IV INTERNATIONAL MEETING OF PHARMACEUTICAL SCIENCES

XII SEMINÁRIO ANUAL DO PCF
II SEMINÁRIO ANUAL DO PROFAR

Abstract book

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STATE UNIVERSITY OF MARINGA

Postgraduate Program in Pharmaceutical Sciences

Programa de Mestrado Profissional em Assistência Farmacêutica

IV INTERNATIONAL MEETING OF PHARMACEUTICAL SCIENCES

XII SEMINÁRIO ANNUAL DO PCF

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NOVEMBER, 26, 27 and 28th

Maringa, PR, Brazil

2022

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ABSTRACTS

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DEVELOPMENT PHARMACEUTICAL CARE IN A PHARMACY SCHOOL: BENEFITS AND CHALLENGES

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Keywords: **Pharmaceutical Care; Pharmacy Services; Delivery of Health Care.**

Introduction: Pharmaceutical care plays a key role in promoting the rational use of medication, besides helping to obtain the desired therapeutic results and acting to improve the health and quality of life (OPAS, 2002). Nonetheless, the benefits of these services extend not only to the patient, but also represent an important step in the process of re-professionalization of pharmacists and in the consolidation of their role as health professionals (ROVERS; CURRIE, 2010). That said, the pharmaceutical profession has a path full of challenges to implement and disseminate the practice of pharmaceutical care in the most diverse fields of professional practice. **Aim:** To evaluate the benefits obtained with the implementation of the pharmaceutical care in a pharmacy undergraduate school in the Midwest of Paraná and the challenges faced in this process. **Methods:** The implementation of pharmaceutical care started in the second semester of 2021 and consisted in offering pharmaceutical orientation, pharmacotherapeutic follow-up and monitoring of blood pressure and blood sugar. These services had as target population patients of the Pharmacy School of the Integrado University of Campo Mourão - PR, who suffers from chronic diseases, presents some complaint or difficulty related to their therapy or clinical condition. The documentation was carried out through Pharmaceutical service forms prepared in Excel. **Results:** In one year, 445 pharmaceutical services were provided to 98 patients, being 344 blood pressure and blood sugar services provided to 44 individuals, followed by pharmaceutical orientations, besides 101 services related to the pharmacotherapeutic follow-up of 54 patients with chronic diseases. From the implementation of these services, the challenges faced were directly related to patient compliance, whereas 12 patients showed no commitment to the follow-up, which is mainly due to the lack of understanding about the purpose of the service and the limited view of the pharmacist's work. However, with the consolidation of the services, a notable increase in the patient's trust in the pharmacist was observed, with 43 patients starting to seek such services and orientations periodically, enabling the creation of a bond between professional-patient in the course of the attendances. **Conclusion:** Although not a recent professional practice, the services related to pharmaceutical care are not yet widely known by the community, thus hindering the patient's understanding and adherence to them. However, the insertion of these services in the pharmacy routine is a big step towards restructuring the image of the pharmaceutical profession, because it shows the benefits generated to the patient's health.

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ESTABLISHMENT OF SUSPENSION CELL CULTURE OF *Cereus hildmannianus* (K.) SCHUM.

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Keywords: Cell culture, Fatty Acid, Elicitation

Introduction: *Cereus hildmannianus* belongs to the *Cactaceae* family. It is used in folk medicine as a healing, cholesterol-lowering and diuretic, and it also has several applications in the food and cosmetics industries. However, these applications are made from the *in natura* plant, which can be a threat to the survival of the species. The suspension cell culture is sustainable alternative process that offers some technical advantages over callus culture, such as low-cost and easily extraction. **Aim:** The establishment of suspension cell culture of *C. hildmannianus* from callus tissues of the species, the elicitation of the cultures with salicylic acid (SA) and evaluation of its lipid profile by gas chromatography coupled to mass spectrometry (GC-MS). **Methods:** *C. hildmannianus* callus tissues were kept in Murashige and Skoog (MS) (1962) medium at a temperature of 30± 1 ºC and a photoperiod of 16 h light/8 h dark, and subcultured every 30-40 days. About 1g of callus was transferred to Erlenmeyers glasses (125 mL) containing 50 mL of MS medium without agar (control culture). Elicitation was performed by adding 50, 100 and 200 µmol of SA to the medium and the cultures were kept in an orbital shaker for two weeks (100 rpm; 30 ± 1 ºC). The cell suspension was lyophilized and 100 mg of this material was added to a assay tube to carry out the direct esterification of fatty acids - 2,0 mL of NaOH (1,5 mol L^{-1}, in MeOH) was added to the tube, placed in ultrasonic vat for 15 min; next, 2,0 mL of H_2SO_4 (1,5 mol L^{-1}, in MeOH) was added, and again placed in ultrasonic vat for 15 min. Then, 1 mL of hexane was added, and the mixture centrifugated at 2000 rpm for 5 min, collecting the supernatant, which contains the fatty acids (this step was performed three times). The lipidic profile was obtained by GC-MS and identified comparing their mass spectra with the NIST 11.0 database (National Institute of Standards and Technology, USA). **Results:** Compared to the control, in which 5 saturated and 1 unsaturated fatty acids were found, the culture elicited with 50 µmol of SA, showed a greater diversity of fatty acids. It was found 6 saturated and 4 unsaturated fatty acids, highlighting the linoleic acid (C18:2n6c), elaidic acid (C18:1n9t), oleic acid (C18:1n9c), and eicosadienoic acid (C20:2). **Conclusion:** The suspension cell culture proved to be a viable alternative for bioproduction of fatty acids, especially unsaturated fatty acids with potential pharmacological application.

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DEVELOPMENT OF PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODEL FOR CANNABIDIOL IN ADULTS

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Keywords: Pharmacometrics, oral administration, PBPK modeling

Introduction: Epilepsy can be defined as a chronic neurological disorder that affects more than 50 million people worldwide. Clinical manifestations are characterized by the presence or absence of seizures. Epilepsy can be refractory to antiepileptic drugs (AEDs), making seizure control difficult. One of the newer AEDs is the cannabidiol (CBD). It is estimated that three quarters of the population living with epilepsy can acquire a better quality of life through the rational and guided use of the AED. Pharmacometrics is defined as "an emerging science whose main objective is the study and development of mathematical models and statistical methods for the optimization of steps during the development and improvement of new drugs". Some pharmacometric tools have been applied to explore the pharmacokinetic profile of drugs in untested conditions. For this, different model approaches can be used to reproduce the plasma exposure. One of these approaches is the Physiologycally-Based Pharmacokinetic Modeling (PBPK), where computer systems simulate the organism through a sequence of equations and physiological properties. **Aim:** The present study aims to develop and validate an oral PBPK model of CBD for adults. **Methods:** Data of pharmacokinetic profile of CBD was obtained by an extensive literature review. Sequentially, the physicochemical and biological properties of CBD were implemented in the GastroPlus software (Simulation Plus) to simulate plasma exposures. To carry out the development of the model for CBD, an average individual (American male, 37 years old, weighing 86.9 kg) was assumed. The simulated plasma exposition after oral administration of 750 mg of CBD was compared to the observed data from Schoedel et al. (2018). The performance of the model was evaluated by mean fold error (MFE) assuming two-fold error as acceptable ($0.5<MFE<2.0$) for the pharmacokinetic parameters area under the curve (AUC), maximum plasma concentration (Cmax) and time to reach the maximum concentration (tmax). **Results:** The input parameters effective permeability (Peff), reaction rate constant (Km) and maximum rate of metabolism (Vmax) of the CYP3A4 enzyme were optimized by Gastroplus. The MFE values for Cmax, tmax and ASCo-t were between 0.67-0.94 and considered adequate. To validate the model, other clinical protocols were simulated and compared with plasma data from the literature (1500mg and 4500mg oral solutions). After the validation of the oral PBPK model for adults, it was extrapolated to a population of 41 individuals, using observed data from the study by Schoedel et al. (2018). **Conclusion:** The simulations showed that the input parameters assumed generate an adequate PBPK model of CBD when the adult physiology was assumed. Other physiological conditions need to be tested as pediatric, geriatric, pregnants and others.

STUDY OF THE RHEOLOGICAL BEHAVIOR OF BIOSTIMULATORS BASED ON CALCIUM HYDROXYAPATITE AND POLYCAPROLACTONE

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Keywords: **Collagen biostimulator; Rheological properties; Calcium hydroxylapatite; Polycaprolactone.**

Introduction: Soft tissue fillers are comprised of a range of materials with differingphysiochemical and rheological (ie, flow) properties. These properties can informtreatment selection for specific anatomic areas, planes of injection, and clinicalapplications. Biostimulators are increasingly used in the dermatological market, withthe aim of preventing and reversing the effects of the skin aging process, acting activelyin the deeper layers of the skin, as well as restoring lost facial volume throughstimulation and formation of new dermal collagen. It is a biomaterial that is, made up ofa material (natural or synthetic) that interacts with the living biological tissues of thehuman body. **Aim:** The aim of the study was to evaluate two biostimulators: Calcium hydroxyapatite (CaHA) and Polycaprolactone (PCL), according to their behaviorthrough rheology. **Methods:** Commercially available CaHA and PCL collagen biostimulators were analyzed with a HAAKE® MARS II rheometer (Thermo FisherScientific, Germany) and evaluated for complex viscosity (η*), viscous modulus (G")and elastic modulus (G') according to standard procedure on a rotational rheometerequipped with a steel plate using the conical plate geometry (C35/2º with a clearance of
0.052 mm) at 25.0 ± 0.5 °C and frequency of 1Hz. **Results:** The data obtained from rotacional experiments show a pseudoplastic behaviour for CaHA and PCL. The great difference observed was an important value of yield stress for PCL (366,3) while for CaHA this value is near from zero. In term of dynamic rheology, the G' values observed for CaHA was 561.9 Pa and for PCL was 616.2 Pa. Meanwhile, the G" was
319.4 Pa for de CaHA and 340.5 Pa for PCL. In both cases, the G' values (elastic modulus) were larger than G"(viscous modulus) showing the elastic predominance of these biostimulators, probably due the spherical particles distributed in the viscous matrix. **Conclusion:** The PCL biostimulator exhibited the highest η*, G" and G' compared to CaHA. These properties will likely support greater lift and support capacity in areas where lasting revolumization is appropriate.

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DETERMINATION OF THE CONTENT OF GALLIC ACID, ELAGIC ACID AND GERANIIN IN SEMIPURIFIED FRACTION OF *Cenostigma pluviosum* var. *Peltophoroides*

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Keywords: sibipiruna, plant extract, phenolic compounds, high performance liquid chromatography.

Introduction: *Cenostigma pluviosum* var. *peltophoroides* is a tree popularly known as "sibipiruna" and widely used in the afforestation of cities. From the stem bark, phenolic compounds, sterols, tannins, flavonoids and saponins have already been isolated and identified, and some pharmacological activities, including healing activity, have been described. Its popular use as a medicinal plant leads us to the need to evaluate its constituents and possible applications in the pharmaceutical area. **Aim:** The objective of this work was to determine the content of substances identified in the ethyl acetate fraction (EAF) of the bark extract of *C. pluviosum* var. *peltophoroids*. **Methods:** The chromatographic profile and identification of the substances gallic acid, geraniin and ellagic acid in the EAF was obtained by high performance liquid chromatography. The mentioned substances were identified by comparing the retention time and UV spectra of the EAF peaks with those of available reference standards and confirmed by adding the standards to the EAF. UltiMate 3000 UHPLC chromatograph (Thermo Scientific, USA) was used, equipped with diode array detector (DAD), Phenomenex® Onix Monolithic C18 column (100 mm × 4.6 mm, 130 Å, 2 µm) and Phenomenex pre-column. Mobile phases: phase A (acetonitrile with 0.05% formic acid) and phase B (water with 0.05% formic acid). Gradient elution: 0-6 min, 10-20% A; 6-10 min, 20-40% A; 10-25 min, 40-10% A. Flow rate 0.5 mL/min; 35 °C and detection at 280 nm. EAF is dissolved in 20% methanol at a concentration of 1 mg/mL. To quantify these substances, standard solutions were prepared and curves were constructed with seven dilutions in triplicate for each substance, adopting the following intervals: gallic acid 2 to 50 µg/mL; geraniin 3.125 to 60 µg/ml and ellagic acid 6.25 to 75 µg/ml. They were analyzed under the same conditions as the EAF. **Results:** For the three standard calibration curves, the coefficient of determination R^2 was greater than 99.47. With the area of the peaks in the EAF, the equation of the straight line, obtained for each curve, it was possible to determine the content of each substance present in the EAF, being: gallic acid 0.807%; geraniin 1.709% and ellagic acid 3.3415%. **Conclusion:** The identification and quantification of substances involved in pharmacological activities can contribute to the discovery of new drugs and their possible mechanisms of action.

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MORPHO-ANATOMICAL EVALUATION OF SPECIES USED IN TRADITIONAL CHINESE MEDICINE

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Keywords: **Botany, morphodiagnosis, *Piper kadsura*, Piperaceae.**

Introduction: Piperaceae Giseke includes five accepted genera. Of these, three genera and 468 species are described in the phytogeographic domains in Brazil. In the world, *Piper* L. includes 2405 accepted species. It is a native genus in Brazil, with 289 species. Of these, 183 are considered endemic. *Piper* species have commercial, economic, and medicinal importance. Economically, its worldwide importance is given by the pepper market, while in medicine, there is used in traditional Chinese medicine, with emphasis on *Piper kadsura* (Choisy) Ohwi, a native species to East Asia, found in Japan, Korea, and Taiwan. **Aim:** Due to the biological potential of this species, this study aimed to describe the morphological and anatomical characteristics of *P. kadsura* stem. **Methods:** Stem samples of *P. kadsura* were fixed for 48 h in FAA50 (5% formaldehyde, 5% acetic acid, and 90% ethanol: water mixture; 50:50, v/v) and storage in 70% ethanol. For morphological analysis, the dried samples were characterized under naked eye and with the use of a stereomicroscope. For analyses by light microscopy (LM), the samples were sectioned freehand in the transverse and longitudinal planes (radial and tangential). The sections were bleached with 30% sodium hypochlorite solution, until fully clarified, washed with distilled water, double-stained with Astra blue and safranin (1:1, v/v), and mounted on semi-permanent slides with glycerin gelatin. **Results:** The stem fragment has a flattened cylindrical shape, with a brown to grayish-brown external surface and longitudinally arranged striations. The inner surface has a grayish-yellow color and evident vascular bundles of a yellowish-white color, arranged radially. Anatomical characteristics include uniseriate epidermis covered by a thick cuticle with a verrucous appearance. Below the epidermis there are 2-3 lamellar collenchyma strata and more internally the collenchyma cortex, where groups of fibers and columnar sclereids are distributed, forming a discontinuous circle. It presents amiliferous cortex with starch grains of the compound type. The vascular bundles are of the collateral type, forming an outermost circle and another 5-8 bundles organized in the medullary parenchyma. The large-caliber vessel elements are scalariform and the others are helical thickening. In tangential longitudinal section, the parenchyma cells have different shapes, from square to rectangular, containing starch grains. **Conclusion:** The morphological and anatomical characteristics observed in *P. kadsura* stem are in agreement with the patterns described for other *Piper* species, such as portions of discontinuous collenchyma and vascular bundles organized in two circles. The distinctive anatomical characteristics of *P. kadsura* are the epidermis covered by verrucous cuticle and the lamellar collenchyma.

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THE USE OF *Cynara scolymus* (ARTICHOKE) BY HYPERCHOLESTEROLEMIC PATIENTS IN A BASIC UNIT IN PARANÁ

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Keywords: *Cynara scolymus*; Phytotherapy; Hypercholesterolemia; Sinvastatina

Introduction: The public health system guarantees safe access to the use of medicinal plants and herbal medicines through strategies such as the analysis and approval of new technologies, among which are herbal medicines. In this context, 12 herbal medicines are part of RENAME (National List of Essential Medicines), including Artichoke (*Cynara scolymus*), a standardized extract with hypocholesterolemic potential that can be considered as an alternative to standardized allopathic treatment. **Aim:** The main objective of the present study was to evaluate the impact on the lipid and hepatic profiles of hypercholesterolemic patients, after pharmacotherapy, with artichoke and sinvastatin. **Methods:** At the participation of a multiprofessional team, with doctors, nurses and pharmacists, the study was clinical, randomized and double-blind, carried out with 30 patients diagnosed with hypercholesterolemia from elective consultations held at a Basic Unit in Terra Boa - PR, selected following pre-defined criteria, treated with Sinvastatin 20 mg/day (tablets, generic drug) and with standardized Artichoke extract (equivalent to 30 mg/day of chlorogenic acid) provided by Catarinense Pharma®. The development lasted 90 days, with individual pharmacotherapeutic follow-up through monthly pharmaceutical consultations and determination of lipid and liver profiles, at the beginning and at the end of the trial. The results were statistically analyzed using GraphPad Prisma 8, applying the normality test followed by Tuckey's test. **Results:** The results were statistically significant in both treatments and revealed that patients treated with Artichoke extract showed improvement in their lipid and liver profiles as much as those treated with Sinvastatin, suggesting that they are substitute specialties. The execution of the study was hampered, especially by the drop in spontaneous demand due to the pandemic of the new coronavirus and the dengue epidemic in Paraná and patients' adherence to pharmacotherapy and the little knowledge of doctors about herbal medicines are points to be highlighted in the study and that suggest strategies for reflection in health teams. **Conclusion:** The results of this study reinforce the possibility of using standardized artichoke extract, a herbal medicine, as a safe alternative to primary health care programs for the treatment of dyslipidemias.

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ASSESSMENT OF ADHERENCE TO TREATMENT IN PATIENTS WITH DIABETES MELLITUS FOLLOWED BY A MULTIPROFESSIONAL TEAM

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Keywords: Patient compliance, Secondary Health Care, multidisciplinary team, chronic diseases.

Introduction: Diabetes *mellitus* (DM) is a chronic metabolic disease characterized by hyperglycemia due to a deficiency in insulin action and/or production. If not properly treated, DM can lead to serious health complications. The treatment of type 2 DM, the most common type of DM, starts with non-pharmacological measures (lifestyle changes, regular physical exercise and a balanced diet), but in most cases requires the use of medication and, in some cases, the use of insulin, in addition to drug therapy. As it is a complex and long-lasting treatment, the possibilities of adherence failure increases, allowing DM to cause serious harm to the patient's health. **Aim:** The objective of this study was to assess pharmacological treatment adherence of DM2 patients, analyzing their understanding of the disease and its treatment. **Methods:** Study with a qualitative and descriptive approach. DM2 patients' data were obtained through electronic medical records and semi-structured, individual and face-to-face interviews. The interviews were carried out by a postgraduate student and pharmacist of the multiprofessional team of the Chronic Care Model (CCM) of the public health system. All participants received detailed information about the study and signed a consent form. The study was approved by the Ethics Research Committee (approval No. 5,435,462/2022). **Results:** 16 DM2 patients were interviewed. They initially did not know they had DM because there were few or no symptoms, eventually receiving the diagnosis. Through the information collected, it was possible to verify patients' difficulties in relation to adherence to DM treatment, their understanding of the disease. Several monitored patients do not have symptoms, reporting low adherence to treatment, indicating greater difficulties in following the recommended diet and performing physical activity. Therefore, the importance of the multidisciplinary team in health promotion was analyzed. This suggests that non-adherence to treatment is related to the absence of symptoms, generating difficulty in understanding the disease and the importance of treatment. The difficulty related to food and physical activity was presented by multiple factors, with the change in lifestyle being a challenge and slow process. **Conclusion:** Non-adherence was frequent in the evaluation of patients with DM2, showing the importance of the performance of the multiprofessional team through proposed interventions and educational actions, to optimize the knowledge about their clinical condition, empowering the user for self-care, contributing to adherence to the treatment of chronic diseases.

