading to microbial growth, drug leakage, and phospholipids hydrolysis. Lyophilization, a dehydration technique that removes water by sublimation, emerges as a strategy to enhance ME stability and prevent drug degradation. The aim of this work was to lyophilize a CBD-containing ME (CBD-ME) and evaluate its physicochemical properties post-lyophilization. The ME, composed of Lipoid® S100 (6.3%), Tween® 80 (14.7%), Miglyol® 812N (11%), and purified water (68%), was homogenized by magnetic stirring followed by sonication, to expedite the process. CBD (150 mg) was added to 10 mL of ME by magnetic stirring overnight. Maltose (5%) was added as cryoprotectant. The CBD-ME was frozen for 24h at  $-80^{\circ}\text{C}$ , followed by 48h of lyophilization. The lyophilized CBD-ME was reconstituted with purified water, heated to  $60^{\circ}\text{C}$ , and evaluated for (i) droplet size, (ii) polydispersity index (PDI), (iii) pH, and (iv) drug content using spectrophotometry at 274 nm. Before lyophilization, the CBD-ME had a droplet size of  $27.72 \pm 0.05$  nm, a PDI of  $0.25 \pm 0.01$ , a pH of  $6.16 \pm 0.07$ , and a drug content of  $14.7 \pm 0.7$  mg/mL. These results confirmed the successful production of CBD-ME. After lyophilization, the droplet size, PDI and drug content were  $52.00 \pm 0.80$  nm,  $0.50 \pm 0.02$ , and  $13.7 \pm 0.3$  mg/mL, respectively. These data suggest that while lyophilization increased droplet size and PDI, likely due to droplet agglomeration, the CBD content remained stable. Thus, lyophilization is a promising method for extending the shelf life of CBD microemulsions.

# Vasconcelos Lopes    Development and characterization of Palmitoylethanolamide-loaded polymeric nanocapsules for the treatment of atopic dermatitis in dogs



## Author

Daniela Vasconcelos Lopes - Universidade Federal do Rio Grande do Sul (UFRGS)  
Diego Fontana de Andrade - Universidade Federal do Rio Grande do Sul (UFRGS)  
Karina Paese - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

FACEPE - APQ-0116-7.08/18



## Keywords

dengue, antivirals, nanoparticles

## Abstract

Canine atopic dermatitis (CAD) is a common inflammatory skin disease in dogs that requires personalized, multimodal treatments. However, current treatments often come with drawbacks, such as side effects, high costs, and a long latency period. In the search for safer and more effective therapeutic options, researchers are investigating the benefits of palmitoylethanolamide (PEA), a natural biolipid produced by cells on demand. While previous studies have focused on oral PEA treatments for CAD, this study explores the use of nanotechnology to develop topical formulations for targeted PEA delivery, offering an innovative approach to treating the disease. Polymeric nanocapsules containing PEA 1mg/ml (NC-PEA) were prepared by interfacial deposition of preformed polymer. Their physicochemical properties, including particle size (laser diffraction and dynamic light scattering), zeta potential (electrophoretic mobility), pH (calibrated potentiometer), PEA content (high-performance liquid chromatography), and encapsulation efficiency (ultrafiltration-centrifugation), were assessed. Blank formulations (without the active substance) were also developed for comparison purposes. Additionally, an analytical method for quantifying PEA was validated in compliance with RDC 166/2017 of the National Health Surveillance Agency. The method was found to be specific, precise, accurate, and linear in the range of 10 to 150  $\mu\text{g/ml}$ . The results showed that NC-PEA had an average diameter of the particle size base on volume weighted D (4,3) of  $241.67 \pm 5.03$  nm, a Span of  $1.74 \pm 0.055$ , a hydrodynamic size (z-average) of  $206 \pm 4$  nm, a polydispersity index of  $0.109 \pm 0.012$ , a zeta potential of  $-15.87 \pm 1.46$ , and a pH of  $4.7 \pm 1.04$ . The PEA content was  $94.84\% \pm 4.22$ , with an association rate of 100%. These findings indicate that NC-PEA possesses suitable physicochemical characteristics for the development of an innovative nanotechnological formulation for the treatment of CAD.

# Nanotechnological Hair Photoprotector: Development and Evaluation of Hair Shaft



## Author

Ana Carvalho - Universidade Federal do Rio Grande do Sul(UFRGS)  
Schmitt, D. L. - Universidade Federal do Rio Grande do Sul(UFRGS)  
Gündel, S. S. - Universidade Federal do Rio Grande do Sul (UFRGS)  
Grudzinski, P. B. - Universidade Federal do Rio Grande do Sul(UFRGS)  
Schuh, R. S. - Universidade Federal do Rio Grande do Sul (UFRGS)  
Paese, K. - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico



## Keywords

hair photoprotection, UV filters, nanotechnology.

## Abstract

Hair plays a fundamental role in aesthetics, style, identity, and personal well-being. However, UV radiation is the primary cause of damage to the hair shaft, leading to the degradation of amino acids in the cortex and cuticle. In this context, the lack of effective options for hair photoprotection is a significant obstacle, as there are no products on the market with satisfactory efficacy. Therefore, the aim of this study was to develop and evaluate a nanotechnological formulation structured with Eudragit® RS100, containing avobenzene (2mg/mL), octocrylene (1.4mg/mL), and  $\alpha$ -tocopherol (2mg/mL). The formulations, both nanocapsules and nanoemulsion, were physicochemically characterized in terms of diameter, zeta potential, and content. Their effectiveness was determined by exposing hair strands to UVC radiation, with or without protection by the developed formulations, and analyzing cuticle photo-induced damage through morphology obtained by scanning electron microscopy. The diameter  $D[4,3]$  ( $\mu\text{m}$ ) was  $0.146 \pm 0.010$  and  $0.257 \pm 0.074$  for nanocapsules and nanoemulsions, respectively, with span values below 2. The z-average (nm) was  $144.0 \pm 13.85$  and  $203.9 \pm 27.9$ , respectively and the zeta potential (mV) obtained was  $+10.64 \pm 2.43$  for nanocapsules and  $-15.13 \pm 3.82$  for nanoemulsions. The content of avobenzene, octocrylene, and  $\alpha$ -tocopherol in the nanocapsules was  $82.29 \pm 1.21\%$ ,  $78.63 \pm 2.94\%$ , and  $85.61 \pm 5.79\%$ , respectively, while in the nanoemulsions, the content was  $85.97 \pm 0.64\%$ ,  $85.40 \pm 3.18\%$ , and  $77.47 \pm 5.38\%$ . Photomicrographs evidenced breakage and detachment of the cuticle structure, with severe surface flaking in the samples treated with water and nanoemulsion. In contrast, no damage was observed in the samples treated with the developed nanocapsules across different analyzed fields. The nanocapsule formulation containing the active substances was able to protect the hair shaft after exposure to UVC radiation.

# Development of Nanoformulation Combining Paclitaxel and Temozolomide: Investigation of the Biological Effects on Glioma Cells



## Author

Danieli Rosane Dallemole - Universidade Federal do Rio Grande do Sul(UFRGS)  
Samanta da Silva Gündel - Universidade Federal do Rio Grande do Sul (UFRGS)  
Silvia Stanisçuaski Guterres - Universidade Federal do Rio Grande do Sul (UFRGS)  
Adriana Raffin Pohlmann - Universidade Federal do Rio Grande do Sul (UFRGS)  
Guido Lenzglenz -Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

Programa de Apoio à Fixação de Jovens Doutores no Brasil FAPERGS/CNPq  
07/2022-23/2551-0000125-0



## Keywords

Cancer; Glioblastoma; Lipid-core nanocapsules

## Abstract

Gliomas are aggressive brain tumors with limited treatment options due to their invasive nature and localization. Drug nanoencapsulation emerges as a promising approach to enhance drug delivery, enabling the targeted delivery of multiple active substances within a single formulation. This approach holds the potential for improving therapeutic outcomes by optimizing drug bioavailability and targeting tumor-specific sites. In this context, the study aims to develop a nanoformulation that combines paclitaxel (PTX, in the core) and temozolomide (TMZ, in aqueous phase), taking advantage of their distinct mechanisms of action, and to evaluate its impact on glioma cell lines. Lipid-core nanocapsules were synthesized by the interfacial deposition of a preformed polymer method. These nanocapsules were characterized by diameter, zeta potential (ZP), drug content, and encapsulation efficiency (EE%). Additionally, an analytical method (HPLC) was validated for the simultaneous quantification of the drugs. The analytical method proved specific and linear for the range of 5-25  $\mu\text{g mL}^{-1}$  and 25-125  $\mu\text{g mL}^{-1}$  concentration of PTX and TMZ, respectively. The precision of the method was confirmed through analyses of repeatability and intermediate precision, with relative standard deviation (RSD) values <2%. Furthermore, the accuracy was validated with recovery percentages ranging from 98-102% and RSD values <2%. The formulation exhibited a unimodal distribution, a diameter of  $179\pm 12$  nm, and low polydispersity indices. The ZP was  $-13.1\pm 1.41$  mV. The PTX content was  $0.11\pm 0.03$  mg  $\text{mL}^{-1}$ , with an EE% of 100%. The TMZ content was  $0.47\pm 0.03$  mg  $\text{mL}^{-1}$ . Cytotoxicity assay demonstrated that the supramolecular structure of the nanocapsule does not reduce cell viability per se, and drug encapsulation did not affect drug efficacy. These findings pave the way to explore the effect of nanoformulation in different cellular phenotypes, such as cell cycle, autophagy, DNA damage, and senescence in glioma cells.

# Evaluation of Contrast Agents for Morphological Characterization of Liposomes



## Author

Laiane dos Santos Ribeiro Machado - Universidade Federal da Bahia (UFBA)  
John Anthony Bonfim Santos - Universidade Federal da Bahia (UFBA)  
Diogo Rodrigo Magalhães Moreira - FIOCRUZ Salvador  
Henrique Rodrigues Marcelino - Universidade Federal da Bahia (UFBA)



## Knowledge Area

Nanotechnology



## Funding

The National Council for Scientific and Technological Development / Bahia State Research Support Foundation



## Keywords

Liposomes, Ethanol Injection, Transmission electronic microscopy

## Abstract

Liposomes are colloidal systems with at least one phospholipid bilayer that can transport lipophilic, hydrophilic, or amphiphilic drugs, providing more stability and modulating their release profile. The morphology of these systems directly influences their stability, encapsulation, and classification, which is why it is essential to know their average size, distribution, and shape. One of the most used imaging techniques is transmission electron microscopy (TEM) by contrast, in which the choice of contrast agent is essential for the analysis's success once some destabilize the liposome bilayer. Thus, the present work aimed to evaluate contrast agents for characterizing liposomes consisting of soy phosphatidylcholine and cholesterol. The liposomes were obtained by the ethanol injection method and analyzed by dynamic light scattering (DLS) and TEM using two different contrast agents (phosphotungstic acid (PTA) and uranyl acetate). The sample preparation for DLS involved dilution in water, while TEM analysis involved a filtration with a 0.45 $\mu$ m membrane and a dilution (1:1; sample:contrast) deposited on the nickel grid (300 mesh) coated with formvar 5%. DLS verified that the vesicles had an average size of 157nm  $\pm$  1 and a PDI of 0.15  $\pm$  0.02. The TEM performed with PTA showed dark-coloured particle and agglomerate structures outside the size range observed in the DLS, while with uranyl acetate, light-coloured vesicular structures with defined edges and size within the DLS range could be observed. With the analysis, we can conclude that the liposomes produced had a good size range and uniformity and that positive contrast (uranyl acetate) is more effective for observing the vesicles.

# Optimizing mRNA delivery with ionizable lipid-enhanced Liquid Crystalline Nanoparticles



## Author

Bryan Wender Debisi - Universidade de São Paulo (USP)  
Pedro Leonidas Oseliero Filho - Universidade de São Paulo (USP)  
Walison Nunes Silva - Universidade Federal de Minas Gerais (UFMG)  
Marcia Carvalho de Abreu Fantini - Universidade de São Paulo(USP)  
Pedro Pires Goulart Guimarães - Universidade Federal de Minas Gerais (UFMG)  
Maria Vitória Lopes Badra Bentley - Universidade de São Paulo(USP)



## Knowledge Area

Nanotechnology



## Funding

Grant #2022/10086-9, São Paulo Research Foundation (FAPESP)



## Keywords

lipid nanoparticle, mRNA vaccine, ionizable lipid

## Abstract

Lipid nanoparticles have emerged as advanced for the intracellular transportation of RNA, as evidenced by the approval of RNA vaccines targeting SARS-CoV-2. The research involved the conjugation of LCNs with ionizable lipids L1, SM-102, and ALC-0315, followed by a comparative analysis of these nanocarriers concerning their physicochemical characteristics, mRNA transfection efficiency, and FLuc-mRNA expression in vivo. The LCNs were developed by the blending of structural lipids, cationic lipid, and ionizable lipids (L1, SM-102, or ALC-0315) in citrate buffer (pH 3), with P407, and subsequently subjected to sonication. The physicochemical characteristics of LCNs was conducted, encompassing measurements of hydrodynamic diameter, PDI, zeta potential, and analysis of structure using SAXS. Following this, LCNs that contained ionizable lipids underwent assessment in vivo in mouse C57BL/6 models, wherein the bioluminescence expression in IVIS was observed subsequent to the IM delivery of 5  $\mu$ g of FLuc-mRNA, with evaluations carried out at 6-hour intervals for a duration of 6 days post-administration. The findings indicated hydrodynamic diameters of 197.7 nm, 201.2 nm, and 196.2 nm, along with corresponding PDI values of 0.209, 0.242, and 0.197. All formulations exhibited positive zeta potential values ranging between +13 and +14 mV. A notable advantage was observed with regards to the expression of FLuc-mRNA in the case of LCN+L1 compared to LCN+SM-102 and LCN+ALC-0315. Particularly, at six hours post-application intramuscularly in animals, LCN+L1 displayed a significantly higher bioluminescence intensity of  $1.28 \times 10^6$  photons/second, as opposed to  $3.98 \times 10^5$  and  $2.24 \times 10^5$  photons/second reported for LCN+SM-102 and LCN+ALC-0315, respectively. LCN+L1 demonstrated more prolonged luciferase expression, than other formulations for at least six days post-dosing. These results show the potential of LCN+L1 as an innovative delivery system for sustained mRNA expression through IM route.



# Nanoencapsulation of etoposide promotes its biexponential release characterized by a burst phase and a controlled phase



## Author

Samanta da Silva Gundel - Universidade Federal do Rio Grande do Sul (UFRGS)  
Sílvia Stanisçuaski Guterres - Universidade Federal do Rio Grande do Sul (UFRGS)  
Adriana Raffin Pohlmann - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Nanotechnology



## Funding

FAPERGS/CNPq 12/2014 (No. 16/2551-0000467-6); INCT-NANOFARMA (FAPESP, No. 2014/50928-2; CNPq, No. 465687/2014-8); CAPES (Finance Code 001)



## Keywords

Controlled release, Dialysis method, Lipid-core nanocapsules

## Abstract

The nanoencapsulation of etoposide, a widely used topoisomerase II inhibitor and chemotherapeutic agent, can overcome its limitations related to low aqueous solubility and facilitate a controlled release mechanism. The objective of this study was to develop and characterize lipid-core nanocapsules and evaluate their in vitro release profile. The nanocapsules were developed using the preformed polymer interfacial deposition method, and the release profile of etoposide, both in solution and nanoencapsulated, was evaluated using dialysis bags. The dissolution medium consisted of PBS (pH 7.4) containing 2% (w/v) Polysorbate 80. At predetermined intervals (up to 72 hours), samples of the medium were collected, and the concentration of dialyzed etoposide was determined using HPLC. The data obtained were fitted to semi-empirical mathematical models using Scientist® 2.0 software. The nanocapsules exhibited a unimodal particle size of approximately 150 nm, a drug content of 0.5 mg/mL, and an encapsulation efficiency of ~99%. Approximately 100% of the etoposide in solution was dialyzed within 6 hours, while about 60% of the etoposide was dialyzed from the nanocapsules. Up to 3 hours, there was no significant difference between the amount of dialyzed etoposide in the solution and in the nanocapsules, which may be related to the distribution of a portion of the etoposide more externally in the nanocapsules. Mathematical modeling demonstrated that the biexponential model (Correlation coefficient ( $r$ ) = 0.998 and Model Selection Criteria (MSC) = 4.842) was the most appropriate to describe the dialysis profile of etoposide from nanocapsules. In this case, the release was characterized by a burst phase (~60) followed by a sustained phase (~33%). Thus, we highlight the promise of this release mechanism, where the initial burst of etoposide release allows for a more immediate therapeutic effect, while the subsequent slow release contributes to prolonging its therapeutic efficacy.

# Citotoxicity evaluation of silica nanoparticles incorporated with chalcones against gastric and breast cancer cells



## Author

Luiz Cezar Barros Simone - Universidade Federal do Espírito Santo (UFES)  
Guilherme José Schwarz Sampaio - Universidade Federal do Espírito Santo (UFES)  
Rodrigo Romagna de Almeida - Universidade Federal do Espírito Santo (UFES)  
Reginaldo Bezerra dos Santos Universidade Federal do Espírito Santo (UFES)  
Rita de Cássia Ribeiro Gonçalves - Universidade Federal do Espírito Santo (UFES)  
Edésia Martins Barros de Sousa - Universidade Federal do Espírito Santo (UFES)  
Gracielle Ferreira Andrade - Universidade Federal do Espírito Santo (UFES)  
Rodrigo Rezende Kitagawa - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Nanotechnology



## Funding

FACEPE - APQ-0116-7.08/18



## Keywords

Nanoparticules, chalcones, tumor

## Abstract

Ways to overcome obstacles in cancer has led to several research aimed at developing system that can increase the effectiveness of treatment and reducing adverse effects, such as nanoparticles. Silica mesoporous nanoparticles (MSN) has demonstrated the capacity of target drug delivery in cancer treatments. Chalcones derivatives, compounds from the flavonoid family, are also tested for their antitumoral and cytotoxic potential. Chalcones derivatives were synthesized using Claisen-Schmidt condensation and had their structure confirmed. MSN were synthesized and the synthetic chalcone utilized was the 3-hydroxychalcone. The study had the objective to evaluate the antitumoral potential of synthetic chalcones and MSN incorporated with chalcones. Cytotoxic activity against gastric adenocarcinoma (AGS) and breast cancer (MCF-7) was evaluated, with fibroblast cells as comparison, using the MTT-tetrazolium method. 3-hydroxychalcone showed cytotoxic activity against AGS and MCF-7 (IC<sub>50</sub> between 47.58±0.16µM and 47.97±2.56µM with selectivity index of 5.78 and 5.75 respectively). The incorporation into the MSN was made using ethyl acetate. The MSN were characterized by scanning electron microscopy (SEM) and by elemental analysis (CHN). SEM showed that the MSN were spherical and that the particles were aggregated. CHN analysis revealed that 1.11% (22.2µg) of the chalcone were incorporated into the MSN. CHN analysis demonstrated that carbon % increased from 5.43% of the pure MSN to 6.54% with chalcone incorporated. The MSN incorporated with 3-hydroxychalcone had cytotoxic activity against AGS and MCF-7 (IC<sub>50</sub> between 53.91±0.85µM and 66.58±1.29µM respectively). These values can be related to the release profile and interactions of the chalcone with the MSN surface. Many works have reported the pharmacological potential of chalcones, but only a few studies report their application in drug delivery systems. The results of this study show the potential of this system in cancer therapy.

# Development and Characterization of Methylprednisolone-Loaded Nanoparticles



## Author

Thiago Medeiros Zacaron - Universidade Federal de Juiz de Fora (UFJF)  
Guilherme Luiz Silva - Universidade Federal de Juiz de Fora (UFJF)  
Maria Fernanda Cobucci Soares de Moura - Universidade Federal de Juiz de Fora (UFJF)  
Helvécio Vinícius Antunes Rocha - FIOCRUZ  
Guilherme Diniz Tavares - Universidade Federal de Juiz de Fora (UFJF)



## Knowledge Area

Nanotechnology



## Funding

CNPq and FAPEMIG



## Keywords

Methylprednisolone, Nanoparticles, Characterization

## Abstract

Severe Acute Respiratory Syndrome (SARS) has gained relevance in the context of the COVID-19 pandemic due to its potential for rapid progression to severe conditions and/or death. Despite extensive use, there is no consensus on the treatment for SARS, and methylprednisolone (MPD) is frequently used for its anti-inflammatory and immunosuppressive activities. However, prolonged use of MPD can lead to undesirable side effects. Nanostructuring MPD could target phagocytic cells involved in the inflammatory process and reduce toxic effects by minimizing the dose required. The bioadhesive and anti-inflammatory properties of chitosan (CS) are well-documented, and its combination with MPD may enhance the desired therapeutic effects. This study aimed to develop and evaluate the suitability of nanostructured carriers for MPD encapsulation. Specifically, chitosan nanoparticles (CsN) and chitosan-decorated nanostructured lipid carriers (NLC-Cs) were developed and characterized. Nanoparticles were characterized for size (mean hydrodynamic diameter), polydispersity index (Pdl), zeta potential (ZP), and encapsulation efficiency (EE). Both formulations exhibited nanometric sizes ( $< 200$  nm), monodisperse behavior ( $Pdl > 0.3$ ), and positive ZP ( $19.5 \pm 2.33$  mV for CsN and  $42.8 \pm 0.84$  mV for NLC-Cs). The EE of MPD was higher in lipid carriers ( $49.5\% \pm 0.09$ ) compared to CsN ( $20.6 \pm 5.28\%$ ), likely due to the greater solubility of MPD in the oily core of the NLCs. Based on these results, NLC-Cs are more promising for MPD encapsulation, given their higher positive charge density, which implies enhanced bioadhesive and anti-inflammatory effects, and their superior drug encapsulation efficiency.

# Evaluation of Antimicrobial Activity of Silver Nanoparticles Synthesized via a Novel Green Synthesis Route from *Plectranthus neochilus* Extract



## Author

Murilo Ricardo Sigal Carriço - Universidade Federal do Pampa (Unipampa)  
Marina Diaz Rodrigues - Universidade Federal do Pampa (Unipampa)  
Fernanda Riffel - Universidade Federal do Pampa (Unipampa)  
Higor Severo Molina - Universidade Federal do Pampa (Unipampa)  
Leonardo Martha Goncalves - Universidade Federal do Pampa (Unipampa)  
Elton Luís Gasparotto Denardin - Universidade Federal do Pampa (Unipampa)  
Rafael Roehrs - Universidade Federal do Pampa (Unipampa)



## Knowledge Area

Nanotechnology



## Funding

Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES



## Keywords

Antimicrobial activity, Green synthesis, AgNP

## Abstract

In this study, we developed a green synthesis route for AgNPs (silver nanoparticles) using an extract from *Plectranthus neochilus*, an aromatic plant with potent antioxidant properties derived from its phytochemical compounds. Our objective was to establish an AgNP synthesis route using the *P. neochilus* extract and assess its antimicrobial potential against four strains. Dried *P. neochilus* leaves (3.5 g) were agitated with a 1:1 ethanol-water solution (100 mL) for 16 hours at 35 °C, followed by filtration. For AgNP synthesis, we diluted 10 mL of the extract in 40 mL of water and 50 mL of silver nitrate (1 mmol/L). The solution was continuously agitated for 48 hours at 50 °C and photo-catalyzed using violet light-emitting diodes. The final formulation was frozen and lyophilized. AgNPs were characterized by UV-Vis spectroscopy, surface charge measurements, dynamic light scattering (DLS), and scanning electron microscopy (SEM). We evaluated the minimum inhibitory concentrations (MIC) using a serial microdilution method in culture broth against 4 strains. The AgNPs exhibited a characteristic plasmonic band at ~426 nm, an average size of  $86.83 \pm 0.58$  nm, a polydispersity index of  $0.192 \pm 0.006$ , and a zeta potential of  $-30.96 \pm 4.23$  mV. The SEM image confirmed their spherical shape. The AgNPs showed a minimum inhibitory concentration (MIC) of 2.31 mmol/L against *E. coli* (ATCC 25922), *S. aureus* (ATCC 25923), and *P. aeruginosa* (Clinical isolate), and 4.63 mmol/L against *P. mirabilis* (ATCC 25933). Notably, the *P. neochilus* extract did not exhibit inhibition ( $CO = 1$  g/L). In summary, we successfully established a green synthesis route for AgNPs with small particle size and spherical shape, providing a high surface area for contact. Although the MIC values for nitrate were lower than those for AgNPs, the concentrations of nitrate used in AgNP synthesis were below the observed MIC, demonstrating the efficiency of AgNPs in antimicrobial activity against the mentioned strains.

# Development and evaluation of Pullulan/Gellan Gum Bilayer Film containing silibinin-loaded nanocapsules for the treatment of atopic dermatitis in a Balb-c mice model



## Author

Taíne de Bastos Brum - Universidade Federal de Santa Maria (UFSM)

Malline Gehrcke - Universidade Federal de Santa Maria (UFSM)

Leticia Cruz - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Nanotechnology



## Funding

National Institute of Science and Technology in 3D printing and Advanced Materials Applied to Human and Veterinary Health - INCT \_3D-Saúde, funded by CNPq, Brazil (Grant #406436/2022-3)



## Keywords

Bilayer polymer film, Atopic dermatitis, Nanocapsule

## Abstract

Silibinin (SB), flavonoid known for its antioxidant and anti-inflammatory action, has been extensively studied to treat inflammatory skin diseases such as atopic dermatitis (AD), a inflammatory skin condition characterized by eczematous lesions, itching and redness, negatively impacting patients' quality of life. Incorporating active compounds into nanostructured systems is a promising strategy to overcome their limitations and increase therapeutic efficacy. Polymeric films offer advantages in treating skin diseases due to their potential to adhere, providing protection and hydration. In this study, a double-layer film composed of gellan gum and pullulan, using a two-step solvent casting method, containing SB-loaded nanocapsules (NC-SB), was developed and evaluated for topical treatment of AD induced by 2,4-dinitrochlorobenzene (DNCB) in animal model. In vitro studies demonstrated that pullulan added bioadhesive properties to films, with forces of  $17,554 \pm 1399$  dyne/cm<sup>2</sup> for vehicle films and  $10,934 \pm 699$  dyne/cm<sup>2</sup> for films containing NC-SB. Incorporation of NC almost doubled the occlusion factor, from  $29.45 \pm 1.47\%$  to  $55.78 \pm 2.35\%$ , from the vehicle films to the one containing NC-SB. NC-SB film exhibited slow release throughout 24 h, reaching  $7.14 \pm 1.34\%$  of released SB, high affinity for skin tissue, free radical scavenging capacity (100%), and non-hemolytic properties (hemolysis:  $0.61 \pm 0.11\%$ ). Treatments with the NC-SB film in vivo in mice attenuated itching behavior (from approximately 200 s to 30 s) and ear edema from approximately 35 mg to 13 mg. Oxidative parameters were modulated by the vehicle films, NC-SB-based films, and free SB (0.6, 0.4, and 0.4 nmol NO<sub>x</sub>/g tissue, respectively) and modulating inflammatory parameters. Finally, the results suggest gellan gum/pullulan bilayer film with NC-SB can mitigate the effects induced by DNCB, protecting the skin against oxidative damage and improving therapeutic outcomes in this AD model.

# Development and Optimization of Insulin/Caseinate/Hyaluronic Acid Nanoparticles by Experimental Design



## Author

Tatiane Patricia Babinski (Unicentro Guarapuava)  
Samila Horst Peczek (Unicentro Guarapuava)  
Andressa Zago (Unicentro Guarapuava)  
Rubiana Mara Mainardes (Unicentro Guarapuava)



## Knowledge Area

Nanotechnology



## Funding

FACEPE - APQ-0116-7.08/18



## Keywords

nanoparticles, insulin, experimental design

## Abstract

Insulin is a peptide hormone that regulates blood glucose levels. This study aimed to optimize the formulation of zein nanoparticles coated with hyaluronic acid (HA) and loaded with insulin (INS) by investigating formulation factors. Using the nanoprecipitation method and a full factorial design, independent variables included concentrations of HA, zein, sodium caseinate, and the organic to aqueous phase ratio. Responses measured were particle size, polydispersity index (PDI), zeta potential, and encapsulation efficiency (EE). Statistical analysis was conducted using Minitab® 18 software, applying ANOVA and multiple linear regression. Nanoparticles exhibited average diameters from 147 nm to 245 nm, PDI from 0.104 to 0.247, zeta potential between -32 mV and -17 mV, and EE from 16% to 59.4%. Global response (GR) combined individual dependent variable responses for optimization. The adjusted linear model had an  $R^2$  of 93.83%, indicating a good fit. ANOVA confirmed model significance ( $p = 0.047$ ) and no significant lack of fit ( $p = 0.579$ ). The organic to aqueous phase ratio (O/A) was the most critical factor influencing nanoparticle characteristics. Optimization using the composite desirability function combined multiple response criteria. The optimal formulation included 2.0% w/v zein, 0.3% w/v HA, 2.0% w/v sodium caseinate, and an O/A ratio of 1:2, achieving a composite desirability of 0.9084, indicating effective optimization. In conclusion, the experimental design methodology effectively optimized zein nanoparticles coated with HA and loaded with INS, yielding a formulation with desirable characteristics for potential therapeutic application. The resulting nanoparticles had diameters below 300 nm, PDI below 0.2, zeta potential around -30 mV, and encapsulation efficiency above 30%, meeting the proposed objectives.

# Peczek Development of Nanostructured Lipid Carriers to Enhance Therapy with Perillyl Alcohol: Improving Oral Bioavailability and Brain Distribution



## Author

Samila Horst Peczek (Unicentro Guarapuava)  
Tatiane Patrícia Babinski (Unicentro Guarapuava)  
Andressa Zago (Unicentro Guarapuava)  
Rubiana Mara Mainardes (Unicentro Guarapuava)



## Knowledge Area

Nanotechnology



## Funding

CAPES



## Keywords

lipid nanoparticles, perillyl alcohol, pharmacokinetics

## Abstract

Perillyl alcohol (POH), a monoterpene, shows promise in the treatment of brain tumors. However, its efficacy is limited due to low oral bioavailability and restricted brain distribution. This study focused on developing nanostructured lipid carriers (NLCs) containing POH to enhance its brain biodistribution. The NLCs were produced by hot homogenization, resulting in spherical particles with an average diameter of 287 nm and high encapsulation efficiency (99.68%). The polydispersity index was 0.143, indicating a uniform size distribution. In vitro release testing of the NLCs showed a biphasic profile: a burst effect with rapid POH release in 8 hours (24.60%), followed by a slower and steady release up to 48 hours (28.76%). Stability studies in simulated gastric and intestinal fluids revealed that NLCs resist pH variations and digestive enzymes. Pharmacokinetic studies in rats demonstrated that encapsulation of POH in NLCs significantly increased the oral bioavailability and brain concentration of the drug compared to free POH. The plasma profile indicated that after oral administration of free POH, the maximum concentration ( $C_{max}$ ) of 40,507.18 ng/mL was reached in 1 hour, dropping to 5,480.12 ng/mL in 24 hours. In contrast, the POH-NLCs reached a  $C_{max}$  of 43,552.17 ng/mL in 4 hours, maintaining 12,999.93 ng/mL after 24 hours. In the brain, the  $C_{max}$  of POH-NLCs was 16,085.07 ng/mL, about twice that of free POH (7,694.15 ng/mL). After 24 hours, the brain  $C_{max}$  of POH-NLCs remained at 7,126.73 ng/mL, while that of free POH dropped to 719.71 ng/mL. The area under the curve ( $AUC_{0-24h}$ ) indicated that the brain bioavailability of POH-NLCs (263,771.20 ng/mL) was 3.6 times greater than that of the free drug (72,104.51 ng/mL). Thus, NLCs present themselves as an effective delivery strategy for POH aimed at the treatment of brain tumors.

# Development Of A Hydrogel Containing 3,3'-Diindolymethane Liposomes Intending For Cervical Cancer Adjuvant Treatment



## Author

Vanessa Neuenschwander Custódio - Universidade Federal de Santa Maria (UFSM)  
Daiane Britto de Oliveira - Universidade Federal de Santa Maria (UFSM)  
Daniele Rubert Nogueira Librelotto - Universidade Federal de Santa Maria (UFSM)  
Letícia Cruz - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Nanotechnology



## Funding

National Institute of Science and Technology in 3D printing and Advanced Materials Applied to Human and Veterinary Health - INCT \_3D-Saúde, funded by CNPq, Brazil (Grant #406436/2022-3)



## Keywords

Liposomes, Cervical Cancer, Nanotechnology

## Abstract

Cervical cancer affects the cells of the cervix, mainly due to the HPV virus. Treatments include chemotherapy agents combined with radiotherapy, but they have significant adverse effects on healthy cells in the body. 3,3'-Diindolymethane (DIM) is a bioactive compound with antioxidant, antitumor, and anti-inflammatory properties, but it faces challenges such as photoinstability. Nanostructured systems like liposomes are being explored to protect and modulate the release of DIM, allowing its incorporation into hydrogels for vaginal application. This study developed and evaluated a guar gum hydrogel containing DIM-loaded liposomes as a potential adjuvant for cervical cancer treatment. Liposomes obtained by lipid film hydration were thickened with guar gum for hydrogel formation. The formulations were evaluated for their physicochemical characteristics and showed suitable results, achieving a size of  $146.10 \pm 1.6$  nm, PDI below 0.2, and a DIM content of  $84.65 \pm 0.24$  %. In the hemolysis test, the liposomes were considered non-hemolytic compared to the free active compound, which showed hemolytic potential. In vitro release was performed using the dialysis bag method, where DIM liposomes exhibited a more controlled release profile, releasing less than 50% of DIM in 12 h. Antiproliferative activity was evaluated on HeLa cells using MTT assay, showing that DIM liposomes reduced cell viability to  $58.68\% \pm 10.94$ . Mucoadhesion of hydrogels was assessed using a modified balance, revealing high mucoadhesive potential on bovine vaginal mucosa. Lastly, the permeation of hydrogels in bovine vaginal mucosa using Franz diffusion cells indicated that hydrogels have the ability to permeate and remain in vaginal mucosa without entering systemic circulation. Based on these findings, the hydrogel containing DIM-loaded liposomes proved to be a formulation with potential for use as an adjuvant in cervical cancer treatment, particularly via vaginal application.



# Evaluation of Curcumin-Loaded Nanocapsules on Survival and Plasma Exposure in Fly and Rodent Models via Time-to-Event and Population Pharmacokinetics Approach



## Author

Flávia Alves França - Universidade Federal de Minas Gerais (UFMG)  
Lays Cordeiro Guimarães - Universidade Federal de Minas Gerais (UFMG)  
Pedro Pires Goulart Guimarães - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Nanotechnology



## Funding

FACEPE - APQ-0116-7.08/18



## Keywords

Nanotechnology; drug-delivery; Pharmacometrics

## Abstract

This study evaluates the effects of curcumin-loaded nanocapsules (NC-CUR, 0.6 mg/mL) on the survival rate of diseased *Drosophila melanogaster* and the population pharmacokinetics (PopPK) in male Wistar rats. NCs were synthesized via nanoprecipitation and characterized for particle size, polydispersity, surface charge, pH, and drug content. Stability was evaluated up to 30 days post-preparation. In survival studies, flies received NC-CUR (10 days, 37 µg/mL). CUR levels in flies were quantified using HPLC-PDA. For PopPK studies, male Wistar rats received a single dose of CUR or NC-CUR intravenously or orally (2 or 6 mg/kg). Blood samples were collected at intervals up to four hours post-treatment. Data analysis utilized MonolixSuite® 2023R1, incorporating time-to-event and compartmental models. NCs exhibited particle sizes < 200 nm, monodispersity, and anionic charge, with slightly acidic pH and 100% drug content. Stability was maintained for 30 days, except for pH, which significantly decreased. Survival analysis with the Weibull model indicated that NC-CUR significantly enhanced survival rates. Higher CUR concentrations were observed in NC-CUR-treated flies. Plasma profiles in rats showed increased CUR exposure with NCs via both administration routes. The final PopPK model, a two-compartment model with linear elimination and proportional error, included first-order absorption for the oral model. Interindividual variability was accounted for in bioavailability, clearance (Cl), absorption rate ( $k_a$ ), intercompartmental clearance (Q), and volumes of central (V1) and peripheral (V2) compartments, with a correlation between Cl and bioavailability. Including NC formulation as a covariate enhanced model fit, indicating faster absorption and reduced V1, V2, Q, and Cl. This study demonstrates that nanoencapsulation significantly improves curcumin's pharmacokinetic properties and survival rates in both flies and rats, highlighting NC-CUR's potential for clinical applications.

# Development of a lipid nanoparticle based mRNA vaccine against Chikungunya Virus



## Author

Ana Cláudia Funguetto-Ribeiro - Universidade Federal do Pampa (Unipampa)  
Camila Pacheco - Universidade Federal der Santa Maria (UFSM)  
Vitória Gallarreta - Universidade Federal do Pampa (Unipampa)  
Clemence Boivin-Champeaux - University of Florida  
Eliana Fernandes - Universidade Federal do Pampa (Unipampa)  
Gustavo Guerra - Universidade Federal do Pampa (Unipampa)  
Francine Johansson- University of Florida  
Sandra Elisa Haas - Universidade Federal do Pampa (Unipampa)



## Knowledge Area

Nanotechnology



## Funding

CNPq (442731/2020-5; 305932/2022-5; 422002/2023-2; 408482/2022-2); FAPEMIG (APQ-00826-21; APQ-02402-23); and MCTI/FINEP—MS/SCTIE/DGITIS/CGITS (6205283B-BB28-4F9C-AA65-808FE4450542)



## Keywords

mRNA Vaccine; Nanoparticle; Chikungunya Virus

## Abstract

**Introduction:** Chikungunya virus (CHIKV) is an arbovirus that has significant implications, as the potential for chronicity, which affects both well-being and economy. Despite being considered a potentially pandemic disease by the World Health Organization, CHIKV lacks a licensed vaccine in Brazil. Thus, the development of an immunizer is a national priority. Recently, nucleic acid vaccines have garnered attention due to their safety and customization potential. Using this, mRNA can be delivered to generate the immune responses in a faster way, when compared to conventional vaccine platforms. Due to the instability and difficulties in delivery of nucleic acids, the use of lipid nanoparticles (LNPs), which protects RNA from degradation, is a strategy to improve the applicability of this technology. Therefore, here we propose the development of an mRNA vaccine against CHIKV using LNPs as a delivery system. **Methods:** LNPs were synthesized by microfluidic mixing and then they were characterized by size, polydispersity index (PDI) and zeta potential using the dynamic light scattering. LNPs transfection efficiency was assessed using L929 cell lineage. The in vivo experiments comprehend a prime and boost scheme in C57BL/6 mice using three different doses of mRNA, followed by a challenge with CHIKV. Weight, pain, viral load, cellular and humoral response, protection and immunogenicity will be evaluated by ELISA, flow cytometry, histopathology and Von Frey test. **Results:** LNP size ranged between 105,8 nm and 136,6 nm across batches. Surface charge was close to neutrality and PDI demonstrated homogeneity. The formulated LNPs could transfect the L929 cells. **Perspective:** To optimize our LNP system, we will evaluate the in vivo delivery of different formulations using barcoded mRNA. With the optimal LNP, we will analyze two distinct types of RNA: one produced in-house, and the other commercially sourced, both encoding the same sequence, allowing us to produce an enhanced vaccine.

# Development and Stability Evaluation of Ketoprofen-Loaded Polymeric Nanocapsules



## Author

Camila de Oliveira Pacheco - Universidade Federal de Santa Maria (UFSM)  
Joane Guterres Ferreira Universidade Federal do Pampa (Unipampa)  
Vitória dos Santos Gallarreta Universidade Federal do Pampa (Unipampa)  
Pedro Santos da Silva - Universidade Federal de Santa Maria (UFSM)  
Taiane Medeiro Cioche - Universidade Federal do Pampa (Unipampa)  
Tamara Ramos Maciel Universidade Federal do Pampa (Unipampa)  
Sandra Elisa Haas - Universidade Federal do Pampa (Unipampa)



## Knowledge Area

Nanotechnology



## Funding

CAPES



## Keywords

Polymeric nanocapsules, Non-steroidal anti-inflammatory drug, Ketoprofen

## Abstract

Ketoprofen (KTP) is a non-steroidal anti-inflammatory drug that inhibits both cyclooxygenase-I (COX-I) and cyclooxygenase-II (COX-II). It is widely used as an analgesic, anti-inflammatory, and antipyretic for the treatment of diseases such as rheumatoid arthritis and osteoarthritis, with a half-life of approximately 4 hours in humans. In the Biopharmaceutical Classification System (BCS), it is classified as a class II drug, making its solubility a critical factor. Combined with its non-selectivity, this makes it a drug of interest for use in polymeric nanocapsules (NCs). NCs are characterized by increasing solubility, prolonging half-life, and providing more controlled release, in addition to targeting treatments. In this context, the objective of this work was to develop and evaluate the stability of polymeric nanocapsules containing ketoprofen (NC-KTP) at 1 mg/mL. NC-KTP was developed using the preformed polymer method, in which the organic phase contained polycaprolactone (PCL), KTP, caprylic acid (TCM), acetone, alcohol, and Span 60, which were solubilized for 20 minutes at 40 °C. After complete solubilization, this mixture was poured into the aqueous phase, composed of polysorbate 80 and water. Following the suspension, the volume was reduced using a rotary evaporator to a final volume of 10 mL. The NC-KTP was characterized for diameter, polydispersity, charge, pH, dosing, and encapsulation efficiency. The NCs demonstrated stability over a period of 60 days, with a diameter of approximately  $330 \text{ nm} \pm 11$ , a span of  $1.49 \pm 0.02$ , a negative charge of  $-31.09 \pm 0.59$ , pH almost 5 and 100% dosing and encapsulation efficiency. Therefore, this study successfully developed and characterized NC-KTP with stable physicochemical properties under ambient conditions for a period of 60 days, suggesting the continuation of evaluation and indicating that the NCs are viable for future studies in vitro and in vivo analyses.

# Development And Characterization Of Nanoemulsions Containing Curcumin



## Author

Marciane Conti Zornita Bortolanza - Universidade Estadual do Centro - Oeste (Unicentro)  
Daniele Fernanda Renzi - Universidade Estadual do Centro - Oeste (Unicentro)  
Emanuele Fermino - Universidade Estadual do Centro - Oeste (Unicentro)  
Najeh Maissar Khalil - Universidade Estadual do Centro - Oeste (Unicentro)



## Knowledge Area

Nanotechnology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq-Brazil).



## Keywords

curcumin, nanoemulsion, stability

## Abstract

Curcumin, extracted from *Curcuma longa*, has been used as a type of spice, but primarily for its biological activities, such as anti-inflammatory effects, activity against tumor cell lines, antioxidants, and antimicrobial properties. However, like many other bioactive molecules, it has limitations regarding its physical-chemical aspects and absorption, which limit its potential pharmacological applications. In this context, biocompatible nanostructured systems emerge as an interesting alternative to enhance the solubility, stability across diverse pH levels, temperatures, and the absorption of these molecules. The aim of the present study was to develop a nanoemulsion containing curcumin using a low-energy method. The nanoparticles were obtained using caprylic acid, glycerol, soy lecithin, tween 20, and curcumin, through phase inversion. The average particle size (AZ) and polydispersion index (PDI) were evaluated using the 90 Plus Particles Size Analyzer. Stability was assessed at room temperature, evaluating the PDI and AZ over 30 days. The developed formulations were obtained through factorial design. Out of the 27 combinations provided by the design, three formulations (F1, F2, and F3) showed an AZ of less than 200 nm. Specifically, F1: AZ of  $113.3 \pm 9.27$  with a PDI of 0.005, F2: AZ of  $115.0 \pm 11.43$  with a PDI of 0.005, and F3: AZ of  $135.2 \pm 30.31$  with a PDI of 0.005. Among the optimized systems, F1 and F2 exhibited the best stability, maintaining it for 28 days, whereas F3 remained stable for a reduced period (14 days). Thus, the formulations achieved exhibit physical-chemical characteristics compatible with a stable nanostructured system.

# Development Of A Nanoemulsion Containing Azelaic Acid



## Author

Aline Camile Stelf Flareço - Universidade Estadual do Centro - Oeste(Unicentro)  
Daniele Fernanda Renzi - Universidade Estadual do Centro - Oeste (Unicentro)  
Emanuele Fermino - Universidade Estadual do Centro - Oeste (Unicentro)  
Najeh Maissar Khalil -Universidade Estadual do Centro - Oeste (Unicentro)



## Knowledge Area

Nanotechnology



## Funding

não possui



## Keywords

Nanotechnology, Azelaic Acid, Melasma

## Abstract

Pathologies such as melasma are among the most commonly reported disorders associated with epithelial tissue. Pharmaceutical industry formulations are developed to alleviate the effects of skin dysfunctions. Azelaic acid (AZA) has keratolytic and depigmenting actions. The combination of AZA with nanostructured systems has the potential to increase cutaneous absorption and efficacy, as well as minimize possible side effects such as itching, burning, hyperemia, and peeling. The aim of this work was to develop nanoemulsions containing AZA and vitamin E. For the development of the nanostructured systems, AZA was incorporated into the formulations in concentrations of 100, 150, 200, and 400 mg, using low-energy methods to obtain the nanoemulsions. AZA was added to the oily phase containing caprylic acid and vitamin E, and subsequently associated with the surfactant tween 80. The aqueous phase, composed of ultrapure water and lecithin, was added to the system, with a final volume of 10ml. The average particle size (AZ) and polydispersity index (PDI) were evaluated. The AZ and PDI (respectively) for 100mg:  $140 \pm 16$  and  $0.273 \pm 0.015$ , 150mg:  $165 \pm 5$  and  $0.198 \pm 0.024$ , 200 mg:  $180 \pm 12$  and  $0.177 \pm 0.03$  and 400mg:  $250.25 \pm 30$  and  $0.297 \pm 0.04$ . The formulation containing 400mg of AZA had its stability assessed through the values of AZ and PDI over a period of 30 days. A decrease in the mentioned parameters was identified when comparing day 01 with day 30: AZ and PDI (respectively):  $176.85 \pm 25$  and  $0.211 \pm 0.020$ . The optimized nanoformulation of AZ shows characteristics compatible with nanometric systems and low cost.

# Development of a 3D GelMA-alginate hydrogel Based platform for drug testing



## Author

Gabriel Henrique Costa da Silva - Universidade Federal de Minas Gerais (UFMG)  
Sérgio Ricardo Aluotto Scalzo Júnior - Universidade Federal de Minas Gerais (UFMG)  
Pedro Pires Goulart Guimarães - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Nanotechnology



## Funding

Postgraduate program in technological innovation, UFMG; FAPEMIG



## Keywords

Hydrogel; Cell culture; 3D Culture

## Abstract

**Introduction:** Identifying therapeutic targets and developing new technologies for treating diseases is increasingly necessary. However, current in 2D culture in vitro models have limitations, as: 2D cultures fail to replicate morphology and cellular behaviors, while animal models are costly and ethically challenging. To overcome these issues, 3D culture has been extensively investigated to be the next generation of in vitro drug testing. Therefore, we aimed to develop a 3D platform based on Gelatin methacryloyl (GelMA) and alginate hydrogel for drug testing. **Methods:** For our 3D platform we used GelMA (10% w/v) and alginate (3% w/v) in ratios of 1:4, 2:4, and 3:4, along with single-polymer formulations. The polymers were diluted in phosphate buffer and cross-linked using UV light for 3 minutes with an 80 mM CaCl<sub>2</sub> solution for 5 minutes. To test the efficiency of our polymer NIH 3T3 murine fibroblasts were cultured, and cell viability, proliferation, and morphology were assessed using resazurin, live/dead assays, and confocal microscopy, respectively. **Results:** The cells remained viable for at least 8 days in the hydrogels, with the lowest viability being 90% in GelMA-only hydrogel. Cell morphology varied with alginate concentration; higher GelMA levels led to stellate morphology within 3 days, while only alginate resulted in spherical cells. Over time, cell proliferation was higher in 3D culture compared to 2D, where all cells died between 3 and 7 days. **Conclusion:** Our results showed that reducing alginate in the hydrogel promoted a more natural cellular behavior, with cells extending within the gel matrix. Alginate concentration didn't significantly affect cell viability. Cells cultured in 3D hydrogel showed sustained proliferation compared to 2D culture, where contact inhibition led to a decline in viability and proliferation. **Next Steps:** The platform will be validated by comparing the efficacy of cell transfection with lipid nanoparticles in 3D and 2D environments.

# Flavonoids loaded Nanostructured Lipid Carrier (NLC) and their antiviral activity for dengue virus.



## Author

Mathias Krindges - Universidade Federal de Santa Maria (UFSM)  
Taine de Bastos Brum - Universidade Federal de Santa Maria (UFSM)  
Letícia Cruz - Universidade Federal de Santa Maria (UFSM)  
Mailine Gehrcke - Universidade Federal de Santa Maria (UFSM)



## Knowledge Area

Nanotechnology



## Funding

National Institute of Science and Technology in 3D printing and Advanced Materials Applied to Human and Veterinary Health - INCT \_3D-Saúde, funded by CNPq, Brazil (Grant #406436/2022-3)



## Keywords

Nanocapsule. Alphatocopherol. Polymer films

## Abstract

$\alpha$ -tocopherol (AT), the active form of Vitamin E, demonstrates potent anti-proliferative, anticarcinogenic, and anti-aging properties due to its strong antioxidant capabilities. However, its poor solubility in water and stability issues pose challenges for incorporating it into topical pharmaceuticals. Polymeric nanocapsules (NC) provide a solution by encapsulating AT, improving its solubility, bioavailability, and stability. Despite typically existing as aqueous suspensions, which may face stability issues, incorporating NC into solid dosage forms as polymeric films proves advantageous for skin application. NC suspensions were prepared using the preformed polymer interfacial deposition method with ethyl cellulose and medium-chain triglycerides. They were characterized for AT content, encapsulation efficiency (EE), pH, particle size, and zeta potential (ZP). Results showed near-theoretical AT content (1 mg/mL) with 99.9% EE, indicating no degradation during NC preparation. The formulations exhibited high antioxidant activity via ABTS radical scavenging assay. Films containing NC were subsequently prepared via solvent evaporation by dispersing 1% of gellan gum and added to the NC suspension. Characterization included AT content, weight homogeneity, thickness, size, and moisture content. AT content in films demonstrated homogeneous distribution (FNC-AT:  $154.51 \pm 4 \mu\text{g}/\text{cm}^2$ , F-AT:  $147.21 \pm 4.10 \mu\text{g}/\text{cm}^2$ ). Films were thin ( $<25 \mu\text{m}$ ), ideal for skin application, maintaining NC's size. The NC effectively protected the AT from photodegradation in the UVC chamber, both in suspension and in film forms, where the remaining amount of the active was 84.52% and 45.0%, respectively. This study successfully associated AT into NC and incorporated them into gellan gum films, providing a promising, photostable pharmaceutical form for topical AT application.

# Polysaccharides Nanocomposite Hydrogel with Sesame Components for Local Cervical Cancer Treatment



## Author

Daiane Britto de Oliveira - Universidade Federal de Santa Maria (UFSM)  
Camila Parcianello Saccol - Universidade Federal de Santa Maria (UFSM)  
Milena Meinerz - Universidade Federal de Santa Maria (UFSM)  
Vinicius Costa Prado - Universidade Federal de Santa Maria (UFSM)  
Marcel Henrique Marcondes Sari - Universidade Federal de Santa Maria (UFSM)  
Daniela Mathes - Universidade Federal de Santa Maria(UFSM)  
Letícia Bueno Macedo - Universidade Federal de Santa Maria (UFSM)  
Daniele Rubert Nogueira Librelotto - Universidade Federal de Santa Maria(UFSM)  
Letícia Cruz - Universidade Federal de Santa Maria(UFSM)



## Knowledge Area

Nanotechnology



## Funding

INCT\_3D-Saúde, funded by CNPq, Brazil (Grant #406436/2022-3) and Rio Grande do Sul State Research Support Foundation (FAPERGS - 21/2551-0002062-8)



## Keywords

Polysaccharides; Nanotechnology; Semissolid dosage form;

## Abstract

Cervical cancer is the third most common malignancy among women worldwide and poses a significant health challenge. Treatment is quite challenging, usually involving systemic chemotherapy and a series of adverse effects. Sesamol (SES) is a phytochemical with promising biological activities, such as anti-inflammatory, antiproliferative, and antioxidant properties. This study aimed to harness this potential by developing a hydrogel containing nanoemulsions loaded with SES, a novel therapeutic strategy for cervical cancer. First, SES was incorporated (SONE-SES) into a previously developed sesame oil nanoemulsion (SONE), showing nanometric size, concentration close to theoretical, and encapsulation efficiency of 67.41 %. The nanoemulsion improved the SES cytotoxic action against the HeLa cell line (IC 50 of 42.06 µg/mL). A similar response was observed for DPPH radical scavenging capacity. The hydrogel was designed considering simulated physiological vaginal conditions, and xanthan and  $\kappa$ -carrageenan gums blended in a concentration of 3.5 % and 2:1 proportion presented the best coverage, retention, and mucoadhesion in the cow's vaginal mucosa. The nanocomposite hydrogel (HG SONE-SES) was prepared by thickening the SONE-SES with gums and maintaining SONE-SES's nanometric size and SES concentration. HG SONE-SES presented a 5.48 mm<sup>2</sup>/g spreadability factor, non-Newtonian pseudoplastic flow, and high mucoadhesion. In the ex vivo permeation, part of the SES was retained in the cow's vaginal mucosa, justifying its topical application. The HET-CAM classified HG SONE-SES as non-irritant, presenting the intended properties for the local treatment. Therefore, the incorporation of the nanoemulsion into the hydrogel was successfully carried out, obtaining a pharmaceutical form that allows vaginal administration of SONE-SES and guarantees efficient performance in delivering SES, which is considered a promising alternative to traditional treatments used in cervical cancer therapy.



# Influence of stabilizers on the properties of gliadin nanoparticles containing insulin



## Author

Beatriz Dagostin Noguchi (Universidade Estadual do Centro-Oeste (Unicentro))



## Knowledge Area

Nanotechnology



## Funding

Fundação Araucária



## Keywords

gliadin, insulin, stabilizers

## Abstract

Influence of stabilizers on the properties of gliadin nanoparticles containing insulin

Nanoparticles are potential carriers for oral insulin administration. The physicochemical characteristics of protein nanoparticles are highly influenced by the type and concentration of stabilizers. In this study, we evaluated two stabilizers, sodium caseinate and apple pectin, at different concentrations (0.5%, 1%, and 2%), and determined their influence on the properties of the nanoparticles such as average diameter, polydispersity index, and zeta potential. The nanoparticles were prepared by nanoprecipitation, their diameter and polydispersity index were measured by dynamic light scattering (DLS), and the zeta potential was measured by electrophoretic mobility. The results showed that the concentration of the stabilizer had a significant impact on the aforementioned properties. Sodium caseinate at low concentrations contributed to a size of 290.2 nm with size homogeneity and a zeta potential of -12.4 mV. Apple pectin at all concentrations produced particles with lower polydispersity, resulting in a value of 0.163 but with a larger diameter of 639.96 nm and particle agglomeration, while the zeta potential was -23.4 mV, being higher compared to the particles made with sodium caseinate. These initial results suggest that sodium caseinate is the better stabilizer for gliadin nanoparticles.

# Antibacterial effect of silver nanoparticles (AgNPs) as a potential healing treatment for complex wounds



## Author

Franciele Garcia Baveloni - Universidade de São Paulo (USP)  
Andréia Bagliotti Meneguim - Universidade de São Paulo (USP)  
Hernane Barud da Silva (UNESP Araraquara)  
Taís Maria Bauab (UNESP Araraquara)  
Marlus Chorilli (UNESP Araraquara)



## Knowledge Area

Nanotechnology



## Funding

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal Ensino Superior – Brasil (CAPES) - Finance code – 001.



## Keywords

Silver nanoparticles, Synthesis, Antibacterial effect

## Abstract

**Objective:** To evaluate the bactericidal action of silver nanoparticles (AgNPs) from strains of *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* present in complex wounds. **Methodology:** (1) Synthesis of AgNPs: an aqueous solution containing 0.025 mM tannic acid (Synth®) and 5 mM sodium citrate (Synth®) was added at boiling temperature, 25 mM AgNO<sub>3</sub> solution (QImis®) was added under reflux. (2) AgNPs concentration by ultracentrifugation: AgNPs were concentrated by the by the sedimentation method (18.000 rpm, 90 min, at 4°C, CR22N HITACHI centrifuge - Thermo Scientific). (3) Characterization of AgNPs: (3.1) Ultraviolet-Visible Spectroscopy (UV-VIS): Varian Cary 500 Scan UV-VIS spectrophotometer was used (wavelength 200 - 800 nm). (3.2) Transmission Electron Microscopy: Dried AgNPs were subjected to analysis on a JEOL JEM model 2100 running at 200 kV. (3.3) Measurement of size, distribution and  $\zeta$  Potential: The diameter, PDI and  $\zeta$  potential of the AgNPs were measured by the DLS Zetasizer Nano NS equipment (Malvern Instruments, Malvern, United Kingdom). (3.4) Minimum Inhibitory Concentration (MIC) determination: *S. aureus* (ATCC 25923), *P. aeruginosa* (ATCC 27853) and *E. coli* (ATCC 25922) were used to determine the MIC, after treatment with AgNPs, using resazurin (0.01%) followed by analysis by spectrophotometer at the length of 590 nm wave (Biotek plates - Synergy model) **Results:** Concentrated AgNPs (117  $\mu\text{g}/\text{mL}$ ) showed a stable yellow color and spherical shape. UV-VIS confirmed characteristic silver plasmonic band at 400 nm and the diameter size was  $24.3 \pm 0.18$  nm, PDI of  $0.25 \pm 0.013$  and  $\zeta$  potential of  $-60.0 \pm 3.07$  mV. The MIC of AgNPs was 58.5  $\mu\text{g}/\text{mL}$  for *E.coli* and 6.74  $\mu\text{g}/\text{mL}$  for *S. aureus* and *P. aeruginosa*. **Conclusions:** The AgNPs were stable, as no signs of aggregation were observed, visualized by the gray color. Furthermore, the potential of topical use of the skin in bacterial control as an alternative treatment for wound healing was verified.

# Nanoparticle Containing Tea Tree Oil And Terbinafine Base As A Therapeutic Strategy For Fungal Nail Infections Caused By Dermatophytes



## Author

Bárbara Marmor Bachinski - Universidade Federal do Pampa)  
Gabriely Antonella Rodrigues Carrazzo (Universidade Federal do Pampa)  
Letícia Marques Colomé (Universidade Federal do Pampa)  
Cheila Denise Ottonelli Stopiglia (Universidade Federal do Pampa)  
Juliano Braun de Azeredo (Universidade Federal do Pampa)



## Knowledge Area

Nanotechnology



## Funding

CAPES - 88887.82144/2023-00



## Keywords

Nanocapsule; Tea Tree Oil; Terbinafine

## Abstract

Onychomycosis is a fungal infection that affects the tissue of the nail, causing scaling and thickening of the affected nail plate. The search for alternative antifungals capable of penetrating nail tissue remains a significant challenge in treating onychomycosis. A promising strategy to control these infections may be using natural compounds combined with synthetic antifungals. Tea tree oil (TTO) is a volatile essential oil mainly derived from the Australian native plant *Melaleuca alternifolia*. Its main constituent is terpinen-4-ol, which is attributed to a broad spectrum of therapeutic antifungal properties. Terbinafine (TBF) is a lipophilic drug belonging to the allylamines class, and its mechanism of action involves inhibiting the epoxidase enzyme of fungal cells. Among the strategies that may enable TBF to penetrate the nail associated with TTO, nanocapsules (NC) stand out. Therefore, this study aimed to synthesize TBF from terbinafine hydrochloride, and develop, and characterize a nanocapsule containing an oily core composed of TTO and TBF, intended for topical use. The NC showed a monomodal distribution profile on a nanometric scale, with an average diameter of 0.236 nm and a Span value (polydispersity) of 0.940, considered suitable for the intended use. The formulation had a pH value of 5.5, classified as suitable for the intended application area. The zeta potential value of the suspension predicts good stability of TBF-TTO NC, with a measured value of -30.72 mV. This study has shown promise for the development of a topical formulation containing nanoparticles that may aid in the treatment of onychomycosis. Future experiments will be conducted to evaluate the antimicrobial activity of NC, TBF dosing, encapsulation efficiency, and nail permeation in bovine hoof models.

# Assessment of meloxicam tissue pharmacokinetics in male rats using polymeric nanocapsules with different surface charges



## Author

Pedro Santos da Silvas (UFSM)  
Camila Oliveria Pacheco (UFSM)  
Kelle Vellasques Pereira (UNIPAMPA)  
Flávia Elizabete Guerra Teixeira (UNIPAMPA)  
Polyana Silveira Pereira (UNIPAMPA)  
Tamara Ramos Maciel (UNIPAMPA)  
Sandra Elisa Haas (UNIPAMPA)



## Knowledge Area

Nanotechnology



## Funding

Pharmacology and Pharmacometric Laboratory (LABFAR); Coordination of Superior Level Staff Improvement(CAPES)



## Keywords

Meloxicam, Nanocapsules, Pharmacokinetics

## Abstract

Meloxicam (MLX) is a non-steroidal anti-inflammatory drug used in the treatment of rheumatoid arthritis and its application for Central Nervous System disorders, such as Parkinson's disease, is under investigation. However, MLX exhibits limitations such as low aqueous solubility and restricted permeability across the blood-brain barrier. To overcome these challenges, the development of polymeric nanocapsules (NC) represents a promising approach. It is known that nanocapsules enhance the solubility and bioavailability of MLX. The aim of this study was to conduct a MLX tissue pharmacokinetics (PK) analysis in rats of NC prepared with different polymers containing MLX. MLX NC (1 mg/mL) were prepared using the nanoprecipitation method, with cationic (EUD) or anionic (PCL) polymers. For the tissue distribution assay, the male Wistar rats were divided into three groups (MLX-F, NC-EUD, and NC-PCL), with intravenous administration (5 mg/kg), and the collection times were set at 0.5, 1.5, 6, 24, and 48 hours. The evaluated tissues were the brain, spleen, lung, heart, liver and kidneys. A liquid-liquid extraction was performed to quantify the samples using HPLC-DAD. A non-compartmental pharmacokinetic approach was used to determine the pharmacokinetic parameters, such as half-life ( $t_{1/2}$ ) and penetration factor ( $F_t$ ), of MLX tissue concentration versus time, using Pkanalix® software. The  $F_t$  for all tissues treated with NC-EUD compared to the MLX-F group, with the brain showing an  $F_t$  of 2 compared to 0.53 for MLX-F and NC-PCL group displayed a permeation of 0.69. The  $t_{1/2}$  for the NCs was longer than that of the MLX-F group, except again in the brain. Through the tissue pharmacokinetic assay, it can be observed that the cationic nanoformulation released approximately 4-fold drug in the brain, and the nanoencapsulation of MLX is a viable alternative to overcome its biological limitations, enabling the development of formulations for Central Nervous System.

# Towards enhanced liposomal nanocarriers: leveraging biomimetic properties to modulate protein corona formation



## Author

Lucas Ribeiro de Sousa (UFG)  
Tácio G. Hayasaki (UFG)  
Mariana A. Salomão (UFG)  
Nathália C. Oliveira (UFG)  
Eliana M. Lima (UFG)  
Sebastião A. Mendanha (UFG)



## Knowledge Area

Nanotechnology



## Funding

CNPQ, CAPES



## Keywords

Nanocarriers, Protein Corona, Liposome

## Abstract

Liposomal nanocarriers are the first generation of approved nanomedicines for clinical use, being fundamental for the development of the latest generation of lipid nanoparticles (LNPs) used for gene therapy and vaccination. However, despite all advancements in LNPs/liposomes formulations, formation of the protein corona (PC) remains a critical implication in their interactions with biological fluids. Surface modification with polyethylene glycol (PEG) is a common strategy to mitigate PC formation; however, it may lead to adverse effects such as accelerated blood clearance (ABC). The latest generation of liposomes explores the integration of cell membrane fragments to tailor the final characteristics of these lipid nanocarriers, including PC modulation. This study investigates the influence of RBC-membrane fragments hybridization with synthetic or purified phospholipid liposomes on hard PC formation. Lipid nanocarriers were prepared using the rotary evaporation method followed by hydration and extrusion through membranes with a diameter of 100 nm. Subsequently, the insertion of PEG2000 was performed via post-insertion, and the hybridization of liposomes with RBC membranes was carried out using the freeze-thaw method. Thermal characterization was performed by isothermal titration calorimetry, and total proteins were quantified using the BCA method. Results demonstrate a significant reduction in PC formation with increased incorporation of membrane fragments into the lipid bilayer of the nanovesicles. Detergent solubilization dynamics is also influenced by the phospholipid-to-cell membrane ratio, impacting nanoparticle stability. Biomimetic liposomes effectively modulate PC formation, potentially enhancing their circulation time as nanocarriers within the body.

# Potential antidepressant effect of red mandarin essential oil



## Author

Katianne Wolf Krawczak (Universidade Franciscana)  
Carolina Cristóvão Martins (Universidade Federal de Pelotas)  
Ketlyn Pereira da Mottamotta (Universidade Federal de Pelotas)  
Rafael Pereira (Universidade Franciscana)  
Ethel Antunes Wilhelm (Universidade Federal de Pelotas)  
Aline Ferreira Ourique (Universidade Franciscana)



## Knowledge Area

Nanotechnology



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Finance Code 001) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (number: 315203/2021-8 fellowship to A.F.O).



## Keywords

Nanoemulsion, Monoamine oxidase, Depression

## Abstract

Depression is a neuropsychiatric disorder that affects millions of people, being one of the main causes of disability in the world. Traditional treatments include drugs that often have significant side effects, fueling the need to search for new therapies. In this context, the objective of this study was to evaluate the antidepressant effect of free and nanoemulsified red mandarin essential oil (*Citrus deliciosa*). To this end, initially *in vitro* tests were carried out to inhibit the monoamine oxidase enzymes (MAO-A and MAO-B), which are fundamental in the degradation of neurotransmitters such as serotonin and dopamine, the reduction of which is associated with depression. Afterwards, the tail suspension test was carried out in Swiss mice, this test induces the phenotypic behavior of immobility, being widely used for screening antidepressant drugs. All experiments were carried out with prior approval from the ethics committee (CEUA 010370/2022-27). The results demonstrated that free and nanoemulsified red mandarin oil inhibited the MAO enzyme, showing greater selectivity for MAO-B. In the tail suspension test, a sex-dependent effect was observed, where males treated with the essential oil had an increase in the latency time for the first episode of immobility and a reduction in the immobility time, indicating a reversal of depressive-like behavior. The results suggest that red mandarin essential oil can effectively modulate MAO-B activity, and this modulating activity possibly contributed to the improvement of symptoms involving depressive-like behavior in mice. These findings indicate that this oil has potential and should be further investigated with the aim of developing a formulation that can act in a complementary way in the treatment of depression.

# Blended $\kappa$ -carrageenan and xanthan gum hydrogel containing ketoprofen-loaded nanoemulsions modulate the inflammatory and oxidative stress parameters in an animal model of rheumatoid arthritis



## Author

Vinicius Costa Prado (Universidade Federal de Santa Maria)  
Marcel Henrique Marcondes Sari (Universidade Federal do Paraná)  
Verônica Ferrari Cervi (Universidade Federal de Santa Maria)  
Vanessa Neuenschwander Custódio (Universidade Federal de Santa Maria)  
Ketlyn Pereira da Mottamotta (Universidade Federal de Pelotas)  
Ethel Antunes Wilhelml (Universidade Federal de Pelotas)



## Knowledge Area

Nanotechnology



## Funding

CAPES and CNPq



## Keywords

Nanoparticles. Polysaccharides. Cutaneous route

## Abstract

Rheumatoid Arthritis (RA) is a chronic autoimmune inflammatory disease that causes joint damage, functional loss, and pain ranging from mild to severe. There are different treatments available for RA, including nonsteroidal anti-inflammatory drugs (NSAIDs), such as ketoprofen (KET). However, gastrointestinal, hematological, and renal disturbances are the most frequent KET adverse effects, mainly in cases of long-term administration, suggesting that cutaneous drug application could be a promising alternative to managing RA. Therefore, the objective of this study was to prepare the hydrogels (HG) made by xanthan gum (XG) and  $\kappa$ -carrageenan (KC) polysaccharides containing ketoprofen (KET)-loaded nanoemulsions (NK) and the evaluation in rheumatoid arthritis (RA) in vivo model. Nanoemulsions containing KET (1 mg/mL) were prepared using the spontaneous emulsification method. Hydrogels were prepared by thickening blended polysaccharides (KC/XG - 2:1) with NK or non-nanoemulsioned KET (1 mg). All nano-based HGs presented nanometric-sized droplets, acid pH, drug content higher than 85%, and a pseudoplastic flow. RA was induced by complete Freund's adjuvant (CFA) intraplantar injection into male and female Swiss mice's left hind paw. Treatments with HGs were applied to the animals' dorsal region for seven days. The CFA injection caused mechanical and thermal sensitivities and increased inflammatory and oxidative biomarkers in paw tissue (edema, myeloperoxidase activity, and lipid peroxidation). Treatment with HG-KET and HG-NK reduced these alterations. Based on technological and pharmacological advantages achieved by nanoencapsulation, it can be inferred that HG-NK is a potentially relevant formulation for treating RA.

# Cryoprotectant screening and freeze-drying optimization of Liquid Crystalline Nanoparticles



## Author

Livia Cirizola Alves Coelho (USP-Ribeirão Preto)  
Bryan Wender DeBiasi (USP-Ribeirão Preto)  
Fabíola Silva Garcia Praça (USP-Ribeirão Preto)  
Maria Vitória Lopes Badra Bentley (USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

National Council for Scientific and Technological Development - CNPq



## Keywords

Freeze-drying, Liquid crystalline nanoparticles, Cryoprotectant

## Abstract

The unique characteristics of Liquid-Crystalline Nanoparticles (LCNs), which exhibit properties that are intermediate between isotropic liquids and crystalline solids, have sparked growing interest in pharmaceutical sciences. These structures have proven effective as nanocarriers for gene therapy using small interfering RNA (siRNA). This study focused on producing LCNs with the aim of ensuring system stability and efficacy after lyophilization through the strategic incorporation of cryoprotectants in aqueous solution (mannitol, glucose, trehalose, and sucrose) at concentrations of 0%, 5%, 10%, 15%, 20%, and 30% w/w. These solutions were added separately with nanoparticles dispersion in ratios of LCNs:crioprotectant solution of 1:2, 1:5, and 1:10. Among the cryoprotectants tested, mannitol aqueous solution at 20% w/w in the ratio of 1:10 showed the best cryoprotective capability, with a sample reconstitution time of  $\leq 1.0$  minute, significantly shorter than the other cryoprotectants evaluated. LCNs without cryoprotectant were not fully reconstituted even after extended homogenization periods. The hydrodynamic diameter and PDI showed a particle size in the range of 174 nm and a PDI of 0.220, comparable to fresh LCNs, which had a size of 175.8 nm and PDI of 0.298. Formulations with higher cryoprotectant concentrations and other ratios showed sizes ranging from 206.1 to 1385.0 nm and PDIs from 0.316 to 1.000. Thus, mannitol aqueous solution at 20% w/w as cryoprotectant at 1:10 ratio of LCN:crioprotectant solution showed promising for preserving the structure of LCNs. These findings underscore the importance of screening cryoprotectant agents in the lyophilization process as strategy to ensure the conservation the stability of lipid nanoparticles, potentially driving significant advancements in drug delivery system.



# Cryoprotectant screening and freeze-drying optimization of Liquid Crystalline Nanoparticles



## Author

Vitória dos Santos Gallarreta (Universidade Federal do Pampa)  
Joane Guterres Ferreira (Universidade Federal do Pampa)  
Camila de Oliveira Pacheco (Universidade Federal do Pampa)  
Sandra Elisa Haas (Universidade Federal do Pampa)



## Knowledge Area

Nanotechnology



## Funding

FAPERGS grant 19/2551-0001970-0, CNPq (no. 309401/2020-8), CAPES (no. 88881.506652/2020-01)



## Keywords

nanotechnology, nanocapsules, anti-inflammatory effect

## Abstract

Curcumin (CUR) is a bioactive compound that is recognized for its neuroprotective, anti-inflammatory and antioxidant properties, despite its short half-life time, low permeability, photosensitivity and pH sensitivity. Meloxicam (MLX), a non-steroidal anti-inflammatory drug, acts inhibiting the COX-2 enzyme but has limited aqueous solubility. The use of polymeric nanocapsules (NCs) is proposed as a strategy to improve the biopharmaceutical characteristics of both drugs. So, we propose a co-nanoencapsulation of MLXCUR, providing controlled release, decreased toxicity and increased solubility and permeability. The aim of this study is to characterize the physicochemical properties and stability over 30 days of MLXCUR and unloaded nanocapsules (UnNC). UnNC and MLXCUR NC were prepared by nanoprecipitation method using the polymer poly- $\epsilon$ -caprolactone (PCL). The parameters evaluated were mean particle diameter (MPD), zeta potential (ZP), SPAN, pH, Drug Content (DC) and encapsulation rate (ER) of the drugs. After characterizing the MLXCUR NC, we obtained that between days 1 and 21 the DMP ranged from 299 to 331 nm, the SPAN remained below 2, respecting a monodisperse system, the pH was slightly acidic as expected, and the zeta potential was negative in agreement with the polymer used. The ER of both drugs was close to 100%. Drug Content of MLX and CUR were  $100.8 \pm 1.8$  and  $104.5 \pm 0.33$ , respectively and didn't show significant differences. There was a decrease in drug content observed for both drugs after 30 days. The UnNC also remained with DMP ranging from 304 to 314 nm, SPAN below 2, slightly acidic pH and negative zeta potential and no differences over 30 days. Then, the physicochemical responses of the nano-coassembly formulation showed satisfactory results for future in vitro and in vivo tests.

# Cytotoxicity evaluation of ferritin-based nanoparticle for EGFRvIII peptide delivery



## Author

Juliana Covolo Marques (USP-Ribeirão Preto)  
Camila Machado França de Almeida (USP-Ribeirão Preto)  
Natália Floriano Paiva (USP-Ribeirão Preto)  
Ana Flávia Gembre Pignata (USP-Ribeirão Preto)  
Wendy Martin Rios (USP-Ribeirão Preto)  
Vania Luiza Deperon Bonato (USP-Ribeirão Preto)  
Fabiana Testa Moura de Carvalho Vicentin (USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

This work was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico [grant number 403588/2021-9]. JCM is recipient of FAPESP fellowship [grant number 2023/13067].



## Keywords

apoferritin nanoparticle, peptide vaccine, vaccine delivery

## Abstract

Variant III of the epidermal growth factor receptor (EGFRvIII) can be applied as a specific tumor antigen in peptide vaccines as it is associated with tumorigenicity, having a high incidence rate in some types of cancer due to increased cell proliferation and inhibition of apoptosis, and it is rarely expressed by normal cells. Ferritin-based nanoparticles can be used as a carrier system due to its self-assembled structure, presenting themselves as an attractive strategy for the development of peptide vaccine delivery systems. The present study proposes to evaluate the cytotoxicity of apoferritin nanoparticles with the EGFRvIII peptide (vaccine formulation) on macrophages and dendritic cells through the *in vitro* study. The vaccine formulation was obtained using the low pH to disassemble apoferritin subunits. The nanoparticle was characterized regarding its physicochemical characteristics of hydrodynamic diameter, polydispersity, zeta potential with the dynamic light scattering (DLS) and nanoparticle tracking analysis (NTA). Cytotoxicity assays were performed on bone marrow-derived macrophages and dendritic cells evaluating apoferritin concentrations from 50 to 500  $\mu\text{g}/\text{mL}$ . The nanoparticles had a size of  $3417,5 \text{ nm} \pm 133,5$  with medium polydispersity index  $0,4 \pm 0,05$ , negative zeta potential ( $-20.6 \text{ mV}$ ) and concentration of  $2,05 \times 10^9 \pm 8,78 \times 10^7$  particles/ $\text{mL}$ . In the cytotoxicity analysis with resazurin, the macrophages viability (around 100%) was observed in cultures stimulated with the formulation at concentrations below  $200 \mu\text{g}/\text{mL}$ . On the other hand, for the dendritic cells the viability was maintained around 100% for all tested concentrations. To summarize, these results are important to define the concentration of the vaccine formulation that does not cause cytotoxicity in future *in vitro* studies.

# Preparation and stability assessment of curcumin-loaded anionic polymeric nanocapsules



## Author

Joane Guterres Ferreira (Universidade Federal do Pampa)  
Vitória dos Santos Gallarreta (Universidade Federal do Pampa)  
Camila de Oliveira Pacheco (Universidade Federal de Santa Maria)  
Sandra Elisa Haas (Universidade Federal do Pampa)



## Knowledge Area

Nanotechnology



## Funding

This work was supported by the CNPq. The authors are grateful for the support provided by the FAPERGS, grant 19/2551-0001970-0, CNPq (no. 309401/2020-8), CAPES (no. 88881.506652/2020-01) and UNIPAMPA.



## Keywords

physicochemical, bioactive compound, anionic nanocapsules

## Abstract

Curcumin (CUR), extracted from the rhizome of the *Curcuma longa* plant, has become a subject of interest in the pharmaceutical industry due to its antioxidant, anti-inflammatory, antitumor, antimalarial and antiviral properties. However, this compound has low bioavailability, poor solubility, and photosensitivity. Nanoencapsulation has emerged as an alternative for improving the limiting technological aspects of promising compounds such as CUR. Polymeric nanocapsules (NCs) are tiny structures that can transport active substances either dissolved in the core or adsorbed on the polymeric wall. In this context, the aim of this study was to prepare, characterize, and evaluate the stability of curcumin nanocapsules using the polymer poly-( $\epsilon$ -coprolactone) (PCL). To this end, nanocapsules containing curcumin (NC-CUR) and nanocapsules without the addition of the drug (UnNC) were prepared by interfacial deposition of the pre-formed polymer. The NCs were characterized for 30 days using the following parameters: mean particle diameter (MPD), SPAN, zeta potential (ZP), pH, absolute drug content and encapsulation rate. The nanocapsules showed adequate physicochemical characteristics between the analyses carried out and showed no significant difference ( $p < 0.05$ ) between the days of analysis until day 21. UnNC had a diameter between 305 and 308 nm, while NC-CUR had a diameter between 246 and 247 nm for 21 days. The SPAN for both NCs remained below 2, the zeta potential ranged from -26.77 to -27.01 and the pH was slightly acidic for both formulations. The drug content and encapsulation rate for NC-CUR was close to 100%. At the end of the evaluation, it was possible to conclude that the systems were within the nanometric scale and had monodisperse characteristics for 21 days. The other physical and chemical responses presented by the formulation proved to be satisfactory for future *in vitro* and *in vivo* tests.

# Self-Nanoemulsifying Drug Delivery System For Nose-To-Brain Transport Of Myrsinoic Acid For Antidepressive-Like Activity



## Author

Anna Carolina Furaer da Rocha (UNIVALI Itajaí)  
Camila André Cazarin (UNIVALI Itajaí)  
Franciele Samanta Bohr Florenço (UNIVALI Itajaí)  
Angela Malheiros (UNIVALI Itajaí)  
Márcia M. de Souza (UNIVALI Itajaí)  
Ruth M. L. Silvar (UNIVALI Itajaí)



## Knowledge Area

Nanotechnology



## Funding

CNPq, CAPES, FAPESC e PPGCF-UNIVALI.



## Keywords

SELF-NANOEMULSIFYING DRUG DELIVERY SYSTEM, NOSE-TO-BRAIN TRANSPORT, MYRSINOIC ACID

## Abstract

Nose-to-brain transport has been proposed as a strategy to increase the bioavailability of drugs for the treatment of CNS disorders. *Rapanea ferruginea* has been demonstrated in vivo antidepressant activity of the ethanolic extract of the bark and its isolated compounds, myrsinoic acids A (MAA) and B (MAB). Nanocarrier platforms, such as self-emulsifying systems (SEDDS) increases solubility and permeability. The present work aimed to develop SEDDS containing AMA isolated from *R. ferruginea* barks and to evaluate the antidepressant potential in silico and in vivo. From the ethanolic extract of the bark of *R. ferruginea*, the compounds MAA and MAB and the mixture of MAB:MAA were isolated, which were characterized by HPLC, NMR of  $^1\text{H}$  and  $^{13}\text{C}$ , TGA, DSC. In silico and in vivo antidepressant-like activity was also evaluated by TST. The development of the SEDDS started with the pseudoternary phase diagram being characterized by visual appearance, internal phase size, polydispersity index, zeta potential, emulsification time, transmittance, physical stability, rheological behavior, evaluation of mucoadhesive strength, and in vitro release of the MAA. The SEDDS were administered IN and evaluated under TST. MAA was obtained with content of 94%, and MAB with > 99%. The MAA at 10 mg/kg showed better antidepressant-like activity in vivo. The SEDDS was obtained by emulsifying in the nanoemulsion form, transparent with bluish reflection, and physically stable. Before dilution in water, it showed mucoadhesive, fluid, and sustained release properties. SEDDS showed the same antidepressant-like activity as the emulsion orally administered. In silico studies suggest the inhibition of the enzyme monoamine oxidase A as a mechanism of antidepressant activity of MA. Predictive safety studies did not detect toxicity. The present work obtain SEDDS with adequate characteristics as a potential vehicle for IN of MAA isolated from *R. ferruginea*, to be used as an antidepressant phytomedicine.

# Impact of Hyaluronic Acid and Beta-Caryophyllene in the Structure and function of Alginate Films



## Author

Millena Mendes de Souza (Universidade Federal do Rio de Janeiro)  
Francisco Alexandrino-Junior (Fiocruz Rio de Janeiro)  
Alexandre Vieira David da Costa (Universidade Federal do Rio de Janeiro)  
Emily Santos de Castro (Universidade Federal do Rio de Janeiro)  
Marcus Vinicius Borges Silva (Universidade Federal do Rio de Janeiro)  
Millena Silva Barbosa (Universidade Federal do Rio de Janeiro)  
Kattya Gyselle de Holanda e Silva (Universidade Federal do Rio de Janeiro)



## Knowledge Area

Nanotechnology



## Funding

FAPERJ (E-26/010.000983/2019)



## Keywords

Sodium alginate films, Hyaluronic acid (HA), Beta-caryophyllene (bC)

## Abstract

The incorporation of hyaluronic acid (HA) and beta-caryophyllene (bC) into sodium alginate (SA) films have the potential to produce a functional wound dressing, i.e., not only acting as a bandage, but also promoting tissue regeneration and repair. However, the presence of these compounds can markedly influence the properties of SA film. Therefore, this study aimed to evaluate how increasing concentration of HA and a lipid nanoemulsion loaded with bC (NE-bC) affected SA films. First, SA films were manufactured by the casting technique, incorporating different concentrations of HA and NE-bC. Thereafter, the samples were characterized by macroscopic aspect, thickness, FTIR, water vapor permeability (WVP) according to the ASTM E96-80, and swelling behavior (SB). The results revealed that the NE-bCP addition turned the transparent SA films into opaque. Moreover, the film thickness was  $1.5 \pm 1.1$  mm ( $n = 54$ ). As the concentration of NE and HA increased, the film thickness also increased. FTIR analysis detected an ester, indicating interaction between HA's COOH group and SA's OH group, suggesting ester formation contributing to cross-linking. The SB analysis suggests that HA significantly influences the diffusion mechanism ( $n$ ) in SA films with NE-bCP. The relation between NE and HA concentrations is linear. HA affects swelling without altering the diffusional mechanism, while increasing NE enhances swelling. HA primarily influences the diffusion mechanism, contributing over 99%. The WVP assay reveals an average WVP of approximately  $-0.484 \pm 0.456$  g.day<sup>-1</sup>.cm<sup>-2</sup>.mmHg<sup>-1</sup>. Increasing NE likely raises hydrophobicity, reducing wettability and WVP. The data suggest bCP-NE reduces WVP, enhancing barrier properties. Higher HA concentrations interact with bCP-NE, causing variable WVP effects. These findings underscore the material's potential for applications needing precise WVP control, like moisture-sensitive pharmaceuticals.

# Influence of Pequi Oil Extraction Methods on the Production of Nanoemulsions for Potential Wound Healing Application



## Author

Lindomara Cristina Félix da Silva (UNB-Brasília)  
Vitória Regina Pereira da Silva (UNB-Brasília)  
Lorrane Ribeiro de Souza (UFLA)  
Jefferson da Silva Oliveira (UFLA)  
Carlos Alexandre Rocha da Costa (UFLA)  
Gilson Gustavo Lucinda Machado (UFLA)  
Eduardo Valério de Barros Vilas Boas (UFLA)  
Marcella Lemos Brettas Carneiro (UNB-Brasília)  
Graziella Anselmo Joanitti (UNB-Brasília)



## Knowledge Area

Nanotechnology



## Funding

This work was supported by CAPES, CNPq, FAP-DF, and UnB



## Keywords

Caryocar brasiliense, Nanoemulsion, Wound healing

## Abstract

Pequi oil (*Caryocar brasiliense*) is known due to its antioxidant and wound healing benefits due to carotenoids, fatty acids, polyphenols, and vitamins. Extraction methods affect these compounds, and nanotechnology enhances absorption, stability, and efficacy. This study aimed to analyze the physical-chemical properties of pequi oil extracted by solvent (OPS), pressing (OPP), and boiling (OPF), produce nanoemulsions with these oils (NEPS, NEPP, NEPF), and evaluate their cytotoxicity in HaCat keratinocyte cells. The study analyzed the acidity degree (AD%), peroxide values (PV), total carotenoid profiles, and antioxidant potential of pequi oil using DPPH, TPC-Folin, and phosphomolybdenum methods. Nanoemulsions composed of Egg Lecithin, Polyethylene Glycol 40, and Pequi Oil were prepared using a tip sonicator under an ice bath and physico-chemically characterized with ZetaSizer (Malvern). Cytotoxicity of NEPS, NEPF, NEPP, OPS, OPF, OPP, and a blank formulation (NB) at 360 and 540  $\mu\text{g}/\text{mL}$  was evaluated in HaCat cells using the MTT assay. PV varied among samples, with OPF at  $5.35 \pm 0.3$ , OPS at  $1.6 \pm 0.06$ , and OPP at  $4.8 \pm 0.5$  meq  $\text{O}_2/\text{g}$ , indicating OPS had the best oxidative stability. However, OPS had the highest residual acidity ( $\text{AD}\% = 4.89 \pm 0.05$ ), while OPF and OPP had GA% values of  $0.47 \pm 0.02$  and  $2.71 \pm 0.11$ , respectively. Carotenoid profiles showed variation with OPF ( $139.7 \pm 0.75$  mg/100g), OPS ( $168.8 \pm 1.66$  mg/100g), and OPP ( $136.5 \pm 7.52$  mg/100g). OPS also exhibited the greatest antioxidant capacity, with averages of  $163.74 \pm 17.62$  for phosphomolybdenum,  $386.54 \pm 8.8$  for TPC-Folin, and  $16.46\% \pm 0.69$  in the DPPH analysis. The nanoemulsions were homogeneous: NEPS  $96.5 \pm 0.3$  nm, PDI  $0.18 \pm 0.02$ , PZ  $-18.7 \pm 1.1$  mV; NEPF  $89.8 \pm 1.7$  nm, PDI  $0.16 \pm 0.03$ , PZ  $-18.0 \pm 1.0$  mV; NEPP  $88.0 \pm 1.5$  nm, PDI  $0.18 \pm 0.01$ , PZ  $-15.1 \pm 1.4$  mV. Both nanoemulsions and free oils showed no toxicity or growth inhibition in HaCat cells, indicating biological compatibility and potential for effective wound healing formulations.

# Cutaneous delivery of different siRNAs for antisense gene therapy of psoriasis: cationic solid lipid nanoparticles as gene carriers



## Author

Ualisson José da Silva (USP-Ribeirão Preto)  
Maria Vitoria Lopes Badra Bentley (USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

Capes PROEX 88887.840590/2023-00.



## Keywords

Gene Therapy, Nanotechnology, Psoriasis

## Abstract

Psoriasis is a chronic inflammatory skin disease, mediated by the immune system, affecting the skin, nails, mucous membranes, and joints, potentially associated with systemic inflammation. Treatment aims for prolonged periods of remission and improved quality of life, but existing therapies have safety limitations for long-term use, complicating disease management. Therefore, there is a search for new treatments targeting specific overexpressed immunopathological targets in psoriasis. RNA interference using small interfering RNAs (siRNAs) of 21-23 base pairs has shown efficacy in controlling overexpressed targets in immune-mediated diseases. In this context, we propose evaluating the silencing of NF- $\kappa$ B, IL-17A, and TNF- $\alpha$  using cationic lipid nanoparticles as a non-viral vector to enhance siRNA bioavailability in the skin. These nanoparticles were characterized by an average size of 83-124 nm and low polydispersity (0.21-0.35), with positive surface charges (10-14 mV) and efficient complexation with siRNA. In vitro skin distribution studies showed that nanoparticles with 0.2% DOTAP promoted penetration and retention of siRNA in the epidermis and dermis for up to 12 hours, compared to nanoparticles with 0.1% DOTAP and free siRNA. In Raw 264.7 and HaCat cells, nanoparticles were cytocompatible below  $5 \times 10^{11}$  particles/mL, with greater siRNA internalization in nanoparticles containing 0.2% DOTAP and increased fluorescence in macrophages inflamed with lipopolysaccharide. These results indicate that cationic lipid nanoparticles overcome extra- and intracellular barriers, providing a basis to evaluate the effects of NF- $\kappa$ B, IL-17A, and TNF- $\alpha$  silencing in cellular models of psoriasis.

# Development of 7-nitroindazole nanoemulsions by high-pressure homogenization technique as a new therapeutic approach for the treatment of sepsis



## Author

Amanda Ellen de Athay (Universidade Federal de Santa Catarina)  
Isabelle Pinheiro Gomes da Silva (Universidade Federal de Santa Catarina)  
Elenara Lemos-Senna (Universidade Federal de Santa Catarina)



## Knowledge Area

Nanotechnology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq - Projeto n. 441453/2018



## Keywords

7-nitroindazole, Nanoemulsions, High-pressure homogenization

## Abstract

Sepsis is defined as a dysregulated host response to an infectious associated with organic dysfunction, constituting the leading cause of death in intensive care units, and nitric oxide plays an important role in the development of sepsis. Our research group has evaluated the potential application of 7-nitroindazole (7-NI), an oxide nitric synthase inhibitor, for treating sepsis. However, this compound has a short half-life and poor aqueous solubility, which limits its clinical uses. Thus, nanoemulsions have been proposed as a strategy to deliver 7-NI. This study employed the high-pressure homogenization technique to obtain 7-NI-loaded nanoemulsions (NE7NI). A 2x3 factorial design was employed to evaluate the effect of the pressure (300 and 500 bar) and number of cycles (5, 10, and 15) (independent variables) on the physicochemical and loading properties of NE7NI. The NE7NI were characterized according to their droplet size, polydispersity index (PDI), zeta potential, drug loading, and encapsulation efficiency (EE) (dependent variables). The mean droplet size and PDI values varied from 205 to 481 nm and 0.348 to 0.494, respectively, while the zeta potential varied between -12 and -15 mV. The drug loading and EE values ranged from 410 to 520  $\mu\text{g}/\text{mL}$  and 64 to 68%, respectively. The analysis of variance (ANOVA) indicated that only the mean droplet size of NE7NI was affected by the change in pressure and the number of cycles of the homogenization process ( $F_{\text{cal}} > F_{\text{crit}}$ ,  $p < 0.05$ ), and no interaction between these two factors was observed. The results showed that with 300 bar pressure, the droplet size was significantly reduced when the number of homogenization cycles increased from 5 to 10 or 15. Likewise, with the increase in pressure from 300 to 500 bar, the droplet size was reduced, keeping the number of homogenization cycles constant at 5 or 15. Since it is possible to conclude that the homogenization process was efficient within the limitations presented.



# Development and characterization of hybrid nanoparticles with cannabidiol and their effect on glioblastoma cells



## Author

Maria Eduarda Almeida Pinto (FCFRP)  
Yasmim Garcia Gonçalves (FCFRP)  
Priscyla D. Marcato (FCFRP)



## Knowledge Area

Nanotechnology



## Funding

CAPES-PROEX



## Keywords

cannabidiol, glioblastoma, nanoparticles

## Abstract

Glioblastoma is a primary malignant tumor of the central nervous system (CNS), responsible for most deaths among patients with primary brain tumors. The standard treatment for glioblastoma includes surgical removal of the tumor mass, fractionated radiotherapy, and chemotherapy with temozolomide, along with corticosteroids. However, these treatments present several side effects, including immunosuppressive effects. Thus, new compounds have been investigated for treating glioblastoma, such as cannabidiol. Cannabidiol (CBD) is a bioactive compound that does not exhibit psychoactive effects in the brain and exhibits antitumor, anti-inflammatory, and antioxidant activities, making it a promising candidate for glioblastoma therapy. However, this compound has low bioavailability and slow and erratic oral absorption. Therefore, the objective of this work is to encapsulate cannabidiol (CBD) in hybrid nanoparticles for the treatment of glioblastoma. The hybrid nanoparticles (HNPs) were prepared using the hot emulsification method followed by sonication and were characterized by dynamic light scattering (DLS), nanoparticle tracking analysis (NTA), and transmission electron microscopy. The HNPs were optimized using a Box-Behnken response surface experimental design, indicating a significant influence of sonication time, oil phase, and surfactant percentages on the size and polydispersity index (Pdl) of the nanoparticles. The optimized HNP-CBD exhibited a diameter of less than 120 nm, low Pdl, positive zeta potential, and high encapsulation efficiency. The HNP-CBD showed a spherical morphology and cytotoxic activity against U87MG glioblastoma cells. Thus, this work demonstrated the potential of HNPs as a CBD delivery system with a pronounced effect on glioblastoma cells.

# Removal of selective serotonin reuptake inhibitor using magnetic graphene oxide: adsorption study and in vitro safety profile



## Author

Franciane Batista Nunes (Universidade Federal de Santa Maria)  
Leonardo Zancanarro Vidal (Universidade Franciscana)  
Altevir Rossato Vianna (Universidade Federal de Santa Maria)  
André Passaglia Schuch (Universidade Federal de Santa Maria)  
Vitoria Fernanda Belmonte Novais (Universidade Federal de Santa Maria)  
Ana Clara Laval Rocken (Universidade Franciscana)  
Alana Torres Viero (Universidade Franciscana)  
Roberto Christ Vianna Santos (Universidade Federal de Santa Maria)  
Cristiano Rodrigo Bonh Rhoden (Universidade Franciscana)



## Knowledge Area

Nanotechnology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPQ (bolsa de mestrado)



## Keywords

Magnetic graphene oxide, citalopram, nanotechnology

## Abstract

Citalopram (CIT) is an antidepressant widely used, hence, this drug is considered an aquatic emerging pollutant. The CIT removal from water can be done using magnetic graphene oxide (GO·Fe<sub>3</sub>O<sub>4</sub> 1:1). Because of this, in this work, CIT adsorption was proposed using graphene oxide (GO) and GO·Fe<sub>3</sub>O<sub>4</sub> 1:1. Moreover, the in vitro safety profile of CIT, GO, Fe<sub>3</sub>O<sub>4</sub>, GO·Fe<sub>3</sub>O<sub>4</sub> 1:1, and CIT-GO·Fe<sub>3</sub>O<sub>4</sub> 1:1 were investigated. The GO was synthesized through the exfoliation and chemical oxidation of graphite. Already the GO·Fe<sub>3</sub>O<sub>4</sub> 1:1 was obtained by the coprecipitation method employing FeSO<sub>4</sub> as the iron source. In CIT adsorption, was used a C<sub>0</sub> = 50.0 mg L<sup>-1</sup>, and adsorbent dosage = 0.5 g L<sup>-1</sup> at 293 ± 1.00 K for 24 hours, the residual solution was measured on a spectrophotometer UV-vis at λ=240 nm. The safety profile of the samples was investigated by MTT and DNA-PicoGreen® assays in BV-2 and VERO cell lines. The concentration of samples used in the in vitro assays were 1, 30, 100, and 300 µg mL<sup>-1</sup>. According to the results, the GO·Fe<sub>3</sub>O<sub>4</sub> 1:1 showed the highest adsorption capacity (q<sub>e</sub>) (97.92 mg g<sup>-1</sup>) and removal percentage (98%). Already the GO shows a q<sub>e</sub>=90.43 mg g<sup>-1</sup> and a removal percentage of 91%. In the in vitro assays CIT showed significant cytotoxicity for Vero and BV-2 cells. For these cell lines, CIT caused a decrease of 40% in cell viability even at 30 µg mL<sup>-1</sup>. Moreover, the CIT was the only treatment that showed genotoxicity in the DNA-PicoGreen® assay. The GO, GO·Fe<sub>3</sub>O<sub>4</sub> 1:1, and Fe<sub>3</sub>O<sub>4</sub> treatments showed great biocompatibility until 100 µg mL<sup>-1</sup>, showing low toxicity at the highest concentration (viable cells 64%, 65%, 73%, respectively). Finally, the CIT-GO·Fe<sub>3</sub>O<sub>4</sub> 1:1 showed cytotoxicity only in the highest concentration employed. That way, the adsorbents showed efficient CIT adsorption and decreased the CIT toxicity on BV-2 and VERO cells. Also, the results allow the accomplishment of further studies employing the GO·Fe<sub>3</sub>O<sub>4</sub> 1:1 on waste management, and drug repositioning.

# Evaluation of the Biocompatibility and Potential for Cell Regeneration of Nanoemulsions Containing Bioactive Compounds from Annatto (*Bixa orellana* L.) in Keratinocyte and Fibroblast Cultures



## Author

Jhenyfer Benício dos Santos (Universidade de Brasília)  
Vitória Regina Pereira da Silva (Universidade de Brasília)  
Graziella Anselmo Joanitti (Universidade de Brasília)  
Marcella Lemos Brettas Carneiro (Universidade de Brasília)



## Knowledge Area

Nanotechnology



## Funding

Fundação de Apoio à Pesquisa do Distrito Federal (FAPDF)



## Keywords

*Bixa orellana*, Cell Viability, Cell Migration

## Abstract

Annatto (*Bixa orellana* L.) presents biocompounds with antioxidant, anti-inflammatory, and regenerative activity. This study evaluated biocompounds such as annatto oil and bixin - a standardized extract of annatto in geranylgeraniol, bixin, and tocopherols. Both compounds were obtained through donation. The biocompatibility of free and nanostructured bixin and annatto oil was analyzed in keratinocytes and fibroblasts within a 24-hour period using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) reduction assay. To verify the potential for tissue regeneration, cell migration assays were performed using the Scratch Assay method. It was observed that after 24 hours of treatment with 125 µg/ml, 62.5 µg/ml, and 31.25 µg/ml of bixin and with a nanoemulsion containing bixin, cell viability was maintained around 100%. However, when free annatto oil was evaluated, there was a significant reduction in cell viability in both keratinocyte and fibroblast cultures. When evaluating the nanoemulsion formulation with annatto oil, a viability of around 100% was observed. According to the migration assay, the groups of bixin and annatto oil nanoemulsions obtained a closure percentage of around 80% and 60%, respectively, with  $P < 0.0001$  and a standard error of bixin at 6 hours of 1.999 and 24 hours of 1.696, and annatto oil nanoemulsion at 6 hours of 4.604 and 24 hours of 5.115. It was concluded that treatments with bixin and with nanoemulsion containing bixin and annatto oil were biocompatible and showed potential for application in technologies related to cell regeneration.

# Hydrogels based on nanoemulsions of Andiroba oil (*Carapa guianensis*): Physicochemical characterization, stability, and evaluation of healing potential in vitro



## Author

Vitória Regina Pereira da Silva (Universidade de Brasília)  
Elysa Beatriz de Oliveira Damas (Universidade de Brasília)  
Atailson Oliveira Da Silva (Universidade de Brasília)  
Carlos Alexandre Rocha da Costa (Universidade Federal de Lavras)  
Gilson Gustavo Lucinda Machado (Universidade Federal de Lavras)  
Lorrane Ribeiro de Souza (Universidade Federal de Lavras)  
Eduardo Valerio de Barros Vilas Boas (Universidade Federal de Lavras)  
Rayssa Ribeiro (Instituto Militar de Engenharia: Rio de Janeiro)  
Valdir Florêncio da Veiga-Junior (Instituto Militar de Engenharia: Rio de Janeiro)  
Marcelo Henrique Sousa (Universidade de Brasília)  
Marcella Lemos Brettas Carneiro (Universidade de Brasília)  
Graziella Anselmo Joanitti (Universidade de Brasília)



## Knowledge Area

Nanotechnology



## Funding

FAPDF process: 00193-00000893/2021-70



## Keywords

Nanotechnology, *Carapa guianensis*, Wound healing

## Abstract

Andiroba oil (*Carapa guianensis*) is described as a pro-healing agent by stimulating cell proliferation and collagen production. Nanostructuring this oil is an alternative for optimizing the occurrence of pro-healing effects. Therefore, the objective of the present study was to develop and characterize andiroba oil nanoemulsions (NeAnd) and incorporate it in a hydrogel matrix (NeAndG) to evaluate its potential healing effects in vitro. Andiroba oil characterization showed the presence of 47.6% of oleic acid, 28.6% of palmitic acid and 9.6% of linoleic acid, acid value of 5.17 mg KOH/g, peroxide value of 1.44 meq O<sub>2</sub>/Kg, and degree of acidity of 2.6%. NeAnd and NeAndG obtained by sonication present, respectively, hydrodynamic diameter (HD) of 129 and 135 nm, polydispersity index (Pdl) of 0.190 and 0.217 and zeta potential (ZP) of -33 and 72 mV. These parameters remained stable on NeAnd stored at 4 °C for 30 days, however, increased in HD was observed at 25 and 37 °C. In contrast, HD decreased was observed in NeAndG stored at 25 and 37 °C. No significant alterations were observed on NeAnd and NeAndG submitted to centrifugation stress. However, pH variation resulted in an increase on HD of NeAnd at pH 11 and NeAndG at pH 3. In thermal analysis, NeAnd degradation occurs at temperature of 300 °C and NeAndG at 430 °C. In MTT analysis, no reduction in cell viability of human fibroblasts (FGH) and keratinocytes (HaCaT) treated for 24h with 90 to 540 ug/mL with NeAnd and NeAndG was observed. However, HaCaT treated with 540 and 360 ug/mL of free andiroba oil showed cell viability of 55.6 and 65.4%. NeAnd promoted HaCaT cell migration of 88.7% and 20% on FGH cells. These results demonstrate the success in the development of nanoemulsions based on Andiroba oil and its incorporation into the gel matrix with similar physicochemical characteristics. Additionally, the biocompatibility and pro-migratory effect evidence the potential use of this formulation as wound healing therapy.

# Development of Rhodamine-Labeled Nanoparticles Coated with Hyaluronic Acid for Ocular Delivery Studies



## Author

Izabella Cristina Bernardo Maríngolo (USP-Ribeirão Preto)  
Gabriela Fávero Galvão (USP-Ribeirão Preto)  
Renata Fonseca Vianna Lopez (USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

Agência CNPq - Edital MCT/CNPq - N° 130751/2024-3



## Keywords

polymeric nanoparticles, topical ocular administration, hyaluronic acid

## Abstract

Polymeric nanoparticles (NPs) offer a promising approach for topical ocular administration due to their ability to sustain drug release and extend retention time. Combined with hyaluronic acid (HA), these NPs can enhance therapeutic efficacy, making them an effective strategy for ocular applications. This study aims to develop rhodamine-label spherical NPs of isobutyl cyanoacrylate (IBCA) coated with HA, characterize their properties, and evaluate their biodistribution and complement system activation in an animal model. Spherical NPs coated with HA were synthesized using the redox radical emulsion polymerization (RREP) method. The synthesis involved IBCA monomer (0.5 mL), cerium ammonium nitrate (2 mL) as a catalyst, polysaccharide HA (136 mg), and rhodamine as a marker. Post-synthesis, the NPs were purified via dialysis using a cellulose membrane with a molecular weight cut-off 3,500. The NPs were characterized using Fourier-transform infrared spectroscopy (FTIR) to confirm HA conjugation and transmission electron microscopy (TEM) to assess NP geometry. The size, zeta potential, and polydispersity index (PDI) of the NPs were measured alongside pH analysis of the dispersions. The RREP method yielded spherical NPs with HA coatings, verified by FTIR, which detected the characteristic functional groups of HA. The NPs had an average size of  $472 \text{ nm} \pm 12.16$ , a PDI of  $0.282 \pm 0.048$ , and a zeta potential of  $-16.5 \pm 2.70$ . The pH of the nanoparticle dispersions was approximately 7, making them suitable for ocular application. Nuclear magnetic resonance (NMR) analysis confirmed the successful incorporation of rhodamine into the NPs. In summary, the NP-HA with rhodamine was characterized to meet the standards for ocular application and is ready for the project's next phase, which involves evaluating biodistribution in a rabbit model.

# Preparation and Physicochemical Characterization of miRNA-loaded Lipid Nanoparticles as a Potential Therapy for Parkinson's Disease



## Author

João Victor Soares Vieira (Universidade Federal de Santa Catarina)  
Máriele Paludetto Sanches (Universidade Federal de Santa Catarina)  
Amanda Ellen de Athayde (Universidade Federal de Santa Catarina)  
Andressa Herrmann (Universidade Federal de Santa Catarina)  
Ana Carolina Irioda (Faculdade Pequeno Príncipe)  
Bassam Felipe Mogharbel (Faculdade Pequeno Príncipe)  
Nathalia Barth de Oliveira (Faculdade Pequeno Príncipe)  
Luis Felipe Costa Silva (Universidade Federal de Santa Catarina)  
Katherine de Carvalho (Faculdade Pequeno Príncipe)  
Elenara Lemos-Senna (Universidade Federal de Santa Catarina)



## Knowledge Area

Nanotechnology



## Funding

CNPq, Projeto n°. 442585/2020-9; FAPESC, Projeto n°. 2023TR000314



## Keywords

miRNAs, Parkinson's Disease, Lipid Nanoparticles

## Abstract

miRNAs are non-coding RNAs related to post-transcriptional gene regulation, playing an important role in the physiological progress of different neurodegenerative diseases. In Parkinson's Disease (PD), miRNAs are involved in various physiological and pathological mechanisms, including immunity and inflammation. In addition, miRNAs can affect the progress of PD by regulating the expression of various microglia genes. However, miRNAs exhibit low stability in biological fluids and a low ability to enter cells to produce a therapeutic effect. To overcome these limitations, lipid nanoparticles (LNPs) containing miRNA that mimic miR-124 were prepared using the ethanol dilution technique. The LNPs consisted of an ionizable (DODMA) and cationic (DOTAP) lipids, a helper lipid (DSPC), a pegylated lipid (DSPE-PEG2000) and cholesterol. Briefly, an ethanolic solution containing DODMA or DOTAP, DSPC, DSPE-PEG2000, and cholesterol was added to an acetate buffer solution pH 4.0 containing the miR-124. The LNPs were formed spontaneously and then submitted to a dialysis against a PBS pH 7.4 overnight. The LNPs were characterized according to their size, polydispersity index (PDI), zeta potential, encapsulation efficiency (EE), and morphology. As a result, LNPs showed a mean size varying from 85 to 100 nm, a PDI lower than 0.3, and a surface charge close to neutrality. The EE was evaluated by the RiboGreen assay and varied from 75% to 95%. Cryo-TEM micrographs showed LNPs displaying a spherical and vesicular structure, with their sizes similar to those obtained by dynamic light scattering. In conclusion, the LNPs exhibited favorable physicochemical characteristics and high EE, indicating significant potential for therapeutic applications. Therefore, these nanoparticles may overcome limitations in miRNAs delivery and hold promise for the treatment of neurodegenerative diseases, such as PD.