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SARS-CoV-2 MAIN PROTEASE: IDENTIFICATION OF NEW PUTATIVE INHIBITORS BY COMBINATORIAL CHEMISTRY & DEEP LEARNING AND MOLECULAR DOCKING APPROACHES

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Keywords: SARS-CoV-2, M^{pro}, deep learning, drug design.

Introduction: Covid-19 pandemic remains a global emergency since March 2020. A global effort has started to find molecules that could disrupt SARS-CoV-2 replication cycle in patients, being its Main Protease (M^{pro}) the most investigated target. Traditional chemoinformatic tools have been used to find M^{pro} inhibitors in chemical libraries with encouraging results. However, there has been little use of more advanced means to investigate the possibilities of structural modifications in sets of designed compounds targeting this enzyme. In this context, combinatorial chemistry (CC) permits the creation of large sets of structures by combining different molecular fragments into a selected scaffold. Then, deep learning (DL) algorithms and molecular docking (MD) screens for the most likely structures, saving precious time and resources. **Aim:** To create a combinatorial library (CL) of analogs planned from lead compound X77 (a broad-spectrum antiviral) and use DL and MD to identify the most likely putative inhibitors of M^{pro}. **Methods:** CL was made by combining a set of scaffolds with several commercial building blocks using SmiLib. DL and MD screenings were performed with Deep Purpose and GOLD, respectively. **Results:** 62,424 analogs were generated, whose structures were designed to be synthetically feasible and practical to obtain. DL and MD recognized the same top 100 structures within CL. A consensus ranking filtered the top 10 most promising ones, all sharing a common building block, recognized by DL and MD as an important structural feature, besides other minor modifications that are acceptable. MD also showed they occupy the same cavities within the enzyme's active site and have similar interaction profile. **Conclusion:** The use of CC, DL and MD showed to optimize the design process of M^{pro} putative inhibitors by exploiting extensive modification possibilities in an accurate and rapid way. The synthesis of the selected analogs is in progress with promising results.

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OBTAINING OF LIMONIN USING EXTRACTION ASSISTED BY ULTRASOUND: A FAST AND SIMPLE METHOD

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Keywords: **Limonin; Antitumor; Antiviral; Ultrasound Extraction.**

Introduction: Limonin, the target compound of this investigation, is present in the human diet through the consumption of orange juice, the most consumed natural juice in the world, Brazil being the world's largest producer of fruit and juice. It's used in other applications, such as research, food and beverages moved 384,5 million dollars in 2018 and tends to grow to US$ 482.6 million up to 2025, this demonstrates that the global limonin market is growing and should continue in the coming years. Limonin is a tetracyclic triterpenoid and one of over 50 *Citrus* limonoids naturally occurring. This compound has had scientific notoriety since 1891 because it demonstrated antiviral (e.g., HIV) and antitumor activities (e.g., breast and uterine cancer). Consider that *Citrus* seeds has high concentrations of this compound, being chosen as source by extraction by Soxhlet apparatus, reflux or ultrasound. Most of the extraction's methods described use oranges or whole seeds, which required several purification steps with expensive equipment. Soxhlet or reflux extraction techniques require a lot of time and solvent. However, it is convenient to look for an extraction with a cleaner starting material, faster, simpler extraction method using less solvents. **Aim:** Obtain limonin by ultrasound-assisted extraction from developing Pera Rio orange seeds and characterize it by ^{1}H and ^{13}C nuclear magnetic resonance (NMR). **Methods:** Seeds of *Citrus sinensis* (Pera Rio orange) in development that husks (integument) ware removed and dried in an oven at 45 °C for 12h. Then, the lipids and fats were extracted by reflux with hexane at 55 °C for 40 minutes and then a crude extract was obtained by acetone extraction in the ultrasound apparatus for 30 minutes. Crude extract had its volume reduced and after was precipitated by addition of hexane as an anti-solvent yield a white solid or powder. For recrystallization, a saturated solution of the crude extract was prepared in dichloromethane and in which slowly added hexane, forming crystals that were dried at room temperature. After this compound was characterized by ^{1}H e ^{13}C NMR. **Result:** From 91 g of dry seeds, 97 mg of limonin crystals were obtained in 30 minutes in the proportion of 1g of seeds to 0.5mL of solvent (1:0.5) quickly, simply and with less solvents when observed with extraction with Soxhlet (3 to 8h; 1 g: 6.25mL) and reflux (3h; 1 g: 6.25mL). Limonin crystals were also characterized by ^{1}H and ^{13}C NMR. **Conclusion:** It was possible to obtain limonin by ultrasonic bath-assisted extraction and confirm its structure by ^{1}H and ^{13}C NMR.

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INFLUENCE OF THE SURFACTANT MIXTURE ON THE FORMULATION DESIGN OF SOLID LIPID NANOPARTICLES CONTAINING CAFFEIC ACID-PHYTALIMIDE

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Key words: Caffeic acid-phthalimide, drug delivery, solid lipid nanoparticles.

NADPH oxidase is a cellular enzymatic system that is involved in the production of reactive oxygen species (ROS) during and even after cessation of ultraviolet (UV) radiation exposure[1]. The UV-mediated ROS production is clearly involved in the pathological skin conditions such as cancer and premature aging. Caffeic acid-phthalimide (CF) is a known inhibitor of NADPH oxidase system, however, the aqueous solubility of CF is low, with an octanol-water partition coefficient (log P) of around 2.27. In addition, it may have inefficient percutaneous penetration due to the relative impermeability of the stratum corneum. Thus, would be interesting to incorporate these substances into new technologies, such as solid lipid nanoparticles (SLNs), which allow an improvement in their characteristics[2], in addition to increasing their permeation and prolonged release of CF in the skin. **Aim:** This study aimed to prepare SLNs, caffeic acid-phthalimide (CF), by hot homogenization method, as a strategy for photoprotection. In addition, evaluate the effect of different preparation methods and the influence of the surfactant mixture in the characterization of SLNs. **Methods:** The influence of the preparation methods of the SLNs with different emulsification processes.The impact of sonication time (3, 5, and 7 min) and different concentrations of Tween 80 were also performed. To maintain the surfactant concentration constant (7.63×10^{-3} mol/L) while reaching a smaller size and polydispersity index (PdI), a mixture of surfactants (Tween 80/Pluronic F-127) was evaluated, varying the molar ratio (85:15, 90:10, 95:05 and 100:0). Moreover, the particle size, PdI, stability, encapsulation efficiency, and drug release was performed. **Results:** SLNs exhibited mean particle size of 160 to 290 nm, PdI of 0.180 to 0.300, and association efficiency between ~95% to 98% with CF. The concentration of Tween 80 in the formulation increased from 7.63×10^{-3} to 1.53×10^{-2} mol/L, showing a decrease in particle size and in the PdI. Interestingly, the formulations containing the surfactant mixture (Tween 80/Pluronic F-127) showed a decrease in particle size and PdI, as the amount of Tween 80 decreased. The formulations were stable for 4 weeks when stored at 25°C. SLNs exhibited a controlled *in vitro* release of CF. **Conclusion:** The results revealed SLNs of CF could be an ideal topical delivery system for photoprotection.

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DEVELOPMENT AND OPTIMIZATION OF MICRONEEDLES CONTAINING ETHANOLIC OR GLYCOLIC EXTRACTS OF PROPOLIS

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Keywords: **microneedles; development; propolis; drug delivery system.**

Introduction: Despite the highly protective characteristic of the skin, it ends up becoming a barrier for the permeation of certain drugs, due to the presence of the stratum corneum and its hydrophilic-lipophilic balance. Microneedles (MN) are a strategy to break this barrier, in a minimally invasive way. By creating temporary micropores, they allow the permeation of the biologically active agent in the deeper layers, which can reach the systemic circulation. Propolis (PRP) is a gum-resin, with a complex chemical composition, displaying many biological and pharmacological properties (antibacterial, antiviral, antifungal, anti-inflammatory, healing and immunomodulatory). However, the existing pharmaceutical dosage forms do not guarantee the PRP availability in an effective way to the patient and, also, do not completely solve the problems of PRP related to taste, odor and stability. Moreover, the administration of PRP extracts by conventional routes has some disadvantages, such as, the flow of liquid or emulsion form throughout the skin. **Aim:** The objective of this work was to prepare and characterize MN containing polyvinyl alcohol: polyvinylpyrrolidone (1:1), poloxamer P407 (P407) (1, 2 or 3%) and ethanolic (4, 8 or 12%) or glycolic (2, 4 or 8%) PRP extract, which would allow the modified and/or controlled release of the biologically active substances of PRP at the site administration, **Methods:** For the development of MN, molds were obtained from polydimethylsiloxane (PDMS). A sample of Brazilian green PRP was obtained, evaluated regard its quality, and the ethanolic and glycolic extracts at 30% (w/w) were prepared. The MN obtained were morphological and mechanically characterized. The mechanical analysis was performed using a texturometer, and *in vitro* release, disintegration and permeation tests were also carried out. **Results:** The extracts showed quality to continue with the work. The results of the mechanical analysis showed that the formulations containing 3% of P407 presented the highest values of compression on a hard surface, which was also confirmed by the height and base values of the morphological analysis as well as by the images obtained by the microscopic analysis. It was possible to design the MN and select the best formulations for specific tests. The chosen MN showed a fast release and disintegration profile, in addition to good skin permeability. **Conclusion:** The MN containing ethanolic extract of PRP showed to be better structured, when compared to the MN containing glycolic extract of PRP. The MN developed proved to be a promising platform for the topical application of PRP.

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MICRONEEDLES FOR BRAZILIAN GREEN PROPOLIS DELIVERY: PREPARATION, MECHANICAL AND *IN VITRO* RELEASE

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Keywords: propolis, poloxamer 407, polyvinyl alcohol.

Introduction: The skin is an organ capable of performing thermoregulation, immunological defense, sensitivity, mechanical barrier against exogenous aggressions and acting by preventing the loss of water and proteins to the external environment. Microneedles (MN) are minimally invasive structures that break the stratum corneum forming microchannels for drug release, which can release the biologically active agent, reaching the blood capillaries. Propolis (PRP) displays anti-inflammatory, antimicrobial, anticancer, antioxidant, antiseptic, anesthetic properties, among others. It is usually used as the form of an alcoholic extract, so administration can be painful and uncomfortable. Therefore, the development of technology to obtain MA containing propolis extract (EPRP), using PVP, PVA and poloxamer407, can be an innovative and viable strategy due to its non-invasive characteristics.
Aim: The aim of this work was to research and prepare MN containing EPRP.
Methods: The formulations were prepared from a polymeric matrix, with different concentrations of polymers and EPRP. The MN were analyzed macroscopically (flexibility, integrity, homogeneity and presence of bubbles), microscopically (light microscope) and compared to the master structure. The content of total polyphenols in MN was determined by Folin-Ciocalteau method. Mechanical resistance (force) was evaluated using a TA-XT plus texturometer and gelatin or Petri dish as base. The EPRP release profile from MN was determined using an apparatus based on the vertical diffusion cells.
Results: The EPRP quality: dryness residue 16.45 ± 0.70 % (w/w); relative density 0.8632 ± 0.0012 g/ml; ethanol content 40.53 ± 0.92% (w/w); pH 4.74 ± 0.04; total polyphenols content 0.72 ± 0.03% (w/w). The MN were mostly rigid, homogeneous, intact, with color patterns and presence of some bubbles. Formulations E3, E6 and E9 presented values of total polyphenols content 0.44 ± 0.014, 0.89 ± 0.03 and 1.14 ± 0.02% (w/w), respectively. The mechanical test using gelatin, the force was 0.0860 ± 0.0437, 0.0870 ± 0.0085 and 0.0982 ± 0,0068 N, for formulations E3, E6 and E9, respectively. Moreover, using Petri dish, the force was 1.29 ± 0.3457, 1.99 ± 0.0657, and 2.17± 0.2112N, for E3, E6 and E9, respectively. The release was fast, and at five minutes, more than 60% of EPRP was released from MN.
Conclusion: MN showed good appearance, structure and uniform composition. The total polyphenol content of MN was in agreement with the amount of EPRP added to the structures. The selected MN provided rapid *in vitro* PRP release.
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EVALUATION OF POSSIBLE ALTERATIONS IN AST/ALT, SOD AND CAT ENZYMES CAUSED IN THE LIVER OF RATS WITH WALKER-256 TUMOR SUPPLEMENTED OR NOT WITH 1% L-GLUTATHIONE.

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Keywords: Oxidative stress, cancer, biochemical analysis**.**

Introduction: Oxidative stress is closely related to the process of cancer initiation and development. One of the main aggravating factors of cancer is cachexia syndrome, in which the tumor competes with the host for nutrients, and is characterized by great weight loss, anemia and weakness, aggravating the body's weakness. One of the pathogenesis also associated with cancer are the modifications generated by oxidative metabolism. Due to their potential damage, free radicals must be rapidly eliminated from the cell's environment. Therefore, different organisms have an endogenous antioxidant system composed of several enzymes and components to maintain the redox balance. Reduced glutathione, a tripeptide found in most tissues, especially in the liver in high concentrations, has an important antioxidant potential. **Aim:** To analyze the possible changes in AST/ALT, SOD e CAT enzymes in the liver of rats bearing Walker-256 tumor supplemented or not with 1% L-glutathione. **Methods:** All procedures were approved by CEUA 8617130120. Adult male Wistar rats (Rattus norvegicus) were randomly divided into 4 groups (n=6): control (C), control supplemented with 1% L-Glutathione (CGT), Walker- 256 tumor (TW) and Walker-256 tumor supplemented with 1% L-Glutathione (TWGT). After the experimental period of 15 days, the animals were euthanized, the liver and blood were collected. Then, the material was processed and the evaluation of serum levels of AST/ALT enzymes and enzymatic activity of SOD and CAT was performed. Statistical analysis was performed using a block design followed by Fisher's post-test. **Results:** For ALT, no statistically significant differences were detected between groups, as well as for CAT and SOD. However, the TW group showed a significant increase ($p<0.05$) in plasma activity only for AST when compared to the C group, on the other hand, the TWGT group showed a significant reduction ($p<0.05$) for AST when compared to TW, approaching the values detected in group C. **Conclusion:** Cancer was not able to affect SOD, CAT and ALT enzymes. However, despite having altered serum AST levels, supplementation with 1% L-Glutathione was able to restore serum levels to the same parameters observed in control animals.

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EPIGALLOCATECHIN-3-GALLATE, A GREEN TEA POLYPHENOL, IMPAIRS THE RAT LIVER MITOCHONDRIAL ENERGY METABOLISM

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Keywords: epigallocatechin-3-gallate,green tea, mitochondrial respiration, oxidative phosphorylation, ROS production.

Introduction: Epigallocatechin-3-gallate (EGCG) is the main compound of green tea with well-described antioxidant, anti-inflammatory, and tumor-suppressing properties. However, EGCG at high doses was reported to cause liver injury, which seems to be related to mitochondrial damage. Nonetheless, the exact molecular mechanisms underlying these effects are not well understood. **Objectives:**To investigate the effects of EGCG on the energy metabolism of rat liver isolated mitochondria. **Methods**: Male albino Wistar rats (200±30 g) were used. All procedures were approved by the Ethics Committee of Animal Experimentation of the University of Maringá (protocol n.2535301019).Rat liver mitochondria were isolated by differential centrifugation and oxygen consumption was quantified at 37^{o}C using an oxygraph. **Results:** Mitochondrial basal respiration was stimulated by EGCG when two substrates, namely glutamate + malate (complex I substrate) and succinate+ rotenone (complex II substrate) were used. In the presence of exogenously ADP (State III), respiration was significantly inhibited by EGCG starting at 250 µM, when succinate was used as substrate, but no inhibition was observed when glutamate + malate was used. State IV respiration (after ADP depletion) was stimulated by EGCG, starting at 500 µM, in the presence of both substrates. As a consequence of both State III inhibition and State IV stimulation, the respiratory control (RC) was inhibited, especially when succinate was used as substrate, reaching a maximum of 77% inhibition at 500 µM. Membrane-bound enzymatic activities of the mitochondrial complexes I, II and IV were measured using disrupted mitochondria in order to extend further knowledge on the EGCG´s actions. Both complexes I and II activities were decreased by EGCG at 1000 µM. On the other hand, oxidation of ascorbate (complex IV) was not affected by EGCG. Mitochondrial membrane integrity was accessed by NADH-driven respiration of intact mitochondria, which was substantially increased by EGCG at 500 µM. Real-time mitochondrial ROS production was also determined. EGCG decreased ROS production at relatively low concentrations, starting at 50 µM. **Conclusion:** EGCG acts both as a mitochondrial inhibitor of complexes I and II and as an uncoupling agent of oxidative phosphorylation. The uncoupling effect can be partially related to the loss of mitochondrial membrane integrity, which is probably not associated to membrane lipoperoxidation.

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EFFECTS OF *TRICHILIA CATIGUA* ETHYL-ACETATE FRACTION ON BLOOD-BRAIN BARRIER INTEGRITY AND WHITE MATTER INJURY AFTER CEREBRAL ISCHEMIA IN BalbC MICE: PRELIMINARY RESULTS.

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Keywords: Bilateral common carotid artery occlusion, blood-brain barrier, white matter, *Trichilia catigua*.

Introduction: Cerebral ischemia (CI) has been characterized by several pathophysiological events including hippocampal neurodegeneration, white matter (WM) injury, and blood-brain barrier (BBB) breakdown. Most of the pathological events have been determined in rodent models of CI. However, the time course of each pathological event in different rodent species is still unknown. **Aim**: The present study aimed to determine the time course of BBB breakdown and WM injury in BalbC mice submitted to CI. Possible neuroprotective effects of the ethyl acetate fraction (EAF) obtained from *Trichilia catigua* were also determined. **Methods:** Male BalbC mice (2 - 3 months old) were used. The local Ethics Committee approved the protocols used in this study (CEUA nº 4596160921). CI was induced by bilateral common carotid artery occlusion (BCCAO) for 20 minutes. The BBB breakdown was evaluated 1, 2, 3, 7, and 21 days after BCCAO. Sham-operated animals underwent the same surgical procedure but without occlusion. Since BBB breakdown occurred more expressively at 7 days after BCCAO the effect of EAF on this outcome was tested at this time. Vehicle or EAF (200 mg/kg, gavage) was given during 7 days, being the first administration at 1 h after BCCAO. Eight hours before sacrifice, the animals were injected (i.p.) with a 2% solution of Evans blue dye (EB; 0.2 mg/kg, 1 ml/kg). EB extravasation was measured by Elisa's technique. Using the Kluver-Barrera staining, WM injury was measured by integrated optical density (IOD) in the corpus callosum 7 and 21 days after BCCAO. The one-way ANOVA followed by Tukey's *post hoc* test was used to quantify the results. **Results:** In BCCAO groups, there was greater EB extravasation compared to the sham group, indicating an effect of CI in increasing BBB permeability. A significant increase in EB extravasation was detected at 7 days after BCCAO when compared to the sham operation ($p < 0.05$). The EAF treatment prevented the BBB breakdown ($p < 0.0001$ vs. vehicle). In the preliminary evaluation of the effect of CI on the WM injury, a greater degeneration was found in the BCCAO at 21 days group compared to the sham group ($p < 0.001$) and BCCAO at 7 days group ($p < 0.05$). **Conclusion:** The greatest BBB breakdown and WM injury occurred at 7 days and 21 days following BCCAO, respectively. Treatment with EAF prevented BBB breakdown in BalbC BCCAO mice.

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POST-ISCHEMIC ADMINISTRATION OF THE ETHYL ACETATE FRACTION OF *TRIHILLIA CATIGUA* PREVENTS INTERRUPTION OF SPATIAL MEMORY, OXIDATIVE STRESS, DENDRITIC MORPHOLOGY AND SYNAPTIC PROTEINS.

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Keywords: Cerebral ischemia, memory, oxidative stress, neuroprotection

Introduction: *Trichilia catigua* (*Meliaceae*) preparations have been shown to have potent antioxidant activity and neuroprotective effect. We originally reported that an ethyl-acetate fraction (EAF) of *Trichilia catigua* when given 1 hour before and 4 hours after TGCI, 4-VO reduced cerebral ischemia-induced learning and memory deficits and antioxidant and anti-inflammatory activities in rats. **Aim:** We investigated whether the administration of the EAF after a cerebral ischemic event would maintain its neuroprotective and antioxidant effects, as well as to assess wether *T. catigua* has neuroplasticity/neurotrophic properties. **Methods:** Rats were subjected to 15 min of transient global brain ischemia (TGCI) and a single dose of the EAF (400 mg/kg) or vehicle (1 ml/kg) was administered by oral route at 1, 4, or 6 h post ischemia and antioxidant status was measured after 24 h of reperfusion. In second experiment, the EAF or vehicle was administered for 7 days after TGCI, and first dose given at 4h or 6h after cerebral ischemia / reperfusion (I / R). Retrograde memory performance was assessed 10-, 17-, and 24-days post-ischemia. Afterwards the brains were examined for neurodegeneration and neuronal dendritic morphology in the hippocampus and cerebral cortex. Another group of ischemic rats received the EAF at 4 h of reperfusion and continued for the next 4 days; their brains were then examined for GFAP and Iba-1 immunoreactivity. Lastly, ischemic rats received EAF at 4 h after ischemia and continued for 6 days, after which the neural plasticity-related proteins were measured in the hippocampus at 7 and 14 days after ischemia. (CEUA nº 7481261017) **Results:** A single EAF administration 1, 4 or 6 h postischemia alleviated the oxidative stress caused by ischemia. Ischemia caused persistent loss of memory (amnesia), an outcome that was consistently ameliorated by the EAF treatment initiated at 4 or 6 h post-ischemia. The 4 h delayed EAF treatment positively impacted the dendritic morphology in neurons that survived ischemia. TGCI reduced the BDNF, SYP, PSD-95, and NeuN protein levels in the hippocampus. Otherwise, EAF normalized the SYP and PSD-95 protein levels. Ischemia-induced neurodegeneration and glial cell activation were not prevented by the EAF treatment. **Conclusion:** The data indicate on the neuroprotective potential of *T. catigua* by demonstrating that postischemia delayed administration of EAF effectively prevented memory impairment and decreased oxidative stress,dendritic deterioration, and synaptic protein loss within a time window of efficacy (TWE) that ranged from 1 to 6 h.

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CHARACTERIZATION OF NANOSTRUCTURED LIPID CARRIERS CONTAINING GERANIOL

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Keywords: **Lipid nanocarriers, particle size distribution, zeta potential, encapsulation**

Introduction: Geraniol is an odorant liquid oily consisting of a complex mixture of labile and volatile compounds that evaporate or decompose easily under high temperatures, low pressure, and the presence of air and light, which shortens its useful life. The nanostructured lipid carriers (NLCs) are an example of an encapsulation system that can be useful to overcome these disadvantages of geraniol and produce biocompatible delivery systems. **Aim:** The objective of this work was to characterize the size measurements, zeta potential (ζ-potential) and polydispersion index (PDI) of NLCs containing geraniol. **Methods:** The NLCs formulations were prepared using cocoa butter, sesame oil and phospolipon 80H as oil phase. Tween 80 and ultrapure water were used as aqueous phase. The F1 (0.311% geraniol), F2 (0.624% geraniol) and F3 (0.935% geraniol) were characterized regarding the particle diameter and PDI by using the dynamic light scattering (DLS) method. The zeta potential (ζ-potential) was measured by means of electrophoretic mobility. These analyses were done in the NanoPlus/Zeta Particle Analyzer equipment (Micromeritics Instrument Corporation, Georgia, GA, USA) with previous dilution with ultra-purified water (1:100), at a temperature of 25 ± 1 °C and a scattering angle of 90˚. The analyses were carried out at least in triplicate. The data were analyzed by one-way ANOVA and post-hoc Tukey's test using the Statistica 10 (StatSoft Inc., Tulsa, OK, USA) software. The results were considered statistically different for p-value ≤ 0.05. **Results:** The particles size values of NLCs were 110.07 ± 1.53^{a} nm (F1), 282.53 ± 5.12^{b} nm (F2) and 117.57 ± 2.74^{a} nm (F3). According to some authors, NLCs with a particle size between 50 and 400 nm, the case of this study, may indicate that the components and preparation procedures were appropriate to prevent the coalescence of nanocarriers. The PDI values were 0.279 ± 0.01^{b} (F1), 0.160 ± 0.03^{a} (F2) and 0.140 ± 0.03^{a} (F3). According to the literature, PDI values below 0.3 denote a homogeneous size distribution. Regarding the ζ-potential, the NLCs containing geraniol had a negative charge ranging from -32.40 ± 0.28^{b} (F1), -35.03 ± 1.08^{a} (F2) and -35.06 ± 0.96^{a} mV (F3). This is an important and useful indicator of stability of NLCs. Particles with ζ-potential values greater than ±30 mV are suggested to have good long-term physical stability due to the phenomenon of repulsion, decreasing the chance of particle agglomeration and the formation of precipitates. **Conclusion:** The NLCs containing geraniol presented small size with a uniform size distribution, and a zeta potential suggestive of a physically stable system.

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EXPLORATION OF DISSOLUTION SAFE SPACE OF LAMOTRIGINE IR USING PHYSIOLOGICALLY-BASED BIOPHARMACEUTICS MODELING (PBBM)

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Keywords: **IVIVR, bioequivalence, virtual bioequivalence, PBPK**

Introduction: Biopharmaceutical modeling techniques have been used to predict and guide the development of new formulations from *in vitro* data, such as the *in vitro-in vivo* relationship (IVIVR) and physiologically-based biopharmaceutics modeling (PBBM).With these tools it is possible to explore a dissolution safe space, that is the dissolution limits to which two formulations are considered bioequivalent to each other. Lamotrigine is a drug used to treat epilepsy and bipolar disorder and the bioequivalence of different formulations present some dissolution issues which may be explained by the safe space. **Aim:** The objective of this work was to explore an IVIVR for lamotrigine immediate release (IR) and to evaluate a possible dissolution safe space. **Methods:** Previously developed and verified physiologically-based pharmacokinetics (PBPK) model for lamotrigine was used. The dissolution data was provided by Prati-Donaduzzi Pharmaceutical Company. The lamotrigine PBBM model was built with dissolution data from flow-through cell apparatus, flow rate of 6 mL/min and FaSSIF medium, and inserted in GastroPlus® as a table of percentual dissolved per time and fitted as z-factor.For the safe space exploration, the final PBBM model was assumed as a reference profile, then the theoretical dissolution profiles were simulated by decreasing or increasing of the percentage of release (5, 10, 15 and 20%) at every reported time point.Predicted AUC_{0-t} and C_{max} parameters were compared to the observed reference parameters. The formulations were considered bioequivalent if 90% confidence intervals (CI) of the mean test/reference for C_{max} and AUC ratios fall within the limits of 0.80-1.25.**Results:** The predicted profiles, called as test formulation, showed mean test/ reference ratio for C_{max} between 0.94 to 1.10 and 90% CI within the range of 0.87 to 1.14. For AUC_{0-t}, mean ratio was between 0.99 to 1.00 and 90% CI within the range of 0.89 to 1.09. All plasma profiles predicted by the PBBM model passed the virtual bioequivalence (VBE), presenting test/reference ratio between 0.80 and 1.25, that is the traditional BE limit for non-narrow therapeutic range drugs. **Conclusion:**The present study indicated the possibility that the lamotrigine IR dissolution profile can vary until 20% of the reference formulation without prejudice to BE.

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EFFECT OF β-MYRCENE ON RESPONSE INFLAMMATORY IN EXPERIMENTAL MODEL OF INFECTION SYSTEMICS IN C57BL/6 MICE

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Keywords: sepsis; inflammation; β-myrcene

Introduction: Sepsis is a syndrome characterized by an exacerbated systemic inflammatory response in response to an infection. β-Myrcene (MYR) is a terpenoid compound of natural origin present in the essential oils of different species of aromatic plants. This terpenoid has several biological activities such as: antimicrobial, analgesic and anti-inflammatory. **Aim:** In this work, the effect of treatment with β-myrcene on systemic inflammation in an experimental model of sepsis induced by ligature and puncture of the cecum (CLP) was evaluated. **Methods:** Male mice of the strain C57BL/6 weighing 20 and 25g, from the Central Animal House of the State University of Maringá, were used. Approved by (CEUA/UEM nº 4628291021). The animals were treated with β-myrcene at doses of (50 mg/Kg, 100 mg/Kg and 200 mg/Kg. After anesthesia - Xylazine + ketamine at a dose of (10:30 mg/Kg), for induction of sepsis the surgery was performed for ligation and perforation by the cecum and leakage of the contents. After 6 hours of CLP induction, the animals were euthanized, the peritoneal cavity was washed with 0.9% saline solution and 20 µl aliquot was diluted in 380 µl of Turk for total and differential leukocyte count. Results were expressed as number of leukocytes per mm^3. **Results:** The results indicated a significant increase of 451% ($P<0.05$) in the number of leukocytes recruited to the peritoneal cavity in sepsis-induced mice (CLP: 10,371 ± 2,599 cells/mm^3) compared to the SHAM group (1,881±285 cells /mm^3). Our results showed that 46% (5,544±1,175 cells/mm^3) of cells after sepsis by (CLP) are polymorphonuclear and that treatment at doses of 100 and 200 mg/kg with MYR promoted a reduction of 46% and 45 % (5,619 ±1,204 and 5,665±811.1) respectively in the recruitment of leukocytes in the peritoneal cavity in relation to the control group (CLP). Treatment with MYR at a dose of 50 mg/kg did not reduce the number of leukocytes that migrated to the peritoneal cavity. **Conclusion:** The results obtained indicate that MYR has an effect on reducing the number of cells migrated to the peritoneal cavity after 6 hours of sepsis induction, in the CLP model.

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DOXORUBICIN-LOADED IRON OXIDE NANOPARTICLES INDUCES OXIDATIVE STRESS IN BREAST CANCER CELLS

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Key-words: oxidative stress, nanotechnology, MCF-7.

Introduction: There are a wide range of biomedical applications for nanotechnology. It is an interdisciplinary and multidisciplinary research area. As the current cancer treatment of choice, chemotherapy has some drawbacks, including drug resistance, lack of selectivity, and accelerated metabolism, all of which reduce its effectiveness (1). In order to reduce side effects caused by anti-tumor drugs in healthy organisms, it is crucial to study the use and mechanism of nanocarriers that can travel to specific targets. In this regard, magnetic nanoparticles are promising candidates because of their physicochemical and magnetic properties (2). **Aim:** Therefore, this work aimed to evaluate the production of oxidative stress by magnetite (NPMag), silica-coated magnetite (NPMag+Si) nanoparticles and doxorubicin-functionalized nanoparticles (NPMag+Dox, NPMag+Si+Dox) on human breast adenocarcinoma cells (MCF-7). **Methods:** DLS and FTIR were used to evaluated the physico-chemical characteristics of the nanoparticles. Cells were exposed to concentrations of 5µg/mL and 10µg/mL of NPMag, NPMag+Si, NPMag+Dox and NPMag+Si+Dox and the equivalent concentrations of 0.3, 0.4, 0.6 and 0.8µg/mL of Doxorubicin (Dox) for 48 h. To search for the ability of these nanoparticles to enhance oxidative stress in cancer cells it was evaluated the reactive oxygen species (ROS) production, nitric oxide (NO), hydrogen peroxide, cell cycle analysis and evaluation of magnetic field targeted drug delivery. **Results:** The DLS data shows that NPMag, NPMag+Si, NPMag+Dox and NPMag+Si+Dox have the hydrodynamic sizes ranges from 120nm to 240nm with a polydispersity index of 0.2. The FTIR shows the presence of Dox in the nanoparticles. The NPMag+Dox and NPMag+Si+Dox induced an increase higher than 80% in ROS, hydrogen peroxide and NO formation compared with the free drug. In addition, NPMag+Dox and NPMag+Si+Dox generated an arrest in the G2 phase of the cell cycle compared with control and they were able to be used in targeted delivery. **Conclusion:** NPMag and NPMag+Si alone did not cause oxidative stress in cells but when conjugated with doxorubicin caused damage to the cancer cells. This indicates the potential of this formulation for drug delivery.

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QUALITY CONTROL OF *ABAREMA COCHLIACARPOS* BARKS.

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Keywords: *Mimosa cochliacarpos*, Quality Control, Brazilian Pharmacopeia.

Introduction: *Abarema cochliacarpos* (Gomes) Barneby & J.W.Grimes (Fabaceae) is a brazilian plant native known as “barbatimão”. Usually found in the northeast and southeast regions, in the Caatinga, and Atlantic Forest biomes. Some of the medicinal properties are antioxidant, antibacterial, wound healing, among others. **Aim:** The aim of this study was to evaluate some quality parameters for milled *A. cochliacarpos* barks. **Methods:** *A. cochliacarpos* barks were collected in January 2020, in Itaporanga d'Ajuda, Sergipe (11º4'41"S, 37º17'23"W). The barks were crushed in a hammer mill. Quality control analyzes such as: moisture content, total ash, and dry residue were performed. For the determination of moisture content, about 1 g of vegetable drug milled on an infrared scale was weighed, which was subjected to a temperature of 105 °C for 45 min. In the determination of total ash, 3 g of the pulverized bark were weighed in previously tared crucibles. Then, the aliquots were placed in a muffle furnace and subjected to a temperature gradient, being 200 °C for 30 min, 400 °C for 60 min, and 600 °C for 90 min. After incineration, the crucibles were cooled in a desiccator and weighed. For the determination of dry residue about 10 g of the pulverized plant drug were weighed. Then the sample was transferred to a round-bottomed flask and 100 mL of extractor liquid (7:3 acetone/water; 50% ethanol; and 70% ethanol) was added. Afterwards, it was refluxed for 1 h under boiling, then the flask was cooled, the solution was filtered and 20 mL were transferred to a weigh filter, previously weighed, the solution was dried in a water bath; then placed in an oven at 105 °C for 3 h. It was then cooled in a desiccator for 30 min and weighed. **Results:** determination of moisture content of *A. cochliacarpos* barks was the average of 11.08%±0.15 (RSD%=1.40); for the determination of total ash, the results were average 2.62%±0.04 (RSD%=1.70). On the residue dried with acetone 7:3; 50% ethanol, and 70% ethanol the average was respectively 2.53%±0.12 (RSD%=4.66), 2.82%±0.10 (RSD%=3.55), and 2.94%±0.06 (RSD%=1.92). **Conclusion:** we concluded that the results were satisfactory according to data researched in the literature.

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CANCER-INDUCED CACHEXIA CAUSES ENTERIC GLIAL CELLS PLASTICITY IN THE JEJUNUM OF WALKER-256 TUMOR-BEARING RATS

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Keywords: **Cancer. Cachexia. Enteric Glial Cells. Plasticity.**

Introduction: Enteric glial cells have a fundamental role in regulating gut functions. Patients with cancer-induced cachexia present gastrointestinal dysfunctions, however knowledge of the effects of cachexia in the enteric glial cells is scarce. **Aim:** Thus, the main goal of this work is to investigate if cachexia induces morphoquantitative changes in enteric glial cells. **Methods:** All procedures described were performed agreeing with international guidelines of ethical regulation and previously approved by the Committee of Ethical Conduct on the Use of Animals in Experimentation (CEUA) of the State University of Maringá – Paraná – Brazil (UEM), CEUA no 8617130120. We performed immunohistochemistry for neurons, enteric glial cells and immune cells in whole-mount preparations and frozen histological sections of the jejunum from 20 Wistar rats, distributed in 4 groups: control, tumor of Walker-256, control administered with 1% L-glutathione, and tumor of walker-256 administered with 1% L-glutathione. Morphoquantitative analyses were made using the Image-Pro® Plus 4.5 and ImageJ® 1.43º software. **Results:** Tumor development caused a significant reduction in neuronal and enteric glial cells populations in both plexuses and an enlargement in the glial body area in the submucosal plexus. There was an increase in enteric glial cells and lymphocyte recruitment on the jejunal mucosa. 1% L-glutathione administration was not able to protect submucosal neurons and the enteric glial cells but yielded partial protective effects for the myenteric populations, causing enteric glial cells density preservation only in the myenteric plexus. **Conclusion:** This study demonstrates for the first time that cachexia development has significant effects on enteric glial cells' plasticity, which may open new pathways to understand the pathophysiology behind gastrointestinal abnormalities in cancer-induced cachexia.

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VIRTUAL BIOEQUIVALENCE STUDIES FOR EVALUATION OF A NOVEL GASTRORETENTIVE RELEASE SYSTEM FOR SILDENAFIL CITRATE

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Keywords: In silico modeling, PBPK, PBBM, modified release formulation, virtual bioequivalence.

Introduction: In silico simulations have been suggested to reduce time and effort in the pharmaceutical development of drug products and predict bioequivalence (BE) outcomes (i.e. virtual BE). Currently, this approach has been successfully predicting in vivo performance of drugs and could be useful in the design of novel modified-release dosage forms (MR) such as gastroretentive drug delivery systems (GRDDS). **Aim:** This work proposes a novel GRDDS for sildenafil citrate and evaluates the proposed formulations through virtual BE studies with GastroPlus™. **Methods:** A compartmental PK model was built using the GatroPlus™ software for virtual bioequivalence of the proposed formulations. The predictive power for the pharmacokinetic parameters of C_{max}, T_{max}, and AUC was proven. The virtual clinical protocol for the conventional IR formulation considered the administration of 20 mg TID (dosing interval of 8 hours), and for the novel formulations the dose was 60 mg once a day (QD). The comparison of plasma exposition between the IR and each GRDDS formulation along 24 hours were performed according to the traditional comparison of BE (IC 90% between 80% and 125% for AUC and C_{max}). **Results:** The virtual BE studies of the proposed formulations and IR formulation was carried out with the previously validated model. By comparing the PK parameters predicted by the virtual BE study, the formulations F1, F2, F3 and F5 failed on BE. While F1 and F2 were reproved on the parameter C_{max}, F3 and F5 failed on both AUC and C_{max} parameters. The formulation F4 showed to be bioequivalent to the reference and was considered the viable formulation to substitute the IR. **Conclusion:** Virtual BE studies have been shown to be an important tool in drug development. It is concluded that gastroretentive systems are a promising alternative for controlling the dose release of drugs such as sildenafil, which have a narrow absorption window due to their solubility characteristics.

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EFFECTS OF THE HYDROALCOHOLIC EXTRACT OF PROPOLIS IN MICE SUBMITTED TO CEREBAL ISCHEMIA

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Keywords: hydroalcoholic extract of propolis, cerebral ischemia, neuroprotection, behavior.