# Lycopene loaded in lipid nanoparticles: physicochemical characterization and lycopene content



## Author

João Victor Soares Vieira (Universidade Federal de Santa Catarina)  
Máriele Paludetto Sanches (Universidade Federal de Santa Catarina)  
Amanda Ellen de Athayde (Universidade Federal de Santa Catarina)  
Andressa Herrmann (Universidade Federal de Santa Catarina)  
Ana Carolina Irioda (Faculdade Pequeno Príncipe)  
Bassam Felipe Mogharbe (Faculdade Pequeno Príncipe)  
Nathalia Barth de Oliveira (Faculdade Pequeno Príncipe)  
Luis Felipe Costa Silva (Universidade Federal de Santa Catarina)  
Katherine de Carvalho (Faculdade Pequeno Príncipe)  
Elenara Lemos-Senna (Universidade Federal de Santa Catarina)



## Knowledge Area

Nanotechnology



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq, Projeto n. 442585/202 Fundação de Amparo à Pesquisa e Inovação do Estado de Santa Catarina - FAPESC, Projeto no. 2023TR0003140-9



## Keywords

lycopene, lipid nanoparticles, nanocarrier

## Abstract

The biological activities of lycopene have been widely studied due to its anti-oxidant, anti-cancer, and neuroprotective properties. The low solubility in aqueous media requires constructing a delivery system when aiming for biomedical applications. In this context, this work aimed to develop a nanocarrier for lycopene based on lipid nanoparticles (NLPs). The organic phase was constructed from DODMA, an ionizable lipid, DOTAP, a cationic lipid, DSPC, DSPE-PEG, and cholesterol as structural lipids, where lycopene was dispersed. In this context, blank NPLs and NPLs with lycopene were prepared by diluting an ethanolic lipid solution in an acetate buffer solution pH 4.0, varying the total concentration of lipids at 12.5 mM, 25 mM, and 50 mM. NPLs were formed spontaneously and subsequently dialyzed against phosphate buffer pH 7.4. All NPLs were characterized in terms of size, polydispersity index, and zeta potential. The results showed the obtaining of NPLs with sizes ranging from 200 to 300 nm and positive zeta potential close to neutrality, depending on the type of cationic lipid used. The incorporation of lycopene into the formulations led to an increase in particle size, its concentration in the formulations was estimated by high-performance liquid chromatography through a calibration curve, and the values found were 36  $\mu\text{g}/\text{mL}$ , 77  $\mu\text{g}/\text{mL}$ , and 75  $\mu\text{g}/\text{mL}$  of lycopene respectively for the formulations containing 12.5 mM, 25 mM, and 50 mM lipids. The morphology of blank and lycopene-containing NLPs was observed by cryogenic electron microscopy. These results lead to the conclusion that the NLPs system are good carriers for the lipophilic lycopene molecule.

# Guar Gum Nanocomposite Hydrogel Containing Alpha-tocopherol: Development and Preliminary Evaluation of Photoprotective Potential



## Author

Kauani Moenke (Universidade Federal de Santa Maria)  
Fernanda Dias Guilherme (Universidade Federal de Santa Maria)  
Daiane Brito de Oliveira (Universidade Federal de Santa Maria)  
Vinicius Costa Prado (Universidade Federal de Santa Maria)  
Leticia Cruz (Universidade Federal de Santa Maria)



## Knowledge Area

Nanotechnology



## Funding

National Institute of Science and Technology in 3D printing and Advanced Materials Applied to Human and Veterinary Health - INCT \_3D-Saúde, funded by CNPq, Brazil (Grant #406436/2022-3)



## Keywords

Human skin, Cutaneous route, Polymeric Nanoparticles

## Abstract

Alpha-tocopherol is an isomer of vitamin E with antioxidant and photoprotective properties. However, it has a high partition coefficient (Log P 10.2), poor water solubility, and is photolabile. Such limitations make alpha-tocopherol a candidate for nanoencapsulation to circumvent them. Nanocapsule suspensions (ethylcellulose as polymeric wall and sesame oil as oily core) containing alpha-tocopherol (1 mg/mL) were prepared by the interfacial deposition of the preformed polymer method. Nanocapsules presented average size in the nanometric range ( $169 \pm 4$  nm), negative zeta potential, alpha-tocopherol content close to the theoretical value (1 mg/mL), and 99% of encapsulation efficiency. The HET-CAM assay classified the nanocapsule suspensions as non-irritating. Nanoencapsulation protected alpha-tocopherol against UVC-induced degradation and had a similar scavenging activity of the ABTS radical when compared to the free form. The UV absorbance spectrum of free alpha-tocopherol (10  $\mu$ g/mL) showed a low-intensity absorbance at the UVB range. Alpha-tocopherol-nanocapsule suspensions increased the UVB light scattering/absorption compared to the free compound. The hydrogels were prepared by thickening nanocapsule suspensions with guar gum (2.5 %). Hydrogels maintained the nanometric size of the nanocapsules and the alpha-tocopherol content at around the initial concentration. Regarding the rheological behavior, the hydrogels were classified as non-Newtonian flow. Hydrogel containing alpha-tocopherol in nanoencapsulated form demonstrated a skin permeation profile similar to the hydrogel containing free compound. Therefore, the nanoencapsulation improved the alpha-tocopherol stability and UVB light scattering/absorption. The hydrogel prepared showed appropriate physicochemical properties for cutaneous application.



# Antiviral Effect of Nanoencapsulated Brazilian Green Propolis Against SARS-CoV-2



## Author

Iasmin Rosanne Silva Ferreira (USP-Ribeirão Preto)  
Isabela Araújo Justino (USP-Ribeirão Preto)  
Ronaldo Bragança Martins Junior (USP-Ribeirão Preto)  
Jairo Kenupp Bastosjk (USP-Ribeirão Preto)  
Alexandre Rodrigues Gaspari (Federal Institute of São Paulo)



## Knowledge Area

Nanotechnology



## Funding

CNPq grants #315601/2023-0; FAPESP grants #2018/13465-5



## Keywords

Brazilian green propolis, SARS-CovV-2, microemulsion

## Abstract

The global COVID-19 pandemic, caused by SARS-CoV-2, continues to pose a significant threat to public health and the economy. SARS-CoV-2 is highly contagious, transmitted primarily through direct contact or inhalation of droplets, and can cause severe respiratory illness and other health complications, including post-acute COVID-19 syndrome. This study explores the antiviral potential of Brazilian green propolis, a natural product rich in flavonoids and phenolic compounds, encapsulated in a microemulsion to enhance its stability and antiviral effects. Microemulsion containing green propolis extract (ME-GP) was prepared and characterized using various physicochemical techniques. Furthermore, the antiviral activity of the ME-GP was evaluated *in vitro* against SARS-CoV-2. The microemulsion showed a size around 217 nm, negative zeta potential and high encapsulation efficiency for artepillin C and baccarin (~99%), and spherical morphology. The ME-GP formulation was tested for its antiviral activity against multiple SARS-CoV-2 variants (WT, Gamma, and Delta) in Caco-2 cells, revealing a significant reduction in viral load (~90%), mainly for the WT and Delta variants. Thus, this study highlights the promising prophylactic and therapeutic potential of nanoencapsulated green propolis for combating SARS-CoV-2 and its variants, providing a natural adjunct in COVID-19 therapy.

# Synthesis and Evaluation of Zinc Phthalocyanine-Linked Nanoparticles for Sonodynamic Therapy



## Author

Tai de Cassia Ribeiro Amaro(USP-Ribeirão Preto)  
Renata Fonseca Vianna Lopez(USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

FAPESP



## Keywords

Sonodynamic therapy, Low-frequency ultrasound, Mesoporous silica nanoparticles

## Abstract

Sonodynamic therapy (SDT) integrates ultrasound with sonosensitizing agents for non-invasive cancer treatment through acoustic cavitation. Low-frequency ultrasound (LFU) enhances cavitation, producing microbubbles that permeabilize cell membranes and activate sonosensitizers. Mesoporous silica nanoparticles (NPs) with adjustable pores can amplify cavitation efficacy. Conjugation of the photosensitizer zinc phthalocyanine (ZnPc) to NPs yields a novel sonosensitizing nanoparticle (ZnPc-NP), capable of generating reactive oxygen species (ROS) upon LFU exposure, leading to tumor cell apoptosis. This study synthesized ZnPc-NP and evaluated its impact on LFU-induced cavitation and sonodynamic activity. The synthesis involved tetraethyl orthosilicate as the silica source, cetyltrimethylammonium bromide as the template and surfactant, octane with ZnPc as the oily phase, L-lysine as the catalyst, styrene as the pore-forming agent, and 2,2'-Azobis dihydrochloride (AIBA) as the polymerization initiator. LFU-induced cavitation was quantified using water's potassium iodide (KI) dosimeter and aluminum pit foil method across different ZnPc-NP concentrations (50 to 500  $\mu\text{g}/\text{mL}$ ). SDT efficacy was assessed in melanoma B16F10 cells treated with varying concentrations of ZnPc-NP and free ZnPc, followed by LFU exposure (40 kHz, 0.5  $\text{W}/\text{cm}^2$ , 1 minute). Cellular viability was measured using the resazurin assay. ZnPc-NP synthesis resulted in spherical, homogeneous nanoparticles. Increasing ZnPc-NP concentrations linearly enhanced LFU-induced cavitation, nearly quintupling with each unit rise in concentration. Moreover, SDT reduced cell viability, highlighting the potential of ZnPc-NP to augment SDT efficacy.

# Fluorescent hybrid nanoparticles as co-delivery system of glycoalkaloids and siRNA and their biological effect on cutaneous melanoma cells



## Author

Yasmim Garcia Gonçalves (USP-Ribeirão Preto)  
Marcelo Kravicz (University of Milano)  
Raul Marques Novais (USP-Ribeirão Preto)  
Bryan Wender Debiasi (USP-Ribeirão Preto)  
Flávio da Silva Emery (USP-Ribeirão Preto)  
Jairo Kennup Bastos (USP-Ribeirão Preto)  
Maria Vitória Badra Lopes Bentley (USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

FAPESP (grants #2018/13465-5, #2017/04138-8, CNPq (grant #407903/2021-6), and CAPES (grant #88887.615169/2021-00).



## Keywords

solid lipid-polymer hybrid nanoparticles, fluorescent probe, cutaneous melanoma

## Abstract

The design of solid lipid-polymer hybrid nanoparticles (SLPH NP) facilitates the efficient co-delivery of drugs with different logP values, such as glycoalkaloids and gene material, to cancer cells. Polyaspartamide copolymers are particularly interesting as polymeric coatings due to their versatile chemical properties, which allow the tunability of hydrophobicity, biocompatibility, stability, and functionality of the nanostructure. In this study, a new fluorescent cationic polymer (P1\*) was synthesized by forming a thiocarbamide bond between the polyaspartamide copolymer and fluorescein isothiocyanate (FITC). The physicochemical characterization of P1\* was performed using <sup>1</sup>H NMR, FT-IR, and fluorescence spectroscopy. The fluorescent SLPH NP, loaded with glycoalkaloid extract (SLPH\*-GE), was prepared via a one-step hot-melt emulsification process followed by ultrasonication and characterized using DLS, ζ-potential, and NTA. Furthermore, siRNA complexation on the surface of the fluorescent nanocarrier was conducted by electrophoretic run and decomplexation by anionic competition with heparin. The results showed that at N/P ratios above 16, the siRNA remained intact during complexation and decomplexation. Additionally, the cytotoxic profile of SLPH\*-GE on human skin fibroblast cells (HFF-1) and human cutaneous melanoma cells (SK-MEL-28) was evaluated. The FITC labeling did not significantly impact the cytotoxicity profile or physicochemical properties compared to the non-fluorescent formulation. Therefore, these findings support further investigation into the biological behavior of SLPH NP in melanoma cells, including cellular uptake and cutaneous permeation profiles.

# Decoquininate-loaded Nanoemulsions: development and anti-malaria effect



## Author

Tainá Santos Souza (Universidade Federal da Bahia)  
Aline Lorena Lourenço dos Santos Miranda (Instituto Gonçalo Moniz)  
Diogo Rodrigo Magalhães Moreira (Instituto Gonçalo Moniz)  
Henrique Rodrigues Marcelino (Universidade Federal da Bahia)



## Knowledge Area

Nanotechnology



## Funding

CAPES, FAPESB.



## Keywords

Decoquininate, Nanoemulsion, Malaria

## Abstract

Decoquininate (DQ) is a drug that has been investigated for its promising effect on the malaria parasitic agent *Plasmodium* spp. However, DQ has a high lipophilicity that prevents its use in humans. This work aimed to validate an analytical method for DQ quantification, test DQ solubility in different lipids, and develop a nanostructured emulsion. The HPLC-DAD quantification method was validated using the ICH Q2(R2). The method was used for the solubility test in lipids, where known amounts of DQ were added to different oil phases. Sonication was used for the solubility assay and later to develop the pseudoternary diagram and emulsified systems. From this diagram, ME-BCO was obtained, and DQ was solubilized (NE-DQ). The formulations were evaluated by their morphology (size, shape and polydispersion) and zeta potential. ME-BCO was stored and assessed over 90 days for stability assessment. The antiparasitic in vivo NE-DQ activity was determined by flow cytometry evaluating the parasitemia of mice infected by *P. Berghei* (CONCEA 019/2021). Then, a linear ( $R^2 = 0.9989$ ), selective, precise and robust method to quantify DQ was developed. Also, the repeatability obtained indicates low variability. As for the solubility, an evident enhancement was observed when using a mix of medium-chain triglyceride and phospholipid. ME-BCO was macroscopically viscous, translucent and homogeneous, and its distribution of droplets with nanometric diameters of  $13 \text{ nm} \pm 1$  was monodisperse. NE-DQ is characterized as viscous, translucent (less than ME-BCO), homogeneous with an average size of  $379 \pm 5 \text{ nm}$ , and polydisperse. ME-BCO remained stable for 90 days. In NE-DQ, a concentration of DQ was found at  $0.3 \text{ mg/mL}$ . Finally, the formulation inhibited parasitemia by more than 94%. Therefore, the developed nanostructured emulsion could deliver DQ efficiently and prevent *P. Berghei* growth. However, we expect to enhance DQ solubility even more to reduce the doses necessary for the treatment.

# Early Development of Liposomal Platforms for BODIPY Incorporation in Skin Cancer PDT



## Author

Nathalia Vasconcellos Nazario (USP-Ribeirão Preto)  
Renata Fonseca Vianna Lopez (USP-Ribeirão Preto)  
Tais de Cassia Ribeiro Amaro (USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

FAPESP 22/03521-0



## Keywords

Photodynamic therapy, Liposomes, BODIPY

## Abstract

Skin cancer is increasingly prevalent worldwide and conventional treatments like surgery, radiotherapy, and chemotherapy suffer from significant drawbacks, such as adverse effects and aesthetic impact. Photodynamic therapy (PDT) has emerged as an innovative alternative, involving a photosensitizer administered followed by specific wavelength light to produce reactive oxygen species (ROS) that selectively target cancer cells. Boron dipyrromethene derivatives (BODIPYs) are promising as photosensitizers due to their excellent photophysical properties and ROS generation ability. However, their hydrophobic nature limits skin penetration, which is crucial for PDT effectiveness. Encapsulating BODIPYs in liposomes can enhance their solubility and cutaneous penetration, offering an efficient topical delivery method. This research aims to develop and evaluate novel BODIPY-based photosensitizers for PDT in skin cancer treatment. Initial efforts involved developing two liposomes based on phosphoethanolamine derivatives (PE) for future conjugation with BODIPYs. Liposomes were characterized for size, polydispersity index (PDI), and zeta potential ( $n=3$ ) and their stability for 7 days was also evaluated. The most promising liposome was encapsulated with a model BODIPY derivative. Liposomes with 2-Dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE) exhibited size of  $274\pm 50$  nm, PDI  $0.26\pm 0.04$  and zeta potential  $-24\pm 1.6$  mV, while those with 1,2-Distearoyl-sn-glycero-3-phosphoethanolamine (DSPE) showed size of  $228\pm 26$  nm, PDI  $0.2\pm 0.06$  and zeta potential  $-26\pm 3$  mV. All presented good stability and BODIPY was successfully encapsulated in DSPE liposomes without significant changes in size, PDI, or zeta potential. Future steps include chemical conjugation of BODIPY with DSPE for liposome preparation and comparison with BODIPY-loaded liposomes already obtained. The efficacy of ROS generation by these liposomes will be studied to understand their behavior in biological systems.

# Personalizing liposome formulations: The Impact of Lipid Composition on Cancer Cell Interaction



## Author

Tacio Gonçalves Hayasaki - Universidade Federal de Goiás (UFG)  
Mariana Arraes Salomão - Universidade Federal de Goiás (UFG)  
Lucas Ribeiro de Sousa - Universidade Federal de Goiás (UFG)  
Laura Gabrielly Pinheiro Vieira - Universidade Federal de Goiás (UFG)  
Sebastião Mendanha - Universidade Federal de Goiás (UFG)  
Eliana Martins Lima - Universidade Federal de Goiás (UFG)



## Knowledge Area

Nanotechnology



## Funding

FAPEG; CAPES; CNPq; INCT NanoFarma.



## Keywords

Liposome, drug delivery, lipid composition

## Abstract

**Introduction:** Liposomes (LP) are among the most explored and versatile drug delivery systems successfully used in the clinic, including in cancer therapies. At present, a vast range of phospholipids is available for the formulation of liposomes, encompassing natural or synthetic, native and modified, alongside other components, such as cholesterol (chol). It has been shown that the surface characteristics of nanocarriers significantly influence their interactions with biological barriers and, ultimately with cells. Nevertheless, the way different tumor cells respond to slight changes in the lipid composition of LPs remains to be understood. **Methods:** LP formulations were prepared using either a natural (SPC) or synthetic lipid (DMPC), with and without 40% chol, prepared by thin-film hydration followed by extrusion. Characterization included size by DLS and membrane lipid dynamics using electron spin resonance (ESR). Human tumor monocyte-like U937 cell line were used as a cellular model and evaluated in vitro studies. **Results:** As expected, the presence of cholesterol increased membrane rigidity for all LPs. In vitro assays demonstrated that the U937 cells responds distinctly to different LPs. Cell viability was higher in the presence of formulations in which chol was part of the lipid bilayer. Regarding cell uptake, unexpectedly, we also found that cellular internalization was dependent on chol content. To investigate the role of cell membrane properties in cell viability, we then hydrated a thin-film of SPC lipid with a cell suspension, which lead to a concentration-depend increase in cell membrane fluidity. These changes were not observed when cells were exposed to LPs at the same lipid concentration [H-I], suggesting an intracellular cell death pathway, currently under investigation. **Conclusion:** This study demonstrated that the lipid composition can modulate LPs bio-interactions, which may help define the best formulations for each type of target cell.

# Combination of iontophoresis and poly (pseudo) rotaxanes for antifungal nail delivery



## Author

Joyce Machado dos Santos - Universidade Federal de Goiás(UFG)  
Ricardo Neves Marreto - Universidade Federal de Goiás (UFG)  
Stephânia Fleury Taveira - Universidade Federal de Goiás (UFG)



## Knowledge Area

Nanotechnology



## Funding

CAPES, CNPq, FAPEG



## Keywords

rotaxanes, iontophoresis, nail permeation

## Abstract

Onychomycosis is a prevalent fungal nail disease that can cause significant discomfort. While oral treatment is the most commonly used approach, it has been linked to adverse effects. Topical antifungal application is an alternative, but the nail is a difficult barrier to transpose. Therefore, this study aimed to combine poly(pseudo)rotaxanes (PPRs) and iontophoresis to enhance drug permeation into the deeper layers of the nail plate. For this, simple and mixed nanomicelles of Kolliphor® (KOL) and Gelucire® (GEL) were prepared, adding 2% terbinafine (TB). 5 or 10% of  $\alpha$ -cyclodextrin ( $\alpha$ -CD) was added to form PPRs. Physical and chemical stability against electrical current was performed. Nail hydration, SEM, and release studies were also carried out with iontophoretic and passive applications. Three formulations proved stable after applying electric current for TB content, pH, and visual aspects. Improvements in nail hydration were achievable solely through the combination of PPRs and iontophoresis. Formulations with higher amounts of  $\alpha$ -CD achieved the highest nail hydration, particularly those containing GEL. Also, greater release was achieved with higher amounts of CDs. Formulations with GEL combined with iontophoresis increased 1.6-fold TB release compared to passive release. Thus, combining iontophoresis and PPRs with 10% of  $\alpha$ -CD seemed promising for nail onychomycosis treatments.

# Development of Nanoformulations and In Vitro Evaluation: New Strategies for Treating Brain Tumors



## Author

Lima, Franciely Rufino de Almeida (USP-Ribeirão Preto)  
Priscyla, Daniely Marcato (USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

CNPq, Projeto n°. 442585/2020-9; FAPESC, Projeto n°. 2023TR000314



## Keywords

Glioblastoma, Nanoparticles, Chemotherapeutic

## Abstract

Glioblastoma (GBM) is the most prevalent and aggressive type of glioma, characterized by a low survival rate. The current treatment for GBM with Temozolomide (TMZ) shows limited efficacy due to resistance mediated by P-glycoprotein (P-gp), which hinders passage through the blood-brain barrier (BBB) and tumor cells. Therefore, there is an urgent need for innovative delivery systems to overcome these challenges. This research aims to develop, optimize, and characterize lipid nanoparticles (NPs) for the co-delivery of chemotherapeutic and natural product, as well as to evaluate their cytotoxic effect on U87MG glioblastoma cells. The NPs were prepared by hot emulsification and sonication, optimized using Box-Behnken design. They were characterized for size, zeta potential, encapsulation efficiency, morphology, thermal profile, and stability. U87MG cells were treated with NPs with and without co-encapsulated compounds, evaluating cell viability by resazurin assay, cellular uptake by confocal fluorescence microscopy, and cell death mechanism by flow cytometry. The optimization showed that surfactants and the proportion of the oil phase significantly influence NP size and PDI. The optimized NPs had a diameter below 150 nm, low polydispersity index, and negative zeta potential. Transmission electron microscopy revealed spherical morphology. High encapsulation efficiency of the chemotherapeutic and natural product was achieved, associated with the appropriate choice of lipid components and low NP crystallinity. The co-encapsulated NPs showed high internalization in GBM cells, contributing to their high cytotoxic activity. Co-encapsulation reduced the IC<sub>50</sub> of the chemotherapeutic by 2.418 times, indicating a chemosensitizing effect of the natural product. The cell death mechanism was predominantly apoptotic. These results highlight the potential of co-encapsulated NPs for GBM treatment, providing a basis for future investigations and clinical applications in nanomedicine.



# Synthesis of an innovative targeting molecule for the development of ligant-specific liposomes towards pulmonary inflammation



## Author

Naiara Ieza Gallo M Benedetti - Universidade Federal de Goiás (UFG)  
Maria Clara Alves de Souza - Universidade Federal de Goiás (UFG)  
Felipe Lange Coelho - Universidade Federal de Goiás (UFG)  
Sebastião Antonio Mendanha Neto - Universidade Federal de Goiás (UFG)  
Eliana Martins Lima - Universidade Federal de Goiás (UFG)



## Knowledge Area

Nanotechnology



## Funding

CAPES



## Keywords

LNPs, Sialic acid, Pulmonary

## Abstract

There is a growing interest in the respiratory tract for drug administration with local and even systemic effects, due to the ease and advantages over other routes, such as the absence of first-pass metabolism. However, this route presents some limitations, it has physiological barriers that protect against the entry of microorganisms, pathogens, and pollutants, thus hindering access to the pulmonary alveoli. In order to achieve drug delivery via nanoparticles to the lungs, several strategies have been developed, including the addition of specific receptors or ligands on the surface of LNPs to facilitate their targeting to the site of action. Examples of these ligands include mannose, a monosaccharide with receptors on macrophages, GALA, a fusogenic peptide, and N-Acetyl-5-neuraminic acid (Neu5Ac), a type of sialic acid with receptors on certain immune cell lineages such as macrophages. In this work, we synthesized a novel molecule to be used for targeting liposomes to inflammatory alveolar cells. Organic synthesis reactions were carried out using Neu5Ac and DSPE-PEG with EDC/NHS as catalysts for 12 hours under a nitrogen atmosphere. The sample was then diluted in milli-Q water and dialyzed using a 1 kDa MWCO membrane. The final compound was obtained by lyophilizing the sample, resulting in a whitish powder. Nuclear magnetic resonance ( $^1\text{H}$  NMR) and thermal analysis using a microcalorimeter, as well as polyclonal antibody testing for sialic acid, were conducted to verify the ligand's affinity for the receptor site. The results from  $^1\text{H}$  NMR suggest that there was indeed coupling between the two molecules, indicated by specific shifts in the Neu5Ac molecule present in the synthesis product spectrum but absent in the phospholipid spectrum, consistent with the microcalorimeter results. The synthesis of molecules that aid in the construction of nanoparticles, enhancing their characteristics and favoring their delivery, is essential for the improvement of new LNPs.

# Phytosomes As Red Propolis Delivery Systems: A Promising Therapeutic Approach For Allergies



## Author

Geovana Carmelina dos Santos Zandona (USP-Ribeirão Preto)  
Valdemir da Costa Silva (UFAL)  
Maria Perpetua Freire de Moraes Del Lama (USP-Ribeirão Preto)  
Irialdo Diniz Basílio Júnior (UFAL)  
Rose Mary Zumstein Georgetto Naal (USP-Ribeirão Preto)



## Knowledge Area

Nanotechnology



## Funding

CNPq



## Keywords

ALLERGIES, PHYTOSOMES, PROPOLIS

## Abstract

Propolis is a natural product with broad pharmacological properties; however, many of its components have low solubility and low ability to permeate biological membranes. Therefore, this study proposes the development of a phytosomal nanocarrier capable of improving the solubility and bioavailability of Red Propolis of Alagoas (RPA) for use in the treatment of allergic diseases via oral route. Phytosomes were prepared by the lipid film hydration method and promising results were obtained for the F4 formulation containing RPA, phosphatidylcholine (PC) and cholesterol in a mass ratio of 1:3:1 and 0.1% Tween 80 (v/v). The physicochemical characterization of F4 showed a particle size of 150 nm, Pdl between 0.1 and 0.2 and Zeta potential around -20 mV, measured by Zetasizer Nano. The flavonoid encapsulation efficiency (EE) was 98% and the total phenolic content was 90%, quantified by the aluminum trichloride and Folin-Denis colorimetric methods, respectively. Nanoparticle tracking analysis (NTA) counted  $6 \times 10^{12}$  particles/mL and infrared results showed overlapping bands characteristic of the components, indicating interactions between PC and RPA. In vitro release studies were performed in PBS buffer with 2% Tween-80. RPA quantification was performed by HPLC through the quantification of vestidiol, one of the RPA markers. The results showed a small increase in the release of RPA in phytosomal form compared to the free extract. The antiallergic potential was evaluated by the enzyme  $\beta$ -hexosaminidase released by mast cells stimulated by calcium ionophore. The results showed that 0.625 mg/mL of RPA in phytosomal form inhibited 75% of the release of  $\beta$ -hexosaminidase, while the extract alone, at the same concentration, could not be used due to low solubility. Thus, it is concluded that the phytosomal formulation F4 increases the solubility and bioavailability of Alagoas Red Propolis, being promising for the treatment of allergies by the oral route.

# Retinal Imaging: Stability and Efficacy of TiO<sub>2</sub>NP-Fluorescein Conjugates



## Author

Marina França Dias (Ezequiel Dias Foundation)  
Rodrigo Ken Kawassa (USP-Ribeirão Preto)  
Lutiana Amaral de Melo (Ezequiel Dias Foundation)  
Robson Raphael Guimarães (USP-Ribeirão Preto)  
Sílvia Ligorio Fialho (Ezequiel Dias Foundation)



## Knowledge Area

Nanotechnology



## Funding

INCT-NANOFARMA (FAPESP, Grant #2014/50928-2 and CNPq, Grant #465687/2014-8)



## Keywords

Fundus Fluorescein Angiography, TiO<sub>2</sub> Nanoparticles, sodium fluorescein

## Abstract

Fundus Fluorescein Angiography is widely used for diagnosing and managing various retinal and choroidal diseases, such as age-related macular degeneration, diabetic retinopathy, and retinopathy of prematurity. This exam allows clinicians to evaluate retinal morphology and vasculature. However, adverse events, including mild to severe reactions to sodium fluorescein, have been reported, and the rapid elimination of the marker can complicate the exam for ophthalmologists. Titanium dioxide nanoparticles have shown great potential in numerous biological applications and possess desirable characteristics for use as carriers for contrast agents. In this work, we developed titanium dioxide nanoparticles conjugated with sodium fluorescein to potentially improve the quality of angiography exams by increasing fluorescein retention time and maintaining fluorescence photostability, leading to more accurate diagnoses. Ultrasmall nanoparticles (size < 5 nm) conjugated with fluorescein (TiO<sub>2</sub>NP-FL) were successfully prepared. Cytotoxicity was evaluated in HUVEC cells using the MTT assay, and a hemolysis test was conducted using rat blood. Scanning laser angiography analysis was performed in rats using HRA+OCT Spectralis equipment after 1, 5, 10, 15, 30, 60, and 240 minutes of IV injection of TiO<sub>2</sub>NP-FL or free fluorescein. Fluorescence intensity was calculated using Image J. Animals that received free fluorescein showed a rapid decline in fluorescence, with a reduction starting at 15 minutes and no fluorescence observed at 240 minutes. In contrast, in the NPTiO<sub>2</sub>-FL treated group, fluorescence intensity remained constant up to 60 minutes, and fluorescence was still visible at 240 minutes. These findings suggest that the nanoparticles were able to increase blood circulation time and contact with the blood-retinal barrier compared to the free molecule, which could improve angiography exams.

**Area**

# **Pharmacology, Pharmacokinetics and Toxicology**

# Characterization of the antitumor action of the ConBr lectin on glioma cells.



## Author

Valeria Da Rosa - Universidade de Santa Catarina (UFSC)  
Rodrigo Bainy Leal - Universidade de Santa Catarina (UFSC)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CNPq



## Keywords

Glioma; lectin; autophagy

## Abstract

Gliomas are primary brain tumors arising from glial cells. Glioblastoma multiforme (GBM) is the most aggressive, due to its infiltrative capacity and resistance to treatments, with the average survival of patients being 15 months. Therefore, it is essential to develop more selective and efficient therapeutic strategies. The molecular changes in GBM include modification of the glycosylation pattern, which can be recognized by glycan-binding proteins, lectins. We have indicated that the lectins purified from the seeds of *Canavalia* and *Dioclea* can trigger antiglioma signaling, decreasing cell viability and inducing autophagy. In the present study, we used glioma cell cultures (C6 lines) exposed to *Canavalia brasiliensis* lectin (ConBr; 10-50  $\mu\text{g}/\text{mL}$ ; 24h), and evaluated cell viability and autophagy in response to lectin treatment. The main results showed that ConBr at concentrations of 30 and 50  $\mu\text{g}/\text{mL}$  (24h) causes a significant reduction (~40%) in cell viability, measured by the MTT method. Furthermore, in the Acridine Orange assay, we were able to observe the induction of autophagy by ConBr. Taken together, the data indicate C6 lineage as a useful model to study the antiglioma activity of lectins. Moreover, additional studies will be performed in order to characterize the role of autophagy and other pathways in ConBr-induced cell death.

# Anti-inflammatory and anti-hyperalgesic properties of delta-3-carene in the experimental acute inflammatory response



## Author

Lucas Luiz Machado - Universidade Federal do Mato Grosso (UFMS)  
Paloma Kênia de Moraes Berenguel Lossavaro - Universidade Federal do Mato Grosso (UFMS)  
João Victor Ferreira - Universidade Federal do Mato Grosso (UFMS)  
Mila Marluce Lima Fernandes - Universidade Federal do Mato Grosso (UFMS)  
Gabriel Silvino de Oliveira Venâncio - Universidade Federal do Mato Grosso (UFMS)  
Joyce dos Santos Lencina - Universidade Federal do Mato Grosso (UFMS)  
Mônica Cristina Toffoli-Kadri - Universidade Federal do Mato Grosso (UFMS)  
Saulo Euclides Silva-Filho - Universidade Federal do Mato Grosso (UFMS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CNPQ, CAPES AND FUNDECT



## Keywords

delta-3-carene, monoterpene, acute inflammatory response.

## Abstract

Acute inflammation is a short-lasting process and one of its characteristics is an edema formation and hyperalgesia. Drugs available for the treatment of inflammatory diseases could cause important adverse reactions, such as kidney damage, gastric injury, and cardiovascular effects. Aromatic plants and natural products, including essential oils, have been used in the treatment of inflammatory conditions, and the constituents of these oils are related to the biological activities of these compounds. Delta-3-carene (CAR) is a monoterpene, one of the main components of pine essential oil, which has demonstrated promising anti-inflammatory activity. The aim of this study was to investigate the effects of CAR on the mechanical hyperalgesia and edema formation in acute inflammation induced by carrageenan (Cg). The experimental protocol was approved by the Ethics Committee in the Use of Animals of UFMS, under registration No. 1.288/2023. Male Swiss mice were treated with CAR (25, 50 or 100 mg/kg, orally), indomethacin (reference drug) or vehicle, 1 hour before intraplantar Cg injection (300 µg/paw) in the right hind paw of all animals. The contralateral paw received saline solution 0.9% injection. The edema formation was determined by the volume difference between the right and left paw, using a digital plethysmometer, in the times of 0.5, 1, 2 and 4 hours after Cg injection. For the evaluation of mechanical hyperalgesia, a digital analgesimeter (Von Frey) was used as a pressure transducer, which records the applied force until the moment of paw withdrawal, 3 and 4 hours after Cg injection. The oral treatment with CAR, in all doses tested, reduced the edema formation and mechanical hyperalgesia in all time points. In conclusion, CAR showed anti-inflammatory and anti-hyperalgesic activities during the acute inflammatory response.

# In vitro genotoxicity evaluation of *Echinodorus macrophyllus* (chapéu-de-couro), a traditional Brazilian medicinal herb



## Author

Inara Carbonera Biazus - Universidade Federal de Passo Fundo (UFP)  
Yasmin Vendruscolo Piton - Universidade Federal do Rio Grande do Sul (UFRGS)  
Luiza Garcia de Souza - Universidade Federal do Rio Grande do Sul (UFRGS)  
Luciane Dellazari da Silva do Prado - Universidade Federal de Passo Fundo (UFP)  
Nicoli da Rosa do Amaral - Universidade Federal de Passo Fundo (UFP)  
Ana Cecília Bezerra Carvalho - Agência Nacional de Vigilância Sanitária  
Ana Maria Soares Pereira - Universidade de Ribeirão Preto (UNAERP)  
Lígia Queiroz Matias - Universidade Federal de Passo Fundo (UFP)  
Solange Cristina Garcia - Universidade Federal do Rio Grande do Sul (UFRGS)  
Jessica Nardi - Universidade Federal de Passo Fundo (UFP)  
Gabriela Göethel - Universidade Federal do Rio Grande do Sul (UFRGS)  
Marcelo Dutra Arbo - Universidade Federal do Rio Grande do Sul (UFRGS)  
Luciana Graziotin Rossato-Grando - Universidade Federal de Passo Fundo (UFP)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

No funding



## Keywords

Chapéu-de-couro, Genotoxicity, 3T3 cell line

## Abstract

**Introduction:** *Echinodorus macrophyllus* (Kunth) Micheli, popularly known as chapéu-de-couro, is a traditional Brazilian medical herb used for kidney and urinary tract diseases. Despite its uses, there are no conclusive studies evaluating the genotoxicity potential of its leaves aqueous extract – the traditional preparation. **Aim:** The aim of this study was to evaluate the in vitro genotoxicity of the leaves aqueous extract of *E. macrophyllus* in 3T3 cell line. **Methods:** The sample was collected in Jardinópolis, SP, Brazil, identified, dried, and processed in a blade mill (SisGen nº A938D92). The leaves aqueous extract was prepared by infusion – traditional preparation – and tested in 3T3 cell culture at concentrations of 5, 10, 20 and 50 mg/mL (herbal drug: water). For the genotoxicity evaluation, alkaline comet assay was performed. The results were expressed as % DNA in the tail for each concentration. MTT reduction assay was used as screening test of cytotoxicity to analyze the viability of working concentrations. For statistical analyses, Shapiro-Wilk test was performed, followed by ANOVA and Bonferroni post hoc test (parametric groups) or Kruskal Walli's test and Dunn's post hoc test (non-parametric groups) ( $p < 0.05$ ). **Results:** A concentration-dependent cytotoxicity was observed. 50 mg/mL reduced more than 90% of cell viability while the traditional used concentration (20 mg/mL) reduced about 40% of cell viability. No genotoxicity effect was detected compared to positive control ( $p < 0.001$ ), neither at most concentrated extract concentration (50 mg/mL). This is the first time this plant species genotoxicity was assessed in 3T3 cell line. **Conclusions:** *E. macrophyllus* leaves aqueous extract was not genotoxic at tested concentrations in the 3T3 cell line. More studies are necessary to evaluate the mechanisms related to cytotoxicity in order to guarantee its safety since it is used in folk medicine.

# Antithrombotic activity of an isoxazolic analogue derived from tetrahydrofuran neolignans



## Author

Isabelly Teixeira Espinoça - Universidade Federal do Mato Grosso do Sul (UFMS)  
Rafael Seiji Na-kano Ota - Universidade Federal do Mato Grosso do Sul (UFMS)  
Maria Eduarda Dias Vedoveto - Universidade Federal do Mato Grosso do Sul (UFMS)  
Leonardo Foglia de Medeiros - Universidade Federal do Mato Grosso do Sul (UFMS)  
Denise Caroline Luiz Soares Basilio - Universidade Federal do Mato Grosso do Sul (UFMS)  
Anna Júlia Papa de Araujo - Universidade Federal do Mato Grosso do Sul (UFMS)  
Diego Bento de Carvalho - Universidade Federal do Mato Grosso do Sul (UFMS)  
Cristiane Yuriko Kawasoko Shiguemoto - Universidade Federal do Mato Grosso do Sul (UFMS)  
Edgar Julian Paredes-Gamero - Universidade Federal do Mato Grosso do Sul (UFMS)  
Adriano Cesar de Morais Baroni - Universidade Federal do Mato Grosso do Sul (UFMS)  
Eduardo Benedetti Parisotto - Universidade Federal do Mato Grosso do Sul (UFMS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CNPq, CAPES, FUNDECT and UFMS.



## Keywords

Cardiovascular diseases, tetrahydrofuran neolignans, platelets

## Abstract

Oxidative stress can cause hemostatic disorders and consequently cardiovascular and thrombotic diseases. Tetrahydrofuran neolignans (NTs) are natural compounds with reported antioxidant and anti-inflammatory activity. The objective of the study was to evaluate the antithrombotic action of an isoxazole analogue of NTs (AINT-4) in an in vitro experimental model. AINT-4 was synthesized by cycloaddition reactions between terminal acetylenes 12 and chlorooximes 13. The SwissADME® and Osiris® software were used to analyze oral bioavailability and in silico toxicity. Blood from voluntary donors, men and women (18 - 40 years old), was used for the experiments after approval by the Human Research Ethics Committee CEP/UFMS (CAAE: 66042722.8.0000.0021). Toxicity in human platelets was evaluated by the Trypan blue exclusion assay after incubation with AINT-4 at different concentrations (9.37 -300 µM), Triton X100 (1%, positive control) or DMSO (0.6%, negative control). Platelet aggregation was performed by turbidimetry in platelet-rich plasma pre-incubated with AINT-4 (9.37-300 µM), ticlopidine (10 µM, positive control) or DMSO (0.6%, negative control). Adenosine diphosphate (ADP) and epinephrine (EPI) were used as agonists. Blood coagulation was determined by prothrombin times (PT) and activated partial thromboplastin (aPTT). Platelet activation was assessed by intraplatelet content of reactive oxygen species (ROS) by fluorescence. AINT-4 has good oral bioavailability, low in silico toxicity and did not exhibit in vitro toxicity. Platelet aggregation was inhibited with both agonists, ADP (mean inhibition of 22.27%) and EPI (mean inhibition of 17.47%), at the tested concentrations. TP was increased to a concentration of 18.75 µM and ROS production showed an average inhibition of 27%. Therefore, AINT-4 has an effect on platelet activation and a consequent antithrombotic effect, providing a basis for research into analogues derived from NTs.



# Effects of Fluoxetine on Melanoma (B16F10) and Breast Adenocarcinoma (4T1) Cell



## Author

Giovani Marino Favero - Universidade Estadual de Ponta Grossa (UEPG)  
Milton de Paula Júnior - Universidade Estadual de Ponta Grossa (UEPG)  
Gabriela Ruva Fagundes - Universidade Estadual de Ponta Grossa (UEPG)  
Felipe de Lara Janz - Universidade Estadual de Ponta Grossa (UEPG)  
Giovani Marino Favero - Universidade Estadual de Ponta Grossa (UEPG)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Fundação Araucária



## Keywords

fluoxetine, melanoma, breast adenocarcinoma

## Abstract

Recent studies have explored the repurposing of fluoxetine, a well-known selective serotonin reuptake inhibitor (SSRI), for its potential anticancer properties. This investigation aimed to evaluate the effects of fluoxetine at dosages ranging from 0.0025 to 0.025 mg/mL on the growth of melanoma (B16F10) and breast adenocarcinoma (4T1) cell cultures. Cultures of B16F10 melanoma cells and 4T1 breast adenocarcinoma cells were treated with fluoxetine at various concentrations (0.0025, 0.005, 0.01, and 0.025 mg/mL). The cell viability was assessed using standard assays, including MTT and trypan blue exclusion, over a 72-hour period. The findings indicated that fluoxetine exhibited a dose-dependent inhibitory effect on cell growth in both B16F10 and 4T1 cell lines. At the highest concentration tested (0.025 mg/mL), a slight but statistically significant reduction in cell viability was observed in comparison to untreated controls. Specifically, B16F10 melanoma cells showed a reduction in viability by approximately 10%, while 4T1 breast adenocarcinoma cells demonstrated a reduction of about 12%. Lower concentrations of fluoxetine (0.0025 mg/mL) resulted in minimal impact on cell growth, suggesting a threshold effect. Fluoxetine, at the tested concentrations, displayed a modest inhibitory effect on the proliferation of melanoma and breast adenocarcinoma cells *in vitro*. These preliminary results support the potential of fluoxetine as an adjuvant in cancer therapy, warranting further investigation into its mechanism of action and efficacy *in vivo*. Understanding the pathways through which fluoxetine exerts these effects could lead to the development of new therapeutic strategies for cancer treatment.

# Evaluation of gabapentin binding to the proteins of the simulated nasal fluid



## Author

Nathalia Aiko Kawamura - Universidade Estadual de Maringá (UEM)  
Gustavo Finatti Sakamoto - Universidade Estadual de Maringá (UEM)  
Monica Villa Nova - Universidade Estadual de Maringá (UEM)  
Andrea Diniz - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Fundação Araucária, project number 584/2023



## Keywords

gabapentin, simulated nasal fluid, protein binding

## Abstract

**Introduction:** Gabapentin (GBP) needs to cross the blood-brain barrier to exert its central effects(1), and the intranasal route is a promising alternative for this purpose.(2) Briefly, mucins are proteins that form the structural basis of nasal mucus and, in order to be absorbed systemically and also available for nose-to-brain delivery, the drug needs to be mucopermeant and not adhere to the mucus.(3) To the best of our knowledge, there is no information on the binding of gabapentin to mucin. Aims: this study aimed to evaluate the binding of gabapentin to the mucin and albumin proteins in the simulated nasal fluid. **Materials and Methods:** Analytical method validation was carried out according to the ICH Q2(R2) guideline.(4) A simulated nasal fluid (SNF) was prepared according to Baumann et al. (2009).(5) The analytical conditions of the HPLC/UV-Vis method consisted in the mobile phase was composed of aqueous trifluoacetic acid 0.05% (pH 2.38):acetonitrile (86:14 v/v), 1 mL/min as flow rate and reading at  $\lambda=210\text{nm}$ . The binding rate of GBP to these proteins was defined by injecting the ultrafiltered in triplicate at the three concentration levels (0.20, 0.45 and 0.80 mg/mL of GBP), by ultracentrifugation using a centrifugal filter unit with nominal molecular weight limit of 10kDa (Merck®, German). **Results:** The analytical method was linear in the concentration range of 0.2-0.8 mg/mL, accurate, precise and robust. The mean  $\pm$  standard-deviation recovery of GBP (%) in the ultrafiltrate was  $143.79 \pm 9.01\%$  (0.20 mg/mL),  $95,15 \pm 4.52\%$  (0.45 mg/mL) and  $99.75\pm 0.33\%$  (0.8 mg/mL), evidencing a low binding rate to proteins (0.25-4.85). These results shed light on the understanding of the behavior of GBP in the nasal cavity and may assist in the development of future GBP nasal formulations. **Conclusion:** This result indicates that GBP has low binding to mucin and albumin, which is important data for contributing to the development of a nasal formulation of the drug.

# Effect of liraglutide in biochemical parameters in ovariectomized LDL-knockout mice



## Authors

Girlandia Alexandre Brasil - Universidade Vila Velha (UVV)  
Lícia Cristina Silva de Lima Oliveira - Universidade Vila Velha (UVV)  
Antonio João Viana Batista - Universidade Vila Velha (UVV)  
Beatriz Astori Paraguassu - Universidade Vila Velha (UVV)  
Tadeu Uggere de Andrade - Universidade Vila Velha (UVV)  
Ewelyne Miranda de Lima - Universidade Vila Velha (UVV)  
Marcella Martins Terra - Universidade Vila Velha (UVV)  
Girlandia Alexandre Brasil - Universidade Vila Velha (UVV)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

FAPES - 884- 2023



## Keywords

western diet, menopause, incretine

## Abstract

Liraglutide is an incretin analogue used to treat diabetes and also is used to treat obesity. Both are chronic disease that rises from some risk factors, such as genetic and hormonal disorders. Womens present a interruption in sexual hormone production in menopause period, which increases the prevalence of that disease. Literature does not present information about the effects of liraglutide in female at this period of life. Our aim was to evaluate the effect of chronic treatment with liraglutide in a mouse model of dyslipidemia and menopause. For that wide type (C57) and LDL-r knockout mice were separated into 5 groups, control groups (C57, LDL and OVX) treated with vehycle (saline, s.c.), treated (LDL-L and OVX-L) that received liraglutide (1,2mg divided into two applications, s.c.). The OVX groups were submitted to billateral ovariectomy and all groups (except C57) received an western diet. All the procedures were approved at CEUA-UVV (668-2023), the animals had access to food and water ad libitum. After 8 weeks the blood were collect to evaluate biochemical parameters (Glucose, Cholesterol - total, HDL, LDL and Triglycerides). After the treatment we observed an increase in plasma total cholesterol, LDL-cholesterol, triglycerides and glucose in all groups that received the western diet and liraglutide treatment were not able to promotes a decrease in that parameter. Our data are a preliminar study, also news ecpériences need to be conduced to better understand that effects.

# Theoretical and experimental input data of physicochemical parameters of LMM6 can misleading prediction of pharmacokinetic properties



## Author

Amanda Antunes Herling - Universidade Estadual de Maringá (UEM)  
João Marcos Barbosa Piai - Universidade Estadual de Maringá (UEM)  
Victor Nery Machado Lippa - Universidade Estadual de Maringá (UEM)  
Gustavo Finatti Sakamoto - Universidade Estadual de Maringá (UEM)  
Andrea Diniz - Universidade Estadual de Maringá (UEM)  
Maria Sueli Soares Felipe - Pontifícia Universidade Católica de Brasília (UCB)  
Érika Seki Kioshima Cótica - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

This study was supported by “Coordenação de Aperfeiçoamento de Pessoal de Nível Superior” (CAPES – Brasília, Brazil) and FAPDF 00193-00001743/2022-64.



## Keywords

Antifungal activity, Physicochemical properties, PBPK modeling

## Abstract

**Introduction:** The 1,3,4-oxadiazolic derivative compound (LMM6) has demonstrated antifungal activity in preclinical studies. Physiologically-based pharmacokinetic (PBPK) modeling and simulation (M&S) have been used to guide in vivo experiments. However, for new compounds, it is common to rely solely on predicted physicochemical parameters. **Objective:** To develop a PBPK model for LMM6 in mice and evaluate the impact of experimental and predicted input data on solubility and lipophilicity on the predicted absorption. **Methodology:** A PBPK model for mice was constructed using GastroPlus v.9.8.2 software, utilizing predicted pharmacokinetic data from ADMET Predictor™. The parameter sensitivity analysis (PSA) was performed using a range of predicted and experimental logP (2.11 - 5.54) and aqueous solubility (2.0-2.93 mg/L) values to assess their impact on predicted intestinal absorption. **Results:** The tested range of aqueous solubility showed no significant variations in predicted intestinal absorption, with a narrow range indicating good agreement between predicted (2.00 mg/L) and experimental (2.93 mg/L) data. However, the logP range tested demonstrated a significant increase in absorption, from 65% at the experimental value (2.11) to 95% at the highest predicted value (5.54). This broad range in logP suggests that its impact on PK prediction is substantial. Relying solely on predicted logP values in PBPK simulations could misleadingly guide viable dosing in preclinical experimental design. **Conclusion:** PBPK simulations are a valuable tool for exploring potential systemic exposures, provided that both experimental and theoretical physicochemical inputs are considered. Incorporating experimental data into PBPK simulations enhances the accuracy of in vivo preclinical experimental designs and provides a more comprehensive understanding of the compound's behavior.

# Neuroprotective effect of cannabidiol and its analogues, PQM-242 and PQM-249, against ethanol-induced neurotoxicity in SH-SY5Y cells



## Author

Carolina Aparecida Faria Almeida - Universidade Federal de Alfenas (UNIFAL)  
Vitor Bruno - Universidade Federal de Alfenas (UNIFAL)  
Jéssyca Milene Ribeiro - Universidade Federal de Alfenas (UNIFAL)  
Alessandra Oliveira Silva - Universidade Federal de Alfenas (UNIFAL)  
Giulia de Assis Braz - Universidade Federal de São Paulo (UNIFESP)  
Felype Valentim Duarte Castelhana - Universidade Federal de São Paulo (UNIFESP)  
Gabriela Salles dos Santos - Universidade Federal de São Paulo (UNIFESP)  
Graziella dos Reis Rosa Franco - Universidade Federal de Alfenas (UNIFAL)  
Cláudio Viegas Júnior - Universidade Federal de Alfenas (UNIFAL)  
Tania Marcourakis - Universidade Federal de São Paulo (UNIFESP)  
Raphael Caio Tamborelli Garcia - Universidade Federal de São Paulo (UNIFESP)  
Larissa Helena Torres - Universidade Federal de Alfenas (UNIFAL)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Ensino Superior; R01 DK103723/DK/NIDDK NIH HHS/United States; R01 DK120862/DK/NIDDK NIH HHS/United States



## Keywords

Ethanol, Cannabidiol, Toxicity

## Abstract

Cannabidiol (CBD) has anxiolytic, antidepressant, antipsychotic and neuroprotective effects, without presenting a psychotic side effect. Therefore, synthetic analogs of CBD become an interesting therapeutic target, including the treatment for alcohol use disorder (AUD). Thus, *in vitro* studies are crucial to verify the toxicity as well as the protective effects of these compounds. Therefore, the aim of this study was to evaluate the neurotoxicity and neuroprotective potential of CBD and its analogs, PQM-242 and PQM-249, against ethanol-induced neurotoxicity in SH-SY5Y neuroblastoma cells. A concentration-response curve (CRC) was obtained for CBD, PQM-242 and PQM-249 (0,1, 1, 10, 100 and 1000  $\mu\text{M}$  of each) to determine the highest concentration without neurotoxic effect (NOAEL). Exposures were performed for 48h in SH-SY5Y human neuroblastoma cells. Subsequently, the NOAEL of each cannabinoid was incubated for 48 hours in the presence of ethanol (250 mM). Cell viability tests were performed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay and annexin V/propidium iodide dye (flow cytometry). Bax and Bcl-2 proteins were analyzed by western blot technique. While NOAEL for PQM-242 and PQM-249 were 100  $\mu\text{M}$ , NOAEL for CBD was 10  $\mu\text{M}$ , being CBD LC is 44  $\mu\text{M}$  and its analogues highest to 600  $\mu\text{M}$ . Thus, the concentration chosen for all substances to continue the experiment was 10  $\mu\text{M}$ . All substances were able to prevent ethanol neurotoxicity through the decrease in both early and late apoptosis. In addition, PQM-242 was able to prevent the increase of proapoptotic Bax level. In summary, these data suggest that CBD, PQM-242 and PQM-249 have demonstrated neuroprotective potential. Therefore, these substances may have an interest potential effect against AUD treatment.