Introduction: Cerebral ischemia (CI) represents an important cause of disability and mortality in the world population, in addition to having a great negative impact on the costs of health systems. Pharmacological treatments for the acute and chronic phases (sequels) of CI are still quite scarce. Propolis has been used as healthy food and for the treatment of various cerebral diseases. Therapeutic properties of propolis include antibacterial, anti-inflammatory, antioxidant, tumoricidal, cytotoxic, and neuroprotective activities. **Aim:** This study aimed to investigate the effects of the hydroalcoholic extract of propolis (HEP) in mice submitted to bilateral occlusion of the common carotid arteries (BCCAO), a model that has been used to mimic conditions of transient CI in mice. **Methods:** All the procedures were approved by the Ethical Committee of State University of Maringá (CEUA nº 3943160921). Male C57/BL6J mice were subjected to BCCAO for 20 minutes. The animals were divided into four experimental groups: BCCAO + Veh, BCCAO + HEP 50 mg/kg, BCCAO + HEP 100 mg/kg and BCCAO + HEP 150 mg/kg. After surgeries, the animals were evaluated using a behavioral test battery during 15 days. Motor, cognitive and emotional functions were evaluated in BCCAO mice treated with vehicle or HEP by gavage during 7 days after reperfusion. The animals were tested in the open field test (OFT), elevated zero maze (EZM) and tail suspension test (TST). Data were analyzed by ANOVA followed by the Tukey's *post hoc* test. **Results:** BCCAO mice exhibited functional impairments as reflected in increased anxiety-like behavior in the OFT and EZM (day 7^{th}) and despair-like behavior in the TST (day 15^{th}) when compared to BCCAO mice that received HEP. BCCAO + HEP 100 mg/kg group exhibited anxiolytic-like behavior, as reflected by an increase in the numbers of entries in the center of the OF. In a similar way, BCCAO + HEP 150 mg/kg group exhibited increase in the open quadrant of the EZM, 7 days after reperfusion. BCCAO + HEP 150 mg/kg group presented a significant decrease in the immobility time in the TST when compared to BCCAO mice, indicating decrease despair-like behavior. **Conclusion:** These findings suggest that short-term treatment with HEP triggered protective mechanisms that might be involved in functional improvements in mice with BCCAO.

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MECHANICAL EVALUATION OF THERMORESPONSIVE AND BIOADHESIVE POLYMERIC BLENDS FOR TOPICAL APPLICATION

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Keywords: **Poloxamer 407; cellulose derivative; binary polymeric systems.**

Introduction: Hydrogels are the most widely used semisolid pharmaceutical forms for topical application. Poloxamer 407 (P407) has often been used to form in situ gels. Since it presents thermoresponsive properties, the systems containing this polymer may change from solution to gel state, when heated above a critical temperature. However, P407 exhibits low bioadhesive capacity and low mechanical properties, which can be modified by incorporation with other polymers. Cellulose derivatives have been able to form polymer blends with P407, with improved bioadhesive and mechanical properties. **Aim:** The aim of this work was to evaluate the mechanical properties (texture profile analysis (TPA), syringability and softness) as well as the bioadhesive strength of binary polymeric systems. **Methods:** Systems composed of 17.5% (w/w) P407 and 0.3% (w/w) of sodium carboxymethylcellulose (B1) or hydroxypropylmethylcellulose (B2) were prepared and, the mechanical analyses were performed using a TA-XTplus texture analyser. In the TPA mode, at 25 and 34 °C, the analytical test was compressed twice within the sample, to calculate the TPA parameters: hardness, compressibility, adhesiveness, elasticity and cohesiveness. In order to study syringability, the samples were placed in 1 mL syringes and fixed to the probe, which was lowered. The work performed to compress the plunger was defined as the work of syringing. For softness analysis, a conical probe was compressed into the sample, and the maximum force required to penetrate the sample was determined as the softness index, at 25 and 34 °C. Bioadhesion was evaluated *ex vivo* using a porcine ear skin attached to the probe, in tension mode, and the force required to detach the formulation from the skin was defined as the bioadhesive force as well as the work of bioadhesion, at 34 °C. **Results:** The TPA of B1 and B2, showed that the temperature influenced all the parameters, except the elasticity, which did not vary across the temperatures evaluated. There was an increasement in hardness and compressibility at 34 °C, being B2 harder than B1. At 34 °C, the systems were both adhesive, and the cohesiveness decreased with increasing temperature. The systems showed low softness values. Considering the work required to eject the formulation from a syringe is useful to characterize the withdrawing of the formulation from the their package, with narrow orifice, B2 showed higher syringing work than B1. There was no difference between the detachment force of the B1 and B2 systems, but evaluating the work of bioadhesion, it was higher for B2. **Conclusion:** The systems presented suitable characteristics at room temperature, showing easy removal of the product from the package and easy application on the skin. Moreover, it demonstrated good bioadhesive performance at body temperature.

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COMPLEXION OF BURITI VEGETABLE OIL WITH BETA-CYCLODEXTRIN CHARACTERIZATION AND SUNLIGHT STABILITY

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Keywords: ***Mauritia flexuosa*, cyclodextrin, thermal analyses, stability.**

Introduction: Buriti, fruit of the *Mauritia flexuosa* palm, is rich in carotenoids and tocopherols, in addition to fatty acids (1). Vegetable oils (VO) are instable, being a factor that restricts their use. In turn, cyclodextrins (CDs) become an alternative to overcome these limitations (2). **Aim:** The complexantion of the buriti VO to the beta-CD, characterize the inclusion complexes (IC) formed and to evaluate color stability against sunlight. **Methods: VO characterization** – The VO was characterized by GC-MS and the compounds were identified by comparing the retention times of each constituent with an analytic standard (3). **Complex formation** – The complex was formed by the kneading methodology in a 1:4 ratio (VO:beta-CD). The physical mixture (PM) was used as a standard for the analyses (2). **Characterization of the IC** – The complex was characterized by DSC and TGA techniques (2). **Color stability against sunlight** – Buriti VO, IC and PM were exposed to sunlight, and on 0, 15 and 30 days color stability was evaluated (4). **Results: VO Characterization**– The majority compound of the buriti VO was oleic acid, with 77% of the total composition. **Characterization of the IC** - The DSC curve of beta-CD presented the first event with peak at 83 ºC, characteristic of beta-CD dehydration. The second and third events were subsequent with peaks at 314 and 331 °C, corresponding to the process of molecular decomposition and consequent removal of carbonaceous material (2). The PM and the kneading showed similar DSC curves to beta-CD. The IC presented an endothermic peak lower than that of pure beta-CD and PM, suggesting that the water present in the beta-CD was replaced by the VO. In the TGA, the mass loss after the first endothermic event was 11.98% for beta-CD, 10.2% for PM and for kneading was 7.74%. Corroborating with the results obtained in the DSC, however, it is possible to suggest that part of the VO was encapsulated in the PM. **Color stability against sunlight –** The VO was degraded 6.82% in the first 15 days and 54.55% after 30 days. The PM showed a decrease of 26.97 and 56.87% at 15 and 30 days, respectively. The IC was stable with a color retention of 97.58% after 15 days and 91.12% after 30 days of sun exposure. **Conclusion:** DSC and TGA techniques were efficient in evidencing the formation of IC between beta-CD and the buriti VO. The protection of the VO by the process of molecular encapsulation by beta-CD proved favorable, ensuring the color stability of the VO.

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LINSEED OIL ATTENUATES LIVER INFLAMMATION INDUCED BY A HIGH-CARBOHYDRATE DIET THROUGH CHANGES IN FATTY ACIDS ACCUMULATION AND COMPOSITION

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Keywords: nutraceutical; anti-inflammatory effect; dietary supplementation; flaxseed oil**.**

Introduction. Liver fatty acids (FA) accumulation and changes in composition are involved in several pathological processes, including non-alcoholic fatty liver disease (NAFLD). NAFLD is characterized by increased FA accumulation and could progress to cirrhosis and liver failure. The main treatment for NAFLD is caloric restriction and body weight loss. Also, linseed oil (LO), a rich source of omega 3 polyunsaturated FA (n-3 PUFA) could prevent the NAFLD progression. **Aim.** We evaluated whether LO modulates the effects of a high-carbohydrate diet (HCD) on FA accumulation, FA composition and liver inflammation. **Methodology.** The control group (HCD-C) received HCD with conventional lipid source i.e., lard (90 %) and soybean oil (10%). The L10 and L100 groups received the HCD with 10% (replacing soybean oil) and 100% of LO (replacing soybean oil and lard) as the lipid source, respectively. The mice were euthanized by decapitation before (Day 0) and after receiving the diets for 56 days. Liver samples were quickly removed and frozen in liquid nitrogen. FA composition was evaluated by gas chromatography. Inflammatory and fibrogenesis gene expression was performed through RT-qPCR. **Results.** Livers from L100 group exhibited a higher ($p<0.05$) liver amount of omega-3 polyunsaturated FA (n-3 PUFA) and lower ($p<0.05$) amounts of saturated FA (SFA), monounsaturated FA (MUFA), and omega- 6 polyunsaturated FA (n-6 PUFA) compared to L10 or HCD-C mice. On day 56, interleukin 10 and type IV collagen gene expression were significantly upregulated and downregulated, respectively in L100. **Conclusion.** We concluded that LO attenuation of liver inflammation in HCD fed mice is associated with increased liver n-3 PUFA levels, so modulating FA composition and deposition in the liver.

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ANTI-INFLAMMATORY ACTIVITY OF B-MYRCENE IN INHIBITING LEUKOCYTE RECRUITMENT, PHAGOCYTIC ACTIVITY OF NEUTROPHILS AND HISTOPATHOLOGICAL ASPECTS

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Keywords: Acute lung injury, essential oil, histology, leukocyte chemotaxis.

Introduction: β-myrcene, a monoterpene, is derived from essential oils of many plants such as lemongrass, verbena, Rosmarinus officinalis and others, which are commonly applied in cosmetic and food industries. Many studies demonstrated pharmacological activities of β-myrcene, as antioxidant, analgesic, antiulcer, anti-inflammatory and antimicrobial activities. **Aim:** The aim of this study was to investigate the anti-inflammatory effects of β-myrcene on leukocyte behavior and pulmonary histology **Methods:** Chemotaxis in vitro was carried out in Boyden chambers using leukocytes from the peritoneal cavity of mice with zymosan-induced peritonitis. The cells were incubated with β-myrcene at the concentrations of 3, 10, 30 and 90 µg/mL for 30 min and fMLP was the chemoattractant. Cell viability, by MTT methods, and phagocytosis assay was performed with β-myrcene at the same concentrations. For the LPA model, the animals were divided into 7 groups: saline, LPS (5mg/kg), LPS + β-myrcene (125, 250, 500 and 750 mg/kg), LPS + dexamethasone (DEX, 1 mg/kg). kg). For the histological analysis, the lungs of the animals, treated or not, were fractionated and submitted to the steps of the histological process. The animal protocol was approved by the Ethics Committee for Animal Experimentation of UEM (CEUA/UEM nº 3919220419). **Results:** Our results showed that β-myrcene promoted a significant decrease in leukocyte chemotaxis when stimulated by fMLP. The treatment with β-myrcene at the concentrations of 3, 10, 30 and 90 µg/mL significantly reduced the phagocytic activity of neutrophils. In addition, treatment with β-myrcene at a dose of 750 mg/kg considerably reduced the change in lung histoarchitecture and presence of leukocytes. **Conclusion:** This study showed that β-myrcene have potential anti-inflammatory effects by reduce migration, phagocytis ability of leukocytes and inhibition of cell migration from lung tissue, as well as reduction in the magnitude of edema.**Acknowledgments:** to CAPES and CNPq for the support and incentive to research.

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MODEL-BASED PHARMACOKINETIC ASSESSMENT OF CANNABIDIOL ADMINISTERED ORALLY IN RATS: DEVELOPMENT AND APPLICATION OF A RAT-PBPK MODEL TO INFORM PREFORMULATION STUDIES

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Keywords: Cannabinoids; Preformulation; Physiologically based pharmacokinetic (PBPK) modeling; Model-informed drug development (MIDD).

Introduction: Cannabidiol (CBD) exerts complex pharmacological actions in several molecular targets, resulting in antiepileptic, anxiolytic, antipsychotic and anti-inflammatory effects that reflect its therapeutic relevance. However, information regarding pharmacokinetic approaches related to CBD is still scarce. **Aim:** This study aimed to determine the pharmacokinetics of orally administered CBD in rats, as well as to assess the impact of different lipid-based preformulations/vehicles on its plasma disposition, and provide a predictive pharmacokinetic background using physiologically based pharmacokinetic modeling and simulation (PBPK M&S). **Methods:** CBD (120 mg/kg) was dissolved in sunflower oil (SFO) and administered by gavage to Wistar rats (CEUA/UEM – protocol number: 5520250918, ID: 002242). Plasma quantification of CBD was performed by UPLC-MS/MS. Modeling and simulations were accomplished in Simcyp® Animal Simulator version 19 software. **Results:** The simulations showed that the use of olive oil, Cremophor® EL:ethanol:saline (1:1:18 v/v), sesame oil, propylene glycol:ethanol:water (80:10:10 v/v), and propylene glycol:ethanol:water (4.5:4.5:1 v/v) as CBD preformulations/vehicles results in the respective relative bioavailabilities (F_{rel}) of 685, 454, 282, 100, and 30% compared to SFO. Pharmacokinetic scenario assessments suggested that administration of CBD in SFO at oral dosing regimens of 50, 120, 250 and 500 mg/kg/day might result in the average steady-state (SS) plasma concentrations ($C_{av,SS}$) of 0.09, 0.21, 0.45 and 0.89 µg/mL, respectively. **Conclusion:** The presented results provide a predictive background concerning CBD exposure in rats, contributing to the planning of preformulation/formulation studies, pharmacological testing methods, and sampling times of biological material in future research involving oral CBD.

Acknowledgments: This study was supported by the Coordination for the Improvement of Higher Education Personnel (CAPES), which granted a postgraduate scholarship to G.F.S. (Process number: 88882.448871/2019-01).

HOW COVID-19 PANDEMIC CHANGED THE MEDICINES, BIOLOGICAL PRODUCTS AND CLINICAL TRIALS REGULATORY SCENARIO IN BRAZIL?

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Key words: Covid-19, Medicines, Regulation, Biological products

Introduction In the Covid-19 pandemic, all health regulatory agencies around the world were expected to accelerate the review pathways for Covid-19 medicine applications to approve the clinical trials or marketing authorizations without waiving the efficacy, safety and quality criteria. In order to achieve that, different strategies were adopted and this was also true for the Brazilian Health Regulatory Agency (ANVISA). **Aim**: the aim of this work was to describe the regulatory policies adopted in Brazil during the COVID-19 pandemic and highlight the main similarities and differences of strategies adopted by ANVISA, Food and Drug Administration (FDA, USA) and the Administración Nacional de Medicamentos, Alimentos y Tecnología (ANMAT – Argentina) in the requirements and timelines for marketing authorization. **Methods**: A literature review was performed using the regulatory agencies' websites published from January 1st 2020 to June 30th 2022. Regulatory procedures and guidance documents for clinical trials, market authorization of medicines or biological products, as well as COVID-19 specific procedures were included. **Results**: A total of 63 of regulatory documents were found. 20 related to policies and 43 guidances were found. ANVISA published 32 new regulatory tools related to strategies for dealing with pandemic situation. Principal improvements was the stablishing a risk-based approach for accelerating pre-clinical and clinical development and emergency-use authorizations. Comparing the regional similarities and differences in the regulation policies, the fast track medicines for emergency-use authorization was ruled out by FDA, but it wasn't in force in Brazil and Argentina before COVID19 pandemic. The final decision on marketing authorization in Argentina is the Ministry of Health responsibility, different of FDA and ANVISA which have their own enforcements laws. This difference in the final decision may affect the timeframe for aproval of the medicines and biological products since political interests can bies a robust evaluation of the medicine´s benefits and risks. **Conclusion**: Anvisa promoted a structural change in regulatory scenario because of COVID-19 pandemic and it agrees with FDA rules.

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POLYPHARMACY OF STATINS IN FEMALE ELDERLY IN THE MUNICIPALITY OF IGUARAÇU-PR

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Keywords: polypharmacy in the elderly; statins; dyslipidemia; adverse reaction; Side effects.

Introduction: Polypharmacy is a common problem in the elderly population, particularly, this population uses multiple drugs with more adverse reactions. Studies indicate that the elderly group is the most medicalized in society, taking into account the increase in the prevalence of chronic diseases that develop with advancing age. Another important factor is the inappropriate use of medications, which can generate risks and harm to the health of patients, so it is important to monitor family members in the treatment of the elderly person, since some medications have adverse reactions and/or side effects, such as the case of statins, a drug available in the public health system at the municipal and state levels. **Objective**: to monitor users who use statins that are available at the state and municipal levels in the basic health unit of the municipality of Iguaraçu - Paraná and to analyze reports of undesirable discomfort resulting from the use of this drug. **Material and methods:** The work was accepted by the Ethics Committee through Plataforma Brasil (CAAE: 63115422.0.0000.0104), it is a descriptive qualitative study based on data collection through a form answered by a sample of 12 patients using statin in the city of Iguaraçu-PR . After collection, the data were analyzed in order to verify the results obtained in accordance with the proposed objective. **Results:** Partial results were obtained based on 9 forms, all patients reported using the drug Atorvastatin 40mg, with most using it for more than a year. The drug was indicated for cholesterol control in 4 patients, the other patients started using it for other conditions, such as infarction, stroke, arrhythmia and catheterization. All indicated an improvement with the treatment and none of them reported any discomfort or malaise. All patients reported the use of other medications, such as acetylsalicylic acid, losartan, carverdilol, hydrochlorothiazide, captopril and others. **Conclusion:** Based on the objective of the study and the results obtained, it can be concluded that the patients did not experience discomfort or malaise with the use of statin-based medication. It was possible to observe that the drug was not only prescribed to patients for the treatment of dyslipidemia, but also for heart problems.

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Mucoadhesive performance of semi-solid systems composed of poloxamer 407 and cellulose derivatives for topical application

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Keywords: **drug delivery systems; mucoadhesion; hydrogel; cellulose derivatives.**

Introduction: Semi-solid hydrogels are pharmaceutical systems composed of polymer and water, that allow intimate contact between the pharmaceutical drug and the application site. Mucoadhesion is defined as the ability to adhere to mucous membranes and remain interacting with it. Cellulose derivatives such as hydroxypropylmethylcellulose (HPMC) and carboxymethylcellulose (CMC) are used in mucoadhesive systems due to their low toxicity and good adhesive performance. Furthermore, polymers that gel with increasing temperature, such as poloxamer 407 (P407), can be mixed to the adhesive polymers in order to guarantee gelation and high viscosity at body temperature. Blending two different types of polymers the systems may combine their properties, being mucoadhesive and thermoresponsive systems. **Aim:** The aim of this work was to evaluate the mucoadhesive performance of semi-solid systems containing 17.5% (w/w) P407 and 0.4% (w/w) HPMC or 0.1% (w/w) CMC with and without a model drug (erythrosine). **Methods:** The mucoadhesive ability of the formulations was evaluated using a TA-XT Plus texture analyzer with tablets of porcine mucin as substrate. They were fixed to a mobile probe, which was lowered at a speed of 1 $mm.s^{-1}$ until reaching the surface of the formulation, at 37 °C, with a contact force of 0.03 N. The substrate and the formulation were kept in contact for 30 s and the probe was withdrawn at 10 $mm.s^{-1}$. The maximum detachment force and the work of adhesion were determined using Texture Exponent 32 software, and performed in triplicate (BASSI DA SILVA et al., 2017b). **Results:** The detachment force of the system containing HPMC, without the model drug, was higher than the system containing CMC. The work of adhesion of both formulations had their values close to each other. Although the addition of erythrosine in the system containing HPMC demonstrated an increase in the detachment force parameter, the work of adhesion of the formulation decreased. On the other hand, for the system containing CMC, it was possible to observe a decrease in both mucoadhesive parameters. **Conclusion:** Except for the detachment force of the HPMC system, all the other parameters had their values decreased with the addition of erythrosine. Nonetheless, even with a reduced performance in comparison to the systems without drug, the formulations maintained suitable mucoadhesive strength for topical application, in line with the literature. The results still suggest the interaction between drug and polymer, which probably reduces mucin-polymer interactions.