# Acute exposure to melatonin affects excitability in the enteric nervous system in healthy conditions



## Author

Fabiana Galvão da Motta Lima - Universidade Estadual de Maringá (UEM)  
Beatriz Bastos de Moraes Thomasi - Michigan State University - East Lansing (MSU)  
Rafaella Lavalle Lacerda de Almeida - Michigan State University - East Lansing (MSU)  
Jacqueline Nelisis Zanoni - Universidade Estadual de Maringá (UEM)  
Brian Gulbransen - Michigan State University - East Lansing (MSU)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Coordenação de Aperfeiçoamento de Pessoal de Ensino Superior; R01 DK103723/DK/NIDDK NIH HHS/United States; R01 DK120862/DK/NIDDK NIH HHS/United States



## Keywords

Calcium-imaging, Neurons, Glial cells

## Abstract

**Introduction:** melatonin is a well-studied molecule and its effects on neurons on the central and peripheral nervous system are extensively described in the literature, however there are no studies focusing if melatonin affects the enteric nervous system and the gastrointestinal tract regulation in health, whereas most studies work on melatonin administration to attenuate pathological processes. Here, we test if melatonin is capable of influencing excitability in the enteric nervous system. **Methods:** calcium-imaging Wnt1 GCaMP5g-tdT mice, males and females, were used to study activity among enteric neurons and glia in samples from healthy animals following pre-incubation with Melatonin (MLT; 50 $\mu$ M, 20min, 37°C) and in control samples (Krebs buffer; 20 min, 37°C). High potassium (K<sup>+</sup>) was used to stimulate neuronal response. We used the software FIJI to process and analyze the average of change in fluorescence in both neurons and glial cells. **Results:** pre-incubation with MLT increased both neuronal responsiveness ( $p < 0.0001$ ) and number of neurons activated ( $p = 0.014$ ) in healthy samples, but did not change their response amplitude ( $p > 0.05$ ). Neuron-to-glia signaling evoked by neuronal depolarization was also affected by MLT, with increased glial responsiveness ( $p < 0.0001$ ). No changes were observed in number of glial cells activated and their response amplitude ( $p > 0.05$ ). Our data also demonstrated that both neuronal and glial responsiveness intensity to MLT is sex-related, with the response in the females being higher than in the males ( $p < 0.0001$ ). **Conclusions:** these data suggests that melatonin affects the enteric nervous system excitability in healthy conditions and demonstrates sex-related differences regarding the response to melatonin exposure, leading to potential changes in the regulation of the gastrointestinal tract homeostasis. These results are something yet to be explored in the field of neurogastroenterology.

# How bioisosteric neolignans can help us to prevent Alzheimer's disease: grandisin-based isoxazole analogue as a possible neuroprotective prodrug



## Author

Gabrielle Teixeira Machado - Universidade Federal de Mato Grosso (UFMS)  
Victor Hugo Bittencourt Andrade - Universidade Federal de Mato Grosso (UFMS)  
Herbert Patric Kellermann Cleveland - Universidade Federal de Mato Grosso (UFMS)  
Egidi Mayara Silva Firmino - Universidade Federal de Mato Grosso (UFMS)  
Ana Beatriz Nogueira da Silva - Universidade Federal de Mato Grosso (UFMS)  
Caroline Dorneles Pereira Portes - Universidade Federal de Mato Grosso (UFMS)  
Daniele Barboza Miranda Guimarães - Universidade Federal de Mato Grosso (UFMS)  
Paola Mayara Valente Coronel - Universidade Federal de Mato Grosso (UFMS)  
Eduardo Benedetti Parisotto - Universidade Federal de Mato Grosso (UFMS)  
Diego B de Carvalho - Universidade Federal de Mato Grosso (UFMS)  
Adriano Cesar de Moraes Baroni - Universidade Federal de Mato Grosso (UFMS)  
Albert Schiaveto de Souza - Universidade Federal de Mato Grosso (UFMS)  
Leonardo Resstel Barbosa Moraes - Faculdade de Medicina (USP Ribeirão Preto)  
Davi Campos La Gatta - Universidade Federal de Mato Grosso (UFMS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Capes



## Keywords

Alzheimer's disease; Grandisin; Neuroprotection

## Abstract

Alzheimer's disease (AD) is a neurodegenerative condition characterized by the deposition of amyloid-beta ( $A\beta$ ) in the brain. Currently, treatments remain ineffective due to the multifactorial nature of the disease. In this context, compounds capable of acting as multi-target drugs, such as bioisosteric neolignans, offer a promising approach to modulating disease-related processes. Grandisin (GRA), a neolignan extracted from *Virola surinamensis*, has shown neuroprotective and anti-inflammatory activity in previous studies. In this study, we demonstrated that the use of isoxazole analogue based on grandisin (ISOX), which is more potent and soluble than GRA, in a behavioral test using an in vivo mouse model of AD, prevented cognitive impairment. Male C57/Bl6 mice (CEUA:1.272/2023) underwent stereotaxic surgery for intracerebroventricular (i.c.v.) injection of  $A\beta$  oligomers or vehicle (10% DMSO). Grandisin (1mg/kg), ISOX (1mg/kg), or vehicle were administered intraperitoneally (i.p.) or orally (p.o.) for 7 days in groups: control (i.c.v.)/vehicle (i.p.),  $A\beta$  (i.c.v.)/vehicle (i.p.),  $A\beta$  (i.c.v.)/GRA (i.p.),  $A\beta$  (i.c.v.)/ISOX (i.p.), and  $A\beta$  (i.c.v.)/ISOX (p.o.). On the 8th day, compound effects were assessed using the Object Recognition Test (ORT), and cortex and hippocampus levels of lipoperoxidation were measured after euthanasia. The  $A\beta$  (i.c.v.)/vehicle (i.p.) group exhibited memory deficits in the ORT compared to the control group ( $p < 0.05$ ). Repeated administration of grandisin (i.p.) prevented memory impairment when compared to control group ( $p < 0.05$ ), whereas ISOX (i.p.) failed to prevent  $A\beta$ -induced impairment ( $p > 0.05$ ) and increased lipoperoxidation compared to control group ( $p < 0.05$ ). On the other hand, oral treatment with ISOX was capable of preventing cognitive impairment ( $p < 0.05$ ). Therefore, we concluded that oral administration of isoxazole grandisin analogue was able to prevent memory impairment induced by  $A\beta$ . These results may suggest a possible prodrug mechanism.

# In vitro hepatoprotective effect of *Achyrocline satureioides* (Lam.) DC, Asteraceae (marcela) in HepG2 cells



## Author

Marcelo Dutra Arbo - Universidade Federal do Rio Grande do Sul (UFRGS)  
Yasmin Vendruscolo Piton - Universidade Federal do Rio Grande do Sul (UFRGS)  
Solange Cristina Garcia - Universidade Federal do Rio Grande do Sul (UFRGS)  
Eduardo Konrath - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Capes Foundation



## Keywords

*Achyrocline satureioides*, ethanol induced injury, acetaminophen induced injury

## Abstract

*Achyrocline satureioides* (Lam.) DC is a medicinal plant native from South America and popularly known as “marcela”. The infusion made with the aerial parts is widely used for liver and digestive-related disorders, mainly in Southern Brazil. Previous investigations conducted with this plant have demonstrated a range of activities, including antioxidant, anti-inflammatory, sedative, antiproliferative, among others. The main constituents of “marcela” are the flavonoids quercetin and 3-O-methylquercetin, followed by luteolin, and achyrobichalcone. The aim of this study was to evaluate the cytotoxicity and protection of aqueous (AE) and hydroethanolic (HE) extracts of this plant in human hepatoblastoma HepG2 cell line. Cells were incubated with 0.1, 1, 5 and 10 µg/mL of each extract during 24 h and the cytotoxicity was evaluated using the MTT reduction and neutral red (NR) up-take assays. The hepaprotection was evaluated incubating the same concentrations of the extracts with 800 mM ethanol or 8 mM acetaminophen. The AE did not present cytotoxicity, however HE decreased cell viability at 5 and 10 µg/mL in MTT reduction and 10 µg/mL in NR up-take assays. In the injury induced by 800 mM ethanol, AE protected the cells at 0.1 and 1 µg/mL in MTT reduction and 0.1 µg/mL in NR up-take assays, while HE protected cells at 0.1, 1, and 5 µg/mL in MTT reduction and 0.1 and 1 µg/mL in NR up-take assays. In the 8 mM acetaminophen induced injury, AE protected the cells at 0.1, 1, and 5 µg/mL in MTT reduction and 0.1 µg/mL in NR up-take assays, while HE protected cells at all concentrations in both assays. In conclusion, *A. satureioides* presented an interesting hepatoprotective effect in vitro, with better results presented by HE, which could be related to the different amounts of flavonoids in each extract. The flavonoids present in the extract should be investigated searching for ingredient responsible for the activity.



# Behavioral tests in Balb/C mice indicate antidepressant effect of the association of rosemary and day lily flower



## Author

Silvia Cristina Fagundes - Universidade de Passo Fundo (UFP)  
Gabriele Luiza Alba - Universidade de Passo Fundo (UFP)  
Nathalia de Souza Rodrigues - Universidade de Passo Fundo (UFP)  
Vitória Citolin Crestani - Universidade de Passo Fundo (UFP)  
Victor Yan Zambenedetti Ilha - Universidade de Passo Fundo (UFP)  
Charise Dallazem Bertol - Universidade de Passo Fundo (UFP)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Capes



## Keywords

Depression, Mice, Herbal medicine

## Abstract

Depression affects many people. Pharmacological treatment has adverse effects. Irisin is effective against this disease. Herbal medicine containing rosemary leaves (*Rosmarinus officinalis* L.) and lily flowers (*Hemerocallis fulva*) increased irisin in the bloodstream by 23%. This study used 40 Balb/C C57Bl/6 mice and aimed to verify the antidepressant potential of the association of herbal medicine in mice with induced depression. Animals were divided into a group, (G1) without depression and without medication, (G2) a depression induced with dexamethasone 64mcg/kg, (G3) a depression induced and treated with a 30mg/kg herbal medicine and (G4) an induced depression treated with fluoxetine 15mg/kg. Animals were submitted for a forced swim test (T1) and tail suspension (T2). T1, the first moment, there was a period of immobility in G3, which reflects a strategy of energy conservation or adaptation environment. G1 There was no statistical difference (ANOVA-Tukey) between the groups G2 ( $P=0.979$ ), G3 ( $P=0.313$ ), G4 ( $P=0.996$ ). Second part, immobility time total registered. G3 had a shorter immobility time em relação G2. G1 had no statistical difference in relation to G2 ( $P=0.957$ ), G3 ( $P=0.109$ ) and G4 ( $P=0.851$ ). G2 ( $P=0.957$ ) was different from G3 ( $P=0.037$ ) and similar to G4 ( $P=0.570$ ). G3 was not statistically different from G4 ( $P=0.453$ ). T2, were observed in a period of 6 minutes, timing 2 times. First, adaptation of the mice to the test environment. G4 remained stationary for longer. But, in a way that is not statistically different. G1 had no statistical difference between the groups ( $P>0.05$ ). This test induce stress, immobility is a strategy to reduce energy expenditure. Secondly, the total time in which the animal remains immobile is recorded during the test. There was no difference between the groups ( $P>0.05$ ). G2 had the shortest time of immobility, indicating hopelessness, but no statistical difference. It is concluded G3 had antidepressant effects similar to the G4.

# Assessment Of The Population Pharmacokinetics Of Colchicine From Optimized Cationic Nanocapsules



## Author

Tamara Ramos Maciel - Universidade Federal de Santa Maria (UFSM)  
Camila de Oliveira Pacheco - Universidade Federal de Santa Maria (UFSM)  
Ana Claudia Funguetto-Ribeiro - Universidade Federal do Pampa (UNIPAMPA)  
Sandra Elisa Haas - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

This work was supported by the CAPES. The authors are grateful for the support provided by the FAPERGS, grant 19/2551-0001970-0, CNPq (no. 309401/2020-8), CAPES (no. 88881.506652/2020-01) and UNIPAMPA.



## Keywords

Cationic Nanocapsule, Population Pharmacokinetics, Malaria

## Abstract

Malaria, a seriously inflammatory disease, causes thousands of deaths worldwide, which is why the anti-inflammatory Colchicine (CC) has aroused interest. However, it has high toxicity. Therefore, new strategies are needed, such as incorporating it into nanocapsule (NC) suspensions. Our research group has been presenting promising results for the treatment of malaria, especially with cationic NCs. The objective of this study was to optimize a cationic NC formulation containing CC, to evaluate population pharmacokinetics (popPK). For this, a factorial design was used with 2 levels and 3 factors: concentration of the cationic polymer Eudragit® RS100, concentration of surfactant Span 80 and presence/absence of TPGS. Resulting in 8 formulations (NC1-NC8), prepared by nanoprecipitation, with 1 mg/mL CC. The NCs were characterized regarding diameter, SPAN, pH, zeta potential, dosage, encapsulation rate and in vitro release. PK studies were performed on the optimized NC in female Wistar rats (CEUA/UNIPAMPA, protocol n° 027/2020), which received an intravenous dose of 0.5 mg/kg of NC or free CC. The collected data was evaluated for PopPK (Monolix®, Simulation Plus). NC7 (highest concentration of Span 80, lowest of Eudragit and with TPGS) had a diameter of 196 nm, zeta potential of 30.41 MV and sustained CC release, therefore selected for biological evaluation. The best PopPK model was two-compartment with formulation as a covariate. NC7 decreased clearance by 14 times in relation to free CC, CC remained predominantly in the central compartment, as it led to a reduction in the distribution volume of the central and peripheral compartments and in intercompartmental clearance. Therefore, increasing the concentration of the medicine in the blood is crucial in treating malaria, as the medicine continues to interact with the parasite for a longer time. In conclusion, these results demonstrate the potential of CC-charged cationic NCs.

# Development and Validation of a Capillary Dried Plasma Spot (DPS) Method for Monitoring Systemic Arterial Hypertension Pharmacotherapy



## Author

Marina Venzon Antunes - Universidade de Novo Hamburgo (Feevale)  
Debora RM Oliveira - Universidade de Novo Hamburgo (Feevale)  
Fernanda Fischer - Universidade de Novo Hamburgo (Feevale)  
Eduarda Roieski - Universidade de Novo Hamburgo (Feevale)  
Andresa Heemann Betti - Universidade de Novo Hamburgo (Feevale)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CNPq, CAPES.



## Keywords

hypertension, dried plasma spots

## Abstract

**Background & Aims:** Adherence to systemic arterial hypertension pharmacotherapy measurement methods include indirect approaches, such as the use of questionnaires, subject to underreporting, and direct methods like drug serum quantification. The present study aims to develop and validate a new LC-MS/MS method for quantification of antihypertensive drugs in dried capillary plasma spots (DPS) as alternative sampling strategy for estimating drug adherence. **Methods:** DPS control samples were prepared by diluting working solutions with blank plasma, then pipetted onto the HealthID® plasma separation device. Sample preparation involved a two-step protocol: Three 5 mm discs cut from the DPS membrane were incubated with bovine serum albumin 0.1%, followed by protein precipitation and methanol extraction, before UPLC-MS/MS. Ionization was conducted via an electrospray source in positive mode, except for hydrochlorothiazide. Mass conditions were optimized for various analytes, and the method was validated according to FDA guidelines for selectivity, precision, accuracy, linearity, sensitivity, stability, and extraction yield. **Results:** The total analytical run time was 10 minutes without interference peaks at analyte retention times. The method demonstrated linearity (0.5-500 µg/mL for amlodipine and enalaprilat; 1.0-1000 µg/mL for atenolol, hydrochlorothiazide, and losartan) with an r-squared value >0.99. Precision and accuracy assessments yielded satisfactory results (CV%: 4.5%-14.6%; accuracy: 89%-113%). Average extraction yields were 75% for amlodipine, 70% for enalaprilat, 101% for atenolol, 82% for hydrochlorothiazide, and 81% for losartan. The analytes remained stable in DPS at 25 °C for 21 days. **Conclusion:** This method offers a simpler, less invasive alternative to traditional blood collection, suitable for pharmacokinetic studies and therapeutic drug monitoring in clinical settings.

# Non-Genomic Effect of Estriol in Rat Thoracic Aorta Involves NO Pathway, Hyperpolarization and Calcium Channels



## Author

Thiago Sardinha de Oliveira - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)  
Renata Anastácia de O. Batista - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)  
Carlos Messias Sousa - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)  
Israel Robson Rocha - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)  
Andréa Renata Malagutti - Universidade Federal dos Vales Jequitinhonha e Mucuri (UFVJM)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CAPES and FAPEMIG APQ-02841-21



## Keywords

Nitric oxide, Potassium Channels, Vasodilation

## Abstract

Hormone replacement therapy (HRT) with estrogen has cardioprotective effects, considering its health benefits. The present study was designed to investigate the vascular effects of estriol (E3) in the thoracic aorta of rats, elucidating the mechanisms underlying the impact of estrogen. Rings of thoracic aorta from male Wistar rats (200-300g) were mounted in organ chambers. Concentration-response curves (1 $\mu$ M - 1mM) were constructed in aortic rings pre-contracted with phenylephrine with endothelium-intact or -denuded. Relaxation responses in intact endothelial rings were performed in the presence of the nitric oxide synthase inhibitor L-NAME (100 $\mu$ M), the cyclooxygenase inhibitor indomethacin (10 $\mu$ M), or the non-selective blocker of K<sup>+</sup> channels TEA (1mM) or CaCl<sub>2</sub>-induced contractions. Experiments were conducted in accordance with CONCEA, approved by CEUA/UFVJM n° 09/2022. Data are presented as mean  $\pm$  SEM of 8 different experiments and analyzed by Student's t-test or one-way ANOVA where appropriate. P values less than 0.05 were considered significant. E3 promoted concentration-dependent relaxation in endothelium-intact and endothelium-denuded aortic rings ( $E_{max}$  = 59.90  $\pm$  3.41% and 29.75  $\pm$  1.46%, respectively). Incubation with the nitric oxide synthase inhibitor (L-NAME) or the non-selective K<sup>+</sup> channel blocker (TEA) reduced E3 relaxation ( $E_{max}$  = 30.07  $\pm$  1.67% and 46.52  $\pm$  0.60%), showing involvement of the NO pathway and K<sup>+</sup> channels in the vasorelaxant effect of E3. On the other hand, inhibiting the cyclooxygenase pathway using indomethacin did not show any effect ( $E_{max}$  = 63.22  $\pm$  3.91%). Concentrations of 0.2 and 1mM of E3 blocked CaCl<sub>2</sub>-induced contractions, elucidating that the endothelium-independent mechanism involves calcium channels ( $E_{max}$  54.73  $\pm$  3.08%; 35.13  $\pm$  1.44%; and 102.00  $\pm$  3.73% of Vehicle, respectively). In conclusion, the results demonstrate that estriol promotes a vasorelaxant effect mediated by NO and K<sup>+</sup> channel pathways and calcium channels.

# Disperse Red dye 60 (DR 60) at environmentally realistic concentrations impact zebrafish (*Danio rerio*) embryo-larval development and locomotor profile



## Author

Bianca de Arruda Leite - Universidade de São Paulo (USP-Ribeirão Preto)  
Danielle Palma de Oliveira - Universidade de São Paulo (USP-Ribeirão Preto)  
Carlos Gravato - Universidade de São Paulo (USP-Ribeirão Preto)  
Daniel Junqueira Dorta - Universidade de São Paulo (USP-Ribeirão Preto)  
Flávia Renata Abe - Universidade de São Paulo (USP-Ribeirão Preto)  
Gabriela Meireles - Universidade de São Paulo (USP-Ribeirão Preto)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Education Personnel – Brazil (CAPES) – Financing Code 001.



## Keywords

Disperse dyes, Behavior, Ecotoxicity

## Abstract

Some of the dyes currently used by the textile, pharmaceutical, food, cosmetic, and photographic industries have mutagenic potential and can be toxic. In addition, most of these dyes resist degradation processes available for treating wastewater, and these processes might generate even more toxic by-products. Despite the large number of available dyes and the large quantity of dyes released into the environment, studies on their toxicity are scarce. Here, we have evaluated and compared the neurobehavioral and developmental impacts of the textile dye Disperse Red 60 (DR 60) on the animal model *Danio rerio* (zebrafish). DR 60 caused changes in ocular structures and changes in behavior. In conclusion, the toxicity of these dyes can be interpreted as a warning for paying greater attention before registering the use of dyes and releasing them into the environment, so that environmental damage and harm to the human health can be prevented.

# Investigating the Role of the Metabolite 2-Hydroxybenzonitrile in Azoxystrobin-Induced Toxicity and Cell Proliferation Mechanisms



## Author

Fernanda Gomes Leite - Universidade de São Paulo (USP-Ribeirão Preto)  
Ivo Ferreira Machado - Universidade de Coimbra  
Carlos Manuel Marques Palmeira - Universidade de Coimbra  
Daniel Junqueira Dorta - Universidade de São Paulo (USP-Ribeirão Preto)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CNPq (Process No 140433/2021-0)



## Keywords

proliferation, fungicide, toxicity

## Abstract

Strobilurins, a class of fungicides derived from the mushroom *Strobilurus tenacellus*, act on the respiratory chain in fungi, effectively controlling pests and holding a significant share of the global market. Azoxystrobin (AZO), the first and most widely used pesticide of its class, undergoes phase I hydrolysis upon metabolism, resulting in metabolites such as 2-Hydroxybenzonitrile (HBN). While AZO has been the subject of environmental studies, toxicological data on HBN remains scarce. This study aimed to investigate the role of HBN in AZO-induced toxicity, focusing on molecular mechanisms involving cell proliferation. We analyzed the effects of AZO, HBN, and their mixture (MIX) on HepG2 cells. Cell viability was assessed using the Live/Dead assay, which revealed significant effects of AZO and HBN at 10  $\mu\text{M}$ , while MIX showed significant effects at 1  $\mu\text{M}$  after 24 hours of exposure. Cell proliferation was evaluated using the SRB assay and microscopy, indicating significant effects of AZO and MIX at 5  $\mu\text{M}$  after 24 hours. Tubulin, a protein crucial for cell cycle and proliferation, was investigated using Western Blot to determine its involvement in the AZO mechanism. AZO showed significant effects at 10  $\mu\text{M}$  after 24 hours. HBN did not show relevant statistical data for proliferation analysis, making it difficult to establish a relationship between HBN and AZO-induced toxicity observed in this study. In conclusion, under the conditions tested, AZO's mechanism of toxicity appears to affect cell proliferation and induce cell death, while HBN appears to play a role in the latter effect. However, further studies are necessary to elucidate the exact mechanism of action.

# Agaricus bisporus Mitigates Hematological Lead Toxicity in Pregnant Rats



## Author

Natasha Lien de Almeida Ibanez - Universidade de Sorocaba (UNISO)  
Erika Leão Ajala Caetano - Universidade de Sorocaba (UNISO)  
Talita Cristina Segato - Universidade de Sorocaba (UNISO)  
Thaís Borim Pickler - Universidade de Sorocaba (UNISO)  
Joana Garrossino Magalhães - Universidade de Sorocaba (UNISO)  
Denise Grotto - Universidade de Sorocaba (UNISO)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Capes



## Keywords

Lead, Agaricus bisporus, Hematological parameters

## Abstract

Lead (Pb) exposure poses severe health risks, especially to vulnerable groups like children, elderly, and pregnant women. Pb can cause liver and kidney damage, cardiovascular diseases, neurological disorders, anaemia, and osteoporosis. Current chelation therapies effectively remove toxic metals; however, these therapies have adverse effects, highlighting the need for safer, natural alternatives. *Agaricus bisporus* (Ab) is a widely consumed edible mushroom rich in bioactive compounds like  $\beta$ -glucans and polyphenols and has shown promising health benefits. Recent studies suggest that mushroom extracts, due to their chitin and chitosan content, can adsorb heavy metals from contaminated water. This study aimed to evaluate haematological parameters in pregnant rats exposed to Pb and to understand the potential of Ab as a protective agent. Healthy female Wistar rats (CEUA-Uniso no 175/2020) were randomly divided into four groups (n = 5/group): Control, Ab 100 mg/Kg, Pb 100 mg/L, and Ab+Pb 100 mg/Kg + 100 mg/L. Pb exposure was administered in water, and Ab was given orally by gavage until the 19th day. On the 20th day of gestation, the animals were euthanized with ketamine, xylazine, and acepromazine, intraperitoneally. Haematological parameters were assessed using an automatic equipment (Hematology XS 1000i WAS, Roche®). A reduction in haemoglobin was observed in Pb-exposed rats compared to the control and Ab groups, as Pb intoxication reduces haemoglobin synthesis by inhibiting enzymes involved in heme production and causing haemolysis. The Pb group showed an increase in red blood cells and elevated haematocrit compared to the control. Although statistical differences were present, the levels were within the expected range for the species. In conclusion, Ab emerges as a viable edible alternative to alleviate lead's toxic effects. This study highlights its potential as a complementary and natural therapy to mitigate lead toxicity on haematological parameters.

# Investigating the toxicity of fipronil desulfinyl using in silico, in vitro, and in vivo methods: is biota in danger?



## Author

Bruno Rossato - Universidade de São Paulo (USP-Ribeirão Preto)  
Arthur Lima de Oliveira - Universidade de São Paulo (USP-Ribeirão Preto)  
Carlos Gravato - Universidade de Lisboa  
Danielle Palma de Oliveira - Universidade de São Paulo (USP-Ribeirão Preto)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CAPES-PROEX 88887.702118/2022-00



## Keywords

pesticides, ecotoxicology, teratogenicity

## Abstract

The application of pesticides is crucial for maintaining a steady agricultural production. Fipronil is a widely used broad-spectrum insecticide, known to degrade into toxic metabolites such as fipronil sulfone, fipronil sulfide and fipronil desulfinyl. It is well-established that fipronil desulfinyl, the major environmental by-product formed through photolysis, is highly stable in the environment. However, toxicological and ecotoxicological data regarding this molecule are not sufficient to determine its true impact. Within this context, we used a combination of in silico, in vitro (HepG2 cells), and in vivo (Danio rerio, zebrafish) methods for its toxicological assessment. The in silico Is-Tox® platform predicted that fipronil desulfinyl induces potential hepatotoxic, mutagenic and ecotoxic effects. Assays using HepG2 cells showed high cytotoxicity (10  $\mu$ M), and DNA damage ( $> 1 \mu$ M). Zebrafish larvae development until 144 hpf demonstrated a higher acute lethality of fipronil desulfinyl, when compared to the parental compound, concomitant with teratogenic effects. Sublethal effects such as yolk sac and pericardial edemas, scoliosis, non-inflation of the swimming bladder, and abnormal extension of the yolk sac were observed. This is also the first work to observe the formation of dorsal protrusions in larvae exposed to concentrations higher than 125  $\mu$ g/L. Morphometric data showed significant reductions of body length, and eye and swimming bladder areas, for concentrations as low as 25  $\mu$ g/L. Histological methods also showed notochord fragmentation, muscular fiber disjunction and epithelial connectivity of the observed protrusions. These findings show that fipronil usage needs to be more carefully monitored in the environment, given the formation of even more toxic metabolites causing effects at extremely low concentrations.



# Pharmacokinetic Evaluation of Curcumin-loaded Nanoparticles in Female Wistar Rats



## Author

Andrieli Rodrigues - Universidade Federal dos Pampas (UNIPAMPA)  
Kelle Velasques Pereira - Universidade Federal dos Pampas (UNIPAMPA)  
Isadora Calone Bitencourt - Universidade Federal dos Pampas (UNIPAMPA)  
Camila de Oliveira Pacheco - Universidade Federal dos Pampas (UNIPAMPA)  
Sandra Elisa Haas - Universidade Federal dos Pampas (UNIPAMPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

LABFAR FAPERGS, grant 19/2551-0001970-0, CNPq (no. 309401/2020-8), CAPES (no. 88881.506652/2020-01), and UNIPAMPA



## Keywords

Nanotechnology, Pharmacology, Nanocapsules

## Abstract

*Curcuma longa*, popularly known as turmeric, contains a bioactive component called curcumin (CCM), which has antiviral, anticancer, antitumor, antibacterial and anti-inflammatory effects. However, due to its short half-life ( $t_{1/2}$ ), photosensitivity and low bioavailability, its therapeutic use is restricted. Under these circumstances, polymeric nanocapsules (NCs) are an option to improve their *in vivo* efficacy by increasing solubility and bioavailability. Consequently, the purpose of this work was to develop NC-CCM and assess its plasma pharmacokinetics in female Wistar rats. NCs were prepared by nanoprecipitation method and characterized by particle size, zeta potential, pH, and drug content. Rat blood was collected from the lateral caudal vein at predetermined times, and the animals were given 2.0 mg/Kg intravenously (NC-CCM and CCM-F,  $n=10$  animals/group). The samples were stored at  $-80^{\circ}\text{C}$  before analysis by HPLC-PDA pre-validated method. The protocol was approved by the Ethics Committee of the Federal University of Pampa (UNIPAMPA-CEUA n $^{\circ}$  017/2022). Characteristics of NC-CCM were anionic Zeta Potential ( $-15.14$  mV), pH close to 6, and particle size of around 200 nm. Drug content and encapsulation efficiency was close to 100%. Following nanoencapsulation, both the volume of distribution ( $V_d$ ) and the Area Under the Curve (AUC) of CCM increased ( $0.0051 \pm 0.001$  and  $0.027 \pm 0.006$  mL/kg for NC-CCM and free CCM, respectively;  $68.83 \pm 11.27$  and  $204.74 \pm 26.61$  h.ng.mL $^{-1}$  for free CCM and NC-CCM, respectively). Clearance decreased after nanoencapsulation. This result suggests that NC-CCM elimination is more slowly. The pharmacokinetic profile of CCM from polymeric nanocapsules was characterized in this work, demonstrating changes in the PK elimination characteristics.

# Safety Assessment of Isolated Cannabidiol from Cannabis Sativa in the Alternative Model *Caenorhabditis elegans*



## Author

Heloísa Padilha - Universidade Federal do Pampa (UNIPAMPA)  
Jean Freitas Reginatto - Universidade Federal do Pampa (UNIPAMPA)  
Julia Dorneles Saleh - Universidade Federal do Pampa (UNIPAMPA)  
Natália Silva Jardim - Universidade Federal do Pampa (UNIPAMPA)  
Alline Campos - Universidade de São Paulo (USP)  
Daiana Silva de Ávila - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Capes



## Keywords

Toxicity, Cannabinoids, Alternative model

## Abstract

*Cannabis sativa* has more than 400 bioactive compounds, and has been used for thousands of years for medicinal purposes and as a recreational drug. Among the main compounds present in this plant are cannabidiol (CBD), an active responsible for the pharmacological profile. The use of CBD for therapeutic purposes covers a wide range of diseases and disorders, and after the discovery of the endocannabinoid system (eCBS) in humans, interest was awakened in investigating the CBD safety and its possible mechanism of action and safety. Besides the several advantages of *C. elegans*, the presence of eCBS in this nematode contributed to the toxicological analyses of isolated CBD. The objective of this study was to evaluate the safety of isolated CBD in *C. elegans*. For the exposure protocol, N2 (wild-type), BY200 *vtIs1(dat-1p::GFP; rol-6)*, and LX929 (*vsIs48 [unc-17::GFP]*) strains were used, maintained in nematode growth media and *Escherichia coli* OP50. The worms were synchronized and treated at the L1 stage, chronically (48h) with CBD concentrations of 10, 150, and 600  $\mu\text{M}$ . After the end of treatment, we analyzed survival, body length and area, brood size and egg production, locomotion capacity by swimming assay. The dopaminergic system was analyzed by neurons marked by fluorescence in BY200 and swimming induced paralysis (SWIP), and the cholinergic system by neurons marked by fluorescence in LX929. We identified that the highest tested concentrations of CBD reduced the worms' survival, locomotion capacity, and body length and area. However, the lowest concentration showed no evidence of toxicity. Finally, we observed that the reproductive system of the worms was not altered by the treatments and a more specific investigation indicated that CBD did not cause damage to the cholinergic neurons and the dopaminergic system. Our research suggests that 10  $\mu\text{M}$  was not toxic to the worm, making it a promising molecule for further exploration in this experimental model.

# Gene expression profiling in Brazilian miners occupationally exposed to crystalline silica



## Author

Ingrid Flesch - Universidade Federal do Rio Grande do Sul (UFRGS)  
Caroline Peruzzi - Universidade Federal do Rio Grande do Sul (UFRGS)  
Shanda Cattani - Universidade Federal do Rio Grande do Sul (UFRGS)  
Simony Costa Beber - Universidade Federal do Rio Grande do Sul (UFRGS)  
Solange Garcia - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

FAPERGS, protocol number 27671.414.17115.26062017, PqG 2017



## Keywords

Crystalline silica, gene profiling, biomarkers

## Abstract

Two million workers are exposed to crystalline silica (CS) in Brazil. CS can trigger non-communicable chronic diseases such as silicosis, a progressive, incurable lung disease diagnosed by imaging tests, with no standardized biomarker of exposure or effect. This study aimed to identify promising biomarkers by gene expression profiling in miners exposed to CS. Subjects were divided into three groups: exposed to CS (n=42), workers with silicosis (n=41) and non-exposed to CS (n=30). 5ml of blood was collected from each subject, mixed with RNALater and stored at -80°C. Samples were shipped to the National Institute for Occupational Safety and Health, Morgantown, WV, USA, for RNA isolation and gene expression profiling. Total RNA was isolated using the Ribopure Blood Kit. NGS library synthesis followed the Low Sample TruSeq Stranded mRNA Sample Preparation Guide with modifications. RNA-Sequencing reads were processed using nf-core/RNAseq v3.9.0 for quality assessment and read alignment. For gene expression analysis, reads were trimmed to remove adapters and low-quality reads using Trimgalore v0.6.7. Significantly differentially expressed genes (SDEGs) had an absolute fold change greater than 1.5 and an FDR p-value less than 0.05. These SDEGs were used for bioinformatic analysis. Gene expression profiling of 25,834 genes revealed 491 significantly altered genes for those exposed to CS, 658 for those with silicosis, compared to the control group, and 17 genes for those exposed to CS compared to those with silicosis. Notable genes include ELANE, DEF4, and FAM20A (upregulated), and DSC1, SLC4A10, and NRCAM (downregulated). ELANE, DEF4, and FAM20A are associated with neutropenia, respiratory diseases, and calcification, respectively. DSC1 is related to autophagy, SLC4A10 to the inflammatory response, and NRCAM, a neuronal cell adhesion molecule, to lung cancer. Some of these genes are involved in silicosis development, indicating their potential as biomarkers of the disease.

# Safety assessment of pesticide and nanopesticide carbendazim using the nematode *Caenorhabditis elegans*



## Author

Aline Castro Silva - Universidade Federal do Pampa (UNIPAMPA)  
Daniel Balbé Nunes - Universidade Federal do Pampa (UNIPAMPA)  
Helena de Souza de Oliveira Barcelos - Universidade Federal do Pampa (UNIPAMPA)  
Estefânia Vangelie Ramos Campos - Universidade Estadual Paulista (UNESP-Sorocaba)  
Leonardo Fernandes Fraceto - Universidade Estadual Paulista (UNESP-Sorocaba)  
Daiana Silva Ávila - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Capes



## Keywords

toxicology, agriculture, nanotechnology

## Abstract

Carbendazim is a systemic benzimidazole fungicide used in agriculture to control a variety of fungal diseases in various crops. Its main mode of action is through interference in the biosynthesis of  $\beta$ -tubulin, an essential component of microtubules, leading to disorganization of the fungal cytoskeleton. However, its extensive use can lead to environmental and health problems due to its persistence in the soil and potential toxicity. The nanoencapsulation of carbendazim using zein nanoparticles, a protein extracted from corn, is a promising strategy for improving the efficacy and safety of this fungicide. *Caenorhabditis elegans*' short life cycle and genetic similarity to mammals allow us to obtain valuable data on the toxicity and environmental effects of pesticides, helping to ensure the safety and sustainability of their use in agriculture. This study aims to verify the toxicological outcomes related to aging in *C. elegans* exposed to carbendazim, as well as to develop safe nanoformulations that mitigate its toxic effects on nematodes. The N2 worms (wild type) were treated from the first to the fourth larval stage (L1-L4) with carbendazim at concentrations of 0.01, 0.05 and 0.1 mg.mL<sup>-1</sup>. After 48 h (L4), the survival rate was assessed and on the first adult day the length, lipofuscin accumulation, swimming movements and intestinal integrity of the nematodes were analyzed. We observed that the highest concentrations of carbendazim caused mortality in *C. elegans* (LC<sub>50</sub> of 0.2 mg.mL<sup>-1</sup>). In addition, a decrease in length, swimming movements and loss of intestinal integrity were observed in the worms exposed to the highest concentration of the fungicide, suggesting a possible acceleration in the ageing of the nematodes. The accumulation of lipofuscin was not altered. Our results indicate that carbendazim was toxic to *C. elegans*. The next step in this study is to deepen the analyses related to ageing and assess whether nanoformulations can reverse the observed damage.

# Effect of Gender on the Safety of a New Colorant – Biochemical Changes in vivo



## Author

Rafaella de Barros Mott - Universidade de Sorocaba (UNISO)  
Talita Cristina Mena Segato - Universidade de Sorocaba (UNISO)  
Erika Leão Ajala Caetano - Universidade de Sorocaba (UNISO)  
Caio de Azevedo Lima - Universidade Estadual de São Paulo (UNESP-Araraquara)  
Valéria de Carvalho Santos Ebinuma - Universidade Estadual de São Paulo (UNESP-Araraquara)  
Denise Grotto - Universidade de Sorocaba (UNISO)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

FAPESP 2022/02015-4



## Keywords

Gender differences, Toxicological Study, Biochemical Parameters

## Abstract

The evaluation of the safety and efficacy of new products is crucial, and assessing both gender is necessary due to biochemical, physiological, and toxicological differences between males and females. Studies show significant variations in metabolism and sensitivity to chemicals, with males often more susceptible to liver injuries. This underscores the need for gender-inclusive toxicological studies for comprehensive product safety evaluation. The purpose of this study was to identify gender differences in biochemical parameters in a toxicity test for a new colorant – Azaphilone – produced by the fungus *Talaromyces amestolkiae*. The preclinical trial was approved by the Ethics Committee (CEUA-Uniso 213/2022). Using male and female Wistar rats, doses of 25%, 50%, and 100% Azaphilone were administered via gavage for 90 days. After euthanasia, peripheral blood was collected for assess hepatic profile (Aspartate aminotransferase - ALT - and Alanine aminotransferase - ALP) and lipid profile (triglycerides and low-density lipoproteins – LDL). Data were analyzed using mean and standard deviation, with Duncan's post hoc test applied. Hepatic parameters showed a pattern in ALT at the control and 25% dosage, where males presented significantly higher values than females. At the 50% dosage, females had higher values than males. For ALP, males consistently had lower values than females across all dosages. Lipid parameters were similar between gender at control and 25% dosages. However, at 50%, males showed higher results, and at 100%, levels were similar between gender. For triglycerides, females had lower levels than males, but at 50%, females experienced a greater increase, while at 100%, males had higher levels again. These results suggest a distinct pattern of response between male and female rats exposed to Azaphilone. While Azaphilone appears safe at certain dosages, gender-specific differences must be considered in safety evaluations.

# Therapeutic Drug Monitoring of Endoxifen for Precision Tamoxifen Dosing in Breast Cancer Patients: The Genotype Dilemma



## Author

Ana Flávia Mendes Batista - Universidade de São Paulo (USP-Ribeirão Preto)  
Letícia Penteado Petrolli - Universidade de São Paulo (USP-Ribeirão Preto)  
Maria Paula Marques Pereira - Universidade de São Paulo (USP-Ribeirão Preto)  
Adriana Rocha - Universidade de São Paulo (USP-Ribeirão Preto)  
Jurandyr Moreira de Andrade - Universidade de São Paulo (USP-Ribeirão Preto)  
Vera Lucia Lanchote - Universidade de São Paulo (USP-Ribeirão Preto)  
João Paulo Bianchi Ximenez - Universidade de São Paulo (USP-Ribeirão Preto)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Fundação de Amparo à Pesquisa do Estado de São Paulo



## Keywords

Endoxifen, Breast Cancer, Therapeutic Drug Monitoring

## Abstract

Endoxifen (END) is considered the most important metabolite of tamoxifen (TAM). Patients undergoing adjuvant TAM treatment with END levels below the threshold of 6 ng/mL may have an increased risk of breast cancer recurrence. Various factors, including genetic polymorphisms, drug interactions, and (non)adherence, lead to significant interpatient variability in END exposure, resulting in a substantial number of patients exhibiting subtherapeutic levels. Since genotyping and phenotyping cannot adequately predict END plasma exposure, therapeutic drug monitoring (TDM) appears to be the best approach for personalized TAM therapy. This study aims to assess the clinical benefits of applying END measurement during TAM therapy in breast cancer patients. Breast cancer patients  $\geq 18$  years who received TAM at a fixed dose of 20 mg daily for at least 3 months were enrolled. TaqMan assays were used for CYP2D6 genotype. The TAM and END plasma concentrations were determined via LC-MS/MS. The pharmacokinetics of TAM and END were evaluated at steady-state during a 24 h interval. A total of 36 patients receiving adjuvant TAM were included in the study. The steady-state plasma concentrations of TAM and END were 145.13 ng/mL (95% CI: 119.43 - 176.35) and 12.15 ng/mL (95% CI: 8.82 - 16.75), respectively. The fluctuation indices at steady-state were 206% for TAM and 154% for END. The metabolic ratio of TAM to END was 11.94. Among the patients, 15% had END plasma concentrations below 6 ng/mL. For those with the normal metabolizer (NM) phenotype, 8.3% were below the efficacy threshold, while 25% of patients with the intermediate metabolizer (IM) phenotype (reduced CYP2D6 activity) had END plasma concentrations below 6 ng/mL. In conclusion, TDM of END provides better identification of patients with low END concentrations compared to CYP2D6 genotyping. Patients can initially start on an individualized dose based on genotyping results, and once steady state is reached, TDM can be performed.

# Evaluation of the antiproliferative action of Uliginosin b using in silico and in vivo models in *Caenorhabditis elegans*



## Author

Maria Eduarda Souza - Universidade Federal do Pampa (UNIPAMPA)  
Flávia Suelen de Oliveira Pereira - Universidade Federal do Pampa (UNIPAMPA)  
Favero Reisdorfer Paula - Universidade Federal do Pampa (UNIPAMPA)  
Stela Maris Kuze Rates - Universidade Federal do Pampa (UNIPAMPA)  
Daiana Silva de Ávila - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CAPES, CNPQ



## Keywords

molecular docking;, cancer, alternative model

## Abstract

Cancer is considered one of the main public health problems, being the second highest cause of death in the world. The use of drugs derived from natural products is already used on the market, but molecules that are more effective and have fewer adverse effects are being sought. In the literature, in vitro studies have already been reported with the potential antiproliferative action of the isolated uliginosin B (ULI), a dimeric phloroglucinol present in species of the *Hypericum* genus. Therefore, the objective of this work was to evaluate its antiproliferative activity in vivo, using the nematode *Caenorhabditis elegans*, and in silico, using molecular docking. Animals of strains N2 and MT4244 (*unc-24(e138)*; *let-60(n1046)* IV) in the L1 larval stage were exposed to ULI at concentrations of 1, 5, 10 and 20  $\mu$ M, in acute exposure (30 minutes). It was possible to observe that ULI was safe in terms of toxicological parameters, and caused a delay in the development of the multivulva (MV) phenotype in worms on the first and second day of adulthood, with significance at concentrations of 5, 10 and 20  $\mu$ M. However, there was no change in the average amount of MV for each worm, as well as in their area. At the in silico tests, the flexible molecular docking method was performed, using iGEMDOCK, demonstrating that ULI has greater affinity for the tyrosine kinase portion of the human endothelial growth factor receptor (EGFR) in its active and inactive form (PDB code 7KXZ and 1M14) compared to *C. elegans* (LET-23) (PDB code 5WNO). It is possible to suggest that ULI delayed the development of the MV phenotype, but without changing the number of tumors, and this can be explained because ULI does not show specificity in the interaction with the receptor in the nematode, as demonstrated in human receptors.

# Potential neuroprotective effect of ketamine in a cortisol-induced cellular stress model



## Author

Nicole Frohlich - Universidade Federal do Rio Grande do Sul (UFRGS)  
Lucas dos Santos da Silva - Universidade Federal do Rio Grande do Sul (UFRGS)  
Carolina Saibro Girardi - Universidade Federal de Ciências da Saúde de Porto Alegre - (UFCSPA)  
Fernanda Petry - Universidade Federal do Rio Grande do Sul (UFRGS)  
Júlia Hansen - Universidade Federal do Rio Grande do Sul (UFRGS)  
Danielle Martins - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

FAPERGS PPSUS (21/2551-0000090-2); FAPERGS PRONEX (16/2551-0000499-4); CNPq; CAPES and PROPESQ/UFRGS.



## Keywords

ketamine, cortisol, neuroinflammation

## Abstract

Major Depressive Disorder (MDD) is a complex and heterogeneous pathology. It is known that stress is involved in its pathophysiology. One of the main problems associated with MDD is resistance to treatments and a high rate of relapse. Given this, ketamine, a fast-acting drug, helps to repair and rebuild brain circuits. However, its neuroprotective mechanism is still poorly understood. Given this, we aimed to verify whether ketamine is capable of reversing the neuronal damage induced by cortisol (cort) in a cellular model using the SH-SY5Y line. First, the cells were differentiated for 7 days with retinoic acid and BDNF. On day 7, 12  $\mu\text{M}$  of ketamine was administered, and on day 8 the cells were exposed to doses of 1125  $\mu\text{M}$  and 1500  $\mu\text{M}$  of cort. Twenty-four hours later, MTT and Sulforhodamine B (SRB) reduction assays were performed to evaluate cell viability. To verify neuronal morphology, immunofluorescence was performed using anti-neurofilament antibodies. To verify the expression of genes responsive to stress and involved in neuroinflammation, perform the RT-qPCR technique. The results were analyzed using one-way ANOVA followed by Tukey's test. Our results suggest that cortisol promotes neuroinflammation in a differentiated SH-SY5Y cell culture with a serotonergic phenotype, through increased expression of NF- $\kappa\text{B}$  and NLRP3 genes and intracellular RS production, impairing BDNF expression, cell viability, and neuronal complexity parameters. Ketamine seems to reduce the expression of inflammatory genes and RS production while increasing BDNF expression, which can be related to the enhanced neuroplasticity and maintenance of neuronal complexity observed. We demonstrated that ketamine acts by reducing neuroinflammation and promoting neuroplasticity, besides blocking the NMDA receptor.



# Evaluation of gene expression associated with pathophysiological modifications in farmers exposed to agrochemicals



## Author

Shanda Cattani - Universidade Federal do Rio Grande do Sul (UFRGS)  
Simony Costa Beber - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ingrid Flesch - Universidade Federal do Rio Grande do Sul (UFRGS)  
Thainá Zanenga Silva - Universidade Federal do Rio Grande do Sul (UFRGS)  
Emerson Cauã dos Santos Silva - Universidade Federal do Rio Grande do Sul (UFRGS)  
Solange Cristina Garcia - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Fundação de Amparo à Pesquisa do Estado de São Paulo



## Keywords

gene expression, agrochemicals, biomarkers

## Abstract

**Introduction:** Brazil is classified as the first country that most uses agrochemicals, being circa of 10 L/brazilian/year. It is known that exposure to these chemical substances triggers several chronic diseases, such as cancer. There are some gene expression associated with pathways of tumoral development, as pathophysiological modifications. **Objective:** Study early biomarker as effect biomarkers to exposure to agrochemicals, gene expressions, involved with oxidative stress and tumoral pathways. **Methodology:** farmers (n=40) and administrative workers (n=40) participated in the study. The separation of peripheral mononuclear cells (PBMCs) was carried out in whole blood using the Ficoll method. The RNA was extracted using the Phenol-Chloroform method. DNase eliminated any contamination, the RNA was converted into cDNA, increasing its stability. Expression quantification was done by RTqPCR (StepOne). The target genes were CXCL2, OGG1 and ITPR3. B-actin was housekeeping gene. **Results:** Despite being preliminary, all gene expressions (CXCL2, OGG1 and ITPR3) were decreased in the farmers compared to the control ( $p < 0.0001$ ). CXCL2 is a chemokine of relevance in the inflammatory process. OGG1 is a DNA glycosylase that repairs DNA damage generated by oxidative stress. ITPR3 is a crucial gene for the regulation of intracellular ions and changes in this gene can affect cell signaling. Thus, response of the inflammation, oxidative stress and signalization were modified. **Conclusion:** The decrease in the gene expressions can affect the efficiency of DNA damage repair and/or the functioning of physiological processes which may be associated with the development of different diseases, including cancer. Furthermore, they provide promising insight into the effects of occupational exposure to chemical agents and reinforce the need to continue studying pathophysiological pathway modifications and their impact on biomarkers as evaluation of risk diseases.

# Genotoxic evaluation in farmers exposed to agrochemicals



## Author

Daiane Domingues - Universidade Federal do Rio Grande do Sul (UFRGS)  
Gabriela Göethel - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ingrid Flesch - Universidade Federal do Rio Grande do Sul (UFRGS)  
Lucas Augsten - Universidade Federal do Rio Grande do Sul (UFRGS)  
Shanda Cattani - Universidade Federal do Rio Grande do Sul (UFRGS)  
Sabrina Nascimento - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Fundação de Amparo à Pesquisa do Estado de São Paulo



## Keywords

Agrochemicals, micronucleus assay, genotoxic effect

## Abstract

**Objectives:** Study on health of the Brazilian farmers, evaluating the genotoxic effect and their potential associations with metals/metalloids in occupationally exposed to agrochemicals. **Methodology:** Samples were collected from 78 farmers occupationally exposed to agrochemicals and workers non-exposed occupationally to pesticides (N=60), tobacco plantations. For the micronucleus assay, epithelial cells from the oral mucosa were collected during a period of high exposure, and the smears were processed using the PAS-Fast Green staining technique on exfoliative cells from the oral mucosa. The concentrations of elements, such as Arsenic (As), Chromium (Cr) and Titanium (Ti) in the blood of farmers, were determined by inductively coupled plasma mass spectrometry (ICP-MS) using a NexIon spectrometer. 300X (PerkinElmer-Sciex, USA). **Results:** The farmers presented increased average plasma levels of Chromium in relation to the control group ( $p < 0.001$ ), as well as their positive correlation to the exposure time ( $p < 0.001$ ). The other metals evaluated did not show a significant difference in their levels in the farmer group in relation to the control group. When evaluating the incidence of micronuclei, a higher average was obtained in the presence of genetic damage in farmers ( $\bar{x} 0.04 \pm 0.20$ ), compared to the group of unexposed individuals ( $\bar{x} 0.02 \pm 0.13$ ). **Conclusions:** The oral cell micronucleus assay is a useful and minimally invasive method for monitoring genotoxicity in individuals exposed to pesticides. Through it, it was possible to observe a higher incidence of genotoxic effects on the cells of the oral mucosa of workers occupationally exposed to agrochemicals in relation to control group. It was also possible to identify the increase in plasma levels of the toxic metal Chromium corresponding to the increase in individuals occupational exposure time.

# Evaluation of renal function biomarkers in farmers exposed to pesticides in tobacco cultivation



## Author

Letícia Campos - Universidade Federal do Rio Grande do Sul (UFRGS)  
Lucas Volnei Augsten - Universidade Federal do Rio Grande do Sul (UFRGS)  
Shanda Aparecida Cattani - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ingrid Flesch - Universidade Federal do Rio Grande do Sul (UFRGS)  
Thainá Zanenga Silva - Universidade Federal do Rio Grande do Sul (UFRGS)  
João Braun Pinto de Queiroz - Universidade Federal do Rio Grande do Sul (UFRGS)  
Isadora de Andrade Arend - Universidade Federal do Rio Grande do Sul (UFRGS)  
Adriana Gioda - PUC-Rio Rio de Janeiro  
Tatiana Dillenbourg Saint ´Pierre - PUC-Rio - Rio de Janeiro  
Marcelo Dutra Arbo - Universidade Federal do Rio Grande do Sul (UFRGS)  
Solange Cristina Garcia - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

CNPq and FAPERGS grant to SCG



## Keywords

pesticides, kidney biomarkers, agriculture

## Abstract

**Introduction:** Agricultural work stands out as one of the highest risk activities, due to direct contact with agrochemicals, which offer potential damage to human health. These substances increase the likelihood of developing chronic non-communicable diseases such as kidney disease, cancer and cardiovascular disease. **Objectives:** To quantify biomarkers of kidney function (mALB, urea and uric acid) and nephrotoxic metals (Pb, Cd and Hg) in farmers exposed to agrochemicals, growing tobacco in RS (n=40, rural workers), compared to the group not exposed to agrochemicals in an urban environment (n=40, urban group). **Methods:** mAlb, urea and uric acid were quantified in plasma using the BS-120 equipment (Mindray®) and the metals Pb, Cd and Hg were analyzed using ICP-MS in whole blood. **Results:** The group of exposed workers showed a higher median mAlb (7 mg/L [3-12]) than the urban group (1 mg/L [0-4.75]) (Mann-Whitney U-test, p<0.001). Urea concentrations in the rural group (26.23 g/24h +- 5.47) were higher than in the urban group (22.2 g/24h +- 6.01) (t-test, p=0.005). The rural group had a higher median uric acid level (0.5 mg/dL [0.3-0.7]) than the urban group (0.1 mg/dL [0.0-0.2]) (Mann-Whitney U-test, p<0.001). The quantification of metals revealed that the concentration of Pb in the group of exposed workers was higher compared to the urban group (t-test, p=0.04), the other metals Cd and Hg showed no differences between the groups studied. **Conclusion:** The results indicate that farmers exposed to agrochemicals have significantly higher concentrations of renal function biomarkers compared to the non-exposed group. In addition, it was possible to observe a higher concentration of the metal Pb in exposed groups. These findings suggest that exposure to agrochemicals is associated with an increased risk of impaired kidney function, highlighting the need for protective measures and continuous monitoring of the health of these workers. **Acknowledgments:** CNPq and FAPERGS.

# Long-Term Repercussions On The Cognitive And Behavioral Record Of Children Post-Anesthetized With Ketamine



## Author

Maria Dinair Gonçalves Batista - Universidade Federal do Pará (UFPA)  
Paulo Monteiro dos Santos Filho - Universidade Federal do Pará (UFPA)  
Jackeline Kerlice Mata Gonçalves - Fundação Santa Casa de Misericórdia do Pará  
Kissila Márvia Matias Machado Ferraro - Universidade Federal do Pará (UFPA)  
Jose Luiz Fernandes Vieira - Universidade Federal do Pará (UFPA)  
Enéas de Andrade Fontes Júnior - Universidade Federal do Pará (UFPA)  
Cristiane do Socorro Ferraz Maia - Universidade Federal do Pará (UFPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Financiado pelo Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), sob o número de projeto: 303196/2022-0



## Keywords

Ketamine, Behavior, Children Post-anesthetized

## Abstract

The use of ketamine as a drug in pediatric sedoanalgesia clinical protocols has been widely discussed. Understanding possible brain damage in development and long-term functional repercussions is still incomplete. Thus, this work aimed to assess what changes occur in the cognitive and behavioral domains in pediatric patients undergoing ketamine sedoanalgesia protocols, as well as the persistence of these changes over the long term after discontinuation of use. A non-randomized clinical trial was conducted using the Denver II Development Screening Test, which consists of 125 items divided into the areas of personal-social, fine-adaptative motor, language and broad motor, grouped into behavioral classes. 19 children from 0 to 5 years of age participated in the study, divided into two groups: G1, consisting of 10 patients who received ketamine, and G2, composed of 9 patients receiving other sedoanalgesics. The number of failures in each area was stratified as a percentage and converted to a table by the Prism Program 8.0. The data were tabulated and the average percentage of the domain variables was calculated after 7 and 15 days, 6 and 9 months of suspension of sedation. The results show that post-anesthetized patients with ketamine showed more pronounced atypical developmental behaviors in the personal-social and cognitive areas, including fine and thick language and motor skills. Furthermore, some atypical developmental responses in the ketamine group persisted for a longer period, compared to the group receiving other sedoanalgesics. This study brings to light information on the long-term effects of ketamine in pediatric patients, revealing a significant impact on cognitive and behavioral areas in a more pronounced and persistent manner. These findings emphasize the need to re-evaluate the use of ketamine in pediatrics, as well as conducting more comprehensive studies to fully clarify the effects of this drug on child development.

# Pharmacokinetics improvements as a tool for side effects reduction



## Author

Julia Gabriele Jesus Ferreira - Universidade de Novo Hamburgo (Feevale)  
Victoria Givankliff Flores - Universidade de Novo Hamburgo (Feevale)  
Patrícia da Fonseca de Morais - Universidade de Novo Hamburgo (Feevale)  
Fernando Dal Pont Morisso - Universidade de Novo Hamburgo (Feevale)  
Juliane Deise Fleck - Universidade de Novo Hamburgo (Feevale)  
Máriele Feiffer Charão - Universidade de Novo Hamburgo (Feevale)  
Cristiane Bastos de Mattos - Universidade de Novo Hamburgo (Feevale)  
Andresa Heemann Betti - Universidade de Novo Hamburgo (Feevale)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Fundação de Amparo à Pesquisa do Estado de São Paulo



## Keywords

Diazepam, Nanotechnology, Pharmacokinetic

## Abstract

Diazepam (DZP), a sedative medication often prescribed for inducing sleep, is notable for its significant residual effects. Therefore, the aim of this study was to enhance pharmacokinetics and mitigate side effects through nanotechnology. The nanocapsules were prepared by the nanoprecipitation method and were characterized for particle size, zeta potential, polydispersity index, pH and content. In vitro release studies were carried out using Franz-type diffusion cells, analyzing DZP nanocapsule and DZP solution, both at the same concentration. The release profiles obtained were evaluated by zero order for release kinetic evaluation. Tiopental (TS) induced sleep test was performed using 4 groups of treatments by gavage: control solution (vehicle); DZP (2 mg/kg), blank nanocapsule and DZP nanocapsule (1 mg/kg). Sixty-minutes after the first treatment, TS (60 mg/kg) was administered to each animal intraperitoneally. Then, the time of loss of the righting reflex (latency), and duration of TS-induced sleeping-time were registered. The nanocapsules had a particle size of  $180\pm 4.0$  nm, polydispersion index of  $0.119\pm 0.01$ , zeta potential  $-28.44\pm 3.3$  mV and pH  $4.05\pm 0.06$ . Content and encapsulation efficiency were  $97.05\pm 1.99$  and 99.56%, respectively. The in vitro release percentage for nano encapsulated DZP was 79,69% while for free DZP, it was 97,29%, throughout a period of 12 hours. Such results demonstrate that nano encapsulated DZP has a more sustained release profile over time. DZP nano encapsulated increased sleeping-time when compared to the free drug, producing a prolonged effect even with half the dose of DZP. Finally, DZP was successfully incorporated into nanocapsules, with high entrapment efficiency and good physicochemical characteristics. This is an innovative formulation with the potential to reduce the side effects of DZP, through the dose reduction and prolonged hypnotic effect, due to improvements in its pharmacokinetic profile resulting from nanoencapsulation

# Use Of Ketamine As Sedoanalgesia In A Pediatric Intensive Care Unit: Evaluation Of Pediatric Delirium And Neuronal Degeneration



## Author

Mary Lucy Ferraz Maia - Universidade Federal do Pará (UFPA)  
Maria Dinair Gonçalves Batista - Universidade Federal do Pará (UFPA)  
Jackeline Kerlice Mata Gonçalves - Fundação Santa Casa de Misericórdia do Pará  
Kissila Márvia Matias Machado Ferraro - Universidade Federal do Pará (UFPA)  
Rommel Mario Rodriguez Burbano - Universidade Federal do Pará (UFPA)  
Emmerson Carlos Franco de Farias - Universidade Federal do Pará (UFPA)  
Jose Claudio Monteiro Rodrigues - Universidade Federal do Pará (UFPA)  
Bruno Goncalves Pinheiro - Universidade Federal do Pará (UFPA)  
Fabio Jose Coelho de Souza Junior - Universidade Federal do Pará (UFPA)  
Enéas de Andrade Fontes Júnior - Universidade Federal do Pará (UFPA)  
Cristiane do Socorro Ferraz Maia - Universidade Federal do Pará (UFPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Financiado pelo Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), sob o número de projeto: 303196/2022-0



## Keywords

Ketamine, sedation, pediatric intensive care unit

## Abstract

In pediatric intensive care unit (PICU) services, anesthetic sedation is often required to promote comfort to patients, and ketamine is commonly used. This study aims to investigate the effects of ketamine in pediatric patients, evaluating the presence of pediatric delirium and a biomarker of neuronal damage. It was conducted a study with 34 patients in an PICU, divided into two groups: G1, comprising 14 patients who received ketamine, and G2, comprising 20 patients who used other sedoanalgesics. Samples were collected on days 1, 2 and 5 after the start of the sedation to evaluate the biomarker S100B, indicator of neuronal damage. The behavioral parameters related to delirium were evaluated using the Cornell Assessment of Pediatric Delirium (CAPD) scale, applied on the 7th and 15th days after the suspension of sedation. The data were submitted to the Kolmogorov-Smirnov normality test and subsequently to the Student t test for comparison between groups. The results indicated a significant difference in the expression of S100B between the groups on all evaluation days: D1 ( $p < 0,0001$ ), D2 ( $p < 0,0001$ ) and D3 ( $p > 0,0001$ ). The evaluation of delirium by the CAPD scale also showed statistically significant differences in the evaluation days: D7 ( $p < 0,01$ ) and D15 ( $p < 0,05$ ) when compared to the control group. Analysing the scale indicators independently, it was noted that 6 of the 8 indicators were increased in the group that received ketamine, with an increase in delirium compared to the control group. This study reveals new information about the effects of ketamine in pediatric patients and launches a warning about its potential negative impact on neurodevelopment. Evidence of increased levels of S100B biomarkers and indicators of pediatric delirium suggest an exacerbation of neuronal and psychological damage. These findings reinforce the need for broader research to assess the safety and feasibility of ketamine use in PICU.

# In Different Periods Of Cerebral Development Are Spatial Learning And Cognitive Flexibility Also Sensitive To The Withdrawal Of Ethanol In Binge Drinking?



## Author

Taiana Cristina Vilhena Carvalheiro Simas - Universidade Federal do Pará (UFPA)  
Luanna de Melo Pereira Fernandes - Universidade Estadual do Pará (UEPA)  
Sabrina de Carvalho Cartágenes - Universidade Federal do Pará (UFPA)  
Leticia Yoshitome Queiroz - Universidade Federal Santa Catarina (UFSC)  
Mayara Arouck Barros - Universidade do Federal do Pará (UFPA)  
Cristiane do Socorro Ferraz Maia - Universidade do Federal do Pará (UFPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Fundação de Amparo à Pesquisa do Estado de São Paulo



## Keywords

Ethanol, Adolescence, Adulthood

## Abstract

Ethanol (EtOH) is the most widely used recreational drug among all age groups and its consumption in the standard binge drinking (BD) has increased in the female gender, especially among underage adolescents and young adults. This has been largely related to the incidence of mental problems and behavioral deficits. In this way, the objective of this work was to identify how different stages of brain maturation are affected by the episodic and intermittent pattern of ethanol on spatial learning and cognitive flexibility through the Water Maze Test. The animals were divided into two groups, an adolescent group and an adult group and the two groups were subdivided into control group (n=10/each) and EtOH group (n=12/each), totaling 44 rats. The administration took place orally (gavage) and consisted of distilled water for the animals in the control groups and ethanol at a dose of 3g/kg/day (20 p/v) for the EtOH groups (3 days on/ 4 days off, for four consecutive weeks), throughout adolescence and adult life. At the end of the last BD cycle, 24 hours after the last administration of H<sub>2</sub>O<sub>d</sub>/EtOH, when there were no more circulating concentrations of this drug in the body, the investigation of the cognitive function of the two age groups was started. Adolescent animals did not show mnemonic impairments associated with learning and spatial flexibility, but temporary motor impairments were evident after ethanol withdrawal and disappeared after days of abstinence. In contrast, adult animals did not demonstrate impairments in learning, flexibility and motor quality after ethanol withdrawal. Our results suggest that components of cortical-subcortical circuits responsible for motor quality, such as the cerebellum and striatum, are more sensitive in periods of cerebral immaturity, such as adolescence, and that the prefrontal cortex and areas of the limbic system are less sensitive to neurotoxic effects of ethanol in binge drinking, even during periods of brain development.

# Toxicological analysis of nanoparticles with bioinsecticidal potential containing geraniol using *Caenorhabditis elegans*



## Author

Daniel Balbé - Universidade Federal do Pampa (UNIPAMPA)  
Aline Castro da Silva - Universidade Federal do Pampa (UNIPAMPA)  
Daniela Teixeira Rodrigues - Universidade Federal de Santa Maria (UFSM)  
Jhones Luís Oliveira - Universidade Estadual de São Paulo (UNESP-Sorocaba)  
Leonardo Fernandes Fraceto - Universidade Estadual de São Paulo (UNESP-Sorocaba)  
Claudia Martinez - Universidade Estadual de Londrina (UEL)  
Daiana Silva de Ávila - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

FAPERGS - Fundação de Amparo à pesquisa do Estado do RS



## Keywords

Ketamine, Behavior, Children Post-anesthetized

## Abstract

Chemical control strategies are the most commonly used methods for managing pest insects in agriculture. However, the irrational use of agricultural pesticides can be linked to human and environmental health damage. Therefore, the application of nanoformulations based on natural products in agriculture has shown promise as an alternative. The present study aimed to determine the toxicity of geraniol nanoparticles (NPs) with bioinsecticidal activity using *Caenorhabditis elegans*. L1 stage worms were chronically exposed (48 hours) to an increasing concentration curve of geraniol emulsion (0.08, 0.16, 0.24, and 0.32 mg/mL) to determine the average lethal concentration (LC50), brood size, body length, body area and swimming movements. Based on the LC50 value of the emulsion (0.1964 mg/mL), the same analyses were conducted on nematodes exposed zein nanoparticle containing geraniol (NZG), control zein nanoparticle (NZC), zein/lignin nanoparticle containing geraniol (NZLG), and control zein/lignin nanoparticle (NZLC). One-way ANOVA followed by Tukey post hoc or Kruskal-Wallis post hoc tests were used for statistical analysis. The results showed that the geraniol emulsion caused significant reduction in the survival of the worms compared to the NPs, suggesting that the NPs were able to reduce the toxicity of geraniol and might be safe for non-target organisms. Additional experiments are being conducted to confirm the safety of the NPs in other parameters in *C. elegans*, as well as to evaluate the potential insecticidal effect of the NPs in *Drosophila melanogaster*.



# Safety assessment of Cannabis sativa extract in the alternative model *Caenorhabditis elegans*



## Author

Julia Saleh - Universidade Federal do Pampa (UNIPAMPA)  
Jean Reginatto - Universidade Federal do Pampa (UNIPAMPA)  
Heloisa Padilha - Universidade Federal do Pampa (UNIPAMPA)  
Daiana Avila - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

Universidade Federal do Pampa



## Keywords

Cannabis, *Caenorhabditis elegans*, safe

## Abstract

*Cannabis sativa* é uma planta composta por inúmeros compostos, sendo o canabidiol (CBD) e o tetrahydrocannabinol (THC) suas principais substâncias. O THC é responsável pelos efeitos alucinógenos causados por *Cannabis*. Por outro lado, o CBD é uma substância química que constitui uma grande parte da planta e não tem efeitos psicoativos. O CBD tem recebido atenção significativa pelos seus potenciais benefícios terapêuticos e tem sido alvo de inúmeros estudos e pesquisas científicas. O modelo alternativo *Caenorhabditis elegans* foi usado para investigar a segurança de um comercial. *Cannabis sativa* Extracto (EXT) contendo 5% de CBD e menos de 0,2% de THC. As estirpes N2 (tipo selvagem), LX929 (vsIs48 [unc-17::GFP]) e BZ555 (eglIs1 [dat-1 p::GFP]) foram sincronizados para obter o mesmo estágio larval, L1. Os vermes foram tratados com o extracto diluído em sulfóxido de dimetil. Os vermes foram expostos a 10 mm, 40 mm e 150 mm de EXT durante 1 hora até ao estágio larval L4. Após 48 horas de tratamento, sobrevivência, área e comprimento do corpo, produção de ovos, postura de ovos, fluorescência das estirpes BZ555 e LX929, e paralisia induzida por dopamina foram analisadas. A taxa de sobrevivência, a produção de ovos e a colocação de ovos não mostraram diferenças significativas em comparação com o controle. Uma diminuição no comprimento e na área do corpo foi observada na maior concentração (150 mm). A quantificação da fluorescência dos neurônios estudados também não mostrou diferenças significativas. O ensaio de paralisia induzido por dopamina não mostrou alterações em nenhuma das concentrações testadas. Assim, é possível sugerir que as concentrações do extrato utilizado mostraram segurança em termos de sobrevivência, produção de ovos, postura de ovos, neurônios colinérgicos e dopaminérgicos. As concentrações mais baixas também provaram ser seguras em termos de tamanho e comprimento, portanto as concentrações de 40 mm podem ser usadas para futuros estudos farmacológicos.

# A elevation in serum potassium levels induced by vasoactive amines in neonates under intensive therapy.



## Author

Andreza Fernandes - Universidade Federal do Rio Grande do Norte (UFRN)  
Daniel Paiva Marques - Universidade Federal do Rio Grande do Norte (UFRN)  
Gabriela Santana - Universidade Federal do Rio Grande do Norte (UFRN)  
Nathalia Beatriz de Oliveira Pedrosa - Universidade Federal do Rio Grande do Norte (UFRN)  
Ayslla Thaisa Guedes Martins - Universidade Federal do Rio Grande do Norte (UFRN)  
Iris Ucella de Medeiros - Universidade Federal do Rio Grande do Norte (UFRN)  
Rand Randall Martins - Universidade Federal do Rio Grande do Norte (UFRN)  
Antonio Manuel Gouveia de Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Rodrigo dos Santos Diniz - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Pharmacology, Pharmacokinetics and Toxicology



## Funding

No



## Keywords

Neonates;, vasoactive drugs;, intensive care unit.

## Abstract

**Introduction:** The neonatal intensive care unit (NICU) frequently requires the use of vasoactive amines to stabilize blood pressure and maintain adequate perfusion in critically ill neonates. However, their use may be associated with complications such as potential effects on serum potassium (K) levels. **Objective:** To investigate variations in serum K levels in neonates undergoing administration of vasoactive amines in NICUs. **Methodology:** A cohort study conducted between March 2023 and March 2024 in an NICU of a public maternity hospital. Inclusion criteria were 336 neonates hospitalized for more than 24 hours and prescribed at least one medication (ethics committee No. 5718250). Daily collection of clinical, laboratory, and pharmacotherapeutic parameters was performed. Serum K levels and doses of the main vasoactive amines dopamine (DOP), dobutamine (DOB), and norepinephrine (NOR) were recorded. Linear mixed-effects regression analysis ( $p < 0.05$ ) was employed to analyze the effect of vasoactive amines on neonatal serum K concentration. Serum potassium was considered the dependent variable; gestational age, glomerular filtration rate, and length of hospital stay were independent fixed-effect variables, with intra-individual variability as a random component of the model. **Results:** Neonates had a mean gestational age of  $33.8 \pm 4.0$  weeks, with respiratory problems associated with prematurity as the primary admission diagnosis (67.5%). The mean serum potassium concentration over the first 30 days of hospitalization was  $4.4 \pm 0.3$  mEq/L (95% CI 4.2 – 4.5). The linear regression model identified DOP and NOR as associated with elevated serum K levels ( $\beta=0.584$ ; SE = 0.196;  $p=0.03$  and  $\beta=0.811$ ; SE = 0.251;  $p<0.01$ , respectively), while DOB led to a decrease ( $\beta= -0.308$ ; SE = 0.141;  $p=0.03$ ). **Conclusion:** These findings underscore the need for rigorous monitoring of potassium levels in neonates receiving these vasoactive amines to prevent and manage events such as hyperkalemia.

**Area**

# **Clinical Laboratory Analysis and Diagnosis**

# Correlation Between Oxidative Stress Markers and Cytokines in Post-Acute Sequelae of COVID-19 (PASC)



## Author

Paola Mayara Valente Coronel - Universidade Federal do Mato Grosso do Sul (UFMS)  
Denise Caroline Luiz Soares Basilio - Universidade Federal do Mato Grosso do Sul (UFMS)  
Isabelly Teixeira Espinoça - Universidade Federal do Mato Grosso do Sul (UFMS)  
Kamylla Fernanda Souza de Souza - Universidade Federal de São Paulo (UNIFESP)  
Paulo Henrique Muleta Andrade - Universidade Federal do Mato Grosso do Sul (UFMS)  
Nathalia Miranda Campos - Universidade Federal do Mato Grosso do Sul (UFMS)  
Rafael Seiji Nakano Ota - Universidade Federal do Mato Grosso do Sul (UFMS)  
Ana Rita Coimbra Motta de Castro - Universidade Federal do Mato Grosso do Sul (UFMS)  
Edgar Julian Paredes-Gamero - Universidade Federal do Mato Grosso do Sul (UFMS)  
Danilo Wilhelm-Filho - Universidade Federal de Santa Catarina (UFSC)  
Renata Trentin Perdomo - Universidade Federal do Mato Grosso do Sul (UFMS)  
Eduardo Benedetti Parisotto - Universidade Federal do Mato Grosso do Sul (UFMS)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

PPS/FUNDECT, CNPq, CAPES and UFMS



## Keywords

post-COVID, oxidative stress, inflammation

## Abstract

COVID-19, caused by SARS-CoV-2, leads to excessive cytokine release, resulting in acute lung injury and death. Sequelae may arise after a severe clinical condition, including pulmonary fibrosis and myocardial damage, increasing morbidity and mortality in the presence of comorbidities. Oxidative stress (OS) plays a fundamental role in the pathophysiology of this disease. We evaluated several biomarkers of OS and inflammation in the blood of individuals with post-acute sequelae of COVID-19 (PASC). 64 patients (men and women) were distributed into 3 groups: healthy individuals (n=20), individuals with acute COVID-19 (symptoms <3 weeks, n=15), and individuals with PASC (symptoms >12 weeks, n=29), after approval by the Human Research Ethics Committee CEP/UFMS (CAAE 37596720.7.0000.0021). Pro-inflammatory cytokines and myeloperoxidase (MPO) activity were analyzed, and also OS markers such as superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase (GST), and gamma-glutamyl transferase (GGT), as well as concentrations of reduced glutathione (GSH), uric acid (UA), thiobarbituric acid reactive substances (TBARS), and carbonyl proteins (PC). Individuals with acute COVID-19 demonstrated increased of IL-6, while individuals with chronic COVID syndrome demonstrated increased of IL-6 and IL-8. SOD and CAT decreased in both COVID-19 groups, while GST values decreased in the acute COVID group. GGT and GSH levels were elevated in the PASC group while decreased in the acute group. UA contents showed high values in PASC individuals. TBARS contents increased in both COVID-19 groups, with higher levels in the acute patient group, while PC contents were elevated in the PASC group. Significant correlations were found between cytokines and OS markers. Individuals with persistent symptoms of COVID-19 experienced a pronounced OS, which may contribute to the severity and complications of the disease. Thus, monitoring OS biomarkers can aid in patient prognosis and management.

# Metabolome/metabolites produced in the vaginal environment in the presence of dysbiosis, HPV persistence and cervicovaginal dysplasia: a scoping review



## Author

Ednéia Peres Machado - Universidade Federal do Paraná (UFPR)  
Helena Hiemisch Lobo Borba - Universidade Federal do Paraná (UFPR)  
Allan Michael Junkert - - Universidade Federal do Paraná (UFPR)  
Idonilton da Conceição Fernandes - Universidade Federal do Paraná (UFPR)  
Wellington Martins de Carvalho Ragassi - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

without funding



## Keywords

Metabolome, HPV, scoping review

## Abstract

Cervical cancer is the fourth most common type of cancer among women. There is a consensus that high-risk HPV infection is not solely responsible for its development, as only 10% of infected women have persistent HPV, which can progress to invasive cancer in 1% of cases. Recently, the relationship between vaginal microbiome, immune system and metabolites in HPV-positive women have been investigated to understand the behavior of the vaginal ecosystem in the presence of high-risk HPV. Primary studies suggest that the vaginal microecology may favor HPV persistence, however, the mechanism is still unclear. **Aim:** To map the available evidence regarding metabolic changes/metabolome in the vaginal environment with dysbiosis and HPV persistence. **Methods:** This scoping review follows the Joanna Briggs Institute and PRISMA extension for Scoping Reviews recommendations. The electronic searches were conducted using Pubmed, Scopus and Web of Science databases. Google Scholar was used to search for thesis and dissertations. Observational studies, in vivo or in vitro, that evaluated metabolic/metabolome changes in dysbiosis and HPV persistence in vaginal microsystem were included, and studies published in non-Roman characters and those that did not contain all three variables (microbiome, metabolome and HPV) were excluded. Two independent reviewers selected the studies and performed data extraction. **Results:** A total of 287 studies were identified. After screening and eligibility, 32 studies were included for data extraction. Partial results from this scoping review demonstrated a distinct metabolomic profile between HPV-positive and HPV-negative cases, with significant differences in the concentrations of biogenic amines, phospholipids, glycogen, glutathione, and other metabolites, varying according to the vaginal microbiota. **Conclusion:** The preliminary data demonstrated a distinct metabolomic profile in the vaginal environment between HPV-positive and HPV-negative cases.

# Seroprevalence Of Syphilis In Blood Donors At The Hemotherapy And Hematology Center Of Espírito Santo – Hemoes



## Author

Larissa Rodrigues de Amorim - Universidade Vila Velha (UVV)  
Claudio Peçanha Júnior - Universidade Vila Velha (UVV)  
Girlandia Alexandre Brasil Amorim - Universidade Vila Velha (UVV)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

Self-funding



## Keywords

Syphilis, Treponema pallidum, Blood Donation

## Abstract

Syphilis is a chronic infectious disease caused by *Treponema pallidum*, which can be transmitted by blood transfusion. Diagnosis, made by treponemal or non-treponemal serological tests, is essential in blood centers due to the high risk of contamination by syphilis and other infectious diseases. In Espírito Santo, transfusions are coordinated by the Espírito Santo Hemotherapy and Hematology Center (HEMOES). Since 2018, syphilis screening has begun using chemiluminescence treponemal testing, followed by non-treponemal testing (RPR). Therefore, our objective was to evaluate the frequency of blood donors positive for syphilis at HEMOES before and after the inclusion of treponemal tests in screening. To this end, a retrospective study was conducted where data from patient records were collected before (2016-2017) and after (2019-2020) the change in syphilis screening protocol. The study was approved by CEP-UVV (CAAE 57233922.9.0000.5064). Data were evaluated using R software (version 4.1.2). In the 2016-17 and 2019-20 periods, HEMOES recorded 173,780 blood donations, with the largest volume concentrated in Vitória (>50%). There was a significant increase in syphilis positive cases in 2019-20 (1489) compared to 2016-17 (506). Vitória also had the highest incidence of syphilis, with rates of 0.26% (2016-17) and 0.84% (2019), compared to Linhares and São Mateus. As of 2019, the prevalence of syphilis has significantly increased across all HEMOES donation sites. The Serra Collection Unit recorded the highest prevalence, with approximately 2.60% of donors testing positive for syphilis. The study revealed that the adoption of treponemal tests increased the detection of syphilis among HEMOES donors, demonstrating greater sensitivity for *T. pallidum* infections. This change was beneficial, increasing the safety of blood recipients and reducing the risk of contamination.

# Role of CD73 in Immunological Modulation and Prognosis of B-cell Acute Lymphoblastic Leukemia: A Retrospective Analysis



## Author

Sacha Krolow Silva - Universidade Federal do Rio Grande Do Sul (UFRGS)  
Camila Kehl Dias - Universidade Federal do Rio Grande Do Sul (UFRGS)  
Maria Fernanda Gonçalves Meirelles Fernandes - Hospital de Clínicas de Porto Alegre (HCPA)  
Vitória Brum da Silva Nunes - Hospital de Clínicas de Porto Alegre (HCPA)  
Mariela Granero Farias - Hospital de Clínicas de Porto Alegre (HCPA)  
Pâmela Portela da Silva - Hospital de Clínicas de Porto Alegre (HCPA)  
Alessandra Aparecida Paz - Hospital de Clínicas de Porto Alegre (HCPA)  
Liane Esteves Daudt - Hospital de Clínicas de Porto Alegre (HCPA)  
Mariana Bohns Michalowski - Hospital de Clínicas de Porto Alegre (HCPA)  
Fabrício Figueiró - Universidade Federal do Rio Grande Do Sul (UFRGS)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

CNPq, CAPES, FAPERGS, Hospital de Clínicas de Porto Alegre FIPE 2022-0094



## Keywords

B-cell Acute Lymphoblastic Leukemia, Measurable Residual Disease, CD73

## Abstract

Cancer continues to challenge researchers and physicians in global efforts to improve public health. Acute Lymphoblastic Leukemia (ALL), characterized by the rapid proliferation of immature lymphoid cells, is the most common type of cancer predominantly affecting the pediatric population. The assessment of Measurable Residual Disease (MRD) through flow cytometry plays a predictive role in monitoring treatment and patient prognosis. The subclonal architecture of the tumor, as well as the expression of ectonucleotidases, such as CD73, in the tumor microenvironment, can influence the immune response, thereby affecting the prognosis in B-ALL. The objective of this study was to explore whether the expression of CD73 in B cells could serve as a promising prognostic indicator during MRD assessments in patients with B-ALL. In this retrospective study, flow cytometry data from 43 patients diagnosed and monitored with B-ALL at the Laboratory Diagnosis Service of the Hospital de Clínicas de Porto Alegre over the past four years (2018 to 2022) were analyzed on days D15, D30, and D45+ post-treatment initiation. This study is authorised on the Plataforma Brasil under CAAE 33989120.1.0000.5327. The MRD analysis shows that lymphocytes represent the largest cell population ( $27.69\% \pm 2.77\%$ ), where a notable decrease in B cells was observed between D15 and D45+ ( $p = 0.0061$ ), along with an increase in T cells during the same period ( $p = 0.0243$ ), suggesting changes in cell composition and dynamics in the immune response. The decrease in CD73+ expression in B cells ( $p = 0.0103$ ), along with the decrease in the MFI of CD73 in B cells during MRD assessments ( $p = 0.0003$ ), particularly between D15 and D45+ ( $p = 0.0002$ ) and D30 and D45+ ( $p = 0.0284$ ), may be associated with a potential positive response to treatment and better prognosis. In conclusion, the results provide promising perspectives for improving therapeutic management and the quality of life of patients with B-ALL.

# CRP as a Potential Method for ASD Diagnosis: A Scoping Review of Biomarkers



## Author

Caroline Folchini - Universidade Federal do Paraná (UFPR)  
Helena Hiemisch Lobo Borba - Universidade Federal do Paraná (UFPR)  
Eduardo Borges de Melo - Universidade Estadual do Oeste do Paraná (UNIOESTE)  
Alexandre de Fátima Cobre - Universidade Federal do Paraná (UFPR)  
Ahmad El Zein - Universidade Federal do Paraná (UFPR)  
Mariana Millan Fachi - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

National Council for Scientific and Technological Development – CNPq; epartment of Science and Technology of Secretariat of Science, Technology, Innovation and Health Complex of Ministry of Health of Brazil –MoH”.



## Keywords

Autism Spectrum Disorder, biomarkers, scoping review

## Abstract

**Background:** Autism Spectrum Disorder (ASD) is a neurodevelopmental condition affecting approximately 1 in every 36 children. Early diagnosis is crucial for effective and personalized treatments. **Objective:** This study is part of a more extensive review to map the scientific evidence on biomarkers for diagnosing ASD in pediatric patients. **Methods:** This scoping review was conducted in accordance with JBI guidelines (OSF Protocol: DOI 10.17605/OSF.IO/EYV8K. Electronic searches were carried out in the Pubmed, Embase, and Web of Science databases (February 2024). Eligible studies included primary interventional or observational studies (with or without a comparator group) that evaluated biological markers (e.g., enzymes, molecules, genes) found in bodily fluids for the diagnosis of ASD and had their main information extracted. Data on the accuracy of methods used to measure biomarkers (including true positives, true negatives, false positives, and false negatives) were collected. Sensitivity, specificity, and ROC curves were constructed using Metadisc2.0 (results reported with 95% confidence intervals - CI). **Results:** Of the 86 articles included for evidence synthesis published between 1986-2023, mainly from the Asian continent (55%), totaling N=37,100. Of these, eight consistently evaluated the C-reactive Protein (CRP) method. The samples used were blood (25%) and serum (25%). The meta-analysis revealed an overall sensitivity of 81% [95% CI 0.76;0.85] and specificity of 82% [95% CI 0.75;0.87]. Sixteen potential biomarkers were mapped using the CRP method, and the highlighted ones were APOE hypermethylation with a sensitivity of 94% [0.84;0.98] and CTRP1 with a specificity of 98% [0.87;1.00]. **Conclusion:** CRP, an easy-to-implement method, presents a promising and practical alternative for aiding in the diagnosis of ASD. This conclusion is particularly true when targeting biomarkers like APOE hypermethylation and CTRP1, which show elevated expression in this population.



# Early postnatal nutritional status and its impact on breastfeeding outcomes



## Author

Fabiola Filippin Monteiro - Universidade Federal de Santa Catarina (UFSC)  
Carolina Dumke de Siqueira - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

FAPESC 466/2018



## Keywords

breastfeeding; lactation; breast milk composition; maternal nutrition

## Abstract

Breastfeeding can be challenging for mothers with overweight or obesity-related chronic low-grade inflammation, negatively impacting newborns. Pre-gestational body mass index is associated with delayed lactogenesis II, the onset of colostrum secretion. This study aimed to evaluate maternal inflammation, metabolic status, and breast milk components postpartum to associate these factors with nutritional and breastfeeding status. Volunteer mothers who delivered at a tertiary maternity hospital were categorized by nutritional status and anthropometric parameters. Serum and breast milk samples were collected 24 and 48 hours after birth to measure inflammatory biomarkers (SAA, leptin, CRP, IL-1 $\beta$ , TNF- $\alpha$ , IL-8, IL-6, MCP-1, IL-10, and IFN- $\gamma$ ), reproductive hormones (prolactin and progesterone), and breast milk composition (total protein, fatty acid, fat percentage, and Kcal). A six-month follow-up assessed breastfeeding outcomes. All facets of this study received approval from HU – UFSC and the Ethical Committee of Universidade Federal de Santa Catarina (CAAE 68008317.4.0000.0121). Breast milk composition remained stable across different maternal ages, nutritional statuses, and types of birth, meeting infant needs consistently. However, a higher concentration of pro-inflammatory biomarkers (SAA, CRP, TNF- $\alpha$ , IL-8, and IFN- $\gamma$ ) compared to the anti-inflammatory IL-10 was found in breast milk. Mothers who were overweight postpartum had newborns with higher birth weights compared to those with healthy post-pregnancy weights. Maternal overweight or obesity-related inflammation can delay lactogenesis II and influence newborn birth weight. Despite these challenges, breast milk remains a stable source of essential nutrients. The presence of pro-inflammatory biomarkers in breast milk suggests a need for further investigation into potential implications for infant health.

# Identification Of Bacterial Genera During The Covid-19 Pandemic In Hospitals In Bagé City, Rio Grande Do Sul



## Author

Darliane Andreis - Universidade Federal do Pampa (UNIPAMPA)  
Cáren dos Santos Corrêa - Universidade Federal do Pampa (UNIPAMPA)  
Cheila Denise Ottonelli Stopiglia - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

No



## Keywords

COVID-19, Antimicrobial resistance, Enterobacteria

## Abstract

In Brazil, the year 2020 was marked by the onset of the spread of SARS-CoV-2 infection. Individuals infected with this virus exhibited weakened immune systems, leading to susceptibility to secondary bacterial infections, especially in hospital settings. This study aimed to assess the prevalence of microorganisms isolated from patients admitted to the Intensive Care Unit (ICU) of two hospitals located in the city of Bagé, in the state of Rio Grande do Sul, between the years 2021 and 2022, considered the pandemic period of COVID-19. Registered by the Ethics Committee for Research with Human Subjects under protocol number 66752623.9.0000.5323. The data were obtained through reports of the results of hospitalized patients' reports, analyzing the identification of bacterial species and the sensitivity profile, issued by the database of the Clinical Analysis Laboratory that provides services to the two hospitals analyzed. The most frequently isolated microorganisms were *Escherichia coli* (37), *Enterobacter* spp. (20), *Acinetobacter* spp. (14), *Proteus* spp. (10), *Klebsiella* spp. (11), *Staphylococcus* spp. (8), *Enterococcus* spp. (8), *Pseudomonas* spp. (7), *Staphylococcus aureus* (4), *Streptococcus alpha-hemolytic* (2), *Citrobacter* spp. (1), and *Streptococcus viridans* group (1). These findings indicate a predominance of secondary infection by Gram-negative bacteria, especially enterobacteria, compared to Gram-positive bacteria. The development of opportunistic bacterial infections may suggest an increase in antimicrobial resistance cases, consequently reducing therapeutic options. The findings of this study contribute to the implementation and promotion of infection prevention and control practices, as well as the rational use of antimicrobials.

# Internal Quality Monitoring and inter-observer agreement of cytopathological tests carried out in the municipal laboratory of Manaus, Amazonas, Brazil.



## Author

Patricia Danielle Almeida - Universidade Federal do Amazonas (UFAM)  
Carlos Henrique L. G. Thomaz Branco - Universidade Federal do Amazonas (UFAM)  
Rita de Cássia Alencar Reffert - Universidade Federal do Amazonas (UFAM)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

Resolution n.002/2023 POSGRAD 2023/2024. Coordinator/Financial Aid



## Keywords

Quality indicators. Internal Quality Monitoring. Pap smears. Performance

## Abstract

**Introdução:** O rastreamento do câncer do colo do útero por meio do exame Papanicolau é a principal ferramenta de detecção precoce e tratamento, entretanto, alguns aspectos epidemiológicos e tipologia do perfil do exame na região ainda são desconhecidos para a compreensão da expressividade dos casos no município de Manaus. **Objetivo:** Investigação por meio de coleta de dados, foi realizado um estudo descritivo, retrospectivo e quantitativo dos resultados divulgados entre os anos de 2019 e 2022, com associação do perfil dos exames emitidos e a avaliação do desempenho dos citologistas atuantes em um laboratório municipal de Manaus, a fim de encontrar inconsistências na qualidade dos resultados. O estudo foi aprovado pelo Comitê de Ética em Pesquisa sob o número CAAE: 77894024.3.0000.5020. **Resultados:** Os achados deste estudo permitiram verificar que os resultados dos exames citopatológicos estão na faixa etária alvo para o rastreamento, porém, quando diagnosticada lesão intraepitelial escamosa de alto grau (HSIL), foram observados erros de seguimento em até um ano (64,16%). Apesar do desempenho laboratorial ser considerado satisfatório, 8 dos 21 principais citologistas apresentaram seus indicadores de desempenho abaixo da média. Destes 8 citologistas, 2 obtiveram resultados de concordância Kappa (k) médios considerados moderados e ruins, enquanto todos os 8 demonstraram problemas de concordância com as terminologias ASC e SIL. **Conclusão:** Os resultados encontrados demonstraram a importância de manter os números epidemiológicos e as pesquisas sobre o perfil dos exames atualizados para serem comparados com outras literaturas. O objetivo do trabalho foi fornecer embasamento para futuros estudos epidemiológicos na cidade de Manaus, visando melhor compreender o cenário atual da cidade em relação ao câncer de colo de útero.

# In Vitro Antifungal Activity Of Non-Steroidal Anti-Inflammatory Agents Against Sporothrix Spp.



## Author

Fernanda Riffel - Universidade Federal do Pampa (UNIPAMPA)  
Gabriela Seibert - Universidade Federal do Pampa (UNIPAMPA)  
Ana Luisa Reetz Poletto - Universidade Federal do Pampa (UNIPAMPA)  
Jennifer Veppo Prade - Universidade Federal do Pampa (UNIPAMPA)  
Débora Nunes Mario - Universidade Federal do Pampa (UNIPAMPA)  
Cheila Denise Ottonelli Stopiglia- Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

CAPES - 88887.820138/2023-00



## Keywords

sporotrichosis, itraconazole, anti-inflammatories

## Abstract

Sporotrichosis is a dermatozoonosis caused by fungi belonging to the *Sporothrix* spp., these microorganisms are thermodimorphic and saprophytic. It is characterized as a subcutaneous mycosis, with contamination occurring through traumatic injury. This infection has been neglected despite reports of resistance to the main antifungal drugs in the therapeutic regimen. This study evaluated the use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as nimesulide, acetylsalicylic acid, and ibuprofen against ten isolates of the species *S. brasiliensis* and *S. schenckii sensu stricto*. The assay was based on the Clinical and Laboratory Standards Institute (M38-A2) - reference method for broth microdilution testing for antifungal susceptibility against filamentous fungi. The NSAIDs were solubilized in dimethyl sulfoxide and diluted in culture broth to concentrations of 8 mg/mL - 0.01 mg/mL. Itraconazole was used as a standard antifungal at a concentration of 16 µg/mL - 0.03 µg/mL. The results showed that the drugs ibuprofen and nimesulide, at Minimum Inhibitory Concentrations (MIC) of  $\leq 1$  mg/mL and  $\leq 2$  mg/mL, respectively, were able to inhibit the growth of eight of the ten isolates evaluated, including microorganisms resistant to the antifungal itraconazole. Acetylsalicylic acid was less effective in treating sporotrichosis compared to the other anti-inflammatory drugs tested, with MIC  $\leq 4$  mg/mL against five isolates, four of which belonged to the species *Sporothrix brasiliensis*. It was concluded that all tested anti-inflammatory drugs demonstrated antifungal activity against the tested strains, with ibuprofen having the lowest MIC. This demonstrated a promising alternative for the treatment of sporotrichosis, potentially in combination with antifungal drugs.

# Partial results of the optimization of an enzyme-linked immunosorbent assay (ELISA) for the determination of thyroid-stimulating hormone (TSH) in capillary blood microsamples



## Author

Julia Paim da Luz - Universidade Novo Hamburgo(Feevale)  
Rafael Linden - Universidade Novo Hamburgo (Feevale)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

CAPES, CNPq/MCTI (408445/2023-8)



## Keywords

TSH, ELISA, Microsampling

## Abstract

TSH is the primary biochemical marker of thyroid function. The gold standard technique for its serum measurement is the ELISA assay, and the sample typically used is serum obtained from venous blood collected by phlebotomy. With technological advancements, minimally invasive collection procedures, such as obtaining capillary blood samples through finger pricking, have emerged as an interesting alternative. These samples can be applied to microsampling devices with passive plasma separation. This study aimed to present partial results of optimizing an ELISA method for quantifying TSH in capillary blood microsamples. The project was approved by the Feevale University Research Ethics Committee (ID: 80820024.1.0000.5348). A kit from Monobind Inc. (USA) was used. Different incubation times, with and without agitation, were investigated using 20  $\mu\text{L}$  samples (instead of the 50  $\mu\text{L}$  recommended). The optimized condition was applied to determine the assay's accuracy and precision. In this evaluation, quality control samples at concentrations of 1.5 (QCL), 3.75 (QCM), and 15  $\mu\text{UL/mL}$  (QCH) were tested in quintuplicate, with three repetitions. The optimized conditions included incubation with the enzymatic reagent for 180 minutes with agitation at 700 rpm, and incubation with the substrate for 30 minutes without agitation (as opposed to the 60 and 15 minutes indicated). Compared to the manufacturer's protocol, the optimized protocol increased absorbances by 174.5%. The intraday precisions were 11.5% (QCL), 9.1% (QCM), and 8.8% (QCH). The interday precisions were 2.2% (QCL), 3.2% (QCM), and 4.5% (QCH). The accuracies were 95.2% (QCL), 99.0% (QCM), and 103.2% (QCH). The modified technique allowed for effective measurement of TSH levels in reduced volume samples, demonstrating accuracy and precision. The next steps of the study will consist of determining TSH in dried plasma extracts derived from capillary blood and comparing these with serum quantifications.

# Emerging Challenges in One Health: Detection of Multidrug-Resistant and Methicillin-Resistant *Staphylococcus haemolyticus* and *Mammaliicoccus sciuri* in Wild Birds in Southern Brazil



## Author

Mateus Rocha Ribas - Laboratório de Microbiologia Molecular Aplicada (MiMA)  
Gustavo Rocha - Laboratório de Microbiologia Molecular Aplicada (MiMA)  
Juliana Lemos Dal Pizzol - Laboratório de Microbiologia Molecular Aplicada (MiMA)  
Victor Felipe Wolleck - Laboratório de Microbiologia Molecular Aplicada (MiMA)  
Vinicius Pais e Oliveira - Laboratório de Microbiologia Molecular Aplicada (MiMA)  
Tainá Bittencourt Klos - Instituto Espaço Silvestre  
Lucas Parra Cesar Nogueira Carreira - Instituto Espaço Silvestre  
Debora Rodrigues de Abreu - Instituto Espaço Silvestre  
Vanessa Tavares Kanaan - Instituto Espaço Silvestre  
Rafael Meurer - Associação R3 Animal  
Franciele Caetano - Associação R3 Animal  
Marzia Antonelli - Associação R3 Animal  
Sandro Sandri - Associação R3 Animal  
Cristiane Kiyomi Miyaji Kolesnikovas - Associação R3 Animal  
Daniel Barboza Capella - Laboratório de Ornitologia e Bioacústica Catarinense (LabOAC)  
Guilherme Renzo Rocha Brito - Laboratório de Ornitologia e Bioacústica Catarinense (LabOAC)  
Cleudson Valgas - Laboratório Central de Saúde Pública de Santa Catarina (LACEN-SC)  
Thais Cristine Marques Sincero - Laboratório de Microbiologia Molecular Aplicada (MiMA)  
Jussara Kasuko Palmeiro - Laboratório de Microbiologia Molecular Aplicada (MiMA)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

CAPES, CNPq/MCTI (408445/2023-8)



## Keywords

Methicillin-resistant Staphylococcaceae, Santa Catarina, Epidemiological surveillance

## Abstract

We assessed methicillin-resistant Staphylococcaceae in wild birds on Santa Catarina Island. Samples were collected from 173 wild-caught birds and 75 birds in rehabilitation centers using oropharyngeal swabs. Samples from R3 Animal Association were collected as part of The Santos Basin Beach Monitoring Project (PMP/BS). This project is a requirement set by Brazilian Institute of the Environment (IBAMA) for the environmental licensing of oil and natural gas production and transport by Petrobras in the pre-salt province under ABIO N° 640/2015. Samples from CETAS-SC were collected under the Public Notice n. 001/2018/IMA, which establishes a partnership between Instituto do Meio Ambiente de Santa Catarina and Instituto Espaço Silvestre to co-manage Santa Catarina Wildlife Rehabilitation Center (CETAS-SC). The process involved enriching swabs in TSB broth supplemented with cefoxitin, then allowing overnight incubation. Samples were plated onto Mannitol Salt Agar with a cefoxitin disk inserted. Colonies located near the disk were selected, identified using MALDI-TOF, and subjected to antimicrobial susceptibility testing via disk diffusion. Confirmation of methicillin resistance was conducted through PCR targeting *mecA*, *mecC* and *SCCmec*. Five isolates of methicillin-resistant *Mammaliicoccus sciuri* were found in five birds from birds at a rehabilitation center and demonstrate resistance to multiple drugs. Additionally, two methicillin-resistant *Staphylococcus haemolyticus* isolates were identified: one a bird from rehabilitation center and other in wild-caught bird, both resistant to multiple antibiotics and harboring *SCCmec* Type I. The results show that the *mecA* gene and *SCCmec* type I are circulating in the wild in a region where MRSA infections are not prevalent. This study enhances our understanding of antimicrobial resistance in Brazilian wild birds and highlights the crucial role of epidemiological surveillance in controlling the spread of resistant bacteria.

# Validation of a bioanalytical method for quantification of dipyrrone serum metabolites by high-performance liquid chromatography



## Author

Heloisa Pamplona Cunha - Universidade de Santa Catarina (UFSC)  
Bruna Soares Marques - Universidade de Santa Catarina (UFSC)  
Iasmim Fermiano Orsi - Universidade de Santa Catarina (UFSC)  
Edson Luiz da Silva - Universidade de Santa Catarina (UFSC)  
Flávia Martinello - Universidade de Santa Catarina (UFSC)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

Fundação de Amparo a Pesquisa de Santa Catarina - FAPESC



## Keywords

dipyrrone metabolites, validation, high-performance liquid chromatography

## Abstract

**Introduction:** Dipyrrone is used for pain and fever relief, known for its accessibility and low cost. After ingestion, it undergoes hydrolysis, yielding metabolites as 4-methylaminoantipyrine(4-MAA), 4-aminoantipyrine(4-AA), 4-acetylaminoantipyrine(4-AAA), and 4-formylaminoantipyrine(4-FAA). The metabolites can interfere with assays of biochemical parameters. A bioanalytical method capable of measuring metabolites in serum is required to understand the pharmacokinetics interference and establish potential associations between in vitro interference and in vivo metabolite concentrations post-dipyrrone ingestion. Objectives: Validate a method described in the literature, with modifications, for the identification and quantification of dipyrrone metabolites in human serum using high-performance liquid chromatography. **Methods:** The project was approved by the University Ethics Committee (CAAE:33933120.8.0000.0121). Serum samples spiked with metabolites were extracted with chloroform and sodium hydroxide. Analysis conditions: C18column (250x4.6mm;5µm), mobile phase of 50mM sodium acetate (pH6.2):acetonitrile (86:14v/v) in isocratic mode, flow rate of 1.25mL/min, detection at 257nm. **Results:** The method demonstrated adequate selectivity and linearity ( $r > 0.99$ ) for all metabolites. Detection and quantification limits met requirements based on concentrations reported in literature after 1g dipyrrone ingestion, except for 4-AA. Serum matrix did not interfere quantification of 4-AAA and 4-FAA; however, matrix effects were observed for 4-AA and 4-MAA. The method was accurate for all metabolites but exhibited adequate precision only for 4-AAA and 4-FAA. For quantifying 4-AA and 4-MAA, is recommended calculate the ratio area using an internal standard. Samples were not stable for subsequent-day analysis. **Conclusion:** The method proved valid for quantifying dipyrrone metabolites in human serum. Adjustments are necessary for improved performance, particularly regarding precision and stability.

# Electrochemical Detection Of Palmitoyl Thioesterase 1 (Ppt-1) - A New Strategy To Diagnosis Of The Neuronal Ceroid Lipofuscinosis.



## Author

Jhenifer Bueno Rosa - Universidade Estadual de Ponta Grossa (UEPG)  
Tayna Prestes Jacinto - Universidade Estadual de Ponta Grossa (UEPG)  
Dhésmon Lima - Mount Saint Vincent University - Halifax - Nova Scotia - Canada  
Karen Wohnrath - Universidade Estadual de Ponta Grossa (UEPG)  
Christiana Andrade Pessoa - Universidade Estadual de Ponta Grossa (UEPG)  
Ana Cristina Puhl - Collaborations Pharmaceuticals - Raleigh - North Carolina  
Juliana Inaba



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

Fundação Araucária



## Keywords

PPT1, NCL1, Immunosensor

## Abstract

Neuronal ceroid lipofuscinosis type 1 (NCL1) is a rare genetic disease resulting from a deficiency in the enzyme Palmitoyl Thioesterase 1 caused by a mutation of CLN1 gene. In this case occurs lysosomal accumulation of lipoproteins in the cells, leading to the pathogenesis. As consequence, progressive neurodegeneration and loss of the physical functions occur in children. Diagnosis is made by clinical and imaging findings which are only observed in advanced stages of the disease, where the lesions are already established and it can't be reversed. In this sense, the immunosensors emerge as an alternative tool, as they are capable of providing useful analytical information for the early diagnosis, promoting early intervention of various diseases, in addition to having a low cost, fast response and easy to use. With this in mind, a biosensor was developed using an oxidized glassy carbon electrode functionalized with protein A. This platform was used for anchoring anti-PPT1 monoclonal antibodies to detect PPT1. The platform was characterized through electrochemical measurements of electrochemical impedance spectroscopy (EIS), cyclic voltammetry (CV) and differential pulse voltammetry (DPV) using the  $[\text{Fe}(\text{CN})]^{6-4-3-}$  probe where it can be observed the incorporation of each monolayer in the device. An analytical curve of PPT1 detection was obtained and a linear relationship ( $y=11.724x+101.89$ ) was observed ( $R^2 0.99$ ). This immunosensor was able to detect PPT1, showed a detection limit of  $0.53 \text{ ng}\cdot\mu\text{L}^{-1}$  and a quantification limit of  $1.62 \text{ ng}\cdot\mu\text{L}^{-1}$ . The biosensor was selective for detecting PPT1 as it was not able to detect another lysosomal protein, the Fucosidase. Together the results demonstrated that this device is a promising tool for detecting and quantifying this PPT1. This system would be applied for PPT1 detection and quantification and this tool would be applied both to research studies as to evaluate the protein activity and promoting early detection of NCL1.



# Reference Change Value for capillary blood glucose: a tool to interpret whether two consecutive laboratory results are significantly different



## Author

Flávia Martinello - Universidade Federal de Santa Catarina (UFSC)  
Kênia Darós Zanette - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

No funding.



## Keywords

Biological Variation, Glucometer, Reference Change Value

## Abstract

**Introduction:** Laboratory tests provide essential information for the medical decision process but are subject to intrinsic variability that affects the generated results. Laboratory test results are interpreted by comparison with reference values or intervals obtained from individuals whose health status is known. This comparison can be cross-sectional (with a population) or longitudinal (with the individual themselves). One of the auxiliary tools in this process is the Reference Change Value (RCV), also known as critical difference, which calculated based on the intraindividual biological and analytical variation of the laboratory parameter. **Objective:** To define the RCV of capillary glycemia using G-TechFree Lite® glucometers. **Materials and Methods:** The study was approved by the ethics committee (CAAE 57812722.2.0000.0121). The coefficient of intraindividual biological variation (CVI) of capillary glycemia was studied using G-TechFree Lite® glucometers (Infopia Co.) in 40 healthy volunteers. Capillary blood samples were collected in fasting state and 30 minutes after a standardized breakfast, at weekly intervals over a period of ten weeks. The glucometer's analytical coefficient of variation (CVA) was obtained by analyzing 400 control sample results. The RCV was calculated using both symmetric and asymmetric methods. **Results and Discussions:** The glucometers showed a CVA of 4.0%, fasting CVI of 3.8% and a postprandial of 10.5%. The symmetric and asymmetric RCV were 15.3% and -12% and + 13.6% for fasting, and 31.1% and -22.9% and 29.7% for postprandial measurements, respectively. **Conclusion:** The RCV is defined as the statistically significant difference between two results from the same individual, taking into account the measurement error. To conclude that the difference between two consecutive capillary glycemia results using a G-Tech glucometer is significant and potentially relevant biologically, the difference must exceed the RCV.