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CONN&ACT: INTEGRATING PHARMACEUTICAL COMPANIES WITH ACADEMIA

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Keywords: pharmaceutical education, pharmaceutical career, pharmaceutical technology

Introduction: The Conn&act project was born by initiative of 8 alumni from the Pharmacy program at State University of Maringá (UEM). They finished their degree in 2005, and since then have been building their careers in pharmaceutical companies. In 2021, during the Covid-19 pandemic, they designed a volunteer project aimed at connecting pharmaceutical students from UEM to private companies. This was motivated by their own past difficulties. Thus, looking to help students by bringing information about possible careers in the pharmaceutical business, they offered their knowledge to academia. Later, a strategy of interaction and training was designed. **Aim:** Connecting and training soft skills in undergrads and postgraduation students for distinct careers in pharmaceutical companies. **Methods:** Web meetings were scheduled twice a month. The first step was the introduction of each alumni tutor, presenting each career´s trajectory. Furthermore, a lecture with a professional in recruiting brought up key points about curriculum vitae, behavior in social media and job interviews. In the second phase of the project, each participant was divided into 8 subgroups (4-6 participants in each group). With each tutor leading one of these groups. The allocation of each participant was motivated by their free manifestation. **Results:** The meetings showed that the students, from undergrad to PhD, knew very little about most possibilities that pharma companies offer. The shared knowledge among students proved to be about sectors related to regular courses, such as Pharmaceutical Technology and Quality Control. However, there are many other possibilities which could be more suited for their abilities. In addition, it was highlighted that most postgraduation students were unaware of the importance of abilities such as critical thinking and extensive writing skills. Some students left the project after realizing what a career in pharmaceutical companies truly demands, and points were made that working at the industry was not best suited for some people. Some professors at UEM are participating in these meetings, and are now better equipped to guide undergraduate students from the base. **Conclusion:** Until this moment, the integration between professionals, professors and students has brought an important focus point to discussing career-related topics, and has primarily given light to how important soft skills are. Lastly, some light was shed on professors about how the academy needs to increase coverage of certain technical points during graduation.

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POPULATION PHARMACOKINETIC MODEL OF KETAMINE IN DOMESTIC CATS AFTER INTRAVENOUS AND INTRANASAL ADMINISTRATION

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Keywords: pharmacokinetic veterinary, pharmacometrics, compartmental analysis, nose-to-brain

Introduction: Ketamine (KET) is an anesthesic drug commonly used in low doses as analgesic in the routine of veterinary medicine. It is known that the bioavailability (BA) of KET is low after oral administration. Nowadays, the intranasal administration has been postulated as an alternative route called nose-to-brain, for drugs targeting the central nervous system. **Aim:** This study aimed to evaluate the pharmacokinetic profile of ketamine in cats after intravenous and intranasal administrations. **Methods:** This study was approved by the Local Ethic Committee (CEUA/UEM Protocol nº 3292020621). Six healthy domestic cats (unknown race, females, and males, weighted 4.63kg ± 0.63 and age 2.83 ± 1.47) participated in this study. A cross-over study design with washout time between treatments was assumed. The arm of the study was intravenous administration group of the racemic ketamine (2mg/kg) and the second arm was the intranasal of the same product (5 mg/kg). For the intranasal administration, a pediatric mucosa tracheal atomizer adapter was used. After administration, blood samples were collected from cephalic vein and the ketamine concentration was measured by a validated method using HPLC-ESI-MS/MS. The pharmacokinetic modeling of plasma data was performed by Monolix software (Simulation Plus). One, two and three compartment body models were evaluated. **Results:** The best structural model was three-compartment parametrized by clearance and volume of distribution with proportional error model. Random effects were not possible to estimate because low amount of data. The BA was fixed as 0.45 according to previous NCA data. The populational pharmacokinetic parameters and relative standard error [RSE] were: a) absorption constant (ka) 0.071 h^{-1} [28%]; Clearance from the central compartment (CL) 0.114 L/h [4.95%]; volume of central compartment (V1) 3.57 L [42.8%], intercompartmental clearance (central to peripheral) Q2 0.59 L/h [71.8%]; volume of peripheral compartment (V2) 3.73 L [27.3%]; intercompartmental clearance (central to deep peripheral) (Q3) 47.8 L [20.6%]; volume of the deep peripheral compartment (V3) 8.84 L [23.4%] and the error model parameter was 0.4 [7.91%]. **Conclusion:** The results provide a population pharmacokinetic model for ketamine in domestic cats following a three compartments body model.

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ANTILEISHMANIAL ACTIVITY AND LIPID PROFILE OF *Lentinus crinitus* BASIDIOCARP

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Keywords: ***Leishmania amazonensis*; Antileishmanial activity; Fatty acids; Linoleic acid; *Lentinus crinitus***

Introduction: Leishmaniasis is a disease that affects millions of people and is an important public health problem. The drugs currently used for the treatment of leishmaniasis present undesirable side effects and low efficacy. **Aim:** To characterize and evaluate the *in vitro* activity of lipid fractions from *Lentinus crinitus* basidiocarp against the promastigote and amastigote forms of *Leishmania amazonensis.* **Methods** Lipids were extracted by maceration to give the lipid crude extract (LCE), then separated into neutral lipids (NL), glycolipids (GL), and phospholipids (PL) by column chromatography. The LCE and fractions were analyzed and quantified by gas chromatography and then evaluated for *in vitro* antileishmanial activity and cytotoxicity against J774A.1 macrophages, after which, the selectivity index was calculated. **Results:** Linoleic, palmitic, and oleic acids were identified as the main components of the LCE and fractions. The NL, GL, and LCE were able to inhibit *L. amazonensis* promastigote and amastigote growth, with IC_{50} values of 56.18, 96.57, and 146.49 µg/ml, respectively for promastigotes, and 22.40, 38.63, and 77.67 µg/ml, respectively for amastigotes. The NL fraction was the most active in inhibiting growth in both forms. Low cytotoxicity values (59.70 to 379.26 µg/ml) were observed for the LCE and fractions compared to the antileishmanial miltefosine (26.06 µg/ml). **Conclusion:** The data indicated that the *L. crinitus* basidiocarp is enriched in polyunsaturated fatty acids, being an excellent source of linoleic acid (ω6). The results indicated the potential value of the LCE and the NL and GL fractions in the treatment of leishmaniasis, which proved to be more active against amastigote forms and being more selective towards the parasites than the host cells. These results provided a significant basis for further investigation into the action of these fractions in the treatment of leishmaniasis.

Acknowledgments: CNPq; CAPES; UNICESUMAR; UEM

COMPLEXION OF OREGANO ESSENTIAL OIL WITH BE[illegible] CYCLODEXTRIN, CHARACTERIZATION OF THE COMPLEXES AND DETERMINATION OF ANTIMICROBIAL ACTIVITY

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Keywords: ***Origanum vulgare,*** **cyclodextrin, thermal analyses, antimicrobial activity.**

Introduction: Oregano is an aromatic plant, whose essential oil (EO) is rich in bioactive compounds that are beneficial to health. The solubility and instability of EOs is a factor that restricts their use, in which cyclodextrins (CDs) become a viable option to improve their applicability. **Aim:** Complex oregano EO with beta-CD, characterize the inclusion complexes (IC) formed and to evaluate the antimicrobial activity. **Methods:** Characterization of OE – The EO was characterized by GC-MS and the compounds were identified by comparison using the NIST 2.0 library. Complex formation – The complexes were formed by the methodologies of co-precipitation and kneading. The physical mixture methodology was used as a standard in the analysis. Characterization of IC – The complexes were characterized by DSC and TGA techniques. Minimum bactericidal concentration (MBC) – Antimicrobial activity was performed following the (CLSI) protocols **Results:** Characterization of OE – The major compound in oregano EO was carvacrol, with a retention time of 19.16 min. Characterization of IC – The DSC curve of beta-CD showed an event from 50 to 113 ºC, with a peak at 84.5 ºC, and is characteristic of the dehydration of beta-CD. The second and third events are subsequent and occur from 270 to 317 °C and 317 to 355 °C, with a peak at 314 and 330 °C, respectively. These events are related to the molecular decomposition process and consequent removal of carbonaceous material (4). The physical mixture presented identical DSC curves to the beta-CD. Both ICs showed no peak of dehydration of beta-CD, suggesting that the water present in beta-CD was replaced by EO. In TGA, the mass loss at the temperature of 113 °C was 11.98% for beta-CD and 16.70% for the physical mixture. For the ICs by kneading and co-precipitation, the mass loss was 6.31% and 3.62%, respectively, corroborating the DSC results. MBC – The oregano-free EO showed a CBM of 250 µg/mL for the microorganisms *Escherichia coli* and *Salmonella enteritidis*. Both ICs decreased CBM to 2000 µg/mL. **Conclusion:** The DSC and TGA techniques proved to be efficient in evidencing the formation of ICs between β-CD and oregano OE. However, the ICs were less active, which may be due to the strong binding with beta-CD and the difficulty in releasing the EO to exert its antimicrobial function, or the use of beta-CD by the microorganism as a carbon source.

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NANOPARTICLES CONTAINING MENADIONE PRESENTS ACTIVITY AGAINST CERVICAL CANCER CELLS

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Keywords: Polymeric nanoparticle, antitumor activity, C33a cell.

Introduction: Globally, cervical cancer is the fourth type more incident in women and the leading cause of death in some countries. The development of the disease may or may not be caused by Papillomavirus (HPV) infection. Despite treatments already implemented in the clinic such as chemotherapy, radiotherapy, and immunotherapy, the survival of these patients is still relatively low. Drug delivery systems have been studied to improve the efficacy and release of chemotherapeutic agents. In this work, the nanoparticles were developed with polylactic-co-glycolic acid (PLGA) or polylactic acid (PLA), which are biodegradable polymers approved by the FDA. These polymers were loaded with menadione (vitamin K_3), since this molecule is a natural quinone-type, and its anticancer activity has already been demonstrated. **Aim:** The objective of this study was to develop the nanoparticles and characterize them, in addition to evaluating their effect on cervical cancer cell lines. **Methods:** The nanoparticles were obtained by solvent evaporation method. It was analyzed the mean size and zeta potential by dynamic light scattering, encapsulation efficiency by the indirect method, and the cytotoxicity assay by the MTT method. **Results:** The nanoparticles of PLA-B, PLA-K, PLGA-B and PLGA-K showed an average size of 306.24 ± 31.83; 297.99 ± 32.39; 209.10 ± 30.19; 215.80 ± 12.93 nm; the polydispersity index was 0.16 ± 0.047; 0.20 ± 0.059; 0.13 ± 0.032; 0.16 ± 0.058 and the zeta potential was of -17.41 ± 3.64; -17.35 ± 4.09; -24.58 ± 3.06 and -22.45 ± 3.51, respectively. The encapsulation efficiency was more than 98% for both formulations. The cytotoxicity assay demonstrated that the nanoparticles exhibited activity against C33a cells when they were charged with menadione, both after 24 and 48h of incubation, presenting IC_{50} values of (µg/mL) 4.68 ± 0.51 and 4.57 ± 0.58 for PLA-K; 7.72 ± 1.17 and 5.80 ± 0.56 for PLGA-K, respectively. **Conclusion:** These results demonstrate that the encapsulation of menadione using the solvent evaporation technique may be an effective strategy for the treatment of cervical cancer, however further studies are needed.

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PREPARATION OF LIPOSOMES WITH THERMOSENSIBLE COPOLYMER WITH SYRINGIC ACID

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Keywords: Liposomes; Syringic acid; Copolymer

Introduction: Liposomes have the capability of entrapping both lipophilic and hydrophilic agents. A variety of bioactive substances have been investigated for the delivery systems using liposomes, like antioxidant activity[1]. Syringic acid (SA) is classified as a phenolic acid derived from hydroxybenzoic acid and it presents antioxidant activity[2]. In addition, thermosensitive molecules can be incorporated into the liposome formulation in order to modulate or alter its properties[1]. **Aim:** Evaluate the role of the thermosensitive copolymer Vac3420 in the release of SA in a liposome formulation. **Methods:** Liposomes were made by the lipid thin film method: DPPC, DSPE-PEG, Cholesterol in the proportion of 65:5:30 mol%, plus 2 mol% of the copolymer Vac3420, SA 2 mg/mL. The SA concentration was performed by HPLC to determine the encapsulation efficiency (EE). The grafting efficiency (GE) of the copolymer was determined by UV-Vis spectrophotometer through a calibration curve. For the SA release, a dialysis membrane (6-8 kD) was used at temperatures of 22 and 40 °C. The characterization of liposomes was performed by Dynamic light scattering and their morphology was observed by CryoTEM. **Results:** The results showed a SA EE of 14% and a %GE of 50% (Vac3420). Regarding the cumulative release of SA, the formulation without cholesterol obtained approximately 20%, with cholesterol 40% and with the copolymer Vac3420 50%. Between temperatures, there were no significant differences. The DLS results showed a particle size of 150 nm, a polydispersity index of 0.05. Through Cryo-TEM, the lipid bilayer can be clearly observed. **Conclusion:** The presence of the copolymer in the liposome formulation generated a greater release of SA, but there were no differences between the temperatures used. In addition, through the methodology used, liposomes with low pDI and interesting size were produced for subsequent application to the skin, with actives such as syringic acid.

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A SYSTEMATIC REVIEW OF EPICATECHIN EFFECT ON BLOOD PRESSURE: METHODOLOGICAL QUALITY ASSESSMENT

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Keywords: **polyphenols, hypertension, cardiovascular disease, natural products.**

Introduction: The high concentration of polyphenols in some foods is directly proportional to their protective effect on the cardiovascular system, as in the case of green tea, grapes and cocoa. **Aim:** Knowing that epicatechin is the major polyphenol in these species, the objective of this study was to evaluate the methodological quality of studies who investigate this effect on blood pressure (BP) and risk factors associated with cardiovascular disease, through a systematic review. **Methods:** The systematic search was performed in PubMed/Medline, Scopus and DOAJ electronic databases, without time and language restrictions, in addition to manual search. Inclusion criteria were: *in vitro*, *in vivo*, *ex vivo* experimental studies and clinical trials that evaluated the effect of epicatechin on BP. The review was conducted according to the PRISMA checklist and Cochrane Handbook recommendations. The methodological quality of preclinical models (*in vitro*, *ex vivo*, and *in vivo*) was assessed using the SYRCLE´s tool and its adaptations, while for clinical trials the RoB2 was used. **Results:** A total of 704 studies were retrieved from the databases, after the exclusion of duplicates, and 5 studies were found in the manual search, totaling 709 studies. In the screening stage (reading of titles and abstracts), 332 studies were selected for eligibility (reading in full). Of these, 62 were included for data extraction and qualitative and quantitative synthesis. Twelve studies (25.00%) *were in vitro* analyses, fourteen studies (29.17%) were *ex vivo* analyses, eighteen (37.50%) were *in vivo* (animal models), and four (8.33%) were clinical trials. Most parameters assessed on study quality by SYRCLES´s and RoB2 were homogeneous, except for the last domain of the RoB2, which showed high heterogeneity associated with a poor absence of conflict of interest or industry sponsorship. In 6 *in vivo* studies the randomization of animals was not cited. **Conclusion:** The studies included presented homogeneous quality standards. The more heterogenic parameter was about the declaration of conflict of interest and the industry sponsorship. This makes the researchers aware of the need to report the presence or absence of a conflict of interest.

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SHORT-TERM PHYSICAL AND PSYCHOLOGICAL STRESS DOES NOT CAUSE LASTING CHANGES IN THE INTEGRITY OF THE CEREBRAL WHITE MATTER IN JUVENILE MALE RATS.

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Keywords: **Predator stress, Immobilization stress, Fornix, Corpus Callosum.**

Introduction: The effect of juvenile stress on brain morphology, and especially the white matter is poorly known, thus in this study we evaluated the effects of two models of stress, physical and psychological in juvenile male rats and their long-term impact on the integrity in the white matter of the brain. The morphological analyses focused on two important regions of brain communication and myelin concentration, the corpus callosum (CC) and fornix. **Aim:** Our objective was to verify if in the long term the morphological responses to two stress models (physical and psychological) would be different, and we analyzed the integrity of the white matter, in the CC in different regions (genu, body and splenium), and in the fornix. **Methods:** Male Wistar rats (n=15) were randomly distributed into three groups: Control (C), Physical Stress (PE) which was Immobilization Stress (n = 5), and Psychological Stress (PE) Predator Exposure Stress (n = 5), kept in a sector animal house under standard conditions with controlled temperature under a 12h /12h light / dark cycle, food and water supplied ad libitum. Stress procedures occurred for three consecutive days starting at 25 days of postnatal life (P25 to P27). For long-term evaluation, at adulthood (P90-P95) brain collection was performed, followed by fixation and processing using the Klüver-Barrera technique. The collected material was captured using high-resolution camera image capture (3CCD Pro-series), and the images represent these regions: anterior (Genu = Bregma 2.28 to 1.56 mm), central region (Body = Bregma - 1.44 to - 4.96 mm) and posterior part (Splenium = Bregma - 5.04 to - 5.16 mm) of the corpus callosum; for the fornix, the regions of the right and left fornix (Bregma -0.36 to -0.60) (Paxinos and Watson, 1998). Images were then quantified using ImageJ software, where the optical density was measured. The statical analyses was made in Graph Prism 8, using One-Way ANOVA and post-hoc Tuckey to compare groups. **Results:** The results obtained in the software ImageJ were report as optic density. This value is the product of area and intensity of black scale in the image, and when plotted in the graph, showed that both stress models studied did not produce changes in integrity in all regions analyzed (regions of the genu, body and splenium of the corpus callosum, and the fornix). **Conclusion:** Our study allows us to conclude that short-term juvenile stress does not cause long-lasting morphological effects when evaluated in the long term in the structure of the white matter, and this adaptation in which neither reductive nor protective changes occurred can be considered a positive adaptation.

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EVALUATION OF THE JEJUNAL INFLAMMATORY RESPONSE OF ARTHRITIC RATS TREATED WITH QUERCETIN-LOADED-MICROCAPSULES

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Keywords: Inflammation, quercetin, rheumatoid arthritis, intestine.

Introduction: Rheumatoid arthritis (RA) is an inflammatory autoimmune disease that is associated with articular and systemic manifestations. The intestine may be a target organ of systemic inflammation caused by the disease, possibly affectting in its structure and functioning. Current conventional therapy for RA has limited effectiveness and numerous adverse effects. In this regard, natural products with anti-inflammatory activitity, such as quercetin, represent promising alternatives to RA therapeutics. **Aim:** To assess the effect of quercetin-loaded-microcapsules 10 mg/kg on the jejunal inflammatory response of rats with RA, through the quantification of B lymphocytes $CD20^+$, macrophages $CD68^+$, mast cells and the total leukocyte population $CD45^+$. **Methods:** Thirty male Holtzman rats were used (CEUA-UEM protocol 4462180216) and divided in 5 groups: Control (C), control treated with quercetin (CQ), arthritic (AIA), arthritic treated with ibuprofen 17.5mg/kg (AI) and arthritic treated with quercetin-loaded microcapsules 10mg/kg (AQ). Arthritic animals were induced by an intradermal injection of complete Freund's Adjuvant. The experimental treatment was daily by gavage during 60 days. After this period, the animals were euthanized the jejunal segment was removed, processed to perform immunohistochemistry for labeling $CD20^+$, $CD68^+$ and $CD45^+$ cells and histological technique, with subsequent staining in Giemsa. Quantification of cells was performed at 30 villi per animal using Image Pro Plus 4® program. **Results:** Immune cells count increased 38% ($p<0,05$) for cells $CD20^+$, 24% ($p<0,05$) for macrophages $CD68^+$, 115% ($p<0,05$) for mast cells and 30% ($p<0,05$) for total leukocyte population $CD45^+$ in the AIA compared to C. Both treatments were able to reduce the density of immune cells by 25% $CD20^+$cells, 21% $CD68^+$cells, 92% mast cells and 24% $CD45^+$ cells for AQ group (vs AIA, $p<0,05$). Ibuprofen treatment reduced by 30% $CD20^+$cells, 24% $CD68^+$cells, 96% mast cells, 24% $CD45^+$ cells (vs AIA, $p<0,05$). The macrophage population increased in CQ 10% ($p<0,05$) in the comparison between groups C and CQ. **Conclusion:** Systemic manifestations caused by arthritis causes an inflammatory response in the intestine, and that treatment with quercetin-loaded-microcapsules showed anti-inflammatory effects by reducing different populations of intestinal immune cells. A slight immunostimulatory effect was evidenced by the increase in macrophage population in healthy animals treated with quercetin.