# Health Evaluation of Endemic Disease Control Agents (ACE) in Santa Catarina state, southern Brazil.



## Author

Roberto Bayestorff Heberle - Universidade Federal de Santa Catarina (UFSC)  
Cristiane Ribeiro de Carvalho - Universidade Federal de Santa Catarina (UFSC)  
Camila Marchioni - Universidade Federal de Santa Catarina (UFSC)  
Liana Conrado França - Hospital Universitário Polydoro Ernani de São Thiago (HU - UFSC)  
Janer Alves Nogueira - Hospital Universitário Polydoro Ernani de São Thiago (HU - UFSC)  
Ana Carolina Ibarra dos Santos - Universidade Federal de Santa Catarina (UFSC)  
Claudia Regina dos Santos - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

Santa Catarina Research Foundation (Fapesc)



## Keywords

Endemic Disease Control Agents, Pesticides, Health Conditions

## Abstract

**INTRODUCTION:** *Aedes aegypti* is the main vector of dengue virus and contributes to the endemic character of dengue in Brazil. The vector control through the use of pesticides is performed by Endemic Disease Control Agents (ACE). The continuous exposure of ACE to pesticides, demands their health monitoring, which includes clinical laboratory exams. **OBJECTIVE:** To evaluate the health state of ACE in Santa Catarina state, through clinical laboratory exams. **MATERIAL AND METHODS:** The participants (n = 96) of this study are ACE from municipalities in Santa Catarina that agreed to participate. They were divided into two groups: applicators (n = 53), who were involved in the use and/or preparation of the insecticides Cielo® or Fludora®, and non-applicators (n = 43), who were not (control). This study was approved by the Ethics Committee for Research with Human Subjects (CEPSH) of Federal University of Santa Catarina (UFSC) under the number 5.318.352. Blood samples were collected from fasting participants in the municipalities of origin and sent to HU-UFSC/Ebserh through the Central Laboratory (LACEN). The hepatic, renal, and hormonal functions were evaluated using 15 laboratory tests for all participants. Data are expressed as mean  $\pm$  SEM and compared between the two groups of volunteers (non-applicator versus applicators) using one-way ANOVA. **RESULTS:** One-way ANOVA analysis revealed significant difference on creatinine levels  $0.89 \pm 0.02$  mg/dL vs.  $0.78 \pm 0.02$  mg/dL ( $F_{n-1} = X$ ,  $p < 0.05$ ) and total T3  $107.59 \pm 3.41$  ng/dL vs.  $124.08 \pm 3.78$  ng/dL ( $F_{n-1} = X$ ,  $p < 0.05$ ). The other biomarkers showed no significant difference, despite the applicator group sometimes presenting values closer to some alteration. **CONCLUSION:** Our study showed that ACE in the applicator group had elevated levels of creatinine and decreased levels of total T3 compared with non-applicator group. These results suggest that continuous exposure to pesticides could impair kidney and thyroid function.

# Diagnosis of enteric parasitosis with a focus on molecular characterization of *Giardia lamblia* and *Blastocystis* sp. in children from the Serrinha community, Florianópolis-SC



## Author

Marina Araújo - Universidade Federal de Santa Catarina (UFSC)  
Júlia Rodrigues de Paula - Universidade Federal de Santa Catarina (UFSC)  
Juliana Gois Nunes - Universidade Federal de Santa Catarina (UFSC)  
Vanessa Galvan - Universidade Federal de Santa Catarina (UFSC)  
Gabriella Rosa Monte Machado - Universidade Federal de Santa Catarina (UFSC)  
Karin Silva Caumo - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding



## Keywords

Molecular epidemiology; Pathogenic protozoa; Nested PCR

## Abstract

*Giardia lamblia* and *Blastocystis* sp. are among the most common protozoa found in human fecal samples and are among the main causative agents of diarrhea in children, especially those living in vulnerable water and food situations. In recent years, the high positivity of *Blastocystis* sp. in fecal samples from laboratory routine, awakens the need for molecular characterization studies for better understanding epidemiology. In this sense, the present study aimed to carry out Nested-PCR for identification and molecular characterization of the protozoa *G. lamblia* and *Blastocystis* sp. from fecal samples from children of the community of Serrinha, Florianópolis-SC. 152 samples were processed, through direct examination, spontaneous sedimentation method and method by Faust et al. Positive fecal samples were selected of *G. lamblia* and *Blastocystis* sp., for DNA extraction and PCR optimization and subsequent sequencing and classification. This study was approved by the Ethics Committee in Research from the UFSC, under CAAE number 59641322.1.0000.0121. In the analysis, it was observed that 64 samples (42%) were positive. The parasites found were: *Blastocystis* sp. (34,8%), *Endolimax nana* (21,2%), *Entamoeba coli* (16,7%), *Entamoeba histolytica*/*E. dispar* (9,1%), *G. lamblia* (7,6%), *Ascaris lumbricoides* (3%), *Iodameba butschlii* (3%), *Hymenolepis nana* (1,5%), *Enterobius vermicularis* (1,5%) and *Entamoeba hartmanni* (1,5%). Of the samples positive for *Blastocystis* sp., 84.8% were confirmed by nested PCR and classified as ST1, ST1b, ST2, ST3, ST3a, subtypes, which are the most related to symptomatic cases. Samples positive for *G. lamblia* were identified as belonging to assembly B, prevalent in human infections and other mammals, considered potentially zoonotic. The results of the present study may contribute to greater epidemiological understanding and surveillance for future control of sources of risk that cause water and food insecurity and directly affect the health of population.

# Relationship between reduced vitamin D and elevated TBARS in individuals with obesity



## Author

Laura Smolski dos Santos - Universidade Federal do Pampa (UNIPAMPA)  
Gênifer Ermindia Schreiner - Universidade Federal do Pampa (UNIPAMPA)  
Camila Berny Pereira - Universidade Federal do Pampa (UNIPAMPA)  
Carolina Pereira de Oliveira - Universidade Federal do Pampa (UNIPAMPA)  
Mohammad Prudêncio Mustafá - Universidade Federal do Pampa (UNIPAMPA)  
Jacqueline da Costa Escobar Piccoli - Universidade Federal do Pampa (UNIPAMPA)  
Vanusa Manfredini - Universidade Federal do Pampa (UNIPAMPA)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

Coordination of Superior Level Staff Improvement (CAPES)



## Keywords

Vitamin D, TBARS, Obesity

## Abstract

Obesity is characterized by excess body fat resulting from multifactorial origins, while vitamin D is a prohormone primarily synthesized through sun exposure. The inverse correlation between vitamin D and a BMI over 30 kg/m<sup>2</sup> links obesity to deficiency of this nutrient. This condition also increases pro-inflammatory adipokines, generating reactive oxygen species and oxidative stress in lipids. The study aimed to explore the relationship between vitamin D and thiobarbituric acid reactive substances (TBARS) in individuals classified as eutrophic, overweight, and obese. The research was approved by the Research Ethics Committee (REC) under registration number 5.308.525. A total of 192 participants were included: 96 men and 96 women, categorized by BMI into eutrophic, overweight, and obese groups. After signing the Informed Consent Form (ICF), venous blood samples were collected for vitamin D (mg/L) and TBARS (nmol MDA/mL) analysis. Data were analyzed with mean  $\pm$  standard deviation, normality test (Shapiro-Wilk). Parametric tests: ANOVA with Tukey; non-parametric tests: Kruskal-Wallis with Dunn ( $p < 0.05$ , GraphPad Prism 8.4). Results indicated that TBARS levels in men were eutrophic 33.62 $\pm$ 11.99, overweight 44.10 $\pm$ 22.77, and obese 46.56 $\pm$ 20.22. In women, eutrophic was 30.70 $\pm$ 13.61, overweight 35.53 $\pm$ 15.30, and obese 40.26 $\pm$ 10.80. For vitamin D levels, in men eutrophic was 27.32 $\pm$ 6.33, overweight 24.71 $\pm$ 5.67, and obese 23.15 $\pm$ 3.94. In women, eutrophic was 24.37 $\pm$ 5.74, overweight 25.15 $\pm$ 4.58, and obese 25.85 $\pm$ 8.88. TBARS levels were higher in obese individuals, while vitamin D levels were lower compared to overweight and normal weight groups. In women, although TBARS were elevated in the obese group, there were no statistically significant differences in vitamin D. Thus, TBARS levels showed an inverse relationship with vitamin D in obese men, suggesting that the inflammatory process of obesity affects the redox status of these individuals.

# Prevalence of pharmaceutical and personal care products and drugs in aquatic environment and occurrence of the antimicrobial resistance in Brazil: a systematic review



## Authors

Izadora Borgmann Frizzo - Universidade Federal de Santa Catarina (UFSC)  
Tainá Larissa Lubschinski - Universidade Federal de Santa Catarina (UFSC)  
Eduarda Mohr - Universidade Federal de Santa Catarina (UFSC)  
Juliana Lemos Dal Pizzol - Universidade Federal de Santa Catarina (UFSC)  
Izabel Galhardo Demarchi - Universidade Federal de Santa Catarina (UFSC)  
Jussara Kasuko Palmeiro - Universidade Federal de Santa Catarina (UFSC)  
Thaís Cristine Marques Sincero - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

his work was supported by the scholarships from the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Brazil) under Grant [Financial code 001]



## Keywords

Water Pollutants, Brazil, Antimicrobial resistance

## Abstract

Pharmaceuticals, personal care products (PPCPs), and drugs can pose potential risks to the environment and health, such as the increased selection and horizontal transfer of genes involved in antimicrobial resistance. However, in Brazil, there is no legislation that mentions or regulates the presence of these pollutants in the environment. This systematic review follows PRISMA and Cochrane recommendations. The search strategy was conducted according to the PECOS acronym and included searches in five bibliographic databases and one gray literature database. A total of 10,675 studies published in the last ten years were obtained. All articles were transferred to My Web EndNote, where 2,809 duplicates were removed. The next step involved the selection of studies using Rayyan QCRI. Titles and abstracts of the studies were independently and blindly screened by two reviewers, resulting in the exclusion of 9,342 studies and the inclusion of 88 studies. Finally, the potentially eligible studies were evaluated in full text, resulting in the inclusion of 60 studies. Preliminary results indicated that among the most frequently investigated pharmaceuticals are hormones, anti-inflammatories, antihypertensives, anticonvulsants, antibiotics, and beta-blockers. Regarding PPCPs, preservatives were more frequent. Few studies have investigated the occurrence of illicit drugs (n = 6). Among these, there was low variability of compounds analyzed (only 4 compounds), with the most frequent being benzoylecgonine, cocaine, and caffeine. Most of the studies focused on the southeastern region (São Paulo and Rio de Janeiro), followed by the southern region (Rio Grande do Sul). These results are relevant for understanding the nature and quantity of these contaminants in order to assist in the planning of regulatory standards that monitor their presence in the environment and, consequently, minimize risks. The next steps will consist of evaluating the quality of the studies.

# Brazilian Epidemiological Data On Syphilis Acquired Before And During The Covid-19 Pandemic



## Author

Rafael Andrade Menolli - Universidade Estadual do Oeste do Paraná (UNIOESTE)  
Isabella Caroline Pilatti - Universidade Estadual do Oeste do Paraná (UNIOESTE)  
Julia Garbin - Centro Universitário Univel  
Ana Claudia Paiva Alegre Maller - Centro Universitário Univel



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

N/A



## Keywords

Treponema pallidum, pandemic, underreporting

## Abstract

Syphilis, caused by the bacterium *Treponema pallidum*, is an infectious disease that represents a major public health problem. It is diagnosed using treponemal and nontreponemal tests in combination, and its treatment is carried out with antibiotics. The objective of this study was to verify the number of syphilis cases in Brazil from 2018 to 2021, comparing periods before and during the COVID-19 pandemic, for the parameters of sex, age group and region of Brazil. This was a cross-sectional and quantitative study of syphilis acquired between 2018 and 2021 based on epidemiological data from bulletins and DATASUS in the public domain. In 2018, 159,329 cases were reported in the country, with the Southeast Region having the highest proportion. In 2021, the number of records was 64,279, a decrease of 40.3%. For gender, in 2018 and 2019, the number of cases was similar, with men having almost 25 thousand more cases in both years. During the COVID-19 pandemic, 2020 and 2021, there was a decrease in the detection of syphilis; however, the male predominance continued. The rate of pregnancy reached 21.8 cases per 1,000 live births in 2019, which is well above the 74.2 cases per 100,000 inhabitants in the general population. The following year saw a reduction, reaching 74.2 cases per 100,000 inhabitants. In 2020, this rate was 54.5 cases per 100,000 inhabitants. In 2018 and 2019, there were approximately 95 thousand cured men and 66 thousand women, respectively. During the pandemic, there was a decrease in the cure rate. Despite the apparent decrease in deaths in 2020/2021 compared to those in the 2018/2019 period, this difference is likely due to the lower number of notifications. There was a notable reduction in the incidence of acquired syphilis during the COVID-19 pandemic, possibly due to the demand it generated, causing other diseases to be underreported.

# Immunological changes in farmers in different agricultural crops



## Author

Simony Costa Beber - Universidade Federal do Rio Grande do Sul (UFRGS)  
Shanda Cattani - Universidade Federal do Rio Grande do Sul (UFRGS)  
Ingrid Flesh - Universidade Federal do Rio Grande do Sul (UFRGS)  
Larissa Cestonaro - Universidade Federal do Rio Grande do Sul (UFRGS)  
Lucas Augsten - Universidade Federal do Rio Grande do Sul (UFRGS)  
Thainá Zanenga - Universidade Federal do Rio Grande do Sul (UFRGS)  
João Queiroz - Universidade Federal do Rio Grande do Sul (UFRGS)  
Marcelo Dutra Arbo - Universidade Federal do Rio Grande do Sul (UFRGS)  
Solange Cristina Garcia - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

Projeto aprovado para SCC, fapergs/PesqGaicho; CNPq)



## Keywords

pesticides, immune system, chronic non-communicable diseases

## Abstract

**Introduction:** Brazil is the country that consumes the most pesticides in the world. Along these lines, studies on the health of Brazilian farmers are very important, especially on pathophysiological changes, such as immunological and inflammation. These changes contribute to the development of chronic non-communicable diseases, such as autoimmune, cardiovascular and allergic diseases. **Objective:** To study inflammatory and immunological/allergic changes through peripheral biomarkers in farmers from different agricultural crops in RS. **Methodology:** the project has already been accepted by the UFRGS Research Ethics Committee (5.752.224) and by the CAAE: 69865417.1.0000.5347. Rural workers occupationally exposed to agrochemicals, being: N=30 on tobacco plantations (T); N=30 soybean/corn plantation (S) and administrative workers N=30 (C), not occupationally exposed to agrochemicals. IgG, IgM, C3, C4 and PCR were analyzed in serum using the Mindray® BS-120 Chemistry Analyzer equipment, using the immunoturbidimetric method, with commercial kits. **Results:** C3 was increased in both groups of farmers compared to those not occupationally exposed ( $p < 0.0040$  and  $0.0137$ ), and group S presented means above reference values. In the tobacco group, IgM was increased compared to the non-exposed group ( $p < 0.0281$ ). The other biomarkers did not show changes between the groups or above the established reference values. The partial results demonstrate that there is a challenge for the immune system and/or allergen response in the groups studied. In this sense, it is important to monitor these workers with frequent laboratory tests for possible progression over time to the development of chronic non-communicable and autoimmune diseases. **Conclusion:** Occupational exposure to toxic chemicals, such as agrochemicals, is a public health problem, studies are essential to support public decision-making and the health of this population, such as technical-scientific studies in the area.

# Neonatal Outcomes Of Pregnant Women With Early Versus Late Preeclampsia



## Author

Marcela Abbott Galvão Ururahy - Universidade federal do Rio Grande do Norte (UFRN)  
Julia Guedes de Araujo Duavy - Universidade federal do Rio Grande do Norte (UFRN)  
Beatriz Maia de Paiva - Universidade federal do Rio Grande do Norte (UFRN)  
Sarah Dantas Viana Medeiros - Universidade federal do Rio Grande do Norte (UFRN)  
Karla Simone Costa de Souza - Universidade federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

None



## Keywords

preeclampsia, neonatal outcomes, maternal parameters

## Abstract

Preeclampsia (PE) is a pregnancy-specific disease that develops from the 20th week of gestation characterized by increased blood pressure ( $\geq 140 \times 90$  mmHg) accompanied by proteinuria and/or target organ dysfunction. PE is associated with both maternal and neonatal morbidity and mortality. Prematurity, low birth weight, respiratory distress syndrome (RDS) and sepsis are the main neonatal outcomes associated to PE. The aim of the present study was to evaluate clinical-laboratorial parameters of pregnant women with early and late PE and the neonatal outcomes. This is a longitudinal, observational and prospective study approved by the Ethics in Research Committee of University Hospital Onofre Lopes (protocol number 3.624.069). Thirty-two pregnant women diagnosed with PE, as well as their respective neonates, were allocated in two groups: early PE (PE onset < 34 weeks of gestation) (n=21) and late PE (PE onset  $\geq$  34 weeks of gestation) (n=11). For the evaluation of biochemical (creatinine, urea, AST, ALT, LDH) and hematological (platelet count) parameters, fasting blood were collected from the pregnant women. Urine samples were also collected for proteinuria determination. Maternal and neonatal data were also obtained from electronic medical records. The early PE group had the lowest number of prenatal consultations (p=0.032), higher values of maternal diastolic blood pressure at admission (p=0.049) and maternal urea (p=0.029), as well as lower gestational age (p=0.004) and birth weight (p=0.021), higher rate of admission to the neonatal intensive care unit (p<0.001), sepsis (p=0.014), RDS (p=0.003) and need for ventilatory support (p=0.027). Thus, the findings of the present study suggest that early PE has an important impact in the neonatal outcomes.



# Evaluation of circulating endothelial cells as possible diagnostic markers in preeclampsia: a systematic review



## Author

Beatriz Paiva - Universidade federal do Rio Grande do Norte (UFRN)  
Arthur Renan de Araújo Oliveira - Universidade federal do Rio Grande do Norte (UFRN)  
Stephany Ann Costa do Rosário - Universidade federal do Rio Grande do Norte (UFRN)  
Jéssica Amanda Moura da Costa - Universidade federal do Rio Grande do Norte (UFRN)  
Matheus Eduardo do Nascimento Barreto - Universidade federal do Rio Grande do Norte (UFRN)  
Rand Randall Martins - Universidade federal do Rio Grande do Norte (UFRN)  
Ricardo Ney Oliveira Cobucci - Universidade federal do Rio Grande do Norte (UFRN)  
Marcela Abbott Galvão Ururahy - Universidade federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Clinical Laboratory Analysis and Diagnosis



## Funding

None



## Keywords

Biomarker, Circulating Endothelial Cells, Preeclampsia

## Abstract

Preeclampsia (PE) affects approximately 5% of pregnant women worldwide. Furthermore PE is associated with several complications which may culminate in maternal and/or fetal death. The identification of reliable diagnostic markers of PE could lead to early intervention and the consequent significant decrease in both maternal and fetal complications. One of the factors involved in the pathogenesis of PE is endothelial dysfunction, causing the release of circulating endothelial cells (CECs). Thus, the aim of this systematic review (SR) was to evaluate the count number of the CECs in blood samples in pregnant women with PE when compared to normotensive pregnant women. PubMed, LILACS, Scopus, Embase, Web of Science, ScienceDirect, Cochrane Library, and Gray-literature were searched. Observational studies (cross-sectional, case-control and cohort), published in any language until July 2022, involving pregnant women diagnosed with preeclampsia and count number of CECs were selected. Two reviewers independently screened the articles by title and abstract, then assessed them for eligibility, extract data and risk of bias using the Newcastle-Ottawa Scale. The extracted data were primarily descriptive and included information on study name, first author's last name, country of origin, year of publication, study design, methods, participants, data related to the patients involved. The guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were followed. A protocol was developed and published on PROSPERO (Registration number 2021 CRD42021226265). In total, 505 articles were identified, 338 were reviewed, and 6 were included. Five studies have shown a statistically significant difference in CECs counts in pregnant women with preeclampsia compared to the control group. The majority studies included in this SR demonstrated that the CECs count may be used as a new biomarker for PE diagnosis, answering the research question.

**Area**

# **Pharmaceutical Policies and Care**

# Contributing To The Quality Of Treatments For Patients With Rheumatoid Arthritis: Construction Of An Application



## Author

Marina Raijche Mattozo - Rover Universidade Federal de Santa Catarina (UFSC)  
Anna Giulia Cruz - Rover Universidade Federal de Santa Catarina (UFSC)  
Bruna Bastian da Costa - Rover Universidade Federal de Santa Catarina (UFSC)  
Nathalia Nunes Loureiro - Rover Universidade Federal de Santa Catarina (UFSC)  
Mariana Bach - Rover Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Santa Catarina State Research and Innovation Support Foundation (FAPESC) N°: 2022TR001393.



## Keywords

Rheumatoid Arthritis, Pharmaceutical Care, Digital Health

## Abstract

Patients undergoing treatment for Rheumatoid Arthritis (RA) are particularly concerned about the risks associated with the use of medications, the impact of the disease on their quality of life, and the existing barriers to systematic monitoring by the healthcare team. Based on this need, the development of an application to help patients with RA began. In this research (2022 and 2023), the characteristics and difficulties presented by patients were raised through interviews. Other information was obtained from researchers, computerized systems and health databases. Therefore, a database was developed in Google Sheets® and validated by health professionals. The Content Validity Index and Cronbach's alpha were used for the analyses. The project was approved by the Ethics Committee (CAAE 74833423.5.0000.0121 - Opinion 6,481,416). The general characteristics of the population were: majority women, over 40 years old, undergoing treatment with three or more medications. Part of this referred to adverse reactions and searching the internet for questions regarding the treatment. Among the needs raised, the management of adverse reactions and the rights of people living with RA stand out. The database was divided into 12 themes, such as: Average response time to treatment; Access to medicines; Management of adverse reactions; Patients' rights; Other services and care. The database was validated by different health professionals (S-CVI = 0.98 and Cronbach's alpha 0.82). The development of this research contributed to a greater understanding of treatments, patients' needs and resources available in the Health System. This research expanded access to information about RA and the care involved, which is being used to create a friendly user interface in the application. It is expected that the application can assist in self-care, improving treatments and prognoses.

# Challenges and strategies for pharmaceutical prescription



## Author

Alana Louise Exterkortter - Universidade Federal de Santa Catarina (UFSC)  
Áurea Elizabeth Linder- Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

None



## Keywords

community pharmacist, rational use of medicines, over the counter

## Abstract

**Introduction:** Community pharmacies are the main entry for health services, where pharmacists play a key role solving people's questions about medicines and giving advice on over-the-counter medicines (OTCs) through pharmaceutical prescription. In Brazil, pharmacists can prescribe OTCs, which are considered low-risk medications when used for a brief period, and they are mostly used for minor health ailments. But, due to easy access to OTCs, self-medication abuse with them is a worldwide concern. Pharmaceutical prescription emerged as a solution for assisting population with minor health illness, helping to solve the overload on public health and to prevent abuse of self-medication, prioritizing rational use of drugs. Despite this, in Brazil, the practice of pharmaceutical prescription is recent (2013), and there are few data about how it works. **Objective:** to better understand how pharmacists prescribe OTCs in Brazil, especially in the State of Santa Catarina, and develop a guideline for prescribing OTCs, unveiling the main concerns raised by these professionals involving the practice. **Methodology:** this research is descriptive and cross-sectional. An online questionnaire was made available and disseminated through flyers with a QR code and through social networks (approved by Plataforma Brasil #6.281.047). From there, information to meet the needs raised by pharmacists was sought in reliable scientific and governmental databases to prepare educational material. **Results:** forty-five pharmacists answered the questionnaire, the majority from Santa Catarina State. An educational material providing information about legislation, mechanisms of action and indications for OTCs prescription, as well as information on anamnesis was prepared and distributed to pharmacists through social networks **Conclusion:** We hope that the dissemination of reliable information to guide pharmacists on their prescription practice can contribute to improve public health in Brazil.

# Pharmacological treatments for Chagas disease: an evidence gap map



## Author

Julia Barbosa Domingues da Silva - Universidade Federal do Paraná (UFPR)  
Helena Hiemisch Lobo Borba - Universidade Federal do Paraná (UFPR)  
Fernando Fernandez-Llimos -University of Porto



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Non funded



## Keywords

Chagas disease, Evidence gap map, Systematic review

## Abstract

Chagas disease, is a potentially life-threatening neglected tropical disease (NTD) affecting about 7 million people worldwide, most of them in Latin American countries. Its management requires access to safe and effective drugs, nevertheless, a low investment in new health technologies is observed. Hence, the goal of this research was mapping the available evidence on current and developing pharmacological therapies for Chagas disease and to present the results in an Evidence Gap Map (EGM). A systematic review (SR) was conducted according to a predefined protocol. The PubMed database was searched in July 2023. Additionally, ongoing clinical trials were searched through ClinicalTrials.gov. Included studies comprised randomized clinical trials (RCT), ongoing phase 1 to 3 clinical trials (CT), and systematic reviews. Six SR, twelve RCT and six ongoing CT were included. Two EGMs were developed: one focusing on the antitrypanosomal drugs and one on the treatment of cardiovascular symptoms. The antitrypanosomal drugs comprised benznidazole, nifurtimox, posaconazole, ravuconazole and allopurinol, which were evaluated for the following efficacy outcomes: mortality, cardiovascular/cerebrovascular parameters and response to therapy. The EGM of symptomatic treatment included antiarrhythmic drugs, antihypertensives, statins and botulinic toxin to treat dysphagia and chagasic achalasia. Efficacy outcomes included mortality, hospitalization, cardiovascular/cerebrovascular parameters, inflammatory markers and esophageal function in chagasic achalasia. Safety outcomes for both EGMs comprised adverse events, treatment discontinuation, liver and renal function, and hematological events. In summary, there are significant gaps in the existing evidence, and the quality of the available studies may limit its application. In addition, there are few studies on new drugs. Therefore, the EGMs may guide researchers regarding further studies on the topic.

# Association between demographic and social variables with the use of health services from the perspective of access to medicines



## Author

Helena Luiza Kirsten Sasse - Universidade Regional de Blumenau (FURB)  
Monica Nunes da Trindade - Universidade Regional de Blumenau (FURB)  
Ernani Tiaraju de Santa Helena - Universidade Regional de Blumenau (FURB)  
Luana Gabriele Nilson - Universidade Regional de Blumenau (FURB)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

PIBIC/CNPq. Projeto n. 317/2023



## Keywords

Effective Access to Health Services, Access to Essential Medicines and Health Technologies, Socioeconomic Factors

## Abstract

The use of health services stems from a complex combination of factors, ranging from need, perception, sociodemographic characteristics and the individual's values. Socioeconomic differences in access and use frame health needs and the search for services. The availability of medicines is an indicator of access, as the lack of medicines weakens the healing, rehabilitation and prevention process. Objective: To analyze the association of demographic and social variables with the search for a pharmacy from the perspective of access to medicines. This is a population-based, cross-sectional epidemiological study of people of both sexes aged between 20 and 79 who took part in the SHIP-Brazil study and sought pharmacy services. Sociodemographic and lifestyle variables were examined. The frequency of visits to the pharmacy was estimated and its association with the variables was obtained using the Chi-square test ( $p$ -value  $< 0.05$ ). There was a predominance of females (58.2%), aged between 20 and 39 years (40.0%), Germanic (61.4%), medium socioeconomic status (SES) (67.1%) and without health insurance (60.2%). Participants reported their level of physical activity as active (63.8%), low risk of alcohol consumption (71.0%) and never smoked (70.0%). Being female ( $p=0.023$ ) and having better SES ( $p=0.001$ ) showed a statistical association with greater demand for the pharmacy. The availability of medicines is an indicator of access that is influenced by socioeconomic, structural and organizational factors. In this study, the predominance of women, young people, people of Germanic origin, with a high SES and no health insurance characterized the profile of the participants who sought out the pharmacy service. Their lifestyles were healthy, with the majority being physically active, with low alcohol consumption and no history of smoking. Being a woman and having better SES were statistically associated with seeking pharmacy services, corroborating the literature.

# Efficacy and safety of biologic therapy in biologic-naïve and biologic-experienced patients with moderate to severe Crohn's disease: a network meta-analysis



## Author

Daniela Gorski - Universidade Federal do Paraná (UFPR)  
Raul Edison Luna Lazo - Universidade Federal do Paraná (UFPR)  
Dalton de Assis de Souza - Universidade Federal do Paraná (UFPR)  
Helena Hiemisch Lobo Borba - Universidade Federal do Paraná (UFPR)  
Fernanda Stumpf Tonin - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

None



## Keywords

Monoclonal Antibody, Interleukin Inhibitors, RCT Comparison

## Abstract

Crohn's is a chronic inflammatory bowel condition with remitting-relapsing course. Biological agents are often used as second-line treatment, yet whose their clinical effects may differ according to patients' prior use of these drugs. Our aim was to synthesize the evidence on the efficacy and safety of biological drugs for treating moderate-to-severe Crohn's disease in adults. A systematic review of randomized clinical trials was performed with searches in PubMed, Scopus, and Web of Science (up to February 2024). Network meta-analyses were conducted using NMA Studio 2.0 to assess clinical remission and serious adverse effects. Results were reported as relative risks (RR) and 95% confidence interval (CI) with additional p-score analysis to rank therapies. This study included 46 studies (n=13,015 patients). In patients with prior biologic use, guselkizumab 200mg demonstrated the highest remission probability (p-score 0.93, RR 5.94 [95% CI 1.95-18.04] vs. placebo), followed by guselkizumab at 600mg (p-score 0.87) and 1200mg (p-score 0.75). Currently recommended drugs such as adalimumab 80/40mg and ustekinumab 6mg/kg/90mg also showed high probabilities to lead to patients' remission (p-scores 0.88 and 0.8, respectively), while ustekinumab 4.5mg/kg was ranked last (p-score 0.14). For treatment-naïve patients, mirikizumab 1000mg was more associated to clinical remission (p-score 0.87, RR 14.33 [95% CI 0.75-275.66] vs. placebo), followed by infliximab 5mg (p-score 0.87); while onecerpt at doses of 50mg and 25mg showed poorer results (p-scores 0.2 and 0.1, respectively). Both guselkizumab and mirikizumab presented reasonable safety profiles (p-score ranging from 0.8-0.49). In conclusion, although not yet recommended in clinical practice, recent drugs such as guselkizumab and mirikizumab (IL23 inhibitors) show promising effects to manage Crohn's disease in both biologic-experienced and treatment-naïve patients.

# Guidelines for the Dispensing of Medications in Community Pharmacies: a scoping review protocol



## Author

Marcelo Rodrigues Reser - Universidade Federal de Santa Catarina (UFSC)  
Luciano Soares - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

None



## Keywords

Guidelines; dispensing; community pharmacies.

## Abstract

**Introduction:** The Brazilian Pharmaceutical Services Policy celebrate 20 years in 2024. It was proposed and approved by pharmacists and health social movements, highlighting its crucial role in this field. However, to become health leaders and drive policy change, individuals need to have the necessary skills and knowledge. To address this, the Integra Project has created and implemented a virtual course, and to assess its effectiveness, a competencies framework was developed. **Objective:** To describe a competency framework elaborated to evaluate learning strategies aiming to train health leaders. **Methods:** The evaluation framework was based on Kirkpatrick's Four Levels of Evaluation and the skills, knowledge, and abilities necessary for a health leader to promote policy change. To be able to evaluate the early and late effects of the training, it was elaborated three surveys to be applied at different time points. Results: The evaluation consists of three surveys. The first survey has 26 Likert scale questions and is given before the training. The second survey has the same questions plus 29 more about course satisfaction (level 1 of Kirkpatrick's evaluation model) and is given after the training. The third survey assesses behavioral changes (levels 3 and 4 of Kirkpatrick's evaluation model) and has 10 closed-ended and 1 open-ended question. The open-ended question aims to capture any changes in professional practice. The third survey is given one year after training completion. Data analysis involves descriptive statistics for the first and third levels and pre-and post-training responses comparison for the second level. The open-ended questions are analyzed using thematic analysis by a deductive approach, considering the intended skills and competencies. **Conclusion:** The evaluation framework was able to capture gained knowledge, skills, and abilities in all levels of KirkPatrick's models as well as early and long-lasting effects of training.



# Competencies framework to evaluate leadership skills on Pharmaceutical Policies



## Author

Fernanda Manzini - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)  
Luísa Arueira Chaves - Universidade Federal do Rio de Janeiro (UFRJ)  
Célia Machado Gervásio Chaves - Federação Nacional dos Farmacêuticos (Fenafar)  
Adelir Rodrigues da Veiga - Federação Nacional dos Farmacêuticos (Fenafar)  
Jorge Antonio Zepeda Bermudez - Fiocruz  
Jorge Carlos Santos da Costa - Fiocruz



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Fiocruz - Projeto: VPPIS-011-FIO-23



## Keywords

Pharmaceutical Services, pharmacy education, health policy

## Abstract

**Introduction.** The Brazilian Pharmaceutical Services Policy celebrate 20 years in 2024. It was proposed and approved by pharmacists and health social movements, highlighting its crucial role in this field. However, to become health leaders and drive policy change, individuals need to have the necessary skills and knowledge. To address this, the Integra Project has created and implemented a virtual course, and to assess its effectiveness, a competencies framework was developed. **Objective:** To describe a competency framework elaborated to evaluate learning strategies aiming to train health leaders. **Methods:** The evaluation framework was based on Kirkpatrick's Four Levels of Evaluation and the skills, knowledge, and abilities necessary for a health leader to promote policy change. To be able to evaluate the early and late effects of the training, it was elaborated three surveys to be applied at different time points. **Results:** The evaluation consists of three surveys. The first survey has 26 Likert scale questions and is given before the training. The second survey has the same questions plus 29 more about course satisfaction (level 1 of Kirkpatrick's evaluation model) and is given after the training. The third survey assesses behavioral changes (levels 3 and 4 of Kirkpatrick's evaluation model) and has 10 closed-ended and 1 open-ended question. The open-ended question aims to capture any changes in professional practice. The third survey is given one year after training completion. Data analysis involves descriptive statistics for the first and third levels and pre-and post-training responses comparison for the second level. The open-ended questions are analyzed using thematic analysis by a deductive approach, considering the intended skills and competencies. **Conclusion:** The evaluation framework was able to capture gained knowledge, skills, and abilities in all levels of KirckPatrick´s models as well as early and long-lasting effects of training.

# Social and technical aspects of municipal pharmaceutical policy management: first analysis of the QUALIFICA.AF-SC



## Author

Patricia Bernardi Sassi - Universidade Federal de Santa Catarina (UFSC)  
Samara Jamile Mendes - Universidade Federal de Santa Catarina (UFSC)  
Rafaela Tavares Peixoto - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

FAPESC - N° 2021TR000703



## Keywords

Pharmaceutical services; Management health; SUS

## Abstract

Pharmaceutical Services (PS) has been consolidated in Brazil as the public policy to guarantee access to medicines. The management of pharmaceutical services in municipalities is a strategic service, considering the challenges of decentralization and municipalization in the SUS. The socio-technical organization has been the subject of studies in the field of pharmaceutical services management. This study analyzed the perception of pharmacists and managers regarding the socio-technical aspects of municipal PS. It is a qualitative study that used the focus group (FG) technique for data collection. Six focus groups were held with municipalities in the state of Santa Catarina, qualified under the structure axis of the Qualifar-SUS Program. The municipalities were grouped using the criterion of participation by PS management in municipal health management activities, with previous information from a national study in 2021. The FGs were conducted face-to-face in three locations in the state. The conversations were recorded. Thematic analysis is being used to find themes based on extensive reading of the transcripts. A total of 35 municipalities with 39 pharmacists and PS representatives took part in the FGs. It was observed that the perception of municipal PS managers considering technical, social and political aspects within the organizations can compromise the development of pharmaceutical services, access to medicines, the application of Qualifar-SUS resources and the structuring of municipal PS. The first analysis revealed: the need to institutionalize PS in a practical way; structuring and recognition of PS in the municipalities; decentralization of actions to the municipalities; and the importance of agreements that strengthen municipal PS. The return of the results to the municipalities will contribute to the advancement of PS management processes, in order to strengthen PS policy and contribute to access and rational use of medicines.

# Estimating The Safety Of Anticoagulation With Warfarin Using The Medication Regimen Complexity Index In Users Of A Health Condition Management Service



## Author

Josiane Costa de Sá - Universidade Federal de Alfenas (UNIFAL)  
Márcia Viviane dos Santos - Universidade Federal de Alfenas (UNIFAL)  
Yasmin dos Santos Louzano - Universidade Federal de Alfenas (UNIFAL)  
Karen Cristina Cassia Roesler da Silva - Universidade Federal de Alfenas (UNIFAL)  
Camila Campos Dutra - Universidade Federal de Alfenas (UNIFAL)  
Raquel Tognon Ribeiro - Universidade Federal de Alfenas (UNIFAL)  
Iara Baldim Rabelo Gomes - Universidade Federal de Alfenas (UNIFAL)  
Leilismara Sousa Nogueira - Universidade Federal de Alfenas (UNIFAL)  
Tiago Marques dos Reis - Universidade Federal de Alfenas (UNIFAL)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

None



## Keywords

Anticoagulants; Pharmaceutical Services; Medication regimen complexity index.

## Abstract

Warfarin is an oral anticoagulant indicated to reduce the primary and secondary risks of thromboembolic events. Due to its low therapeutic index, it requires continuous monitoring. Drug and/or food interactions and the medication regimen complexity can also affect the effectiveness and safety of the treatment and require frequent adjustments to the warfarin dose. The medication regimen complexity index (MRCI) determines the complexity of therapeutic regimens and taking into consideration factors such as formulation, number of drugs, dose frequency and instructions on necessary care during administration. Studies have associated MRCI with higher hospitalization rates and lower quality of life. The objective of this study was to estimate the safety of the anticoagulation in warfarin users using the MRCI. This is a cross-sectional study that evaluated the MRCI of 10 patients followed from March to June 2024 in the anticoagulation management service offered at the university pharmacy of a public university in the south of Minas Gerais, Brazil. The MRCI contains 65 items covering three sections (pharmaceutical formulation, dosing frequency and additional instructions) and was calculated for each patient. Scores between 2.0-5.0 for adults and 2.0-7.0 for the elderly are considered low complexity. MRCI scores greater than 13.0 for adults and 15.0 for the elderly indicate high complexity. Most patients were female (70.0%), and mean age was 56.10 (SD=13.0). The median for MRCI was 11.5 (IQR 7.0 to 26.0) points for adults and 26.0 (IQR 23.0 to 30) points for the elderly. Considering the group of adult patients, 42.9% had highly complex pharmacotherapy and among the elderly it was 100%, which may reflect difficulty in controlling the International Normalized Ratio. Thus, an increased risk of thromboembolic and hemorrhagic events in the group is estimated. Future studies will be conducted to evaluate a possible association between time in therapeutic range (TTR) and MRCI.

# Drug donations: A scoping review of the benefits and challenges



## Author

Felipe Felizardo Mattos Vieira - Universidade Federal do Paraná (UFPR)  
Maria Luiza Soares - Universidade Federal do Paraná (UFPR)  
Fernanda Stumpf Tonin - Universidade Federal do Paraná (UFPR)  
Inajara Rotta - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

None



## Keywords

health inequities, health services accessibility, access to essential medicines and health technologies

## Abstract

Inequity in access to medicines is a persistent problem, particularly in low- and middle-income countries. Drug donations represent a commonly employed strategy to mitigate these disparities. This scoping review aimed to answer the questions: How do drug donation programs operate in Brazil and other countries? What are the public health impacts of these donations? Do these donations contribute to reducing inequities in access to medicines? This study was reported following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement for Scoping Reviews (PRISMA-ScR), and the review protocol was registered in the Open Science Framework (10.17605/OSF.IO/TPV36). Searches in the Scopus and PubMed databases were performed to identify pertinent articles, regardless of study design. Books/book chapters, literature reviews, guidelines and articles published in non-Roman characters were excluded. The selection of studies was performed by two independent reviewers with possible discrepancies being resolved by a third reviewer. From the initial 899 publications identified through title and abstract screening, 167 were selected for full-text review and 40 publications were included in this review. These publications spanned a 33-year timeframe, which allowed us to understand the evolution of drug donation programs in at least 20 different countries. The findings revealed different impacts on local public health and implications for guaranteeing access to medicines. Among the publications, we identified 14 related to drug donation programs that contributed to access to essential medicines, especially for patients with precarious financial situations, or related to specific endemic diseases. The drug donations can play a valuable role in addressing inequalities in access. However, most studies have highlighted that careful planning, implementation and monitoring are essential to maximize the benefits and minimize the potential damage.

# Overview of notifications in Pharmacovigilance at a High Complexity University Hospital



## Author

Letícia Demétrio Simão - Universidade Federal de Santa Catarina (UFSC)  
Isabel Machado Canabarro - Universidade Federal de Santa Catarina (UFSC)  
Filipe Carvalho Matheus - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

No funding.



## Keywords

Pharmacovigilance; notifications; university hospital

## Abstract

Pharmacovigilance is a science aimed at detecting, evaluating, understanding and preventing adverse effects or any other problems related to medicines. The aim of this study was to analyze pharmacovigilance notifications recorded at a highly complex university hospital in southern Brazil. The methodology consisted of a descriptive, cross-sectional and retrospective study, using the pharmacovigilance notifications recorded in the HU database between January 2019 and December 2023. All reports of drug-related incidents and adverse events within this period were included and those lacking relevant information (name of drug, type of incident, outcome, among others) were excluded. The data was categorized as the type of incident, the drug involved, the Potentially Dangerous Drug (PPM), whether the incident affected the patient, the degree of harm, the patient's outcome and the actions taken. In total, 1480 notifications were analyzed. The results showed a high incidence of administration errors (27.71 %); prescription errors (21.01 %) and loss of medication (11.62 %). The majority of incidents affected patients (56.89%), but did not result in harm (56.35%). MPP's (31.75%) and antimicrobials (21.55%) were involved in general incidents and antineoplastics were more present in spillage incidents (100%) and extravasations (42.10%). The majority of the procedures involved communicating to managers (30.40%) and referral professionals (30.67%). The study concluded that pharmacovigilance plays a crucial role in identifying risks related to the use of medicines, highlighting the importance of ongoing educational actions to prevent incidents. The research suggests improving the quality of records and strengthening reporting systems to ensure an effective response to incidents, as well as emphasizing pharmacovigilance in pharmacy courses. In summary, this study highlights the importance of pharmacovigilance for patient safety, with a view to the safe use of medicines.

# Social, Humanistic And Technical Aspects Of The Management Of Pharmaceutical Services In The Municipalities Of Santa Catarina Qualified In Qualifar-Sus Program



## Author

Rafaela Tavares Peixoto - Universidade Federal de Santa Catarina (UFSC)  
Samara Jamile Mendes - Universidade de São Paulo (USP)  
Patrícia Bernardi Sassi - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

FAPESC - Termo de outorga de apoio financeiro N° 2021TR000703



## Keywords

Management of Pharmaceutical Services; Qualifar-SUS; Sociotechnical System

## Abstract

Evaluative systems in health have been increasingly used with of strengthening public policies, especially when discussing pharmaceutical policies. The literature shows that it has been an advance in practices related to Pharmaceutical Services (PS), mainly related to regulations, structuring, and technical activities. Social and political aspects are poorly studied and considered in the planning and implementation of PS actions and services. The theme management of municipal Pharmaceutical Services based on a logic of sociotechnical organization[1] has been receiving more attention when studying the implementation of the municipal PS policy, because it's based on access and rational use of medicines and on the needs of people and society. The objective of this work was to evaluate the management of PS in the municipalities of Santa Catarina qualified in the Qualifar-SUS program using a sociotechnical approach. A quantitative analysis was carried out in a sample of 99 municipalities in the state of Santa Catarina that answered the QUALIFICA-AF study questionnaire, and that were qualified for structure axis of the Qualifar-SUS program. The sample was analyzed according to the degree or participation in activities related to management. As result, it was observed that municipalities have a high MHDl average and mostly small population size. There is a predominance of formalization of the position of PS coordinator, greater participation and insertion of PS in the Municipal Health Plan, in addition to greater follow-up and planning of use Qualifar-SUS resources among those with a higher degree of participation. It was concluded that the greater the participation and integration of PS in activities related to the management of the health system, better the development of the municipal PS policy. Parameters needs to be established to monitoring and evaluating PS management to participatory municipalities can be a strategy to implement PS within the Health System.

# The effects of nutrition and supplementation for children and adolescents with sickle cell disease: a systematic review and meta-analysesations: A scoping review of the benefits and challenges



## Author

Bruna Cardoso Orsi - Universidade Federal do Paraná (UFPR)  
Daniela Gorski - Universidade Federal do Paraná (UFPR)  
Naila Emilia Krul - Universidade Federal do Paraná (UFPR)  
Fernanda Tonin - Universidade Federal do Paraná (UFPR)  
Roberto Pontarolo - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

No funding



## Keywords

Sickle Cell Disease, Supplements, Systematic Review

## Abstract

**OBJECTIVES:** Sickle Cell Disease (SCD) patients' nutritional status is often compromised, therefore, supplementation is required to reduce the incidence of complications. The aim of our study is to assess the impact of supplementation in SCD-associated complications. **METHODS:** PubMed, Scopus and Web of Science databases were used on searches for this systematic review. Randomized controlled trials (RCT) including nutrition and supplementation interventions used as complementary therapy for children and adolescents with SCD were included (PROSPERO CRD42024532369). The data for outcomes of interest (efficacy, safety, incidence of SCD-related complications) were pooled by means of pairwise and network meta-analyses with surface under the cumulative rating curve analysis. The results were presented as risk ratio or mean differences with 95% credibility intervals; p values  $\leq 0.05$  were considered significant. **RESULTS:** Nineteen RCTs were included in this study (n=1,856), analyzing 9 different dietary supplements on various dosages and forms of administration. Supplementation with DHA and EPA (n=3) and L-arginine (n=4) presented significant improvement in pain intensity and vaso-occlusive crisis (VOC) compared to usual care/placebo ( $p < 0.05$ ). Citrulline (n=1) ( $p < 0.005$ ), vitamin A (n=2), and lime juice (n=1) ( $p < 0.001$ ) may improve SCD-related complications. Vitamin D3 (n=6) were evaluated for various outcomes, all demonstrating at least one beneficial effect. **CONCLUSIONS:** The statistical analyses indicates that the complementary use of some supplements (DHA, EPA, L-arginine and vitamin D3) can enhance the management of vaso-occlusive and pain crises. These supplements are often affordable, can additionally contribute towards the reduction of opioid use and shorten patients' hospital stays, especially in low/middle-income countries. Although further studies are needed to refine these findings, practical guidelines and decision-makers may benefit from updated evidence.

# Use of Benzodiazepines among State School Teachers in Espírito Santo: Evaluation of Prevalence and Degree of



## Author

Bruna Lopes Antonucci - Universidade Federal do Espírito Santo (UFES)  
Yohan Cancelheri Mazzini - Universidade Federal do Espírito Santo (UFES)  
Kimberly Domingos Schneider - Universidade Federal do Espírito Santo (UFES)  
Guilherme Rocha Pereira - Universidade Federal do Espírito Santo (UFES)  
Kérlin Stancine Santos Rochal - Universidade Federal do Espírito Santo (UFES)  
Dyego Carlos Souza Anacleto de Araújo - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

FUNDAÇÃO DE AMPARO À PESQUISA E INOVAÇÃO DO ESPÍRITO SANTO



## Keywords

Benzodiazepines, Mental Health, Teachers

## Abstract

**Objective:** To evaluate the use of benzodiazepines (BZDs) among teachers in the state education network of Espírito Santo. **Methodology:** A cross-sectional study was conducted with teachers from the Regional Education Superintendence of Carapina in Espírito Santo. The sampling was performed by clusters, with each school considered a primary sampling unit. Data collection was carried out in person. The self-administered questionnaire included sociodemographic data and a profile of BZD use. The Benzodiazepine Dependence – Self Report Questionnaire (BENDEP-SRQ PV) was used to assess the severity of dependence on BZDs. The BENDEP-SRQ PV score varies between from 15 to 75 points, with individuals scoring between 31 and 50 points classified as "potentially dependent" and those scoring  $\geq 51$  points classified as dependent. The data were presented using descriptive statistics. The project was approved by the Human Research Ethics Committee. **Results:** 453 teachers participated in the study, the majority of whom were: cisgender women (63.1%; n=286); heterosexual (87.2%; n=395); of white ethnicity (46.3%; n=211); with a family income between 3 to 5 minimum wages (50.5%; n=229); married (47.5%; n=215); with a specialization (66.0%; n=299). Among the teachers, 6.8% (n=31) use BZDs, with 38.7% of these having used them for more than two years (n=12). The most commonly used drugs were Clonazepam (64.5%; n=20) and Alprazolam (21.2%; n=7). It is important to note that five teachers reported using BZDs without a medical prescription. The BENDEP-SRQ PV was answered by 24 of the 31 BZD-using teachers, with 41.7% (n=10) of them classified as "potentially dependent" and 12.5% (n=3) classified as dependent. **Conclusion:** A significant portion of the teachers in the state education network of Espírito Santo use BZDs, with cases of self-medication and associated risk of dependence.



# Evaluation of drug interactions in an electronic prescription system of primary care in Vitória (ES), Brazil



## Author

Veronica da Fonseca Almeida - Universidade de Vila Velha (UVV)  
Carolina Dutra Degli Esposti - Universidade Federal Espírito Santo (UFES)  
Rita de Cássia Ribeiro Gonçalves - Universidade Federal Espírito Santo (UFES)  
Eliane de Fatima Almeida Lima - Universidade Federal Espírito Santo (UFES)  
Denise Coutinho Endringer - Universidade Federal Espírito Santo (UFES)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Own Resource



## Keywords

Drug interactions, Electronic Prescription, Basic Care

## Abstract

Drug interactions (DI) are clinical events in which the effects of one drug are altered by the presence of another drug. In other words, when two drugs are administered to a patient at the same time, they can act independently or interact with each other, increasing or decreasing the therapeutic or toxic effect of one or the other. The objective was to evaluate drug interactions in an electronic prescription system in primary care in Vitória (ES), divided into two stages: 1) Description and evaluation of the 2,119 drug interactions contained in the system by the researcher, following the criteria of the Micromedex, Lexicomp and Memed databases; 2) Evaluation of the interactions by a group of pharmacists in three rounds. This is an implementation research, where the analysis and quantification of the Well-Being Network (RBE) database was initially carried out, using the Micromedex®, Lexicomp® and Memed® data reference tools, to evaluate all the interactions already existing in the primary care network of the municipality. In total, 2,119 interactions were organized and evaluated in a Microsoft Excel® spreadsheet, reporting the classification according to severity and level of documentation. In the second stage of the study, the database was evaluated in 842 quantified DI. Thus, the interactions were reclassified, 61.1% (n=475) as Serious; 30.2% (n=235) as Moderate; 5.3% (n=41) as Mild and 3.5% (n=27) as Contraindicated and 64 DI were excluded. In the second round of evaluation, of the 778 DI's, 60.7% (n=481) were Serious, 30.9% (n=235) as Moderate, 4.9% (n=39) as Mild and 3.4% (n=23) as Contraindicated. Finally, the database had 545 interactions, of which (n=331) 62.3% were Serious; (n=162) 30.5% Moderate; (n=31) 3.2% Contraindicated, (n=21) 4% of the Mild type. Thus, it can be concluded that the use of information technology has become an essential tool to reduce the prevalence of recurrent IMs at the time of medical prescription.

# Strategies to Ensure Access to Leprosy Medications in Rural Municipalities of Amazonas



## Author

Genize Kaoany Alves Vasconcelos - Universidade Federal de Santa Catarina (UFSC)  
Amanda Mamed de Gusmão - Universidade Federal de Santa Catarina (UFSC)  
Rana Andressa Castelo Branco Feitosa - Universidade Federal de Santa Catarina (UFSC)  
Marcelo Campese - Universidade Federal do Amazonas (UFAM)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

None



## Keywords

Public Policies, Pharmaceutical Services, Leprosy

## Abstract

**Introduction:** The study is part of the project "Access to Medicines in the Amazon: Influence of the Amazon Factor on Pharmaceutical Policies and Services," funded by the Amazon+10 Initiative. Given the vast territorial expanse of Amazonas, comprising 62 municipalities, and its low population density, challenges arise in accessing public health policies, including ensuring diagnosis and treatment for leprosy patients. In 2023, Amazonas reported 310 new cases of leprosy, with 204 (65.8%) occurring in 42 municipalities in the interior. **Objective:** To identify strategies to ensure access to medicines for leprosy patients in the interior municipalities of Amazonas. **Methodology:** Data were obtained through interviews with managers, users, and health professionals (prescribers, pharmacists, and coordinators of the leprosy program). Additionally, visits were made to therapeutic support points in both urban and rural areas, with an emphasis on riverside communities in 12 municipalities. **Results:** Clinical follow-up and obtaining a month's supply of medications are generally carried out at health units in the municipal headquarters. The headquarters also house banking institutions and commerce. The population seeks to optimize trips by combining health services with monthly trips to withdraw social benefits and acquire subsistence products. In situations where travel is challenging due to long distances, seasonal droughts, or the user's physical and financial limitations, certain municipalities rely on the support of rural Community Health Agents (ACS). These agents facilitate the delivery, supervise the first dose, and monitor treatment adherence. **Conclusion:** Despite logistical challenges, geographical barriers, and infrastructure limitations that hinder the distribution of medicines in the region, strategies such as the involvement of ACS in communities have contributed to ensuring access to medicines, particularly in areas distant from health units.