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POSTISCHEMIA TRICHILIA CATIGUA A. JUSS (MELIACEAE) MICROEMULSION ALLEVIATES MEMORY DEFICIT, OXIDATIVE STRESS, AND DENDRITES DETERIORATION.

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Keywords: Global cerebral ischemia, *Trichilia catigua,* Microemulsion, Neuroprotection.

Introduction: We previously observed that a lyophilisate, ethyl-acetate fraction (EAF-L) of the plant *Trichilia catigua* A. Juss. (Meliaceae) prevented the learning/memory impairments, oxidative stress, neuroinflammation, and deterioration of dendritic morphology that were caused by transient, global cerebral ischemia (TGCI). In those studies, however, a dose as high as 400 mg/kg of the EAF-L was necessary, which limits the clinical relevance of those findings. **Aim:** Here, we evaluated whether 100 mg/kg doses initiated 4 hours postischemia and continued for the next 1, 4, or 7 days as an EAF microemulsion (EAF-ME) could maintain its neuroprotective efficacy. **Methods:** Naive rats (CEUA no 2102271119) were trained in a radial maze task, subjected to TGCI, then tested several weeks later for retrograde memory performance. In other groups, the activities of the superoxide dismutase (SOD) and catalase (CAT) enzymes, as well as the levels of protein carbonylation (PCG) and lipoperoxidation (TBARS) were assayed as markers of oxidative stress 24 h after ischemia. Analysis was also done for GFAP and Iba-1 immunoreactivity as neuroinflammation markers in the hippocampus and cerebral cortex. Lastly, rats were examined 14 days after TGCI for disruption of dendritic morphology in the hippocampus, and pre-frontal cortex (PFC). **Results:** The EAF-ME 100 mg/kg treatment alleviated the disruption of memory when the data of latency and working memory errors were examined cumulatively ($p < 0.05$), but not longitudinally ($p > 0.05$). All oxidative stress markers triggered by ischemia were prevented with the EAF-ME treatment ($p < 0.001$ to 0.05). The number of dendritic branches was partially preserved branches in the CA1 and PFC regions ($p < 0.01$ to 0.05), as well as the number of spines in the CA1 region ($p < 0.05$). No change occurred at all in the CA3 region ($p > 0.05$). The EAF-ME treatment did not alleviate the neuroinflammation markers analyzed ($p > 0.05$). **Conclusion:** The data not only confirm the neuroprotective properties of *T. catigua*, but indicate also that its potential applicability in the field of cerebral ischemia can be increased through the development of appropriate drug delivery systems that could improve the poor oral bioavailability of the *T. catigua* polyphenolic constituents.

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SUPPLEMENTATION WITH MICROOEMCAPSULATED QUERCETIN PRESERVED SIZE OF nNOS-IR NEURONS IN THE JEJUNUM MYENTERIC PLEXUS AFTER CHEMICALLY INDUCED COLORECTAL CARCINOGENESIS IN RATS

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Keywords: **Colorectal cancer; enteric nervous system and probiotics.**

Introduction: The enteric nervous system (ENS) is responsible for determining the patterns of peristaltic movements in the gastrointestinal tract and controlling secretions. Inhibitory motor neurons release neurotransmitters such as nitric oxide (NO). During colorectal carcinogenesis, oxidative stress can lead to nitrosylation (3-NT) of neuronal proteins. **Aim:** To perform the morphometry of neurons that are immunoreactive to the nitric oxide synthase enzyme (nNOS-IR) and the quantification of 3-NT-IR in the myenteric plexus of rats chemically induced to colorectal carcinogenesis supplemented with microencapsulated quercetin and *Bifidobacterium animalis*. **Methods:** After approval by CEUA (n°1126010419) the animals were randomly distributed into 5 experimental groups (N=8): control(C), colorectal cancer (CRC) (CR), CCR administered with probiotic *Bifidobacterium animalis* ($5x10^{-7}$ UFC) (CP), CRC administered with microencapsulated quercetin (10mg/Kg) (CQ) and CRC administered with microencapsulated quercetin and probiotic *Bifidobacterium animalis* (CQP). The CRC was induced by 1,2 dimethylhydrazine (DHM) (40mg/Kg) intraperitoneal injection twice a week for 2 weeks. Fourteen weeks later, the jejunum was collected and processed for immunohistochemical reactions for nNOS and 3-NT. Morphometric analyses of 100 nNOS-IR neurons and 3-NT-IR were performed in 32 images per animal, followed by statistical analysis. **Results:** Our data showed a significant reduction of 19.22% in the mean size of nNOS-IR neurons in the CR group compared to the C group. Among the different administrations used, CQ and CQP showed a significant difference compared to the CR group, with an increase in 23.51% and 17.46%, respectively. The CP group did not present significant differences when compared to the CR group. By analyzing the number of 3-NT-IR cells, we found an increase of 25.01% in CR group compared to the C group. When comparing with the CQ, CP and CQP did not present significant differences when compared to the CR group. **Conclusion:** Colorectal carcinogenesis promoted a reduction in the size of nNOs-IR neurons and a significant increase in 3-NT. Supplementation with microencapsulated quercetin was able to preserve the size of nNOS-IR cells although it did not reduce protein nitrosylation.

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CHARACTERIZATION OF PHARMACEUTICAL INTERVENTIONS IN DIABETIC PATIENTS

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Keywords: **diabetes, pharmaceutical intervention, pharmacotherapy.**

Introduction: Among the CNCDs, diabetes mellitus (DM) ranks fourth in number of deaths, accounting for 1.5 million deaths per year. In Brazil the disease is the fifth place among the main causes of death. Pharmaceutical assistance (PA) is an efficient practice in health systems that promotes patients' adhering pharmacological treatment, providing a significant improvement in the quality of life. The implementation of a pharmacotherapeutic follow-up, an integral part of PA, can be considered a viable alternative in optimizing the treatment of CNCDs.
Aim: The aim of this study is to identify and classify pharmaceutical interventions necessary to improve the efficacy of pharmacological treatment of patients diagnosed with type II DM.
Methods: An intervention study was conducted in primary health care units of the Unified Health System (SUS) of two cities of Paraná state, enrolling 32 patients with type II DM. We use as a collection instrument and record data a standard questionnaire, elaborated specifically for this type of study. It was filled out through face-to-face consultations and the addition of constant data in the patient medical records.
Results: During the follow-up, 326 interventions were performed, of which 167 (51%) were information or counseling to the patient, 56 (17%) about disease monitoring, 41 (13%) related to change or suggestion of change medicines, 35 (11%) supply materials for better treatment or clarification on pharmacotherapy and 27 (8%) referrals to other services or professionals. Among the interventions related to changes in pharmacotherapy, 25 were adjustments in the frequency or times of administration, without dose modification, 7 had changed in doses and 9 replacement the medicines or started new ones. All patients had at least one type of intervention and 75% had interventions related to modification of pharmacotherapy, in cases of dose change or pharmacotherapy replacement, a suggestion letter was sent to physicians and all were accepted.
Conclusion: The large number of pharmaceutical interventions performed in the follow-up of patients with diabetes, considering mainly of those related to the change in pharmacotherapy, shows the importance of PA in primary health care, especially in patients with CNCDs in whom the success of pharmacotherapy reduces morbidity and mortality, improves the quality of life and prevents the disease progression, as well as, the need for more complex and costly treatments in public services.

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ANTIFUNGAL ACTIVITY OF ALGINATE MICROPARTICLES CONTAINING BERBERINE AND FLUCONAZOLE INCORPORATED INTO VAGINAL CREAM AND ARTIFICIAL SALIVA

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Keywords: **Berberine, *C. albicans*, Synergism, Fluconazole, Candidiasis.**

Introduction: Vulvovaginal candidiasis (VVC) is an infection of the vulva and vagina caused by *Candida* spp. while oral candidiasis is the most prevalent fungal infection diagnosed in the oral cavity of humans. Although there are more than 200 *Candida* species, *C. albicans* stands out due to its prevalence rate in humans under normal and infected conditions. Berberine (BBR), an isoquinolinic alkaloid extracted from *Coptis chinensis*, has been shown to have benefits in antifungal treatments, while fluconazole (FLU) is a well-tolerated and safe antifungal triazole with good efficacy against *Candida* spp. **Aim:** The objective of this work was to evaluate the antifungal activity of alginate microparticles containing BBR and FLU produced by spray dryer technique, to incorporate the produced microparticles in two pharmaceutical forms: vaginal cream and artificial saliva, analyzing its stability, physical-chemical analysis and microbiological tests. **Methods:** The microparticles were produced by spray-drying technique to encapsulate Berberine and Fluconazole substances; morphological analysis, scanning electron microscopy, minimum inhibition concentration test, anti-biofilm effect in the formation phase, inclusion of microparticles in the base of vaginal cream and artificial saliva, physicochemical, microbiological tests of the final products and also quantification of BBR and FLU components in the microparticles by RMN technique**. Results:** It was possible to observe oval microparticles with small holes in their structure being compatible with the literature, for the microbiological tests the microparticle showed a promising antifungal effect demonstrated through scanning electron microscopy, being possible to verify the reduction of fungal growth and damage in the structure of the microorganism. The vaginal cream and artificial saliva formulations containing the microparticle showed adequate stability to the tests submitted, approved physicochemical analysis, excellent microbiological tests, showing a promising antifungal effect even for biofilms in formation. RMN quantification showed a value of 1.77 mg/ml FLU and 1.97 mg/ml BBR. **Conclusion:** We can conclude then, that the microparticle produced containing BBR and FLU showed efficient encapsulation as well as its structure, presented antifungal properties in its isolated form and also incorporated into pharmaceutical formulations: vaginal cream and artificial saliva. The prepared formulations proved to be stable and also showed satisfactory results against *Candida albicans*.

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IMPACT OF THE COVID-19 PANDEMIC ON CHILDREN BEING TREATED FOR ADHD

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Keywords: **ADHD, METHYLPHENIDATE, COVID-19 PANDEMIC**

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is a syndrome normally diagnosed in schoolchildren by their parents or teachers based on the children's behaviors. Social isolation and remoted education implemented during the COVID-19 pandemic might have had an impact on patients with ADHD health and wellbeing. **Aim:** The aim of this study was to investigate the knowledge of caregivers of children/adolescents with ADHD and the consequences of the treatment during social isolation due to the COVID-19 pandemic. **Methods:** This qualitative study addressed the active relationship of interviewees with reality. Eight caregivers of children diagnosed with ADHD treated at the Unified Health System in the municipality of Califórnia, Paraná, Brazil were interviewed. **Results:** The school had an essential role in the screening of most children with ADHD. All eight interviewees mentioned that their children had used methylphenidate at some moment during the treatment. Adherence-wise, only two interviewees reported that their children never discontinued their pharmacological treatment, with four reporting that their children discontinued methylphenidate use during vacations. Because of the pandemic, the children in this study had their in-person classes canceled and stayed home, having online classes instead. This change in the educational system had important consequences for children, particularly those with ADHD, as having to stay home caused some behavioral disorders. Due to social isolation, children stayed home, and two interviewees reported their children were more restless. Likewise, two interviewees said their children were more anxious because of closed schools, as they did not spend their energy playing with other children and lacked close contact with friends, distractions, and other physical activities. Increased nervousness and aggressiveness were other behavioral changes observed. Evidence suggests that when children and adolescents are away from the classrooms, they are less physically active and have greater screentime and sleep problems and poorer eating habits, leading them to gain weight and lose cardiorespiratory fitness. Thus, during social distancing, the effects on adolescents' health are probably more intense because they are confined at home, with no outdoor activities or interaction with their friends. **Conclusion:** The interviews indicated that schools played an important role in noticing the children's atypical behavior. After diagnosis, all interviewees chose to use methylphenidate. Restlessness, anxiety, and nervousness increased during the pandemic and were reported by interviewees.

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COVID-19 in the ICU: drugs used in patients with acute renal failure undergoing dialysis treatment

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Keywords: *COVID-19; Pharmacovigilance; Renal insufficiency.*

Introduction: Patients infected with the SARS-CoV-2 virus present implications resulting from the systemic inflammatory response, evolving with cardiac and renal impairment. Renal endothelial damage caused by the virus can lead to acute renal failure (ARF). However, ARF can be attributed to processes such as sepsis, contrast agents, post-surgical causes, nephrotoxic drugs, and others.**Objective:** To analyze the drugs used in patients with COVID-19 admitted to the intensive care unit (ICU) who underwent hemodialysis (HD).**Methods:** Cross-sectional, retrospective and documentary study were carried out at the Maringá University Hospital between May/2020 and May/2022. Data were obtained from electronic medical records. The identified drugs were analyzed for their nephrotoxicity profile on the Drugs.com website. **Results:** Of the 380 patients eligible for the study, 102 (27%) underwent HD and were part of the studied sample. Of these, 51% were men. The age ranged from 24 to 92 years with an average of 66±14. The average length of hospital stay was 20±19 days and 76% (77) of the patients died. A total of 113 different drugs were used, with cardiovascular action, antimicrobials, sedatives and analgesics being the most used groups. The most used drugs among HD patients were Norepinephrine and Ceftriaxone, both of which can cause nephrotoxicity or otherwise affect the renal/urinary system. Although it is not yet possible to establish a direct causality between their use and the need for HD, this use may have contributed to the outcome presented.**Conclusion:** The study points to the need to deepen knowledge about the relationship between drug therapy, coronavirus infection and HD in critically ill patients. In this scenario, pharmacovigilance actions are essential to reduce care risks and thus promote higher quality care and patient safety.

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EVALUATION OF THE CONSUMPTION OF MEDICINES OF THE STATE PROGRAM "PARANÁ SEM DOR" IN THE BASIC PHARMACY OF THE MUNICIPALITY OF NOVA PRATA DO IGUAÇU-PR

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Keywords: **medicines; pain; pharmacy**

Introduction: The International Association for the Study of Pain (IASP) defines pain as an "unpleasant sensory and emotional experience, associated with actual or potential injuries or described in terms of such injuries, its classification can occur in two types: acute, with known cause and limited duration, chronic when it lasts more than three months with unknown or ill-defined cause". This condition is considered one of the major public health problems because it presents a growing demand for health services. **Objective:** To evaluate the consumption of medicines from the Paraná state program without pain in the Basic Pharmacy in the municipality of Nova Prata do Iguaçu -PR. **Methods:** This is a descriptive, quantitative and exploratory study to evaluate the consumption profile of the drugs codeine 30 mg and gabapentin 300 mg available in the "Paraná sem Dor" program. Data collection was carried out through the reports compiled from the Pharmaceutical Assistance System of the Ministry of Health, during the period April to September 2022, using a standard form for data collection.The study was approved by the Standing Committee for Ethics in Research Involving Human Beings (COPEP) of the State University of Maringá, report no 5.464.328. **Results:** The results obtained refer to 161 patients, 58.5% of whom use gabapentin 300 mg, 16.7% use codeine 30 mg and 24.8% use both together, with varying daily doses. Regarding treatment time, 22.4% of patients use the medication for less than 1 year, 67.1% for 1 to 5 years and 10.5% for 5 to 10 years. Of the total number of patients, 106 are women and 55 men, aged between 20 and 89 years, with a prevalence of non-specific rheumatism comorbidities, followed by fibromyalgia and back pain. **Conclusion**: Pain is one of the main factors that negatively impact the physical and psychological health of patients. In this research, we can observe the prevalence of time of medication use between 1 and 5 years, generating a large consumption of pain medication, with prevalence among women. It was possible to observe the main pathologies that affect patients, and through this information it is important to plan actions that allow an improvement in the clinical condition and reduction of the consumption of these drugs, aiming at a better quality of life for individuals.

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TUMORAL WEIGHT IN A549 CELL LINE TUMOR BEARING RATS ADMINISTERED WITH 10 mg/kg MELATONIN.

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Keywords: **Cancer, Weight Loss, Antitumoral.**

Introduction: The A549 cell line is a cell line from lung cancer. The melatonin is the main hormone produced by the pineal gland, it acts as an antioxidant and has immunomodulatory properties, playing an important role in blood composition. It also has important atoxic, oncostatic, angiogenic, differentiating and antiproliferative properties against solid and liquid tumors. Also, melatonin is proven to be an efficient treatment for cancer. **Aim:** The aim of this study is the evaluation of the tumor size in rats induced with A549 lineage tumor in the right flank and the administration with melatonin (10 mg/Kg). **Methods:** The experiments with animals were approved by CEUA/UEM under the number 8812040521. 28 Wistar rats were divided in 4 groups randomly (n=7): Control group (C), control administered with melatonin 10 mg/kg (CM), rats with A549 lineage tumor (A), and rats with A549 lineage tumor administered with melatonin (AM). The animals from the cancer groups (A and AM) were inoculated with the A549 cells, in a $1x10^7$ concentration, while the other groups were inoculated with PBS. After the 14-day experimental period, the tumors were collected and fixated with buffered formalin. **Results:** All the A group rats (cancer groups) presented tumoral mass, while in the AM group (cancer groups administered with melatonin), 2 of the animals didn't present any tumoral mass. The mean value of the A group was 0,1102 g, while the mean value of the AM group was 0,0463 g. The statistical analysis (T test) showed no significant difference comparing groups A and AM (p=0,131). **Conclusion:** The tumor induction was effective and the tumoral mass was present, confirming the efficiency of the A549 line inoculation. The melatonin administration did not alter significantly the tumor size.

Acknowledgments: To CAPES for the financial support.