# Remote Rural Municipalities In The Amazon: Challenges Of Pharmaceutical Practice



## Author

Ilvia Silva Gomes - Universidade Federal de Santa Catarina (UFSC)  
Wilson Sabino - Universidade Federal do Oeste do Pará (UFOPA)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)  
Marina Rajjche Mattozo Rover - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

FAPESC(SUP2022350000016); CNPQ(401966/2023-2); FAPESPA



## Keywords

Pharmacists, Remote Rural Health, Access to Health Services

## Abstract

Inequalities in access to health services and the unequal distribution of professionals, including pharmacists, persist over time and affect many municipalities in vulnerable situations, such as remote rural municipalities (MRR). This results in weaknesses for the area and enormous challenges for professionals. The objective of this study is to describe the role of pharmacists in the Brazil's National Health System (SUS) in MRR of the Brazilian Amazon. This is an excerpt from one of the qualitative stages of the project "Access to medicines in the Amazon: the influence of the Amazonian factor on Pharmaceutical Services," a cross-sectional, descriptive study with a quantitative and qualitative approach, conducted in 2024, in which pharmacists working in two MRR were interviewed. The questions ranged from developed activities to the challenges faced. The municipalities had populations ranging from 24,000 to 35,000 inhabitants and had 3 pharmacists with a 40-hour weekly workload. Both MRR had a Central Pharmaceutical Supply, a municipal pharmacy, a hospital, and a testing and counseling center. Pharmacists needed to provide all these services and also assumed responsibilities for the management of medical and hospital supplies and other materials. They sought to organize their activities in the services, however, logistical and managerial activities stood out from patient care activities, which was one of the weaknesses highlighted in the study. Furthermore, they had difficulties in participating in training in the area, both due to the high demand for work and the need to travel to the municipalities where these are offered. Thus, it appears that in MRR there are many challenges for the development of pharmaceutical services. Investments are needed, for example, through programs that can not only attract and retain professionals in these locations, but also to strengthen and train the workforce in order to obtain better health results.

# Prevalence of Burnout and Associated Factors Among State School Teachers in Vitória: A Cross-Sectional Study



## Author

Yohan Cancelheri Mazzini - Universidade Federal do Espírito Santo (UFES)  
Bruna Lopes Antonucci - Universidade Federal do Espírito Santo (UFES)  
Beatriz Nicoli Ferreira - Universidade Federal do Espírito Santo (UFES)  
Ana Clara Garcia Marton - Universidade Federal do Espírito Santo (UFES)  
Sthefany Brito Salomão - Universidade Federal do Espírito Santo (UFES)  
Kérlin Stancine Santos Rocha - Universidade Federal do Espírito Santo (UFES)  
Dyego Carlos Souza Anacleto de Araújo - Universidade Federal do Espírito Santo (UFES)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Fundação de Apoio à Pesquisa do Espírito Santo - FAPES



## Keywords

Burnout, Mental Health, Teachers

## Abstract

**Objective:** To assess the prevalence and factors associated with burnout among teachers in state schools located in the municipality of Vitória, Espírito Santo. **Methods:** A cross-sectional study was conducted in four state schools in Vitória-ES, selected by random draw. Teachers away from teaching duties or on leave were excluded. Data were collected between January and February 2024, in person, using a questionnaire that included sociodemographic variables and the Oldenburg Burnout Index (OLBI). The OLBI consists of 13 items, divided into two domains: emotional exhaustion and disengagement from work. Each item was evaluated using a 4-point Likert scale. A sum score of the domains  $\geq 4.73$  results in a high risk of burnout. Descriptive and inferential statistics were used for data analysis. Inferential analyses were considered statistically significant when  $p \leq 0.05$ . The study was approved by the Human Research Ethics Committee. **Results:** A total of 109 teachers participated in the study, with 56.0% being cisgender women ( $n=61$ ), 87.2% heterosexual ( $n=95$ ), 55.0% white ( $n=60$ ), 38.5% married ( $n=42$ ), 23.9% taught at night ( $n=26$ ), and 27.5% had another job ( $n=30$ ). A high risk of burnout was observed in 59.6% of teachers ( $n=65$ ) and showed a statistically significant association with the variable "having children" ( $X^2=4.483$ ;  $df=1$ ;  $p<0.05$ ). Teachers at high risk of burnout had a shorter professional tenure compared to those at low risk of burnout ( $14.3 \pm 8.0$  years vs  $19.9 \pm 11.4$  years [ $t(99)=2.746$ ;  $p<0.01$ ]). There was no significant difference in the average workload between teachers at high risk of burnout and those without risk. **Conclusion:** More than half of the teachers in the study showed a high risk of burnout, with teachers with children being more likely to experience burnout. Furthermore, experience may play a protective role against burnout.

# Evaluating the Cost-Effectiveness of Pharmacological Therapy in Early Alzheimer's Disease in Brazil



## Author

Price Udo Price - Faculdade de Ciências Farmacêuticas Ribeirão Preto (FCFRP-USP)

Robert HeggieRobert - University of Glasgow

Leonardo Régis Leira Pereira - Faculdade de Ciências Farmacêuticas Ribeirão Preto (FCFRP-USP)

Julio Cesar Moriguti - Faculdade de Ciências Farmacêuticas Ribeirão Preto (FCFRP-USP)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

CAPES



## Keywords

Alzheimer's Disease; Lecanemab; Donanemab; Donepezil; AChEIS, QALYs

## Abstract

Alzheimer's Disease (AD) is the most common form of dementia, leading to disability and death in older adults. Given the high costs of treatment and limited healthcare resources in developing countries, evaluating the cost-benefit and effectiveness of these treatments is crucial. Also, assessing patients' improvement of independence and maintenance of quality of life due to these treatments according to the disease progression is essential. This study aimed to evaluate the cost-effectiveness of no pharmacological treatment/best supportive care, the standard of care (SoC – AChEIs/Donepezil), Donanemab, and Lecanemab antibodies on slowing down disease progression in early (MCI/Mild) AD patients from the perspective of the Brazilian Public Health System (SUS). We developed a decision analytic model to replicate the natural history of AD patients, incorporating costs and quality adjusted-life years (QALYs) data from a Brazilian setting and, where necessary, data from the literature. None of the interventions (SoC, Donanemab, and Lecanemab) dominated the BSC. However, the SoC had the lowest cost per QALY (\$5,288.75), compared to Donanemab (\$1,225,304.30), and Lecanemab (\$2,092,3422.72), respectively. Considering the stipulated threshold of \$15,094 per QALY gained by CONITEC, the SoC falls within this threshold. Hence, it is considered a cost-effective strategy for treating early AD.

# Dispensing Ontology for Supporting Clinical Pharmaceutical Services



## Author

Luciano Soares - Universidade Federal de Santa Catarina (UFSC)

William Bonner Lopes de Almeida - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

FAPESC - PPSUS N° 16/2020



## Keywords

Dispensing, Pharmaceutical Services, Ontology

## Abstract

Medication dispensing involves complex interactions among various technologies, including the medicines provided, technical and management routines, and professionals with specific qualifications. Pharmaceutical clinical services require the development of technologies designed to organize the capture, enhance the interpretation, and optimize the recording of information related to pharmacotherapy. As knowledge representations, ontologies implement abstractions capable of describing a particular system in terms of its subjects and relationships, making them highly applicable in real-world scenarios. This study aims to present preliminary data on modeling a domain specifically tailored to support medication dispensing, a crucial aspect of pharmaceutical care. The study defined the domain scope based on a medication dispensing service model built by the UFSC Pharmacy School (FEUFSC). The concepts derived from this model led to the definition of classes, properties, and relationships necessary to represent the knowledge produced in medication dispensing. We analyzed these definitions through their implementation in FEUFSC's pharmaceutical service to characterize their ability to represent reality within the scope of the ontology. The institution's ethics committee approved the project. The ontology not only enrolls the dispensing process and its stages as entities of information content but also defines a key component, the characterization of treatment outcomes involving medications dispensed by the service. These outcomes, crucially, result from the clinical action produced by the pharmaceutical work interacting with the patient. The production of this content drives an investigation process of factors capable of modifying effectiveness and safety, providing a comprehensive understanding of the factors influencing medication dispensing outcomes and contributing significantly to developing technologies that help pharmacists improve medication use.

# Evaluation of the drugs used by patients attending a Pharmacotherapy Outpatient Clinic



## Author

Bernardo Sá de Aguiar - Universidade Federal de Santa Catarina (UFSC)  
Letícia Demétrio Simão - Universidade Federal de Santa Catarina (UFSC)  
Francine Spigolon Stella - Universidade Federal de Santa Catarina (UFSC)  
Júlia Maria Borges Evaldt - Universidade Federal de Santa Catarina (UFSC)  
Lucas Eduardo de Souza - Universidade Federal de Santa Catarina (UFSC)  
Lara Júlia Sopelsa - Universidade Federal de Santa Catarina (UFSC)  
Valentina Ribeiro Pires da Silva - Universidade Federal de Santa Catarina (UFSC)  
Tatiana Herrerias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

ProEx/UFSC



## Keywords

Evaluation of pharmacotherapy, Polypharmacy, Pharmaceutical care.

## Abstract

**Introduction:** The inappropriate use of several drugs concomitantly increases the risk of adverse reactions, drug interactions and intoxications, generating health complications and possibly even leading to death, so it is necessary to evaluate pharmacotherapy in order to reduce the risk of health complications. **Objective:** To assess the main classes of medication used by patients seen at the UFSC Pharmacotherapy Evaluation Outpatient Clinic. **Materials and methods:** Participants in projects related to physical activities and education/training carried out at the university between March and June 2024 were seen. For the pharmaceutical consultations, the Ministry of Health's adapted Pharmacotherapeutic Form was used and BP and blood glucose were measured. After the assessment, guidance was given on medication and health problems, as well as interventions and referrals. **Results and discussion:** 12 patients were seen, aged between 24 and 78, 11 women and 1 man. A total of 62 drugs were taken (5.2 drugs/patient): antihypertensives 14 (22.5%), NSAIDs 11 (17.7%), antidyslipidemics 10 (16.1%), antidiabetics 8 (12.9%), vitamin supplements 7 (11.2%), mental health 4 (6.4%), 5-alpha-reductase inhibitor 1 (1.6%), antirheumatic 1 (1.6%), monoclonal antibodies 1 (1.6%), muscle relaxants 1 (1.6%), hormones 1 (1.6%), potassium pump inhibitors 1 (1.6%), others 1 (1.6%). With regard to the source of the drugs obtained by the 12 patients, 1 (8.3%) obtained them exclusively privately, 2 (16.3%) obtained them exclusively publicly and 9 (75%) obtained them both ways. **Final considerations:** Polypharmacy was frequent in the study population and with it problems related to medicines. One of them was lack of adherence to treatment, either due to lack of use or incorrect use. These problems reflect the lack of control and progression of diseases, as well as being an important risk factor for other events.

# Evaluation Of Pharmaceutical Interventions In An Outpatient Pharmacotherapy Clinic



## Author

Júlia Maria Borges Evaldt - Universidade Federal de Santa Catarina (UFSC)  
Letícia Demétrio Simão - Universidade Federal de Santa Catarina (UFSC)  
Francine Spigolon Stella - Universidade Federal de Santa Catarina (UFSC)  
Bernardo Sá de Aguiar - Universidade Federal de Santa Catarina (UFSC)  
Lucas Eduardo de Souza - Universidade Federal de Santa Catarina (UFSC)  
Lara Júlia Sopelsa - Universidade Federal de Santa Catarina (UFSC)  
Valentina Ribeiro Pires da Silva - Universidade Federal de Santa Catarina (UFSC)  
Tatiana Herrerias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

ProEx-UFSC



## Keywords

Avaliação de farmacoterapia, Polifarmácia, Atenção farmacêutica.

## Abstract

The inappropriate use of medicaments increases the risk of adverse reactions, drug interactions and intoxications, generating health complications and possibly even leading to death. It is necessary to evaluate pharmacotherapy in order to reduce the risk of health complications. To evaluate the pharmaceutical interventions carried out on patients treated at the Ambulatório de Farmacoterapia da UFSC. Participants in projects related to physical activities and education/training carried out at the university between March and June 2024 were seen. For the pharmaceutical consultations, the Department of Health's adapted Pharmacotherapeutic Formulary was used and blood pressure (BP) and blood glucose (BG) were measured. After the assessment, guidance was given on medication and health problems, as well as interventions and referrals. Twelve patients were seen, aged between 24 and 78, 11 women and 1 man. Changes were made to the dosage (schedule) to improve adherence in 33.3% of the patients, and for 75% a medication taking schedule was given. All the patients received guidance on medication and health habits, as well as the need to adhere to their treatment (100%), not interrupting treatment on their own (100%), drug interactions (41.6%), self-medication (50%), correct storage (8.3%) and obtaining medication through the courts (8.3%). In 50% of the patients, BP was found to be above the recommended values and 66.6% were given a diary to monitor their pressure. BG was measured in 75% of the patients, with 33.3% above the recommended values, and 16.6% were given a glycemic diary for monitoring. With regard to referrals to other professionals, there were 5 medical referrals, 6 to the nutrition clinic and 2 to psychotherapy. Polypharmacy was frequent in the study population and with it problems related to medication. These problems lead to lack of control and progression of diseases, as well as being an important risk factor for other events.



# Accidents caused by venomous animals in municipalities of the State of Amazonas: reports from health professionals



## Author

Amanda Mamed de Gusmão Lobo - Universidade Federal de Santa Catarina (UFSC)  
Genize Kaoany Alves Vasconcelos - Universidade Federal de Santa Catarina (UFSC)  
Rana Andressa Castelo Branco Feitosa - Universidade Federal do Amazonas (UFAM)  
Marcelo Campese - Universidade Federal do Amazonas (UFAM)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Fapesc e TO2022TR2174; Fapeam Amazônia+10; resolution n. 23/2022



## Keywords

Health Equity, Venomous Animals, Antivenins

## Abstract

**Introduction:** Accidents caused by venomous animals are relevant to public health due to their severity and high frequency in Brazil. In the Amazon State, the large territorial extension, low demographic density and types of transport influence the availability of antivenoms to the population, this research is part of the project “Access to medicines in the Amazon: influence of the Amazon factor on pharmaceutical assistance” financed by the Amazônia +10 Initiative. **Objective:** To report the availability of antivenom in municipalities in the interior of the state, and the difficulties about the acquisition, transportation and distribution in the region. **Methodology:** Descriptive study using semi-structured interviews with public service health professionals in 13 municipalities in Amazonas, about the availability of antivenin serum and how the request, supply, transport and distribute in the municipality, as well as the main difficulties faced to guarantee access. The interviews were recorded and the audios were evaluated by the research team. Results: Antivenoms were available in all hospital located in the urban perimeter. However, most accidents occur in rural areas, forcing patients to travel through rivers during 6h to 36h depending on the type of transport, which can worsen the injury or even lead to death before the first care. In addition, health professionals reported logistical difficulties to receiving serums in some municipality due to regional characteristics, in some cases taking weeks to arrive which can lead to shortages. **Conclusions:** The results demonstrate the need for a specific polity for Amazon region regarding the distribution chain and the population's access to treat accidents caused by venomous animals, in order to search for alternatives that promote equity in the health of this population.

# Vaccines For The Child Population: Supply And Cost Analysis



## Author

Clarice Chemello - Universidade Federal de Minas Gerais (UFMG)  
Sueyder Drumond Carvalho Victor - Universidade Federal de Minas Gerais (UFMG)  
Carlos Eduardo de Oliveira Pereira - Universidade Federal de Minas Gerais (UFMG)  
Ana Rafaela Pires Lira - Universidade Federal de Minas Gerais (UFMG)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

no funding



## Keywords

children; immunization programs; public health

## Abstract

Vaccination is an important strategy for controlling vaccine-preventable diseases since the first days of life. Brazil has a consolidated vaccination program through the policies by the Ministry of Health, by the creation of the National Immunization Program (PNI), which guides vaccination in the country. Brazil has two models for the vaccination schedule, the public system, free through the Unified Health System (SUS), and the private system, which in addition to the recommendations of the PNI, also includes the guidelines recommended by the Brazilian Society of Immunizations (SBIIm). Thus, this study aimed to evaluate the public and private childhood vaccination schedule in Belo Horizonte regarding vaccine availability and costs. To do so a cross-sectional study was carried out in 2023 using public databases and private clinics' websites, as well as pharmacy and drugstore based on the PNI and the SBIIm. Additionally, a comparison was made between the available immunizations and the prices charged in private establishments, considering the factory price and the maximum retail price. The results showed that the SUS is able to meet a significant portion of the basic vaccination needs of the pediatric population, although the SBIIm offers a broader schedule by including private options. The costs related to the final consumer price demonstrate that the population's access to vaccines available on the private calendar is still not financially accessible to everyone, which corroborates the importance of the PNI for national public health. Pharmacies have a lower overall average price than private clinics. Furthermore, the consumer usually pays more for the service than for the vaccine itself, needing a more effective regulation, given that the population will not purchase the input for self-application. Future research on the relationship between vaccine availability and vaccination coverage is important as they are directly related to public health indicators.

# Computerized Notification System: Pharmacovigilance As A Technology To Improve Access To Information And Ensure Quality In Federal University Hospitals In The Ebserh Network



## Author

Serena Pireneus Oliveira Borges de Pina - Universidade de Brasília (UnB)  
Aline Matilde Ferreira dos Santos - Universidade de Brasília (UnB)  
Matheus Lopes da Silva - Universidade de Brasília (UnB)  
Bruno Pereira de Melo - Universidade de Brasília (UnB)  
Helaine Carneiro Capucho - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

CNPq



## Keywords

Pharmacovigilance, patient safety, medications errors

## Abstract

Pharmacovigilance aims to prevent, eliminate, or reduce adverse events (AEs) related to medicines and vaccines. VigiHosp is a computerized health surveillance system present in federal university hospitals linked to the Brazilian Hospital Services Company (EBSERH), which is used to collect data from voluntary and anonymous AE notifications and based on this data, generate improvements in the quality of health services, by supporting decisions about care practices and promoting patient safety. This work aims to analyze notifications of medication errors (ME) and characterize their severity, using VigiHosp as a research instrument and data source. This study has a cross-sectional, retrospective, and qualitative epidemiological nature, and was approved by the FS/UnB Research Ethics Committee. Data collection involved document analysis, carried out at VigiHosp, of notifications received in 2022, whose reports were generated in an Excel spreadsheet. In the first half of the year, 1,605 ME-related incidents were reported. Regarding severity, 1,574 (n=98%) were non-serious incidents, that is, they did not cause prolonged hospitalization or disability for the patient, but 31 (n=2%) incidents were serious, including 2 deaths (0.1%), which prolonged hospitalization and/or cause permanent or temporary disability to the patient. In the second half of the year, 641 (n=39%) ME were reported, totaling 2,246 ME notifications this year. Regarding the severity of this semester, 622 (n=97%) incidents were considered non-serious, however, there were 19 (n=3%) serious incidents. Because of the above, one can observe the potential and quantity of existing notifications, from mild to fatal incidents, useful as support to prevent AEs, which have already occurred or may happen again, thus improving patient care behaviors to guarantee access to an excellent healthcare system.

# Incorporation of Fourth Industrial Revolution (4IR) Themes into the Pedagogical Projects of Courses (PPC) Based on the Current Curriculum Guidelines (DCN) for Undergraduate Pharmacy Courses - Resolution CNE/CES No. 6/2017



## Author

Paulo Roberto Boff - Universidade Federal de Santa Catarina (UFSC)  
Norberto Rech Binetti - Universidade Federal de Santa Catarina (UFSC)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Não Há



## Keywords

Pharmaceutical education in Brazil, Innovation in medicines and pharmaceutical services, Fourth Industrial Revolution

## Abstract

**Introduction:** The Fourth Industrial Revolution (4IR) is transforming various sectors, including pharmacy, through the integration of digital, physical, and biological technologies. This study investigates how undergraduate Pharmacy courses in Brazil are adapting to these technological changes and the challenges faced in training professionals for this new era. **Methodology:** A protocol was used to identify the integration of 4IR themes into the Pedagogical Projects of Courses (PPC). Based on the Technology and Health Innovation axis of the National Curriculum Guidelines for Pharmacy (DCN), established by Resolution CNE/CES No. 6/2017, the study analyzed whether themes related to the 4IR were incorporated. Ten PPCs with ratings of 4 and 5 in SINAES/ENADE, covering different regions of Brazil, were examined. **Results:** Regarding the presence of conceptual approaches related to the 4IR in the PPCs, 30% showed strong evidence, 26% showed partial evidence, and 44% showed no evidence. For theoretical and practical pedagogical approaches connected to the 4IR, 82% of PPCs showed partial evidence, 18% showed no evidence, and no course showed strong evidence. Concerning the integration of emerging technologies and CT&I structures, 70% of PPCs showed no evidence, 30% showed partial evidence, and no course showed strong evidence. **Conclusion:** Although there is an effort to include new technologies and pedagogical practices, there is still no integration of strategies and content aligned with the challenges of the 4IR, such as artificial intelligence, nanotechnology, 3D printing of medicines, innovation, startup creation, and entrepreneurship associated with technology and pharmaceutical services. Continuous investment in modernizing educational infrastructure and training teachers is necessary to ensure education aligned with the demands of the 4IR, aiming to improve competitiveness and innovation in the Brazilian pharmaceutical sector.

# Role of the Pharmacist in Caring for People Living with HIV/AIDS: User Perspectives from a Medicines Dispensing Unit within Primary Health Care



## Author

Isabel Cardoso de Carvalho - Universidade Federal de Santa Catarina (UFSC)  
Fernanda Manzini - Universidade Federal de Santa Catarina (UFSC)  
Alessandra da Silva Kulkamp - Universidade Federal de Santa Catarina (UFSC)  
Leandro Ribeiro Molina - Departamento Municipal de Saúde de Florianópolis  
Vanessa de Bona Sartor - Escola de Saúde Pública de Florianópolis  
Luísa Vitória Gehrke - Escola de Saúde Pública de Florianópolis  
Fabíola Michele Gessner - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

There is no funding agency.



## Keywords

Primary Health Care, People living with HIV, Pharmaceutical Services

## Abstract

The decentralized model of care for people living with HIV/AIDS in Primary Health Care (PHC) has been consolidated in diagnosis and medical care, but challenges remain in the area of Pharmaceutical Services. This study sought to understand the experience of people living with HIV/AIDS treated at a Medicines Dispensing Unit within PHC. This was a qualitative study, with in-depth interviews conducted with seven people living with HIV/AIDS at the Saco Grande Health Center in Florianópolis/SC, the only Health Center to offer this pharmaceutical service, due to a local initiative by the professionals. The results highlight the benefits of interprofessional collaboration, such as increased access to health services and strengthening the bond with users. People living with HIV/AIDS access the pharmacy service for other health needs, allowing pharmacists to gain insights that go beyond antiretroviral medication. Reception by the pharmacist after the HIV diagnosis is mentioned as a support to overcome the emotional upheaval. Initial care provides clarification to ensure that users understand the next steps in treatment, promoting safety in the therapeutic process. Pharmacists are part of the Family Health Teams and are thus more integrated into the user care process. Pharmacists carry out dispensing, evaluate pharmacotherapy, request clinical monitoring tests and participate in HIV prevention strategies. The care provided by the pharmacists at this Medicines Dispensing Unit contrasts with the experience of users in other health services, where unfamiliarity with the professionals is common. From the reports, it is possible to identify that the services are organized in such a way as to promote access, comprehensiveness, coordination and longitudinality. It is essential that the pharmacist's role in caring for people living with HIV/AIDS in PHC goes beyond medicines management, incorporating the principles of PHC.

# Social Participation role in Sustainable Economic Health Developing



## Author

Vinícius André Boff - Universidade Federal de Santa Catarina (UFSC)  
Fernanda Manzini - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Projeto Integra, funding by Fundação Oswaldo Cruz and Pan American Health Organization.



## Keywords

Social Participation; Public Health Policies; Health Councils.

## Abstract

**Introduction:** In Brazil, the right to health is guaranteed mainly by the Unified Health System, which has as one of its guidelines social participation in the planning, evaluation and proposition of health policies, to ensure that they are aligned with social needs. Health Councils and Health Conferences are one of the forms of social participation. In this way, health is a strategic area for national development and combating health, social and political difficulties. **Method:** This is an ongoing document analysis study, which analyzes reports from state health conferences held in 2023 in all Brazilian states. The initial search was carried out on the website of the state health councils and state health departments, and a request was subsequently made to the National Health Council (NHC) for reports that were not found. To analyze the reports, keywords related to Science, Technology and Innovation, Pharmaceutical Assistance and Health Surveillance are being searched for in the guidelines, proposals and motions of the reports, followed by categorization of the findings. **Results:** 12 reports were found on the websites and 15 were requested from the NHC. These results demonstrate difficulties in accessing information related to social control in health. The themes are also presented in different formats in the construction of the documents, indicating inequality in the understanding of the areas of study by social participation. After analyzing the reports, we intend to verify the relationship between what was proposed at the Conferences and the Health Plans. **Conclusion:** As an ongoing study, we point to the need to improve the transparency of social control documents in order to facilitate access to information by the population. This study also hopes to contribute to improving public health policies, strengthening and qualifying social participation so that it can be more effective in building the Unified Health System and sustainable economic development.

# Experiences and Initiatives on Physiologically Based Biopharmaceutics Modeling (PBBM) in the Brazilian Regulatory Context



## Author

Luiza Novaes Borges - Agência Nacional de Vigilância Sanitária (ANVISA)  
Eduardo Agostinho Freitas Fernandes - Agência Nacional de Vigilância Sanitária (ANVISA)  
Érico Miroro de Oliveira - Agência Nacional de Vigilância Sanitária (ANVISA)  
Víctor Gomes Pereira - Agência Nacional de Vigilância Sanitária (ANVISA)  
Andrea Diniz - Universidade Estadual de Maringá (UEM)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

No funding received for this work.



## Keywords

modeling and simulation; PBBM; regulatory science

## Abstract

Physiologically Based Biopharmaceutics Modeling (PBBM) combines a representation of the organism, mechanistically describing the gastrointestinal tract and variability in physiologically relevant factors, with critical attributes of the drug substance and product influencing in vivo dissolution and absorption. PBBM use is growing in drug product development and regulatory sciences, addressing quality-related and biopharmaceutics questions and enabling patient-centric drug developments. This study aims to facilitate drug product submissions to ANVISA, supported by PBBM analyses, through a situational and proactive analysis of the scientific and regulatory landscape. International collaborations on PBBM best scientific and regulatory practices, as well as the initiative of ANVISA-Academia working group and its experiences with PBBM analysis, are being considered. Results highlight that regulations concerning biopharmaceutics and quality topics in Brazil, such as quality by design (QbD), dissolution assays, in vitro in vivo correlations (IVIVC), bioequivalence, and biowaiver, do not yet integrate modeling and simulation (M&S) techniques like PBBM. Propositions for a systematic revision of regulations to provide necessary updates with flexibility, considering M&S as an evolving field, are presented. To apply these concepts and knowledge, three pillars need to be structured at ANVISA and in the pharmaceutical industries to effectively integrate PBBM analysis into regulatory decision: enhanced pharmaceutical development, structured biopharmaceutics analyses, and pharmacometrics analyses. This structure demands application of multidisciplinary workflows and roadmaps to be applied by various sectors, thematic working groups, or newly created specific sectors. The suggested strategies can strengthen ANVISA's capabilities, enabling regulatory review of PBBM reports and fostering science- and risk-based decisions for patient benefit and international regulatory convergence.

# Self-Reported Side Effects By Elderly Users Of Benzodiazepines



## Author

Marlon Silva Tinoco - Universidade Federal de São João del-Rei (UFSJ)  
Aline Istefane de Camargos Ramos - Universidade Federal de São João del-Rei (UFSJ)  
Silvio José Elisei Carvalho Júnior - Universidade Federal de São João del-Rei (UFSJ)  
Luciana Soares Rodrigues - Universidade de Formiga (UNIFOR-MG)  
Mariana Linhares Pereira - Universidade Federal de São João del-Rei (UFSJ)  
André Oliveira Baldoni - Universidade Federal de São João del-Rei (UFSJ)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ): 304131/2022-9.; Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES): 001.; Fundação de Amparo à Pesquisa do Estado de Minas Gerais: APQ-01107-21 e APQ-01189-22.



## Keywords

Aged, Benzodiazepines, adverse effects.

## Abstract

Benzodiazepines, widely used across the planet, are lipophilicity drugs that accumulate in the body of elderly people, causing well-known adverse reactions described in the literature, such as memory impairment, increased risk of falls, car accidents, increased hospitalizations, and others. In view of this, this study aims to analyze the self-reports of elderly users of benzodiazepines regarding the presence of Side Effects possibly related to this class of medications. An interview was carried out to recruit elderly benzodiazepine users who were candidates for a deprescription process, and in this context questions were asked about the presence of forgetfulness, history of recent falls, car accidents and recent hospitalization. Elderly people using benzodiazepines were identified by teams from the respective basic health units and the collection was carried out by the research team in a small city in Minas Gerais, Brazil. 49 elderly patients using benzodiazepines were identified. 13 (26.5%) patients reported two or more falls in the last year. More than half of the patients (53.1%) reported some forgetfulness confirmed by a family member, and 11 (22.4%) elderly people noticed a worsening of this forgetfulness in recent months and 9 (18.4%) stated that there was a worsening in the development of their activities of daily living. Only 1 (2%) patient reported a car accident, but the vast majority do not even have the habit of driving vehicles. Among the elderly, 7 (14.9%) were recently hospitalized. The presence of these Side Effects is already well described in the literature, however the irrational use of benzodiazepines by elderly people remains prevalent and puts their quality of life at risk. Therefore, it is necessary to adopt measures to gradually withdraw these potentially inappropriate medications for the elderly, in order to promote a rational use of this medication and more appropriate approaches to the health of the elderly.



# Cannabidiol As An Orphan Drug In The Treatment Of Rare Diseases: A Study Of Ema Registration Applications



## Author

Matheus Lopes da Silva - Universidade de Brasília (UnB)

Aline Matilde Ferreira dos Santos - Universidade de Brasília (UnB)

Serena Pireneus Oliveira Borges de Pina - Universidade de Brasília (UnB)

Helaine Carneiro Capucho - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Não há.



## Keywords

Cannabidiol, CBD, Orphan designation

## Abstract

Cannabidiol (CBD) has aroused interest in the medical and scientific community in recent years due to its possible therapeutic effects. Originating from the *Cannabis Sativa* L. plant, CBD is a non-psychoactive substance that is still being widely studied due to its potential benefits in the treatment of a variety of diseases, from anxiety disorders to epilepsy. At the same time, rare diseases present significant challenges for both patients and drug developers. Due to their low prevalence, obstacles such as difficulties in developing clinical trials and the high cost of developing such specific treatments end up not arousing too much interest in the pharmaceutical industry. To alleviate this problem, regulatory agencies such as the European Medicines Agency (EMA) have established protocols for so-called "orphan" drugs, which are used for the diagnosis, prevention and treatment of rare diseases. In this context, CBD is gaining strength as a valuable option for the treatment of various rare diseases. This study aims to analyse the applications for registration of CBD as an orphan drug for rare diseases, the specifics of these applications, as well as the main diseases in which these applications are made. After analysing the applications for orphan drug registration, using the EMA's public database as a research base. Considering the number of positive registrations over the years, with the first application registered in 2014 for the treatment of Dravet syndrome. In 2022, there were four applications for different conditions, such as 22q11.2 deletion syndrome, fragile X syndrome (FXS) and epidermolysis bullosa. In this way, as well as proving to be a good ally in the treatment of a wide range of diseases that go beyond those related to the Central Nervous System, CBD seems to be promising in the treatment of rare diseases, thus allowing patients with such diseases to have therapeutic alternatives.

# Validation Of The Modeling Proposal For Evaluation Of Toxicological Information And Assistance Centers Of Brazil's National Health System



## Author

Ana Paula da Rocha - Universidade Federal de Santa Catarina (UFSC)  
Luana Gabriele Nilson - Universidade Federal de Santa Catarina (UFSC)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

O presente trabalho foi realizado com apoio da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Código de Financiamento 001.



## Keywords

Poison Control Centers, Health Evaluation, Validation Study

## Abstract

**Introduction:** Toxicological assistance is essential for public health, it guarantees the diagnosis and treatment of intoxications and poisonings, prevents worsening, promotes education, health recovery and saves lives. Brazil has 32 Toxicological Information and Assistance Centers (CIATox), integrated into the Urgency and Emergency Network of the Unified Health System - SUS. The project "Qualification of Assistance and Surveillance of Poisonings in the SUS" aims to evaluate these Centers, identify needs and propose improvements. This summary presents the initial results of the validation of the model and evaluation matrix proposed for CIATox. **Methodology:** The project involves evaluability, case studies and formative and summative assessments. The theoretical-logical model and evaluation matrix were constructed based on a literature review, document consultation and initial diagnosis of CIATox. They are organized into dimensions of structure, processes and results. The first stage of validation involved the application of a questionnaire with 59 questions online. The responses were tabulated and categorized by context. **Results:** The evaluation instruments detail structural and procedural components, expected results and effects of CIATox service. The matrix comprises 56 indicators divided into 20 structural, 24 process, and 12 results indicators. Results: We received 30 responses, including 2 suggestions for new titles for the model and 17 proposals in the evaluation matrix, for the inclusion of normative documents and more service results and the semantic alignment of work processes. Considerations will be discussed at Consensus Conferences, to validate the instruments and application at the Centers. **Discussion:** The engagement of the actors was and is fundamental, as it leads to the precision, relevance and consensus of the instruments, reflecting the reality, needs and effectiveness of the service.

# Characteristics of the management and operationalization process in Toxicological Information and Assistance Centers (CIATox) in Brazil



## Author

João Vítor Burtet - Universidade Federal de Santa Catarina (UFSC)  
Ana Paula da Rocha - Universidade Federal de Santa Catarina (UFSC)  
Filipe Carvalho Matheus - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq): project number 40916C/2023 - 7



## Keywords

Suicide attempt, Medicines, Pharmaceutical services

## Abstract

**Introduction:** The 32 Toxicological Information and Assistance Centers – CIATox, are specialized and public Brazilian units, which also provide assistance to the large volume of poisonings by chemical agents. It is estimated that 20% of all suicides worldwide are directly related to the use of medicines and pesticides, which makes these poisonings a global public health problem. **Objective:** to identify the characteristics of the management and operationalization process in 10 Brazilian CIATox regarding matrix support for suicide attempts. **Method:** The exploratory study was carried out through a semi-structured interview containing 17 guiding questions with employees in 10 Brazilian CIATox, 2 from each Brazilian region. The inclusion criteria of centers in the study were: having a psychiatrist/psychologist on staff or having psychosocial support in cases of attempted suicide and the scope of care and the number of cases treated in 2020. In Brazilian regions where there was a center with the first criterion, the selection of the second center was made based on which had the lowest number of cases in 2020 and the lowest coverage, while in regions where there were no centers with the first criterion, those with the greatest coverage and number of cases were selected, followed by those with lower scope and number of cases. Ethical approval (64280222.8.0000.0121). **Results:** respectively, the centers included in the research after applying the inclusion criteria were: in the South region (CIT-RS and CEATOX-Cascavel), Southeast (CCI-São José dos Campos and CIATox-ES), Northeast (CIATox-Bahia and CIATox-João Pessoa), Central-West (CIATox-Goiás and CIVITOX-MS) and North: (CIT-AM and CIT-Belém). **Conclusions:** potentialities and weaknesses were identified in the structure of these centers, which will contribute to the development of innovative normative guidelines for the implementation of strategies that add to intersectoral efforts to suicide prevention in the country.

# Frameworks of Interprofessional Competencies in Healthcare: A Comparative Analysis



## Author

Ana Paula Veber - Universidade Estadual de Ponta Grossa (UEPG)  
Isabel Cardoso de Carvalho - Universidade Federal de Santa Catarina (UFSC)  
Marina Raijche Mattozo Rover- Universidade Federal de Santa Catarina (UFSC)  
Fernanda Manzini - Universidade Federal de Santa Catarina (UFSC)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite- Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

National Health Fund, Ministry of Health, Brazil, TED 113/23



## Keywords

interprofessional education, residency programs, professional competence

## Abstract

Interprofessional education (IPE) in health aims to improve collaborative practice, meaning that workers from different health professions and with different professional backgrounds can collaborate effectively to develop joint practices, aiming for positive impacts on health systems. For that, the development of various competencies is necessary. Considering the absence of methodologies for evaluating IPE strategies in the country, it is essential to identify which competencies have already been studied concerning the effectiveness of health education and professional qualification actions as part of ongoing efforts to improve health systems. An exploratory research was carried out with document analysis aiming to identify and compare frameworks for interprofessional competencies in health available in the literature. Official documents available on websites of governmental entities, universities, and associations were included. So far, 7 frameworks have been identified: 1 from WHO (World Health Organization), 2 from Canada, 2 from Australia, 1 from the UK, and 1 from the USA, published between 2008 and 2023. The WHO framework provides a comprehensive understanding of how collaboration among health professionals can be implemented globally. The Canadian documents define domains applicable in different contexts, allowing adaptations to local and institutional needs. In Australia, documents promotes essential skills for safe and efficient collaborative practices. In the United Kingdom, guidelines encourage the introduction of interprofessional learning into multiprofessional courses, while the USA document sets out core competencies aimed at promoting interprofessional collaborative practice. Through the analysis and comparison of these documents, it is expected to propose a guiding model for evaluating the development of interprofessional health competencies among graduates of Multiprofessional Health Family and Family and Community Medicine Residency programs.

# Elaboration of a protocol to optimization of antibiotic therapy by augmented exposition in critical care patients according to the antimicrobial susceptibility test.



## Author

João Vitor Burtet - Universidade Federal de Santa Catarina (UFSC)

André Igor Oliveira Prado - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Recursos próprios dos pesquisadores.



## Keywords

antimicrobial drug resistance; critically ill; pharmacokinetics

## Abstract

**Introduction:** Appropriate antimicrobial therapy is essential in critical care patients, especially when it's directed against a microorganism where high minimum inhibitory concentrations are required. The optimization of the antimicrobial use is essential, through appropriate selection, dose and administration. Since the March 2021 BrCAST update, which changed the reporting of dose cutpoints for antimicrobial susceptibility testing from "intermediate" to "susceptible, increased exposure", it has been highly important to set standards for achieving increased exposure to provide effective and safe antimicrobial therapy. **Objectives:** To create a protocol for optimizing the use of antimicrobials at Polydoro Ernani de São Thiago University Hospital (HU/UFSC). **Methods:** It was performed an Integrative Review at the database Pubmed/MEDLINE, searching for the terms ("name of the antimicrobial") AND (critically ill) AND (pharmacokinetics) AND (dosing), published from 2016 to 2021. Additionally, it was searched at the application Sanford Guide to Antimicrobial Therapy© **Results:** From a total of 200 articles, 49 were included and 151 were excluded by four criteria: specific populations (34); validation of methods (15); renal replacement therapy (38); without adequate information (64). The protocol was elaborated containing information about the antimicrobials, referred to dose, administration, special situations when the use can be adapted. **Conclusions:** The data found highlighted some main pharmacological points, such as the prolonged infusion of beta lactams showing probability of target attainment in higher levels than intermittent infusion, and the use of higher dose regimens to penetrate some infectious sites. Beyond the protocol elaboration, it was possible to raise some issues concerning antimicrobial resistance, antimicrobial stewardship, and the key role of clinical pharmacists in these activities.

# Analysis of time between drugs incorporation and the first dispensing considering rheumatic diseases



## Author

Talyta Dolores do Bonfim César - Universidade Federal do Paraná (UFPR)  
Astrid Wiens Souza - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

sem financiamento



## Keywords

avaliação de tecnologia em saúde, assistência farmacêutica, custos e análise de custos

## Abstract

The National Committee for Technology Incorporation (CONITEC) was created following the publication of Law No. 12,401/2011, whose function is to advise the Ministry of Health on the incorporation, exclusion or alteration of new medicines, products and procedures, as well as the drafting and/or alteration of Clinical Protocols and Therapeutic Guidelines. Also in 2011, Decree No. 7.646 was published, regulating its composition, competencies and operation, setting a deadline of one hundred and eighty days from the publication of the decision to incorporate the health technology, for the new medicine to be offered to the Unified Health System (SUS). The aim of this study was to analyze the time elapsed between the publication of the latest drugs incorporated for rheumatic diseases (rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis) in the Specialized Component of Pharmaceutical Assistance, group 1A, and their first dispensing in the SUS. The date of publication of the drugs incorporated since 2016 was extracted from the CONITEC website. The date of first dispensing was verified from the data available on the SABEIS (Open Room of Health Intelligence) platform. It was found that the time taken for the first dispensation of the incorporated drugs (Upadacitinib, Baricitinib, Tofacitinib, Golimumab, Certolizumab pegol and Secuquinumab) ranged from a minimum of 316 days to a maximum of 784 days, longer than the time stipulated by Decree 7.646, causing damage to the effectiveness of the pharmacological treatment, since the availability of the drug to the user is essential for proper treatment. This demonstrates the need to review pharmaceutical assistance procedures in order to find the main causes which make it difficult to comply with the law in that hinder compliance with the law in optimizing the start of treatment.

# Assessing Interprofessional Competencies in Primary Health Care: A Scoping Review



## Author

Ana Caroline Machado - Universidade Federal de Santa Catarina (UFSC)  
Ana Paula da Rocha - Universidade Federal de Santa Catarina (UFSC)  
Fernanda Manzini - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Ted 113/23 - Fundo Nacional de Saúde



## Keywords

Interprofessional Competencies, Primary Health Care, Interprofessional Education

## Abstract

**Introduction:** Health professionals need preparation and support to work effectively in collaborative practice teams to address increasingly complex health needs. Interprofessional education and interprofessional collaborative practice are essential strategies for developing the necessary interprofessional competencies (IPC) for collaborative practice. While assessment tools measuring IPC are widely used in educational settings, their application in primary health care is unknown. **Objective:** This review aims to identify the available tools for assessing IPC in primary health care. **Methods:** A scoping review was conducted by searching nine databases. Data extracted included publication details and descriptions of assessment tools. The tools were further evaluated to determine which IPC was addressed. **Results:** The search strategies retrieved 895 records. After selection, 19 studies with 12 different assessment tools were included for analysis. The studies (n=19) were published between 2016 and 2024, mostly conducted in the United States and involving Nursing, Medicine, and Pharmacy. Nine tools were validated by the authors or previous studies. The most utilized tools were the Interprofessional Collaborative Competency Attainment Survey (ICCAS), the Japanese version of the Self-Assessment Scale of Interprofessional Competency (JASSIC), and the Interprofessional Education Collaborative (IPEC) Competency Self-Assessment. The IPC assessed are related to interprofessional communication; collaboration; roles and responsibilities; ethics and conflict resolution; patient-centered care, and leadership. **Conclusion:** This review offers a comprehensive overview of the most common assessment tools and IPC assessed in primary health care settings. Faculty, health professionals, and researchers should identify the most appropriate tool according to the context in which it will be used. The results will provide the baseline for the 'Fui Residente' project.

# The role of Social Service In The Pharmacy Of Dispensing The Specialized Component Of Pharmaceutical Assistance.



## Author

Danuza Barros Gomes - Universidade Vila Velha (UVV)  
Girlandia Alexandre Brasil - Universidade de Vila Velha (UVV)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Não se aplica



## Keywords

Specialized Component of Pharmaceutical Assistance, Social Work, professionals

## Abstract

**Introduction:** Ensuring access to medicines involves urgent care and is a constitutional right. The Brazilian health policy becomes a space for action and work of various health support professionals, including the social worker, however, the role of this professional in pharmaceutical care is still little known, which makes our study relevant. **Aim:** Analyze the role of Social Work in the pharmacies dispensing the Specialized Component of Pharmaceutical Assistance in the State of Espírito Santo. **Methods:** This is an exploratory and descriptive study using a quali-quantitative approach. Data collection and analysis was carried out between October/2021 and March/2022. **Results:** In all, 76% of respondents reported that they work with social workers in the team and most (92.11%) know what activities they perform in the citizen pharmacy, with reception being the main activity reported (n=19). As for social workers, they reported that there is no way to measure the activities they perform, and there is not much unanimity in the instruments used in their practice. However, they report participating in discussion spaces (57.14%) and all believe that the work they do is important. As for the challenges, professionals report that the very strict protocols, the small number of social workers and the non-consideration of their opinions for the provision of diets and medicines as some of the points that need to be improved, however, most report that they observed improvement in the service since they started their activities. **Conclusion:** The professionals of the dispensing pharmacies teams understand the work process of the social service and value the institutional space that the professional occupies. Furthermore, the theoretical-methodological relevance materialized in the action mediated by the social service professional in the routine of the service was confirmed, considering the pharmaceutical assistance policy a legitimate space for social service action.



# Uncovering the conditions for implementing clinical pharmaceutical services with interprofessional collaboration: a scoping review



## Author

Tereza Cristina Pamplona Mosimann Busnardo - Universidade Federal de Santa Catarina (UFSC)  
Mayara Alessandra Schmitz - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

None



## Keywords

clinical pharmaceutical services, interprofessional collaboration, implementation

## Abstract

Internationally, pharmaceutical assistance values improve equitable access to safe and effective medicines and "person-centered" care, services in collaboration with other health professionals. In this Collaborative Care model, pharmacists, in addition to assuming responsibilities for performing their work, are also considered members of a team and have an active voice in the system. This study analyzed published experiences on clinical pharmaceutical services developed with interprofessional collaboration (CIP) at a global level and what conditions are necessary to implement it. A scoping review was carried out on the databases: PubMed, Scopus, Web of Science, SciELO and Embase. The research was carried out in pairs, and disagreements were resolved with a third researcher. Endnote 20 was used to eliminate duplicates and Rayyan to select articles. The full analysis of 53 articles is in process. Data extraction is mapping results to show potential driving factors in the intervention implementation process using the Consolidated Framework for Implementation Research (CFIR). In innovation we found interventions to improve the quality of therapy in general and carry out diagnostic tests, which provided access and prevention of the worsening of pathologies. In the internal configuration, we see trained clinical pharmacists undergoing continuing education. Most operate under collaborative practice agreements or communicate quickly with the prescriber via software, telephone or fax, providing rapid clinical decisions that benefit the patient. Discussions of clinical cases are also routine. As for external configuration and individuals, companies provide a work structure and time for dedication to the clinic, some even pay the professional better. Implementation is always evaluated and many projects are carried out in partnership with universities.

# A Trigger Tool for Optimising the Detection of Drug-Related Problems in High-Risk Pregnant Women: Development and Validation



## Author

Gabriela Santana Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Larissa Cândido Gomes da Silva - Universidade Federal do Rio Grande do Norte (UFRN)  
Priscilla Karilline do Vale Bezerra - Universidade Federal do Rio Grande do Norte (UFRN)  
Daniel Paiva Marques - Universidade Federal do Rio Grande do Norte (UFRN)  
Andreza Kelly Fernandes da Silva - Universidade Federal do Rio Grande do Norte (UFRN)  
Gabriela de Freitas Jorge - Universidade Federal do Rio Grande do Norte (UFRN)  
Andreia Suelle Moura Fonseca - Universidade Federal do Rio Grande do Norte (UFRN)  
Francisca Sueli Monte Moreira - Universidade Federal do Rio Grande do Norte (UFRN)  
Rand Randall Martins - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Coordination for the Improvement of Higher Education Personnel (CAPES) and National Council Scientific and Technological Development (CNPq) - Finance Code 001



## Keywords

Drug-related problems, High-risk pregnancy, Trigger tool

## Abstract

**Introduction:** This study aims to develop and validate a trigger tool for optimising the detection of Drug-Related Problems (DRPs) in hospitalised high-risk pregnant women, as current tools were not specifically designed for this context. **Methods and Material:** The study was divided into two stages. The tool development stage (January to December 2019) involved a descriptive analysis of medication consumption reports to identify monitoring parameters. The validation stage (February 2020 to July 2022) consisted of an observational and prospective study to determine the occurrence of DRPs in high-risk pregnant women. Two groups (test and standard) collected data to validate the tool. The data were analysed using descriptive and inferential statistics with Stata version 15. **Results:** In the development stage, the most relevant monitoring parameter involved respiratory changes (9.7%), gastrointestinal disorders (8.6%), abdominal pain (7.2%), and changes in heart rate (6.8%). These parameters corresponded to the "triggers" for optimising pharmacotherapy during high-risk pregnancy. The tool exhibited considerable sensitivity (74.1%; 95% CI 67.7 - 81.1), specificity (70.7%; 95% CI 63.4 - 78.0), accuracy (95% CI 65.3 - 79.7), and a high positive predictive value (PPV = 87.0%; 95% CI 81.6 - 92.4). However, its lower negative predictive value (NPV = 50.9%; 95% CI 42.9 - 58.9) may underestimate the detection of some DRPs, particularly those related to safety. In the validation stage, the test and standard groups identified a proportion of total DRPs (61.7 vs. 72.5%;  $p = 0.381$ ), respectively, although the test group detected fewer effectiveness-related DRPs (58.4 vs. 82.6%;  $p = 0.05$ ), safety-related DRPs (11.4 vs. 47.7%,  $p = 0.001$ ), and other DRPs (0.7 vs. 6.0%,  $p = 0.012$ ). **Conclusions:** The tool can be used as an initial screening tool to identify DRPs in hospitalised pregnant women, given its moderate sensitivity and acceptable positive predictive value.

# Self-perception of health in individuals with Diabetes Mellitus: profile and associated factors



## Author

Luanna Gabriella Resende da Silva - Universidade Federal de São João del-Rei (UFSJ)  
Marlon Silva Tinoco - Universidade Federal de São João del-Rei (UFSJ)  
Mariana Linhares Pereira - Universidade Federal de São João del-Rei (UFSJ)  
Maria Teresa Herdeiro - Universidade de Aveiro  
André Oliveira Baldoni - Universidade Federal de São João del-Rei (UFSJ)



## Knowledge Area

This work was supported by the Research Support Foundation of the state of Minas Gerais (FAPEMIG - APQ-01107-21), by the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES - 001), and by the National Council for Scientific and



## Funding

sem financiamento



## Keywords

Diabetes Mellitus, Patient Satisfaction, Drug Therapy

## Abstract

**Background:** Diabetes Mellitus (DM) affects 537 million adults worldwide, causing one death every five seconds. The monitoring of individuals with DM is a crucial part of optimizing pharmacotherapy. Self-perception of health serves as an indicator of overall well-being and treatment adherence, which is important for its success. **Aim:** To measure the level of health self-perception in individuals with DM before they begin monitoring with a pharmacist. **Methods:** This study is part of a larger project (training in Clinical Pharmacy). This is a cross-sectional study that included patients with DM treated in the SUS of municipalities where pharmacists completed the aforementioned training. They completed a structured sociodemographic questionnaire, which included the following question: "How do you perceive your health compared to that of others your age?" We compared the response variable (health perception) to the following explanatory variables: sex, age group, ethnicity, family income, type of DM, and whether they had Systemic Arterial Hypertension (SAH) or not. We performed independent samples t-tests and ANOVA for comparing means. **Results:** We recruited 399 patients (67.7% female) from 16 municipalities in Minas Gerais, Brazil. The median age was 64 years (range 55-71). Approximately 41% perceive their own health as "fair", but the age group 50-59 years is associated with a self-perception of "poor" health ( $p=0.02$ ). Additionally, Type 2 DM was the most prevalent type (89%), and 79% also had SAH. **Conclusion:** The study evidenced that the majority of individuals with diabetes mellitus (DM) classify their own health as fair, but that the age group 50-59 had a "poor" self-perception, suggesting that factors beyond the analyzed variables impact the health of individuals with DM. Further studies involving this age group are necessary to investigate a possible causal relationship between these variables.

# Experience report on the Temporary Center for Receiving, Storing, and Distributing Medicine Donations during the May 2024 Flood in Rio Grande do Sul



## Author

Isabela Heineck - Universidade Federal do Rio Grande do Sul (UFRGS)  
Camila S. Muneretto - Instituto do Câncer Infantil  
Ruy C. R. Beck - Universidade Federal do Rio Grande do Sul (UFRGS)  
Diogo Pilger - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

No funding



## Keywords

Pharmaceutical Services, Floods, Pharmaceutical Centers

## Abstract

Extreme weather events are becoming more frequent and contingency plans need to be prepared and adapted to the new times. In May 2024, Rio Grande do Sul experienced its worst floods in history, leading to a significant humanitarian crisis. The Faculty of Pharmacy of the Federal University of Rio Grande do Sul played a crucial role in the relief efforts by establishing a center for collecting and distributing donated medicines to the affected areas. This operation involved approximately 250 volunteers, including pharmacists, professors, technicians, and pharmacy students. The operation was set up in the designated area of the Faculty building, where the volunteers handled the reception, assessment, registration, storage, and dispatch of the medicines. Additionally, a software management system was developed in partnership with UFCSPA to manage the flow of incoming and outgoing donated items and requests from the shelters. Over a period of 20 days, the center sent medicines to 180 shelters, 42 institutions, 21 hospitals, and 32 health centers in the affected municipalities. They received 1528 orders for medicines, and 88% of them were successfully fulfilled, resulting in the distribution of 787,204 items, including capsules, tablets (770,818) syrups, suspensions, and solutions (12,057). The center's efforts were crucial in supporting pharmaceutical services in the capital and other affected areas. This underscored the importance of planning pharmaceutical service strategies during climate and humanitarian crises.

# Twenty years of medicines economical market regulation in Brazil



## Author

Valdete Aparecida de Melo - Universidade Federal de Santa Catarina (UFSC)  
Dayani Galato - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Coordination for the Improvement of Higher Education Personnel – Brazil (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES)



## Keywords

drug price, acces to essential medicines, drug market regulation chamber

## Abstract

**Objetives:** Interpret and describe possible advances perceived in the text of the public consultation of the Secretariat for the Defense of Competition and Competitiveness of the Ministry of Economy (SEAE) 2/2021, which had the proposal to review the Resolution of the Drug Market Regulation Chamber (CMED) 2/2004, referring to the regulation of medicine prices. **Methodology:** Analytical-descriptive documentary research, of an exploratory nature, which resulted from the search for possible interrelationships between the legal texts consulted. **Results:** The text of the public consultation covered Res. 2/2004 and Statement 9/2016, which deals with the pricing criteria for non-new biological medicines (BNN). The public consultation kept the marketing guidelines unchanged to justify the inclusion of medicines in different price categories, the structuring of prices through External and Internal Price Referencing (REP and RIP), the fixed list of countries as a reference for searching for international prices and provisional price conditions, provided for in Res. 2/2004. Furthermore, there remains a lack of inclusion of pricing criteria for radiopharmaceuticals, advanced and genetic therapies, as well as synthetic and biological medicines that do not have an international price and/or comparators in Brazil. The BNN pricing suggestion is only a 20% discount in relation to the price of the biological originator, however, there is an absence of criteria for pricing the BNN when the originator does not have a health registration in Brazil, in addition to the absence of criteria for pricing the originator. **Conclusions:** During the 20-year period of validity of Res. 2/2004, significant changes occurred in the global medicines market, and regulatory advances observed in other countries, in relation to periodic price reviews and/or due to line extensions for new indications, as well as flexibility in the basket of countries for international prices, may be adopted in Brazil.

# How Can Pharmaceutical Services Improve Medication Adherence in Elderly Patients with Non-Communicable Chronic Diseases? A Systematic Review



## Author

Vinícius Soares Ribeiro - Universidade Federal do Paraná (UFPR)  
Luan Diniz Pessôal - Universidade Federal do Paraná (UFPR)  
Thais Teles de Souza - Universidade Federal da Paraíba (UFPB)  
Walleri Christini Torelli Reis - Universidade Federal da Paraíba (UFPB)  
Ana Carolina Melchioris - Universidade Federal do Paraná (UFPR)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

This work was funded by the Public Call n. 03 Produtividade em Pesquisa PROPESQ/PRPG/UFPR grant n. PVG13351-2020



## Keywords

Health Services for the Aged, Medication Therapy Management, Chronic Disease

## Abstract

Non-Communicable Chronic Diseases (NCDs) pose a significant challenge to health systems, particularly in low and middle-income countries, as they are the leading causes of global mortality. Managing NCDs often involves the use of medications, but adherence to these treatments is low, especially among the elderly. Pharmacists play a crucial role by providing clinical services and applying various resources in the medication use process to improve adherence and the effectiveness of pharmacotherapy. However, there are gaps in the characterization and evaluation of these methods. This systematic review, conducted in March 2024 following PRISMA guidelines and Cochrane Collaboration recommendations, registered under PROSPERO CRD42023432053, focused on identifying and evaluating resources used by pharmacists in clinical settings to promote medication adherence in elderly patients with NCDs, including conditions such as hypertension, diabetes mellitus, and dyslipidemia. The databases PubMed/MEDLINE, Scopus, Scielo, and Google Scholar were searched, initially yielding 2,357 records. After screening, 10 studies were deemed eligible. The identified resources were categorized into four main groups: tools (30%), contact approaches (30%), medication dispensing (30%), and applications (10%). The results indicated significant improvements in patient adherence, such as with the use of medication organizers, dosage calendars, home visits, home delivery, synchronization programs, and family educational support applications. Despite the promising results, only home delivery programs, synchronization programs, and applications showed a lower risk of bias. The review highlighted the need for more research with robust methodologies to optimize and validate these pharmaceutical interventions, ensuring better adherence to pharmacotherapy in elderly patients with NCDs.

# Communication with users: an analysis of websites for the specialized component of pharmaceutical assistance in Brazilian states



## Author

Ana Liani Beisl Oliveira - Fiocruz

Vera Lucia Luiza - Fiocruz

Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Research comprises doctoral thesis Fiocruz student, CAPES scholarship holder.



## Keywords

Drugs from the Specialized Component of Pharmaceutical Care, E-government, Access to Information

## Abstract

Considering the importance of the government's digital communication with users, this article aims to analyze the websites of all federative units in Brazil in order to identify whether the information presented on CEAF services is sufficient, updated and in line with the digitalization of public services. The websites of the 26 study health departments and the district secretariat were analyzed based on indicators organized into four functions (navigability, service maturity, content and execution), organized in an information matrix, for which data were collected in May 2024. A score expressed as a percentage of what was observed in relation to the maximum expected was calculated. At the national level, function scores ranged from 53.1% (CEAF Execution) to 72.5% (Content). In the Execution function, the North and Southeast achieved the worst and best scores, with 20.8 and 76.5%, respectively. In the Content function, the North again had the worst score with 41.9% and the South the best, with 88.9%. Within the CEAF Execution function, the sub-function "Adequacy to electronic format" had the worst average result in Brazil (28.9%; min-max. 0.0% to 100%). In view of the findings, it is concluded that there is still a great disparity between the SES websites in Brazilian states, but there are partial gains with the availability of updated stock information and the possibility of requesting CEAF medicines through some websites.

# Mapping antidote availability policies and guidelines: a scoping review protocol



## Author

Barbara Rahn - Universidade Federal de Santa Catarina (UFSC)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

No funding



## Keywords

Poisoning, Antidotes, Health Policy

## Abstract

**Introduction:** In most cases of poisoning, symptomatic and supportive treatment is appropriate in the initial approach. However, using the correct antidote, appropriately and at the right time, can save lives. The rational use of antidotes contributes to reducing mortality, hospital stays and costs. **Objectives:** The study aims to map policies and guidelines for the availability and logistics of antidotes used in the treatment of acute and chronic poisoning. **Methods:** This scoping review and policy mapping will be carried out following the JBI Manual for Evidence Synthesis and reporting will follow the PRISMA-ScR tool. The study will have the following guiding questions: What are the policies and guidelines that guide the logistics and availability of antidotes in the world? What are the available antidotes that compose these policies and guidelines? What logistics strategies for distributing antidotes are proposed in these policies and guidelines?. Data collection will consist of four stages: review and extract policies and guidelines on the availability and/or logistics of antidotes in government websites or recognized organizations in the area; develop a systematic search strategy for scientific databases; search reference lists of documents already included; and merge all documents into a data repository. The protocol has been registered in the Open Science Framework website. **Results:** The database search retrieved a total of 2.842 studies and 17 policies were identified in a local or national context: Canada, United Kingdom, United States of America, Spain, Ireland, Sweden, Australia, Swiss, New Zealand, Malaysia, Denmark, Nova Scotia, United Arab Emirates, Hong Kong, Santa Catarina (Brazil), Campinas (Brazil), Espírito Santo (Brazil). The results of the study search and inclusion process will be reported in full in the final scoping review. **Conclusion:** We believe the results of this scoping review will support the development of a national guideline.



# Cost of stress ulcer prophylaxis in critical ill patients: effects of pharmaceutical recommendations



## Author

Cássio Alexandre Oliveira Rodrigues - Universidade do Rio Grande do Norte (UFRGS)  
Nara Ruth Freitas e Paiva - Universidade do Rio Grande do Norte (UFRGS)  
Ana Beatriz Dantas Gomes - Universidade do Rio Grande do Norte (UFRGS)  
Vaneska Silveira de Paiva - Hospital do Coração de Natal  
Antônio Manuel Gouveia de Oliveira - Universidade do Rio Grande do Norte (UFRGS)  
Rand Randall Martins - Universidade do Rio Grande do Norte (UFRGS)  
Francisca Sueli Monte Moreira - Universidade do Rio Grande do Norte (UFRGS)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Research comprises doctoral thesis Fiocruz student, CAPES scholarship holder.



## Keywords

Clinical pharmacy, Critical care, Pharmacoeconomics

## Abstract

**Introduction:** Among the various roles of pharmacists in intensive care units (ICUs), rationalizing healthcare costs is notable. In this context, stress ulcer prophylaxis in critically ill patients using proton pump inhibitors (PPIs) can reveal significant cost differences between the parenteral approach and sequential oral therapy (SOT). **Objective:** To evaluate the impact of pharmaceutical recommendations for SOT on the costs of stress ulcer prophylaxis in critically ill patients. **Methodology:** A quasi-experimental cost-minimization trial involving adult patients admitted to an ICU. Patients were divided into two groups (control and intervention), each consisting of 86 patients (from January to December 2023). Unlike the control group, the intervention group (IG) had a clinical pharmacist who assessed the appropriateness of switching from parenteral PPIs to SOT and recommended this change to the multidisciplinary team. Direct costs in Brazilian Reais for both approaches were calculated, and their means were compared using Student's t-test and Pearson's chi-square test, with significance set at  $p < 0.05$ . This study was approved by the Research Ethics Committee of the Hospital Universitario Onofre Lopes, under CAAE number 29834320.4.0000.5292. **Results:** In the IG, the suggestion to switch to SOT was accepted for all patients, whereas this substitution occurred in only 15 patients in the control group (100% vs. 17.4%;  $p < 0.01$ ). Patients in the IG had a significantly shorter duration of parenteral PPI therapy compared to the control group (4.4 vs. 10.0 days,  $p < 0.01$ ). The total final cost for gastric ulcer prophylaxis was R\$176.73 in the IG, compared to R\$14,198.28 in the control group ( $p < 0.01$ ). **Conclusion:** Pharmaceutical care recommending SOT for stress ulcer prophylaxis in critically ill patients results in a significant reduction in costs, a shorter duration of parenteral PPI use, a greater adoption of SOT compared to conventional approaches.

# Profile Of Interventions Performed During Pharmacotherapy Monitoring In An Intensive Care Unit



## Author

Cyntia Elizabeth Fonseca Bosco Galvão - Secretaria de Estado de Saúde do Distrito Federal  
Brasília  
Dayani Galato - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

No funding pharmacists



## Keywords

pharmacists, intensive Care Units, evaluation of results of therapeutic interventions

## Abstract

**Introduction:** Critically ill patients require specialized care provided by a multidisciplinary team. Pharmacotherapy, which is often complex, requires monitoring by pharmacists. **Objectives:** To analyze the profile of interventions performed by pharmacists in an intensive care unit (ICU) during pharmacotherapeutic monitoring. **Methods:** A retrospective cohort study carried out in an eight-bed adult intensive care unit of a public hospital in the Federal District. Pharmaceutical interventions carried out between January 2022 and December 2023 by clinical pharmacists were analyzed. The interventions resulting from the daily monitoring performed by a routine pharmacist and a resident were collected from a standardized spreadsheet for recording clinical pharmacy indicators. Ethics Committee approval No. 58120322.0.0000.5553. **Results:** A total of 1,466 interventions were conducted over the course of the study period, with 902 occurring in 2022 and 581 in 2023. This was due to the temporary closure of the facility for refurbishment. In 2022, the most common interventions were related to the addition of medication (n = 222; 24.7%), followed by the discontinuation of medication (n = 86; 9.6%), other signs and warnings (n = 75; 8.3%), and the increase of dosage (n = 70; 7.8%). In 2023, there was a higher frequency of drug additions (n = 158; 27.2%), followed by dosage increases (n = 59; 10.2%), dosage decreases (n = 56; 9.5%), and drug suspensions (n = 46; 7.9%). The drugs that were most frequently involved in interventions in 2022 were quetiapine (n = 48; 5.3%), bromopride (n = 32; 3.6%), and pantoprazole (n = 31; 3.4%). In the subsequent year, the most frequently encountered drugs were methadone (n = 43; 7.5%), meropenem, vancomycin, and polymyxin B (n = 28; 4.9%). **Conclusions:** Given the level of adherence to the proposed interventions, it was possible to contribute to the pharmacotherapy of patients in terms of delirium and pain management and antimicrobial use.

# Social determination of health and the relationship with pharmaceutical services and access to medicines: a scoping review in the context of primary health care (PHC)



## Author

Samara Jamile Mendes - Universidade Federal de Santa Catarina (UFSC)  
Patricia Bernardi Sassi - Universidade Federal de Santa Catarina (UFSC)  
Rafaela Tavares Peixoto - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

CNPq post-doctoral Fellowship 151549/2022-2



## Keywords

Social determination of health, Pharmaceutical Services, Primary Health Care

## Abstract

The analysis of the social determination of health is an opportunity to study the living conditions of individuals and population groups and their relationships with the health situation, the social, economic, cultural, ethnic/racial, psychological and behavioral factors that can influence responses of health. The objective of this study is to identify social determinations in pharmaceutical assistance and access to medicines in the context of PHC. This is a scoping review of the literature, according to the Joanna Briggs Institute protocol. The question is: what does the scientific literature present about social determinations in pharmaceutical care in the context of PHC? The databases in the search were: Medline via PubMed, Scielo, Lilacs, Scopus via Elsevier and Embase. The protocol was registered in the Open Science Framework repository. The inclusion criteria are: (1) whose setting is PHC; (2) that address municipal pharmaceutical management; pharmaceutical management in PHC; pharmaceutical logistics; purchase of medicines; pharmaceutical care; pharmaceutical services; pharmaceutical workforce in municipal PHC; pharmacy work processes; access and use of medicines; medicine access policies; (3) which include the debate on determination or social determinants. As exclusion criteria, articles from the hospital context and/or levels of care other than PHC were used. 2,180 studies were selected, 544 of which were duplicates, 53 articles were included during the eligibility process using the inclusion and exclusion criteria. The most frequent countries among the studies were Brazil and England, the others present are Saudi Arabia, USA, Kuwait, Sweden, Australia and Ireland. The years of publication varied between 2000 and 2023 (largest number). Explicitly, 8 articles have the concept of social determination of health, the others present factors that affect the use and access to medicines, as well as strategies for the development of pharmaceutical assistance in PHC.

# Pharmaceutical care in the quality of life of patients using the capecitabine and oxaliplatin (CAPOX) protocol for the treatment of colorectal câncer



## Author

Camille Nigri Cursino - Universidade Federal Fluminense (UFF)  
Patrícia Kaiser Pedrosa Caval - Universidade Federal Fluminense (UFF)  
Ana Clara Duarte dos Santos - Universidade Federal Fluminense (UFF)  
Ariela Dutra Norberto de Oliveira - Universidade Federal Fluminense (UFF)  
Larissa dos Santos Sebold Marinho - Universidade Federal Fluminense (UFF)  
Larissa Rodrigues Nascimento - Universidade Federal do Rio de Janeiro (UFRJ)  
Thaís Amorim Nogueira - Universidade Federal Fluminense (UFF)  
Sabrina Calil-Elias - Universidade Federal Fluminense (UFF)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

FAPERJ - 7a EDIÇÃO DO PROGRAMA PESQUISA PARA O SUS: gestão compartilhada em saúde - PPSUS\_ E-26/210.459/2021



## Keywords

Pharmaceutical care, quality of life, colorectal neoplasms

## Abstract

**Introduction:** Colorectal cancer and its treatment can influence the patient's social, productive, and financial life. Quality of life (QoL) is an important outcome measure for evaluating treatment results from the patient's perspective. Objective: To measure the health-related quality of life of patients taking CAPOX who receive pharmaceutical care. **Methods:** Multicenter, prospective study. Patients taking CAPOX aged between 18 and 80 years were included. Patients who did not complete their treatment and who died were excluded. The EQ-5D was used to assess QoL at two different times, at the first pharmaceutical consultation at the start and end of treatment. The EQ-5D has five dimensions: mobility, self-care/personal care, usual activities, pain/illness, and anxiety/depression. The Ethics Committees of the respective institutions approved this study. **Results:** 22 patients were included in the study. Of these, half (11) were female and 86.4% were aged between 40-69 years. The majority (81.8%) had 4 or more years of schooling. Concerning the tumor, 36.4% had metastases. In addition, 11 patients (50%) had some comorbidity. All the patients had at least one adverse event during treatment, with an average of  $3.7 \pm 1.8$  events per patient, most of which were classified as mild to moderate. The majority of patients reported no problems with mobility, self-care/personal care, and usual activities before and after treatment. Concerning pain/malaise, half of the patients reported no problems. And 68.2% and 54.5% reported some anxiety or depression problems before and after treatment, respectively. When comparing before and after, only usual activities showed a statistically significant improvement ( $p=0.02$ ). **Conclusion:** Pharmaceutical care prevented the aggravation of adverse events, which probably meant that the quality of life of these patients did not worsen throughout their cancer treatment.

# The role of pharmacists in the context of rare diseases: a scoping review



## Author

Cássia Cunico - Universidade Federal de Santa Catarina (UFSC)  
Matheus Nascimento Fuchina - Universidade Federal de Santa Catarina (UFSC)  
Marina Raijche Mattozo Rover - Universidade Federal de Santa Catarina (UFSC)  
Rafael Santos Santana - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

No funding



## Keywords

Rare Disease, Pharmaceutical Services, Public Health

## Abstract

**Background:** Rare diseases are a group of clinical conditions poorly understood, that often manifest in childhood and have a significant impact on quality of life and life expectancy. Advances in innovative therapies and their high price further increase the need for specialized assessment and directions for better access to and management of treatments. **Objectives:** Identify and summarize the evidence on the role of pharmacists and their impact in the field of rare diseases. **Methods:** JBI Methodology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist was used. Three electronic databases were consulted to search for published literature. The list of rare diseases for the search was established by consulting consultative documents from the health systems of Brazil, the United Kingdom, Ireland, the United States, and China. The protocol for the methodological approach has been previously published. **Results:** 48 studies fully met the eligibility criteria. Most were observational studies from 10 countries and 10 rare diseases. Most were conducted in academic settings, hospitals or specialized care centers. The studies have limited characteristics and lack specificity. The pharmaceutical services most commonly performed by pharmacists included educating and counseling patients and caregivers (n = 40; 83.3%) and prescription monitoring and medication review service (n = 37; 77.1%). **Conclusions:** Despite the immense advances in the development of new medicines for rare diseases, the literature is limited in its report on the development of pharmaceutical care services. It is essential to invest in pharmaceutical services to provide technical support for rational use of medicines, and establish evidence for health systems and services to recognize their usefulness and subsidize public policies to expand the provision and funding of pharmaceutical services for rare health conditions.

# Assessment of the sociodemographic profile of patients using the continuous glucose monitoring sensor in the glycemic management of patients benefiting from dispensing via the public health system in the state of Espírito Santo.



## Author

Fernanda Domingues Gomes Martins - Universidade de Vila Velha (UVV)  
Girlandia Alexandre Brasil Amorim - Universidade de Vila Velha (UVV)  
Denise de Amorim Loura Macedo - Universidade de Vila Velha (UVV)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding



## Keywords

Diabetes Mellitus; Continuous glucose monitoring; Sociodemographic profile; Diabetes mellitus;

## Abstract

Diabetes Mellitus (DM) is a prevalent disease worldwide, with high mortality rates, posing a significant challenge to public health. Brazil ranks as the sixth country with the highest number of adults with DM, approximately 15.7 million. Diagnosis is based on measuring plasma glucose, using criteria such as fasting blood glucose, postprandial glucose, and glycated hemoglobin (HbA1c). Effective glycemic control is essential for reducing long-term complications. The difficulty in managing the disease makes glycemic control challenging, favoring the occurrence of micro and macrovascular complications. Self-monitoring of blood glucose represents a significant advancement in diabetes treatment, allowing for more precise control. The FreeStyle Libre (FSL) system is a device that offers advantages such as a reduction in hypoglycemia frequency and improvement in glycemic control. The State of Espírito Santo (ES) has invested in continuous glucose monitoring devices for patients, aligning with the principle of comprehensiveness in the Unified Health System (SUS). This study aimed to investigate the sociodemographic profile of patients benefiting from glucose monitoring sensors for glycemic management. An exploratory-descriptive, retrospective study was conducted, analyzing electronic medical records of patients who used the continuous glucose monitoring sensor (case group - S) and diabetic patients without the device (control group - C) between January 2020 and December 2022. Group S included 108 diabetic patients with ongoing processes for the FSL sensor, and in group C, 108 diabetic patients with ongoing processes for insulin were randomized. It was found that 46.6% of patients were female and 53.7% were male. The urban population tends to develop more DM. Patients cared for by the SUS have a higher average HbA1c when compared to patients in the private system. The impact of the prescription origin (public vs. private) on the average HbA1c was statistically significant.

# The perspective on pharmaceutical care in the community shelter of the University of Rio Grande do Sul - The public health emergency



## Author

Isabeli Brum Ginar Telles - Universidade Federal do Rio Grande do Sul (UFRGS)  
Vinicius Jardim Rodrigues - Universidade Federal do Rio Grande do Sul (UFRGS)  
Eduarda Fernandes de Mello - Universidade Federal do Rio Grande do Sul (UFRGS)  
Diego Gnatta - Universidade Federal do Rio Grande do Sul (UFRGS)  
Fernanda d'Athayde Rodrigues - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Universidade Federal do Rio Grande do Sul



## Keywords

pharmaceutical care, climate crisis, interprofessional

## Abstract

**Introduction:** The state of Rio Grande do Sul was hit by the biggest climate crisis in its history, with more than 400 cities affected by the flood. Between May 4th and June 14th, a community shelter was set up at School of Physical Education, Physiotherapy and Dance of the Federal University of Rio Grande do Sul for 660 people, including 169 children and 68 immigrants. **Objective:** Describe the experience of pharmacists and students volunteers in an emergency shelter, during the calamity situation with an interprofessional health staff. **Methodology:** Description of the work of pharmacy, made up by both students and teachers in a health unit in the shelter. **Results:** Was adapted a field basic health unit to meet the needs of the shelter with an interprofessional health staff including nurses, pharmacists and doctors, made up by both students and teachers. The team was able to care for the population with case discussions, prescriptions adjustments, adapting treatments to each case. The care service was established according to demand from the sheltered community, in the first weeks, the staff provided 24-hour care, after the hours of service were staggered by needs. Prescriptions were retained for each treatment, amounting to 1.725 during the period the health center was working. The presence of the pharmacist allowed the existence of a pharmacy supplied by donations and the unit supplied 333 medicines of which only 91 were covered by a list of essential medicines for Porto Alegre, named REMUME. In addition, active search for patients adhering to antiretroviral therapy was made, as the directly observed treatment was one of the most resolute practices, helping patients with difficulties in the management of their treatments. **Conclusions:** Pharmaceutical counseling is the mainstay of Pharmaceutical Assistance, a place to listen to the sheltered community, ensure access to treatments and medication adherence, understanding their particular characteristics and weaknesses.

# Drug-Drug Interactions In Neonatal Intensive Care And Associated Clinical Outcomes



## Author

Daniel Paiva Marques - Universidade Federal do Rio Grande do Norte (UFRN)  
Andreza Kelly Fernandes da Silva - Universidade Federal do Rio Grande do Norte (UFRN)  
Gabriela Santana Oliveira - Universidade Federal do Rio Grande do Norte (UFRN)  
Nathalia Beatriz de Oliveira Pedrosa - Universidade Federal do Rio Grande do Norte (UFRN)  
Áyslla Thaisa Guedes Martins - Universidade Federal do Rio Grande do Norte (UFRN)  
Jadson da Silva Alves - Universidade Federal do Rio Grande do Norte (UFRN)  
Iris Ucella de Medeiros - Universidade Federal do Rio Grande do Norte (UFRN)  
Rand Randall Martins - Universidade Federal do Rio Grande do Norte (UFRN)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Coordination for the Improvement of Higher Education Personnel (CAPES) and National Council Scientific and Technological Development (CNPq) - Finance Code 001



## Keywords

Neonates, Intensive Care Unit, Drug-Drug Interaction

## Abstract

**Introduction:** Neonatal intensive therapy involves the administration of multiple medications to treat critical conditions in neonates. Thus, this study aims to assess the profile of Drug-Drug Interactions (DDI) and their potential associated clinical outcomes. **Methods and Material:** A cohort was conducted between March 2023 and March 2024 in a Neonatal Intensive Care Unit (NICU) at a teaching maternity hospital in Natal/RN (23 beds). It included 365 patients using at least one medication, excluding readmissions (approval from Research Ethics Committee no. 5867920). Daily clinical, laboratory, and pharmacotherapeutic parameters were collected. DDI were classified according to Micromedex and grouped by potential common outcomes, with their incidences presented with 95% confidence intervals (CI). The influence of length of stay and number of medications on the incidence rate of DDI in neonates was analyzed using mixed-effects linear regression. In the analysis of the potential influence of DDI on selected outcomes such as heart rate (HR), respiratory rate, creatinine clearance, urine output, and urea, Student's t-test was employed ( $p < 0.05$ ). **Results:** 255 (69.9%) neonates experienced 1 or more DDI during hospitalization, predominantly involving antimicrobials (58.6%), potentially associated with arrhythmias (27.4%), nephrotoxicity (18.3%), and Central Nervous System Depression - CNSD (16.8%). The incidence of DDI related to arrhythmia and CNSD tended to decrease with length of stay ( $\beta = -0.106$ ;  $p < 0.01$  and  $\beta = -0.088$ ;  $p < 0.01$ , respectively), while the risk of nephrotoxicity increased with treatment duration ( $\beta = 0.097$ ;  $p < 0.01$ ). DDI potentially related to arrhythmia increased HR by 5.9% ( $p < 0.001$ ), those associated with nephrotoxicity decreased glomerular filtration by 44% ( $p < 0.001$ ), and those related to CNSD decreased HR by 6% ( $p < 0.001$ ). **Conclusion:** DDI were significantly associated with arrhythmias, nephrotoxicity, and CNSD, negatively impacting critical clinical parameters.



# Acess to medicines for rheumatoid arthritis in the Unified Health System: a brazilian's patient perspective



## Author

Emilia Vitória da Silva - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding



## Keywords

sociodemographic factors, pharmaceutical assistance, Rheumatoid arthritis

## Abstract

**Introduction:** In Brazil, through the Specialized Component of Pharmaceutical Assistance (CEAF), including immunobiological medicines representing an annual cost of 6 million Brazilian reais (BRL) or the Ministry of Health. The objective of this study is to understand the perspective of Brazilian patients with rheumatoid arthritis regarding access to medications provided by CEAF. **Method:** This is a cross-sectional, descriptive study with data collected through an electronic form on the Survey Monkey platform. A pilot study was conducted from May 13 to June 19, 2024. Descriptive statistics of the data were performed. **Results:** A total of 201 respondents participated in the pilot project. Among the respondents, 92.1% (n=175) have rheumatoid arthritis. 26.3% (n=50) have lived with the disease for 10 to 15 years, 24.2% (n=42) live with chronic pain, and 16.3% (n=31) have hypertension. Regarding access to medications, 20.9% (n=39) obtain them entirely through the SUS, while 51.9% (n=97) need to supplement their treatment by purchasing from private pharmacies. 47.6% (n=89) report spending between R\$100 and R\$400 on medication purchases, resulting in a high impact (29.9%; n=56) on the family budget. Additionally, 46.2% (n=85) state they use medication without medical indication, with analgesics (55.4% of respondents), anti-inflammatories (29.4%). The use of symptomatic medications with a medical prescription is reported by 79.73% (n=146), including 35.33% (n=65) anti-inflammatories, 32.61% (n=60) analgesics, 29.35% (n=54) oral corticosteroids, and 22.28% (n=41) opioid analgesics. Of the total respondents, only 15.79% (n=24) reported being attended by a pharmaceutical professional when receiving medications from the CEAF. **Conclusion:** The results of this study can guide public policies to improve access to medications, increasing the percentage of those who use CEAF, thus reducing the impact on the family budget and enhancing pharmaceutical care to minimize self-medication."

# The profile of sedatives and analgesics used in a COVID-19 intensive care unit of a university hospital in southern Brazil.



## Author

André Igor Oliveira Prado - Universidade Federal de Santa Catarina (UFSC)  
Diogo Mariz - Universidade Federal de Santa Catarina (UFSC)  
Paola Andréia Santos - Universidade Federal de Santa Catarina (UFSC)  
Filipe Carvalho Matheus - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

None.



## Keywords

sedatives, intensive care unit, COVID-19

## Abstract

**Introduction:** The COVID-19 pandemic has brought great difficulties in managing critically ill mechanically ventilated patients. It was observed markedly higher sedation needs compared to other critically hospitalized and mechanically ventilated patients. **Objective:** To describe the profile of sedatives and analgesics in critically ill patients with confirmed COVID-19, under mechanical ventilation in the Intensive Care Unit (ICU) of an university hospital in southern Brazil. **Methods:** A descriptive retrospective study on the use of sedative and analgesic drugs was carried out. From 497 patients with confirmed COVID-19, admitted from March 2020 to December 2021, in an adult respiratory intensive care unit in a university hospital in southern Brazil, data from 165 patients were collected, drawn at random. Inclusion criteria was the use of mechanical ventilation and the access to data from the medical records. The variables were age; sex; length of stay; type of discharge; and the sedative and analgesic drugs used during the ICU stay. The study was approved by the Human Research Ethics Committee of the Federal University of Santa Catarina (CEPSH-UFSC) under CAAE number 56237422.0.0000.0121. **Results:** 55.15% were male, and the average age was 55.22 years. The most common diagnosis on admission was Severe Acute Respiratory Syndrome (23.63%). The average ICU stay was 12.15 days. 14 different sedatives and analgesics were used. The most common were fentanyl (79.39% of patients), midazolam (72.12%) and propofol (66.67%). Regarding the outcome, a total of 74.54% were discharged, 24.24% died and 1.21% were readmitted. **Conclusions:** The mortality rate in this cohort is among the lowest reported so far. The use of a safe and effective deep sedation strategy certainly contributed to this outcome, and calls for a more analytic view over the characteristics of the use of these drugs in this scenario, pointing to future trends for a more efficient and safer use of the deep sedation.

# Evaluation of the clinical impact of continuous glucose monitoring sensor use on glycemic management in patients benefiting from public health system dispensation.



## Author

Fernanda Domingues Gomes Martins - Universidade de Vila Velha (UVV)  
Girlandia A. Brasil Amorim - Universidade de Vila Velha (UVV)  
Anelise Souza Gava - Universidade de Vila Velha (UVV)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding



## Keywords

Diabetes Mellitus; Glycemic control; Continuous glucose monitoring;

## Abstract

Diabetes Mellitus (DM) is a disease with high mortality rates and effective glycemic control is essential to reduce long-term complications. The FreeStyle Libre (FSL) system is a device that offers advantages in improving this control. However, the literature lacks investigations into the real benefits perceived by patients. This study aimed to investigate the clinical impacts of adopting this device, aiming to improve the glycemic management of patients benefiting from the Unified Health System (SUS). An exploratory-descriptive, retrospective study was carried out, analyzing electronic medical records of patients who used the sensor (case group - S) and diabetic patients without the device (control group - C) between January 2020 and December 2022. The study was approved by the CEP-UVV (64014522.1.0000.5064) and SESA/ES. Group S included 108 diabetic patients with ongoing processes for the FSL sensor, and in group C, 108 diabetic patients with ongoing processes for insulin were randomized. Descriptive statistics and non-parametric tests were used to evaluate associations between variables. A significant difference was considered when  $p < 0.05$ . Group S recorded lower HbA1c rates compared to group C ( $p < 0.05$ ), suggesting better glycemic control. Comparative analysis between groups S and C revealed statistically significant differences in HbA1c between groups from T0 onwards ( $p < 0.05$ ). In group S, HbA1c showed a tendency to reduce at T1, T2, T3 and T4, but without statistical significance. Time in range (IRR) ranged from 50.20% (T2) to 57.1% (T4). The results indicated that the group that used the FSL continuous glucose monitoring sensor showed better glycemic control, evidenced by the reduction in HbA1c. However, despite these improvements, the percentage of patients achieving goals remained relatively low.

# Dissatisfaction with Pharmaceutical Services in primary health care and non-adherence to medication for hypertension



## Author

Poliana Vieira da Silva Menolli - Universidade Estadual do Oeste do Paraná (Unioeste)  
Edmarlon Giroto - Universidade Estadual de Londrina (UEL)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

This research received no funding. PNAUM-Funding: Brazilian Ministry of Health (SCTIE/MS – Process 25000.111834/2, Decentralization of FNS Resources).



## Keywords

pharmaceutical services, satisfaction assessment, Hypertension

## Abstract

The relationship of users with health services and professionals creates judgments and beliefs that influence health decision-making. The experience can be positive (satisfaction) or negative (dissatisfaction). Satisfied users are more adherent to treatments. Pharmaceutical services (PS) are activities in primary health care (PHC) for medication logistic and Clinical care for positive results in health. Affordable, quality PS promotes user satisfaction. Objective: to analyze the association between user dissatisfaction with PS and intentional non-adherence to hypertension medications. Methods: cross-sectional study with data from PNAUM Services (National Survey of Access, Use and Promotion of Rational Use of Medicines in Brazil), carried out from July to December 2014. Interviews of users aged 18 or over who used medication for hypertension and SUS pharmacies were analyzed. The dependent variable was intentional non-adherence obtained by the question “Do you stop using any medication prescribed by your doctor?” with “yes” and “no” answers. The independent variable was dissatisfaction with the PS Accommodation dimension (difference between the services offered and the expectations and needs of users in the quality of dispensing, quality of the medicine, ambience and interpersonal relationships) obtained through item response theory. Logistic regression was performed by crude and adjusted odds ratios (ORs). Results: 2,248 users were evaluated. Most respondents were women (73%) satisfied with PS (satisfaction levels above 70%). Intentional non-adherence was observed in 13.0% of respondents. Dissatisfied users were more non-adherent to Hypertension medication, with rates three times higher than satisfied users. In the adjusted analysis, dissatisfaction with the Accomodation dimension was associated with intentional non-adherence (OR 3.270; 95% CI 2.308-4.634). Conclusion: dissatisfaction with the Accomodation dimension was associated with intentional non-adherence.

# Discharge of Patients with Spinal Cord Injury: Sociodemographic and Pharmacotherapeutic Profile



## Author

Emília Vitória da Silva - Universidade de Brasília (UnB)  
Alliny do Nascimento Martins - Secretaria de Estado da Saúde do Distrito Federal  
Eric Ferreira Santana - Universidade de Brasília (UnB)  
Kamila Soares Lopes - Secretaria de Estado da Saúde do Distrito Federal  
Débora Santos Lula Barros - Universidade de Brasília (UnB)  
Rinaldo Eduardo Machado de Oliveira - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

CAPES - Coordenação de Aperfeiçoamento de Pessoal de Nível Superior



## Keywords

Spinal Cord Trauma, Patient Discharge, Drug Utilization

## Abstract

**Introduction:** Spinal cord injuries result in partial or total loss of motor, sensory, and autonomic functions, with complications as neuropathic pain. The objective of this study was to describe the sociodemographic and pharmacotherapeutic profile of patients with spinal cord injuries at the time of hospital discharge, admitted to a specialized health unit for rehabilitation and long-term care. **Method:** This is a retrospective cross-sectional observational study, involving inpatients with spinal cord injuries hospitalized in the healthcare unit between January 2022 and December 2022. The study analyzed variables such as sex, age, marital status, education level, type of injury, etiology, admission information, and prescriptions at discharge to determine medication consumption. **Results:** Out of a total of 50 patients, 84% were male, with the most prevalent age group being between 29 and 50 years (n=24; 48%). Additionally, 42% were single and had a low level of education, with incomplete primary education (34%). The main causes of injuries were motor vehicle accidents (28%) and falls from great heights (26%). The average number of medications prescribed at discharge was  $5.2 \pm 8.32$  per patient, totaling 419 prescribed medications. The most frequently prescribed medications were gabapentin (n=89; 21%), dipyron (n=73; 17%), omeprazole (n=55; 13%), ondansetron (n=47; 11%), and lactulose (n=39; 9%). **Conclusion:** The profile of patients with spinal cord injury predominantly includes males with low levels of education, in the economically active age group, and injuries that are largely preventable. Regarding pharmacotherapeutic profile, the data indicate polypharmacy and align with protocols for treating major health conditions such as pain, gastric discomfort, nausea, vomiting, and constipation, the latter resulting from neurogenic bowel. These findings are crucial for guiding discharge strategies, particularly in improving access to medications.

# Assessment of Facilitators and Barriers in Implementing Pharmacy Services: A Sociotechnical Study in the Context of Judicialized Medicines



## Author

Rafaela Rafognatto Andregueti - Universidade Federal de Santa Catarina (UFSC)  
Natália Weber Besen - Universidade Federal de Santa Catarina (UFSC)  
Luciano Soares - Universidade Federal de Santa Catarina (UFSC)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Fapesc



## Keywords

implementation science, pharmaceutical care, sociotechnical

## Abstract

Concerns regarding judicialized medicines go beyond financial impacts, encompassing inadequate monitoring of patients' health. Although judicialization can safeguard rights to healthcare, financing medicines without proven efficacy can put patient safety at risk. The implementation of effective pharmaceutical clinical services in judicial pharmacies is crucial and challenging, requiring adequate monitoring of processes. A sociotechnical systems approach guided the implementation in a University Pharmacy (UPh). Data collection from March to May 2023 used SEIPS (Systems Engineering Initiative for Patient Safety) to analyze work system interactions. Responses from pharmacists and professors highlighted key themes in SEIPS regarding facilitators and barriers. Barriers identified were related to the culture shared by users, who do not understand the need to schedule appointments due to their familiarity with the on-demand pharmaceutical service. As UPh is a training place for undergraduate students and judicialized medicines often come from prescriptions for the treatment of rare or complicated health conditions, the lack of predictability can hinder overall quality of clinical assessment. Facilitators for users to adhere to scheduling appointments include understanding the benefits and offering flexibility. Another barrier is related to the current structure of the workforce, particularly the high turnover of students in training. For pharmacists, these challenges can impact job satisfaction and increase concerns about the technical responsibilities of the profession. Although pharmacists and professors share common concerns about the organization of service at UPh, their perspectives reflect distinct operational and educational priorities. Bringing these perspectives together could improve service provision and educational experiences, benefiting both users and students in the UPh environment.

# Access to Evidence Based Heart Failure Treatment: A Nationwide Study in Brazil



## Author

Luísa Preiss Marques da Rocha - Universidade Federal do Rio Grande do Sul (UFRGS)  
Kathleen Asturian - Universidade Federal do Rio Grande do Sul (UFRGS)  
Isabel M. Canabarro - Universidade Federal do Rio Grande do Sul (UFRGS)  
Lídia Einsfeldl - Universidade Federal do Rio Grande do Sul (UFRGS)  
Diogo Pilger - Universidade Federal do Rio Grande do Sul (UFRGS)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

There was no funding allocated to this project



## Keywords

Heart Failure;; Drug Therapy;; Access to Essential Medicines and Health Technologies.

## Abstract

Heart failure (HF) affects over 64 million people worldwide and drug treatment consists of 4 different pharmacological classes with evidence-proved benefits, reducing both mortality and hospitalizations. This study aims to describe, through an exploratory analysis, access to HF treatment drugs in Primary Health Care in Brazil, via Unified Health System (SUS). Based on the Municipal Lists of Essential Medicines (REMUMEs) available in the public domain, we collected data from HF drugs available from the nationwide metropolitan regions. A total of 387 municipalities were included. Half of the cities (197, 50.9%) had a publicly available REMUME. Lists' lowest availability was found in the northeast region (40, 34.2%) and the highest in the south (67, 78.8%), with the majority (121, 61.4%) being updated in the last 2 years. The presence of Angiotensin Converting Enzyme Inhibitors were identified in 92.4% (182), Angiotensin II Receptor Blockers in 80.2% (158), cardioselective beta-blockers in 91.9% (181), other drugs reached 87.8% (173). Most frequent medications in each pharmacological classes were enalapril (176 – 89,3%), losartan (157 – 79,7%), carvedilol (173 – 87,8%), spironolactone (169 – 85,8%), furosemide (178 – 90,4%) e digoxin (171 – 86,8%). Overall analysis showed that none of the cities simultaneously had all 4 therapeutic classes for the comprehensive treatment, which are recommended by the Brazilian guidelines. Three classes were combined available in 77.7% (153), 2 of them in 15.7% (31) and 6.6% (13) of lists' had just one HF drug class. Ivabradine, sacubitril-valsartan (from the specialized component of pharmaceutical assistance, "CEAF" and the "Programa Farmácia Popular, PFP") and dapagliflozin/ empagliflozin were not identified. The lists analyzed show important variability between medications provided and there is only full coverage of HF treatment considering CEAF and PFP, reinforcing the challenge of access.

# Adverse Drug Reactions Caused By The Use Of Cannabidiol And Related To The Central Nervous System: An Overview Of The Data Provided By Vigiaccess



## Author

Aline Matilde Ferreira dos Santos - Universidade de Brasília (UnB)

Serena Pireneus Oliveira Borges de Pina - Universidade de Brasília (UnB)

Matheus Lopes da Silva - Universidade de Brasília (UnB)

Helaine Carneiro Capuchoh - Universidade de Brasília (UnB)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

CAPS; UNB



## Keywords

Pharmacovigilance. Adverse events. Cannabidiol.

## Abstract

Patient Safety is considered by the World Health Organization (WHO) to be a fundamental element in preventing risks, errors, and damages. Its cornerstone is knowledge about errors and adverse reactions regularly and continuously. Adverse drug reactions (ADRs) are unexpected and unintended responses related to the use of medications. Through notification systems and databases, pharmacovigilance identifies patterns of adverse reactions and potential health risks, contributing to the protection of health and promoting safer and more effective medication use. VigiAccess is a pharmacovigilance system aimed at collecting, analyzing, and monitoring ADRs. Its main objective is to ensure the safety and effectiveness of medicines on the market, identify and evaluate possible side effects, contribute to health damage prevention, and improve the quality of pharmacological treatment offered to the population. Currently, cannabidiol (CBD) is introduced as a therapeutic alternative in disease treatment. Known for its non-psychoactive property, CBD does not cause euphoric effects and appears to be effective in treating various diseases related to the Central Nervous System (CNS). However, it is still necessary to elucidate its effects, ideal dosages, and adverse reactions. This work aims to create an overview of the main adverse reactions caused by cannabidiol, related to the CNS and reported in VigiAccess. As a result, around 6,227 reactions were identified. Of these, 4,006 were epileptic seizures; 909 drowsiness; 203 lethargy; 172 sedation; 171 generalized tonic-clonic epileptic seizures; 143 dizziness; 123 headache; 111 hypersomnia; 99 epilepsy; 81 tremor; 68 psychomotor hyperactivity; 46 impaired memory; and 35 amnesia. Given the variety of reactions identified, most of which interfere with individuals' quality of life, the importance of such monitoring is notable, as well as reinforcing the relevance of pharmacovigilance to ensure the safety of such product users.



# Clinical and Pharmacotherapeutic Profile of Patients Undergoing Invasive Mechanical Ventilation in an ICU COVID-19



## Author

Tadeu Uggere de Andrade - Universidade de Vila Velha (UVV)  
Danilo Hugo Brito - Universidade de Vila Velha (UVV)  
Girlandia Alexandre Brasil - Universidade de Vila Velha (UVV)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Fundação de Amparo à Pesquisa e Inovação do Espírito Santo (FAPES; 291/2021) e CNPq (314722/2021)



## Keywords

INVASIVE MECHANICAL VENTILATION, COVID-19, PAVMI

## Abstract

The impact of the COVID-19 on the world's population, especially for those patients who developed the most severe form requiring admission to the Intensive Care Unit (ICU) and invasive mechanical ventilation (IMV), was devastating. Within the context of health care, there was the problem of complications related to health care, as an important factor that worsens the prognosis of patients on IMV, in addition to this, there was an increase in the consumption of antimicrobials that have a direct impact on the hospital microbiota. The objective of this study was to trace the clinical and pharmacotherapeutic profile of patients with COVID-19 admitted to IMV and correlated with secondary drugs and the use of antimicrobials. This was a retrospective observational epidemiological study from April/2020 to April/2021, about these patients and their clinical evolution. The profile was traced through the collection of information described in the patients' computerized records: gender, age, presence of comorbidities and use of drugs to control or treat them, use of antimicrobials before hospitalization, occurrence of pneumonia associated with IMV, days on corticosteroids, renal injury, use of antimicrobials in the ICU and microorganisms isolated in biological cultures. For statistical analyses, IBM SPSS Statistics version 24 and MedCalc version 19.4.1 programs were used. The results revealed that 69.2% of the patients were male, with a mean age of 68 years, 88% had documented comorbidities and 81% used home-use medications, 59% were diagnosed with VAP and a mortality rate of 45%. It concludes the negative impact of PAVMI's in relation to death and also reiterates the importance of corticosteroids in relation to survival. As it is the first work at the state level that aims to identify this niche of patients, it is suggested that the institution create an antimicrobial management program, according to the profile of the unit and patients.

# Clinical and Pharmacotherapeutic Profile of Patients Undergoing Invasive Mechanical Ventilation in an ICU COVID-19



## Author

Vanessa Maria Correa - Universidade Federal de Santa Catarina (UFSC)  
Carolina Camargo de Araujo - Universidade Federal de Santa Catarina (UFSC)  
Livia Maria de Souza Gonçalves - Universidade Federal de Santa Catarina (UFSC)  
Karyme Damarys Rodrigues Calisto - Universidade Federal de Santa Catarina (UFSC)  
Marina Raijcher Mattozo Rover - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)  
Filipe Matheus Carvalho - Universidade Federal de Santa Catarina (UFSC)  
Luciano Soares - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

Nonexistent



## Keywords

Graduate assessment, Pharmaceutical Policies and Services, Postgraduate

## Abstract

The Política Nacional de Assistência Farmacêutica (PNAF - National Pharmaceutical Policy) introduced an innovative approach that focused on the needs of patients, creating demand for the training of pharmacists in this new reality. The Postgraduate Program in Pharmaceutical Policies and Services (PPGASFAR), a pioneer in the field since 2011, has a network structure that brings together universities from different regions of the country. To ensure continuous improvement, the Coordination for the Improvement of Higher Education Personnel (CAPES) is leading the systematic evaluation of the programs in Brazil. This research aims to construct and validate a model and a tool to evaluate the contributions of PPGASFAR to its graduates. The first step was to create the model and the assessment tool. The model was designed to emphasize a humanized and multidimensional approach, addressing traditional indicators and valuing the experiences and trajectories of graduates (currently 170 masters and four doctors). The instrument, a semi-structured questionnaire, explores socio-demographic aspects and the influence of PPGASFAR on the graduates' careers based on the categories of the Kirkpatrick evaluation method (reaction, learning, behavior, and results) and the CAPES guidelines (training process, knowledge, and impact of political, educational, economic, and social programs). The model and the instrument are currently being validated using the Delphi method. This approach involves identifying academic outcomes, considering the publications produced and their quality; management outcomes, considering professional and service qualifications; and social outcomes, from the perspective of access to medications and pharmaceutical services. The research intends to promote continuous improvements of the program's curriculum by systematically identifying qualification successes and gaps, deepening the impact on human resource training and knowledge production in pharmaceutical sciences.

# Health monitoring for elderly people using wearable electronic devices: a scoping review on privacy and confidentiality with recommendations for developers and other stakeholders



## Author

Silvio Barberato Filho - Universidade de Sorocaba (UNISO)  
Alan Martinez Kozyreff - Universidade de Sorocaba (UNISO)  
Lívia Luíze Marengo - Universidade de Sorocaba (UNISO)  
Fabio da Silva Moraes - Universidade de Sorocaba (UNISO)  
Cristiane de Cássia Bergamaschi - Universidade de Sorocaba (UNISO)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

University of Sorocaba



## Keywords

Elderly. Privacy. Confidentiality.

## Abstract

**Introduction:** Monitoring elderly health via wearable electronic devices is beneficial but faces ethical and regulatory challenges. Despite aiding in emergencies like falls, concerns about user privacy and data confidentiality persist. **Objective:** To systematize recommendations for developers of wearable electronic devices used in elderly health monitoring, and for other stakeholders, focusing on privacy and confidentiality. **Method:** The search was completed in October 2023 in the databases MEDLINE (PubMed), Embase, Scopus, The Cochrane Library, Web of Science, Epistemonikos, and Virtual Health Library. Studies that simultaneously addressed wearable electronic devices, elderly individuals, health monitoring, privacy, confidentiality, or data protection were included. We excluded studies that did not provide any recommendations for developers or other stakeholders aimed at increasing user privacy protection and data confidentiality. Results were presented as a narrative synthesis. **Results:** A total of 1,037 records were identified in the databases, and 12 studies published between 2014 and 2022 were included. The main findings were addressed in topics, including: privacy and confidentiality in monitoring the health of elderly individuals using wearable electronic devices; barriers and facilitators for the adoption of wearable devices in monitoring the health of elderly individuals; recommendations for developers of wearable devices in monitoring the health of elderly individuals and for other stakeholders. **Conclusion:** The application of wearable electronic devices for health monitoring in elderly individuals presents complex ethical, regulatory, and technological challenges, particularly in relation to privacy and confidentiality. The collaboration between developers and other stakeholders is crucial for implementing robust security measures and establishing effective regulatory standards that provide comprehensive user protection.

# Integrating Clinical Pharmacy Principles: Description of Judicialized Medicine Dispensation in a University Pharmacy



## Author

Natália Weber Besen - Universidade Federal de Santa Catarina (UFSC)  
Rafaela Rafognatto Andregueti - Universidade Federal de Santa Catarina (UFSC)  
Luciano Soares - Universidade Federal de Santa Catarina (UFSC)  
Mareni Rocha Farias - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

FAPESC - Fundação de Amparo à Pesquisa e Inovação de Santa Catarina



## Keywords

Dispensation, pharmaceutical care, judicialized medicines

## Abstract

Soares et al. (2021) propose a model for a drug dispensing service that considers access as an essential factor, including user reception, bonding, accountability, pharmaceutical management, and clinical aspects, with rational drug use as an objective. The model focuses on dispensation services, demanding the reorientation of practices and tools to enhance service efficiency and effectiveness. Our work aims to describe and analyze the degree of compliance of a pharmaceutical dispensing service of judicialized medicines implemented in a University Pharmacy. The workflow begins with patient reception, where personal documents are verified and data checked through a management system. Each patient undergoes a case study and treatment assessment by an attendant at a service counter, cross-referencing data, checking medication availability in stock, and assessing the validity of court orders. The dispensation process starts with the verification of prescriptions by a pharmacist, followed by digital storage and the physical dispensing of medications through the pharmacy's management system. Multiple checks are conducted to ensure accuracy in dosage, quantity, batch numbers, and expiration dates. Patient safety and treatment efficacy are paramount, with attendants empowered to intervene and resolve any issues related to pharmacotherapy. Ongoing patient monitoring and follow-up after dispensation are integral components of the service. This includes documenting treatment outcomes, addressing patient queries, and scheduling future medication pickups. This service model emphasizes patient-centered care, safety, and adherence to clinical standards. It reflects the structured approach advocated by Soares et al., which underscores the importance of multidisciplinary collaboration and continuous patient management in optimizing health outcomes.

# Interprofessional Competencies in Primary Health Care in Brazil: a scoping review



## Author

Alessandra da Silva Kulkamp - Universidade Federal de Santa Catarina (UFSC)  
Fernanda Manzini - Universidade Federal de Santa Catarina (UFSC)  
Gabriele Fritsch Oliskowski - Universidade Federal de Santa Catarina (UFSC)  
Sabrina de Miranda Carlin - - Universidade Federal de Santa Catarina (UFSC)  
Silvana Nair Leite - Universidade Federal de Santa Catarina (UFSC)



## Knowledge Area

Pharmaceutical Policies and Care



## Funding

FAPESC - Fundação de Amparo à Pesquisa e Inovação de Santa Catarina



## Keywords

Interprofessional competencies, collaborative competencies, primary health care

## Abstract

**Introduction:** Interprofessional education and interprofessional collaboration practices have stood out worldwide to overcome the challenges of addressing population health issues. Primary Health Care (PHC) in Brazil is based on teamwork; however, there is no consensus in Brazil on the necessary interprofessional competencies required to work in PHC. **Objective:** To identify publications that describe the interprofessional competencies necessary to work in Primary Health Care (PHC) in Brazil. **Method:** A scoping review was conducted in nine databases. The PCC acronym was used to define the inclusion and exclusion criteria: Population: Healthcare professionals and interprofessional teams. Concept: Necessary interprofessional/collaborative competencies. Context: Primary Health Care in Brazil. The data extraction includes bibliometric results and the list and description of identified competencies, the framework used if applicable, and the methods of competency evaluation. **Preliminary Results:** The research strategies retrieved 1,296 studies. After selection, 30 studies were included. Most of them are qualitative studies. Only the most recent studies used the specific term "interprofessional competency." The most frequent competencies are interprofessional communication, teamwork, and patient-centered care. A second round of review will be conducted on the reference lists of the included studies to identify more studies with the same thematic focus. **Conclusion:** This review is part of a research project named #FuiResidente and is important for developing an understanding of the studies that have PHC in Brazil as a scenario and for identifying the necessary interprofessional competencies.