EXPLORING SEX DIFFERENCES IN FUNCTIONAL AND NEUROPATHOLOGICAL OUTCOMES AFTER CEREBRAL ISCHEMIA IN MICE

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Keywords: Cerebral ischemia, Neurodegeneration, Cognitive deficits, Sexual dimorphism

Introduction: Although recent studies have begun to reveal sex-dependent differences in affective, cognitive and neurodegenerative brain conditions, the gender differences in response to transient global cerebral ischemia is still not clear. **Objective**: In the present study, we tested whether bilateral common carotid occlusion (BCCAO) an animal model of global cerebral ischemia, result in different behavioral and neuropathological outcomes in male and female C57BL/6. **Methods**: This study was approval by the Ethycal Comitte 7995230420. Male and female (90 days) C57BL/6 mice were used. BCCAO was induced for 20 min. Seven days after the reperfusion, the animals were evaluated for locomotor activity, memory, anxiety- and despair-like behaviors using the open field, object location test and forced swimming, respectively. Nissl's and Kluver Barrera's staining were used to analyze hippocampal neurodegeneration and white matter injury, respectively. Blood-brain barrier integrity was measured by Evans Blue extravasation. Male and female mice were tested for 21 days. Depressive and anxious behaviors were observed between 7 and 21 days after BCCAO injury, regardless of gender. **Results**: Cognitive deficits, behavioral helplessness were observed only in males. Significant hippocampal neurodegeneration in the CA1 and CA3 sectors was observed only in male animals. Similarly, white matter injury was detected in the corpus callosum of BCCAO male mice. In both male and female, there was an increase in EB extravasation, indicating no sexual dimorphism related to BBB integrity. **Conclusion**: BCCAO results in anxiety and despair behaviors in male mice, inferring that they are more vulnerable to functional and neuropathological outcomes associated with BCCAO than female mice.
Acknowledgments: CAPES

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EVALUATION OF TEXTURAL MECHANICAL PROPERTIES AND MICELLE SIZE OF POLYMERIC SYSTEMS CONTAINING MELOXICAM FOR NASAL ADMINISTRATION

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Keywords: texture profile analysis, micelle size, meloxicam, nose to brain

Introduction: The treatment of neurological diseases is complex, considering the drug needs to cross the blood-brain barrier to exert its action. One strategy studied to improve the brain drug delivery is the combination of thermoresponsive and mucoadhesive polymers in a platform for intranasal administration. **Aim:** The aim of this work was to evaluate the texture profile and the micelle size of polymeric systems containing poloxamer 407 (P407), hydroxypropyl methylcellulose (HPMC) and meloxicam intended for intranasal administration for the brain drug delivery. **Methods:** Systems were prepared containing 17.5% (w/w) of P407, 0.1 and 0.4% (w/w) of HPMC, and 0.05 and 0.15% (w/w) of meloxicam. Drug-free systems were also prepared for comparison purposes. Texture profile analysis was performed in triplicate and at temperatures of 25 °C and 37 °C using the TA-XT plus equipment, in which an analytical probe was compressed twice inside each sample, generating a graph of force *versus* distance and force *versus* time, used to calculate the hardness, compressibility, adhesiveness, elasticity and cohesiveness of the systems using Exponent 3.2 software. The micelle size analysis of systems were accomplished by diluting in purified water and evaluated at 2 mg/ml in an angle of 90º at 37 ºC using a Litesizer 500 equipment. All analyzes were statistically compared using analysis of variance (ANOVA), with the Statistica 10 software. **Results:** The increase of temperature significantly affected the hardness, compressibility, adhesiveness and cohesiveness ($p < 0.05$), which were increased at a temperature of 37 ºC. Regarding the HPMC concentration, the formulations with 0.4% (w/w) displayed a significant lower hardness and compressibility ($p < 0.05$) than the systems containing 0.1% (w/w), while adhesion, cohesiveness and elasticity did not change ($p > 0.05$). As the meloxicam content increased, the hardness of formulations increased ($p < 0.05$). Both systems did not change the adhesion properties with diferente amounts of meloxicam. Moreover, compressibility, cohesiveness and elasticity, were not significantly influenced by the drug presence ($p > 0.05$). The average size of system micelles was 22.76 ± 0.4368 nm, that was not influenced by different concentrations of HPMC and meloxicam. **Conclusion:** The polymeric systems containing meloxicam displayed improved mechanical textural characteristics and micelle structure considering the nasal administration.

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UHPLC METHODOLOGY DEVELOPMENT FOR *MONTEVERDIA ILICIFOLIA* SEMIPURIFIED FRACTION

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Keywords: ***espinheira-santa*, liquid chromatography, methodology development.**

Introduction: *Monteverdia ilicifolia* (Mart ex Reissek) Biral, a Celastraceae family member, is popularly known as *espinheira-santa*, *cancorosa*, among others. In Brazil is widely used to treat gastric ulcers. *M. ilicifolia* presents a complex composition, containing terpenes, triterpenes, essential oils, tannins, glycolipids, and alkaloids. HILIC (Hydrophilic Interaction Liquid Chromatography) is a type of partition chromatography which the stationary phase is polar. This column is based on an organic/inorganic hybrid particle synthesized with dihydroxypropyl groups. Its use is indicated in the polar and high molecular weight compounds separation. **Aim:** In this work was to develop a UHPLC methodology for semipurified fractions of *M. ilicifolia* rich in high molecular weight compounds using a HILIC column **Methods:** The extraction process was carried out from *M. ilicifolia* dry leaves by turbo extraction to obtain the acetone: water (7:3, v/v) extracts. The extracts were partitioned with ethyl acetate and water. The aqueous fraction (10 mg/ml) was analyzed using a diol phase analytical UHPLC column (YMC Triart Diol-HILIC;150 x 3.0 mm; 1.9 µm) in a UHPLC Thermo Ultimate 3000. **Results:** The methodology which presented the best aqueous fraction profiling used a gradient elution, as the mobile phase the mixture of methanol and water, and acetonitrile, both mobile phases acidified with formic acid 0.5%. The flow was set as 0.7 ml/min. The oven temperature was varying between 35 to 45 ºC, but the temperature set up at 45 ºC demonstrated a better extract separation. **Conclusion:** This work allowed the development of a methodology capable of characterizing a semipurified extract from *M. ilicifolia*, which is rich in higher molecular weight compounds, that are difficult to separate using a reverse-phase HPLC column.

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EFFECTS OF MICROENCAPSULATED QUERCETIN ON THE CELLS IMMUNOREACTIVE TO SEROTONIN IN THE EXPERIMENTAL MODEL OF RHEUMATOID ARTHRITIS

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Keywords: **rheumatoid arthritis, quercetin, immunoreactive cells, serotonin.**

Introduction: Rheumatoid arthritis (RA) is a systemic inflammatory disease that affects the joints and also organs such as the intestine. Conventional treatment of RA consists of non-steroidal anti-inflammatory drugs, like ibuprofen, but these are known to cause harmful side effects. Elevated levels of serotonin (5-HT) in the intestine could assist in the restoration and homeostasis of the mucosa as well as exert a pro-inflammatory action. Quercetin is a natural compound with antioxidant properties and the potential to treat RA. **Aim:** to evaluate the density of 5-HT immunoreactive cells in the colonic mucosa of arthritic rats. **Methods:** Thirty-three 50-day-old male Holtzman rats were randomly assigned to five groups: control (C), quercetin-treated control (CQ), arthritic (AIA), ibuprofen-treated (AI) arthritic, and quercetin-treated arthritic (AQ). RA was induced by intradermal injection of complete Freund's adjuvant containing 0.1 mL of 5% Mycobacterium tuberculosis suspension in the plantar region of the left hind paw. The CQ and AQ received quercetin-loaded microcapsules by gavage at a dose of 10 mg/kg, while the AI group received ibuprofen at a dose of 17.5 mg/kg also by gavage for sixty days. After euthanasia, the colon was collected, processed for quantitative analysis to reveal 5-HT immunoreactive cells in the mucosa**. Results:** In the 5-HT-IR quantification analysis, the AIA group significantly reduced -20% in the mucosal layer comparing to C. AQ showed a significant increase of 20.9% next to AIA, in the same way the AI that increased significantly 30.6% compared to AIA. The CQ showed a significant reduction of -13% compared to C. **Conclusion:** Quercetin prevented the changes caused by rheumatoid arthritis, more consistently with values similar to control animals. Furthermore, microencapsulated quercetin was more effective than ibuprofen in preventing these changes in parameters that indicate colonic atrophy.

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ANALYSIS OF MUSCLE MASS, FAT MASS AND CACHEXIA INDEX OF RATS SUBMITTED TO CARCINOMA LINEAGE A549 ADMINISTERED WITH MELATONIN

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Keywords: cancer, cachexia index, melatonin, muscle mass and fat mass

Introduction: Lung cancer (LC) is found in different types of variants, including LC lineage A549 in a preclinical test adapted by the xenograft form in mice that were inoculated with a modified human cell culture. Melatonin is from the group of indolamines that is produced by the pineal gland, its benefits are the possibility of combating oxidative stress, inflammation, cellular apoptosis and the restoration of tissue function, which in several studies has proven effective in the treatment of cancer. Cachexia, observed in some cancer cases, differs from anorexia because it is a syndrome that results in a constant and involuntary loss of muscle, adipose and skeletal tissue. **Aim:** Assess muscle and fat weight in healthy rats, tumor-bearing rats and the effect of groups treated with daily melatonin use, as well as the cachexia index, to determine if there was cancer-associated cachexia. **Methods:** Study groups were randomly divided into 4 sets (n=7): control (C), control administered with melatonin 10 mg/kg orally (CM), tumor-bearing rats lineage A549 (A), tumor-bearing rats lineage A549 administered with melatonin 10 mg/kg orally (AM). The animals in the A and AM group were inoculated subcutaneously in the right flank with a 1x107 concentration of A549 cells, while the control groups inoculated with PBS undergoing the same protocol stress. After the daily administration period of 14 days, the animals were killed and, in sequence, the muscles and fats were collected for analysis. It was also calculated the cachexia index for each rat. **Results:** In the evaluated muscle masses of the C, CM, A and AM groups, there were no significant differences in their mass when comparing the study groups. However, the evaluated fat masses showed a significant reduction when comparing the C and A groups, when comparing C and CM and when comparing A and AM. The calculation of cachexia index showed that 6 rats developed cancer associated cachexia, 4 from group A and 2 from group AM. **Conclusion:** After analyzing the data collected, the experimental model of cancer lineage A546 was not effective in inducing cachexia in the timespan of 14 days, remaining a cancer model.

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ANALYSIS OF SUBPOPULATION OF NADPH-D POSITIVE NEURONS IN THE STOMACH OF RATS INDUCED TO COLORECTAL CARCINOGENESIS

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Keywords: **enteric nervous system, myenteric plexus, NADPH-diaphorase, *Bifidobacterium animalis*, 1,2-dimethylhydrazine (DMH).**

Introduction: Colorectal cancer (CRC) is one of the most common types of cancer. In this pathology, we observe oxidative stress and dysbiosis, which affect the Enteric Nervous System (ENS), present on the gut wall. Quercetin is a flavonoid with antioxidant effect, among others, which makes it a promising treatment for CRC. *Bifidobacterium* strains have been studied in the treatment of CRC because they play a role in the maintenance of microbiota homeostasis. **Aim:** To evaluate the effect of colorectal carcinogenesis on the NADPH-d-positive myenteric neurons in the stomach of rats, as well as the effect of the treatment with microencapsulated quercetin, *Bifidobacterium animalis* subtype lactis probiotic and the association of both. **Methods:** Male rats were divided into 5 groups (n=6): control (C), colorectal carcinogenesis (CR), colorectal carcinogenesis administrated with *Bifidobacterium animalis* probiotic $5x10^7$CFU (CP), colorectal carcinogenesis administrated with microencapsulated quercetin 10 mg/Kg (CQ) and colorectal carcinogenesis administrated with microencapsulated quercetin and *Bifidobacterium animalis* probiotic (CQP). CRC was inducted by injections of 1,2-dimethylhydrazine (DMH). We collected the stomachs for histochemistry technique to visualize NADPH-d positive neurons, which were quantified and measured. **Results:** In the quantification, there was a significative reduction of 14,66% in the mean of neurons comparing group CR to C ($p<0,05$). Despite the increase of 7,24% in the mean of NADPH-d neurons in the group CP compared to CR, there was no statistical significance. Comparing CR to CQ, there was an increase of 19,30% ($p<0,05$) in the mean and an increase of 36,84% ($p<0,05$) compared to CQP. In the morphometric analysis, there was a significant increase of 7,98% in the mean of the neuronal area of the group CR compared to C. Comparing group CR to the different treatments, there was a significant reduction of 5,88% ($p<0,05$) compared to CP, reduction of 7,01% ($p<0,05$) compared to CQ and reduction of 12,02% compared to CQP. **Conclusion:** Microencapsulated quercetin and *Bifidobacterium animalis* subtype lactis probiotic can be promising in the treatment of CRC effects in nitrergic neurons, acting in the maintenance of important gastric functions such as gastric relaxation and inhibitory reflex.

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TEXTURAL MECHANICAL PROPERTIES OF POLYMER BLENDS AIMING VETERINARY APPLICATIONS IN CATS

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Keywords: mucoadhesion, texture profile analysis, poloxamer 407.

Introduction: Buccal administration site may be suitable for local and systemic administration. This administration route represents an alternative way to anesthetic drugs, since they are mainly administered as parenterals for cats. Polymer blends containing poloxamer 407 (P407) and mucoadhesive polymers, including Carbopol 974P® (C974P) and polycarbophil (PCB), have already been studied for human buccal use with improved mucoadhesive, rheological and mechanical properties. The mucoadhesive polymers differs by the cross-linking density which impacts in the mechanical properties. **Aim:** The aim of this study was to prepare and evaluate the textural mechanical properties of polymer blends containing P407, C974P or PCB for future veterinary application in cats. **Methods:** Polymer blends were composed of 15% (w/w) P407 and 0.25% (w/w) C974P or PCB. The texture profile analysis (TPA) was accomplished using a TA-XTplus Texture Analyzer. The formulations were evaluated in TPA mode and at 5, 25 and 37 °C, using a cylindrical polycarbonate probe. The parameters (hardness, compressibility, adhesiveness, elasticity, and cohesiveness) were derived from force-time and force-distance plots. The effects of temperature and mucoadhesive polymer type (C974P or PCB) on textural parameters were statistically evaluated by two-way ANOVA. **Results:** The increase of temperature significantly increased the hardness, compressibility, adhesiveness, and elasticity of formulations ($p < 0.05$), due to its adhesive and thermoresponsive properties. The effect of polymer type provided increased hardness, compressibility, adhesiveness, and elasticity values ($p < 0.05$) for C974P because of its higher cross-linking degree than PCB. **Conclusion:** The formulations demonstrated suitable and promising textural mechanical properties for the development of new veterinary drug delivery systems.

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ANALYSIS OF THE REGULATION OF THE INCENTIVE TO ORGANIZE PHARMACEUTICAL CARE IN PARANÁ

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Keywords: Healthcare policy; Pharmaceutical Assistance; Program Evaluation ;

Introduction: The Incentive to the Pharmaceutical Assistance Organization (IOAF) was implemented by the Paraná State Health Department from 2012 with the objective of contributing to the organization of Pharmaceutical Assistance (AF) and thus qualifying the access and rational use of medicines. The program is based on the transfer of resources to the structuring and costing of AF services in the municipalities. **Aim:** Analyze the organization and regulation of the IOAF from 2012 to 2021. **Methods:** This is an evaluative research, of a documentary nature, which started from the systematization of the resolutions and deliberations that implement the program, seeking to analyze the changes over time and their completeness in front of the theoretical framework of the evaluation of health policies and systems. **Results:** The IOAF was implemented in 2012, initially for 111 municipalities, with the transfer of funding through membership and counterparts, that were: having a pharmacist, preparing and updating essential medication list and implementing a computerized system. In the following year, the resource was extended to municipalities with up to 20,000 inhabitants, covering 312 municipalities, with financial resource for funding and later resources for capital. In 2014, all municipalities in Paraná were considered eligible, with variation in values from year to year, according to budget availability and pacts. Since its implementation, the incentive provided for the need to build an Application Plan and subsequent accountability through the Management Report. With the progress of the program, it strengthened the monitoring of the use of resources by the Health Regionals, which became part of the regulation from 2015 and, from that, the amount of resources used was considered as an adjustment criterion in the subsequent transfers, implemented in 2019. As of 2020, it also considered the size of the municipality for the proportional distribution of resources. While the incentive was consolidated over the years, on the other hand, the definition of objectives, goals and counterparts remained poorly established, making it difficult to induce the organization of municipalities, with evolution over time, and the mesure program impact. **Conclusion:** It is a relevant and strategic program, with no equivalent at the federal level, but which can be improved in light of the foundations for organizing public policies and programs to expand their institutional benefits.

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CHEMICAL CHARACTERIZATION OF EPIGALLOCATECHIN-3-*O*-GALLATE ISOLATED OF *Limonium brasiliense* RIZHOME

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Keywords: **flavan-3-ol, polyphenol, phytochemistry, phytochemical**

Introduction: *Limonium brasiliense* (Boiss.) Kuntze, Plumbaginaceae, is a native and not endemic herb of the coastal region of the Southeast and the South States from Brazil, popularly known as "baycuru, guaycuru or guaycurá". The rhizome of *L. brasiliense* is employed in folk medicine for the treatment of menstrual disorders and genitourinary infections, and it has been demonstrated antioxidant, neuroprotection, and antibacterial activities. The major compounds present in ethyl acetate fraction of *L. brasiliense* included phenolic compounds, as flavan-3-ol and proanthocyanidins. **Aim:** This study aimed to isolate, quantify, and identified the compound epigallocatechin-3-*O*-gallate (EGCG) of ethyl acetate fraction (EAF) by chromatographic, spectrophotometric, and spectroscopic techniques. **Methods:** The plant material was collected in 2013 on the Ilha dos Marinheiros (31°59′33″ S, 052°10′43″ W) in the city of Rio Grande, Rio Grande do Sul, Brazil. Samples of the reproductive phase are held in the Herbarium of the Universidade Estadual de Maringá (HUEM) under registration number 27725, and CNPq authorization number 010252/2015-0. Dried and powdered *L. brasiliense* rhizome was extracted with 70% acetone (1:10, w/v) by turbolysis, obtained the crude extract (CE). The CE was partitioned with ethyl acetate (1:10, w/v), resulting in the EAF (28.22 g). The EAF (15.0 g) was fractionated by column chromatography. The isolated compound (F#10) was analyzed by UHPLC-ESI-QTOF-MS/MS, by nuclear magnetic resonance (NMR) 1D (^{1}H) (Bruker, model Avance III, 300 MHz, CD_3OD); by polarimetry for optical determination (Jasco, model P2000; methanol at 25 °C and cuvette of 0.1 dm at 589 nm); circular dichroism (CD) (Jasco, model J-815; methanol at 20 °C and cuvette of 5 mm at 200-400 nm). **Results:** The EGCG was obtained in subfraction F#10 (817.2 mg) and represents 9.88% of the EAF. The analyses by UHPLC-MS/MS showed the peak at 8 min and protonated ion at *m/z* 459.0909 $[M+H]^+$ and fragments of *m/z* 289.0702, 139.0386 compatible with $C_{22}H_{19}O_{11}^+$ (error: -2.6 ppm). The chemical shifts in ^{1}H NMR [δ 4.97 (1H, *s*, H-2), δ 5.53 (1H, *m*, H-3), δ 2.85-2.99 (2H, *dd*, H-4), δ 5.98 (2H, *s*, H-6 and H-8) ring A, δ 6.52 (2H, *s*, H-2' and H-6') ring B, δ 6.96 (2H, *s*, H-2" and H-6") gallate], indicated this compound to be epigallocatechin-3-*O*-gallate. Optical rotation $[\alpha]_D^{25^\circ}$ -136.973 (methanol, c 1) and the CD spectrum (methanol, c 28 µg/ml) showed a negative Cotton-effect between 220-240 nm and a negative Cotton-effect at 280 nm characteristic to 2*R*,3*R* configuration. **Conclusion:** The results were consistent with the EGCG, a phenolic compound isolated and identified in previous works of our research group and data of the literature.

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MORPHO-ANATOMICAL EVALUATION OF *Trichilia* SPECIES STEM BARK

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Keywords: **Botany, morphodiagnosis, Meliaceae.**

Introduction: *Trichilia pallida* Sw., Meliaceae, popularly known as "baga-de-morcego" and "catiguá", is a plant with distribution from southern Mexico to Tropical America. *T. pallida* is rich in terpenoids, including limonoids. **Aim**: To perform a morpho-anatomical evaluation of *T. pallida* stem bark. **Methods**: Stem bark samples of *T. pallida* were collected in forest fragments in the cities of Maringá (HUEM 37891) and Terra Boa (HUEM 37892), Paraná State, Brazil, authorization nº 27711/2022; IBAMA-SISBIO and SISGEN registration under nº A8B4204. The samples were fixed in FAA50 (48 h) and storage in 70% ethanol. For morphological analysis, the dried samples were characterized under naked eye and with stereomicroscope. For analyses by light microscopy, the samples were sectioned freehand in the transverse and longitudinal planes (radial and tangential), bleached with 30% sodium hypochlorite solution, double-stained with Astra blue and safranin (1:1, v/v), and mounted on semi-permanent slides with glycerin gelatin. Histochemical tests were performed. **Results:** The dried sample, collected in Terra Boa, revealed a stem bark with recurved shape, while samples from Maringá have a slightly recurved shape. For both samples, the outer surface is rough, due to the presence of numerous greenish-brown lenticels, in addition to showing longitudinally arranged striations. The inner surface is smooth and light yellow, with thin striations in the longitudinal. The fracture is granular on the outside and fibrous on the inside. In cross-section, there is a presence of a poorly developed periderm, with 5-10 layers of tabular cells, with thin walls and brownish-brown content. Below the periderm, groups of sclereids with branched ends are observed. The cortical parenchyma is composed of cells of different shapes, ranging from rectangular, square to polygonal. In this region, some cells have rounded endings and starch grains are observed. In the inner region of the cortex, there are groups of fibers of two to many elements, with simple ends and very apparent lumen. Parenchymatous rays from one to a few layers of cells are observed. Calcium oxalate druses are distributed in the cortical and phloem regions. In the tangential longitudinal section, fibers are surrounded by a crystalline sheath. Histochemical tests demonstrated the presence of phenolic compounds in the periderm and starch grains. **Conclusion:** The results demonstrated the main botany characteristics of *T. pallida* stem bark.

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AUTOPHAGY AND BRAIN ISCHEMIA: EFFECTS OF CANNABIDIOL

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Keywords: autophagy, ischemic stroke, cannabidiol

Cerebral ischemia (CI) is a condition where cerebral blood flow is interrupted, and it can be focal when a clot obstructs a cerebral vessel preventing the passage of blood to a region of the brain or global when all the blood supply to the brain is blocked. Patients who survive cerebral ischemia may develop cognitive deficits and sensory and motor impairments. Cannabidiol (CBD), the major non-psychotomimetic component of the *Cannabis sativa* plant, has been shown to exert neuroprotective effects after several cerebral ischemia. Although the mechanisms of CBD's effects are not completely understood, they appear to involve a reduction of oxidative stress and neuroinflammation. CBD neuroprotective actions may also interfere with autophagic processes. However, previous works indicate that autophagic processes can present both beneficial or deleterious effects following CI. This work aimed to investigate whether autophagy is involved with CBD neuroprotective effects following bilateral common carotid occlusion (BCCAO) in mice. Male C57/BL6J mice were subjected to sham or 20 min of BCCAO surgeries. This experiment was approved by the Ethical Committee (CEUA nº 2233130521). Cannabidiol (10 mg/kg), the autophagy inducer rapamycin (RAPA; 0.25 mg/kg), and the autophagy inhibitors 3-methyladenine (3-MA; 20 mg/kg) and chloroquine (CRQ; 3.5 mg/kg) were administered 1 h before, and 1 h, 24 h, and 48 h after sham or BCCAO surgeries. Combined injections between CBD, RAPA, 3-MA, or CRQ were performed. After the pharmacological treatments, the animals were submitted to the open field test (OF) and object location test (OLT) to evaluate the locomotor activity and spatial memory, respectively. In the OF, BCCAO animals treated with CQ presented decreased locomotor activity when compared to sham operated animals. In the OLT BCCAO animals treated with CBD or RAPA presented a higher discrimination index when compared to ischemic animals. The same happened with BCCAO animals that received CBD+RAPA. However, the autophagy inhibitors associated with CBD (i.e., CRQ or 3-MA) did not improve spatial memory of BCCAO animals in this task. These results suggest that activation of autophagy plays an important role in hippocampal-mediated spatial memory and that CBD may act similarly that an activator of autophagy.

Acknowledgments: CNPQ, CAPES

EFFECT OF YLANG-YLANG (Cananga odorata) ESSENTIAL OIL ON THE HYPERALGESIA, EDEMA FORMATION AND HISTOPATHOLOGICAL ALTERACTIONS IN ZYMOSAN-INDUCED ARTHRITIS MODEL

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Keywords: essential oil, ylang–ylang, experimental arthritis, inflammation.

Introduction: The use of anti-inflammatory drugs becomes limited in therapy due to the adverse effects. Several biological activities have been described for Ylang-ylang essential oil (YEO). **Aim**: To evaluate the effect of YEO on edema formation, mechanical hyperalgesia and cartilage destruction in zymosan-induced arthritis model. **Methods**: Swiss male mice were orally treated with YEO (50, 100 and 200 mg/kg), dexamethasone (1 mg/kg) or vehicle (saline solution and Tween 1%) (n=5 animals/group). One hour after pre-treatment, 200 µg of zymosan diluted in 10 µL of sterile saline were injected into the mice joint cavity of the right knee. Mechanical hyperalgesia was evaluated at 3 and 4 hours after arthritis induction, using a digital analgesimeter (Von Frey, Insight®). The knee joint edema formation was evaluated at 4 and 6 hours after arthritis induction, using a digital micrometer. Histological analysis was performed 7 days after zymosan-induced arthritis (animals were treated daily with YEO at dose of 200 mg/kg). The right knee joint was collected and sent for histological analysis. **Results**: The zymosan injection induced mechanical hyperalgesia at 3 and 4 hours. In these times, only the YEO treatment (200 mg/kg) reduced mechanical hyperalgesia in 52.38% and 81.75%, respectively, compared to control group. The YEO treatment at doses of 50 and 100 mg/kg did not significantly reduce the mechanical hyperalgesia in any tested times The YEO treatment showed anti-inflammatory activity, promoting a significant reduction in knee edema formation at de doses of 100 and 200 mg/kg, in all tested times. The dexamethasone treatment promoted a reduction of mechanical hyperalgesia and knee edema formation in all-time points tested. In histological analysis, discontinuity the surface the cartilage, disorientation of chondrocytes columns, cells death, proliferation (clusters) and hypertrophy were observed in the arthritic animals. The YEO (200 mg/kg) and dexamethasone treatment, for 7 days, promotes a reduction of cartilage damage to grade 1, where the cartilaginous surface is intact, with a homogeneous matrix. **Conclusion**: YEO has anti-inflammatory activity, reducing knee joint edema formation, mechanical hyperalgesia and reduced cartilage destruction in mice submitted to zymosan-induced arthritis model.

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CONTRADICTIONS, INCREASE AND PERSISTENCE IN THE CONSUMPTION OF INEFFECTIVE MEDICINES FOR "TREATMENT" OF COVID-19 IN THE MUNICIPALITY OF APUCARANA/PR IN THE YEARS 2020 AND 2021

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Keywords: COVID-19, Pharmaceutical Assistance, Medicine Use

Introduction: The COVID-19 pandemic has presented to managers, to health professionals, and to the population countless challenges. In the area of healthcare, the use of medicines in a scenario of evidence production and misinformation has led to the irrational consumption of products without efficacy and with unwanted effects for individuals and the community. **Objectives:** To analyze the consumption of medicines supposedly related to the treatment of COVID-19 in the municipality of Apucarana/PR during the years 2020 and 2021. **Methods:** This is a Medicine Utilization Study, with a quantitative approach, based on the number of medicine units distributed monthly by the municipality's Central Supply Office to health care units from January 2019 to December 2021.The following medicines were evaluated: Azithromycin 500mg, Ivermectin 6mg, systemic use corticosteroids (Dexamethasone 4mg, Prednisone 5 and 20mg and Prednisolone 3mg/ml) and Oseltamivir 75mg.The data were tabulated in Microsoft Excel and analyzed in aggregate, with the percentage of annual growth compared to the baseline (2019). **Results:** With the effervescence of cases and incipient production of studies on the subject, the year 2020 was marked by an increase in the consumption of the analyzed medicines compared to the year 2019. Composing the basic scheme of the "covid-kit", the Azithromycin 500mg and Ivermectin 6mg were increased by 73% and 124%, respectively. Oseltamivir 75mg, the antiviral medication of choice for Influenza A, followed the same trend with a 56% growth. In 2021, even with the significant increase in cases, the three medicines had a gradual decrease in consumption, returning to the levels of 2019, which can be explained by the production and dissemination of evidences about their lack of effectiveness. Systemic use corticosteroids, however, continued their upward trend, being 14% in 2020 and 31% in 2021, even without evidence of their application in light cases and moderate cases, which also characterizes an unnecessary practice. C**onclusion:** It was possible to characterize the increase in the consumption of ineffective medicines, as well as to observe a peculiar effect in 2021, with a reduction in the consumption of items without efficacy and intensification of others whose efficacy is limited to the outpatient context, reinforcing the need for the qualification of tools for the Rational Use of Medicines as an element for integrality of health care.

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THE USE OF PSYCHODRUGS BEFORE AND DURING COVID-19 PANDEMIC

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Keywords: COVID-19 Pandemic. Psychopharmaceuticals. Antidepressants. Benzodiazepines.

Introduction: With the COVID-19 pandemic, the emergence or worsening of mental disorders was observed, motivated by direct action of the virus or by stress due to changes in the socioeconomic context. The treatment of depressive and anxiety disorders includes psychotherapies and the use of psychotropic drugs. In the pandemic, the use of psychotropic drugs may have increased due to the increase in disorders. **Aim:** Examine the use of psychotropic drugs before and during COVID-19 pandemic. **Methods:** This study was conducted at Farmácia Básica Municipal de Paranavaí/PR, where data were collected regarding psychotropic drugs (PS), with an emphasis on antidepressants (AD) and benzodiazepines (BZD) from 2019 to 2021. The year 2019 was considered as a reference, due to the little impact of the disease in Brazil. The year 2020 was analyzed as a period of more intense and restrictive isolation, while the year 2021, as a period of resumption of economic activities and greater movement of people. The variables included the number of patients seen, the number of visits at the pharmacy, and the number of dispensed drugs. This study was approved by the Research Ethics Committee (opinion No. 5,295,815). **Results:** When analyzing the number of patients treated for use of any PS, a reduction of 6.7% (2020) and 2.4% (2021) was observed. For the use of AD, there was a reduction of 6.8% (2020) and an increase of 2.6% (2021). For BZDs, the decrease expressed 6.9% (2020) and 10.1% (2021), compared to 2019. Regarding the number of PS visits, there was a reduction of 5% (2020) and a slight increase of 1% (2021). For AD, there was a decrease of 4.5% (2020) and a significant increase of 10.4% in 2021. For BZD, the decrease expressed 0.8% (2020) and 2.7% (2021), all compared to the year 2019. Considering the number of items dispensed in the years 2020 and 2021 in relation to 2019, an increase was observed. For PS, the increase was 2.8% (2020) and 16.4% (2021). For AD, there was an increase of 3.2% (2020) and 30.6% (2021). For BZDs, the increase represented 11.5% (2020) and 12.1% (2021). **Conclusion:** It was observed that even with the decrease in the patient´s attendance and/or pharmacist-provided medication, there was an increase in the use of PS dispensed, indicating a possible increase in mental disorders caused by COVID-19 pandemic. Studies are needed to know the prevalence of mental disorders, as well as the management of treatment through the use of PS associated with psychotherapy.

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EPIGALLOCATECHIN-3-*O*-GALLATE FROM *Limonium brasiliense* INHIBITS THE MUCOADHESION OF *Porphyromonas gingivalis*

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Keywords: ***Limonium brasiliense*, *Porphyromonas gingivalis*, mucoadhesion.**

Introduction: *Limonium brasiliense* (Boiss). Kuntze (Plumbaginaceae), popularly known as baicuru, is used in Brazil for the treatment of menstrual disorders. The crude extract has specific inhibitory activity against *Porphyromonas gingivalis* (Pg). Pg is a pathogen strongly involved in chronic and aggressive forms of periodontitis, that is a complex microorganism-induced inflammation of periodontal tissue, and if left untreated leads to the destruction of the tooth supporting system with eventually tooth loss, and this microorganism is also related with Alzheimer disease, cardiovascular disease, and other systemic problems. **Aim:** The aim of this work was evaluating the activity of Epigallocatechin-3-*O*-gallate (EGCG) from *L. brasiliense* against mucoadhesion of *Pg* in KB cells. **Methods:** The crude extract of the rhizomes was obtained by turbo-extraction with acetone:water 70:30 (v/v) and was partitioned with water and ethyl acetate (ethyl-acetate fraction - EAF). EAF was fractioned by Sephadex LH20 column, obtaining EGCG. The antiadhesion activity was analyzed by plate fluorimetric assay in KB cells (ATCC CCL-17), using coincubation methodology (90 min) with FITC (fluorescein isothiocyanate) previous labeled bacteria. **Results:** EGCG showed results in a 79 ± 3% reduction of bacterial adhesion to KB cells in a concentration of 30 µM and 75 ± 3% at 20 µM. **Conclusion:** EGCG showed promising effect against *Pg* adhesion in KB cells. *L. brasiliense* can be used to prevent periodontal disease caused by *Pg* and improve the systemic health of population.

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CLINICAL MONITORING OF VANCOMYCIN IN THE ICU OF A SCHOOL HOSPITAL: PHARMACIST IMPACT

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Keywords: Clinical pharmacist; drug therapy monitoring, pharmaceutical care.

Introduction: One of the guidelines advise the minimum concentration (trough) of vancomycin ≥10 µg/mL prevent the resistance, and minimum concentrations of 15 – 20 µg/mL may enhance the results and must be monitored due the nephrotoxicity risk. Thus, the vancomycin dosage is widely recommended to reach greater effectiveness on the use of this antimicrobial. **Aim:** Evaluate the vancomycin dosage in patients at the intensive care unit (ICU) of the Regional University Hospital of Maringá (HUM) and comprehend the impact of the pharmaceutical intervention on this monitoring. **Methods:** A descriptive retrospective study was performed with patients that received the vancomycin between July 2019 and June 2020. The data was obtained researching the electronic medical history of the patients at the system of Health Assistance Management of the Unique Health System (GSUS). The study was approved by ethic committee (CEP) of the State University of Maringa, protocol n° 36827420.3.0000.0104. **Results:** It was included 28 patients, being 17 males (60.71%) e 11 (39.29%) females; with average age of 53 years old (18–89). The ICU admissions were motivated mostly by sepsis (46.4%), pneumonia (35,7%), meningitis (7.14%) and other infections (3.57%). The average of admission was 46.7 days. In relation to the vancomycin, it was observed the accomplishment of 77 dosages on the studied period, with an average of 2.75 dosage/patient. Considering the trough concentration, most of it was >20 µg/mL (40.26%), approximately 30% was in the therapeutic window for severe infection (15-20 µg/mL) and 23.38% for moderate ones (10-15 µg/mL), only 6.49% underdoses (<10 µg/mL), the average trough concentration was 20.57 µg/mL, with minimum and maximum of 5 and 71,.5 µg/mL, respectively. Related to the total of dosage, approximately 50% was out of the therapeutic (12.99% below e 37.66% over). The dose adjustment was performed by the pharmacist in 51.9% of the sceneries, of which 35% were successful and no induction of nephrotoxicity was seen during the treatments. The greater prevalence of dose adjustment was between the age range of 60 to 69 and 70 to 79 years. **Conclusion:** The dose adjustment was performed in most of the cases, showing the positive impact of pharmaceutical intervention and that there was an increase on the serum levels of the vancomycin, according to each patient's need. Hence, the pharmacist is essential to establish protocol that are most adequate to the health institution.

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COMPARATIVE ANALYSIS OF EXTRACTS OF *Chenopodium quinoa* Willd. OBTAINED BY DIFFERENT SOLVENTS

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Keywords: **Fatty acids; Gas chromatography; Quinoa residue;**

Introduction: *Chenopodium quinoa* Willd. grain is a native species of the Andes, currently known and marketed worldwide for being rich in nutrients, vitamins, minerals and essential amino acids, in addition to being an ingredient in cooking. In recent years, researchers have reported several bioactivities for quinoa grain extracts, such as antioxidant, antifungal, immunomodulatory and anticarcinogenic effects. BRS Piabiru quinoa, developed by EMPRAPA, is the first quinoa adapted to the Brazilian climate. Currently, BRS Piabiru quinoa is the most cultivated in our country, mainly in the Cerrado. Quinoa husks are by-products generated during the industrial processing of grains, where most of these peels are discarded due to the possibility of the presence of bitter saponin compounds. Although the quinoa grain has been extensively studied, the literature on industrial quinoa bio-waste is quite scarce. **Aim:** The present study aimed to optimize the extraction of the residue from the grain of *Chenopodium quinoa* BRS Piabiru, the Brazilian quinoa, and itschemical profile by Gas Chromatography Coupled to Mass Spectrometry (GC-MS) of the obtained extracts. **Methods:** The quinoa husk residue was dried and then tritured with a knife mill. The extraction was performed by Soxhlet, for each 10 g of sample, 250 mL of solvent were used for 2 hours. The following solvents were tested: water (H_2O), 50 % ethanol solution in water (EtOH50%), 70 % ethanol solution in water (EtOH70%) and pure ethanol (EtOH99%). Then, the different extracts obtained were filtered, rotaevaporated, frozen and lyophilized for yield calculation and analysis in (GC-MS). **Results:**It was possible to verify that the Soxhlet extraction with the solvent EtOH70% performed a higher extraction yield (16.8 %), compared to EtOH50% (9.9 %), H_2O (5.4 %) and EtOH99% (4.1 %). Furthermore, the GC-MS analysis revealed that the EtOH99% extract obtained a greater variety of identified compounds (8 compounds), followed by EtOH70% (7 compounds), EtOH50% (7 compounds) and H_2O (6 compounds). In addition, the ETOH70% extract revealed a greater amount of substances from the class of fatty acids, phytosteroids and alkaloids: palmitic acid (C16:0), oleic acid (C18:1n9c), stearic acid (C18:0), tricosanoic acid (C23:0) and oxalic acid (organic acid), β-Sitosterol, Stigmasterol, Nonadecone. **Conclusion:** Therefore, the characterization of the samples by GC-MS revealed that residue from the quinoa peel, which is currently discarded by the industry, presents bioactive compounds of interest, revealing the possibility for application in the pharmaceutical, cosmetic and food industries.

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COMPARATIVE ANALYSIS OF *Humulus Lupulus* L. EXTRACTS OBTAINED BY DIFFERENT SOLVENTS

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Keywords: **Bioactive compound; Gas chromatography; Hops;**

Introduction: Hops (*Humulus lupulus* L.) is a popularly plant known as one of the main ingredients in beer production. The plant has the botanical characteristic of being a vine, perennial and dioecious, that grows preferentially in temperate climates in the northern hemisphere. However, only the female plant has a commercial value, because its cone synthesizes a superior amount of secondary metabolites such as essential oil, polyphenols and bitter acids (α and β-acid), which in turn are responsible for adding aromatic notes and bitterness in the drink. However, these substances also have some bioactive properties and folk medicine uses them for the treatment of pathologies such as sleep disorders, anxiety and insomnia. **Aim:** This study aimed to optimize the hop cone extraction by ultrasound-assisted extraction (UAE) comparing with different solvents (acetonitrile, chloroform, ethanol, methanol) and obtain the chemical profile by Gas Chromatography coupled with Mass Spectrometry (GC-MS) of the obtained extracts. **Methods:** The hop cone (Cascade variety) was obtained from a producer from Lajes Santa-Catarina. After receiving the plant material, it was dried and reduced in size with the aid of a knife mill. The extraction was performed by UAE, using 1.0 gram of the hop cone, added 20 ml of extractor liquid (acetonitrile, chloroform, ethanol or methanol) and under the following conditions: frequency of 30 kHz, temperature of 35°C and time of 35 minutes. Then, the different extracts were filtered and lyophilized for yield calculation and analysis in GC-MS. **Results:** It was possible to verify that the UAE with the chloroform solvent performed a higher extraction yield (23.44%), followed by the methanol (17.54%), acetonitrile (15.62%) and ethanol (8.8%). The GC-MS analysis revealed that the chloroform extract obtained a greater variety of identified compounds (44 compounds), followed by the methanolic (35 compounds), ethanolic (32 compounds) and acetonitrile (31 compounds). Furthermore, the chloroform extract revealed a greater amount of substances from the sesquiterpene hydrocarbon class such as: α-copaene, β-copaene, humulene and α-salinene. **Conclusion:** Therefore, the characterization of the samples by GC-MS revealed that the chloroform solvent showed a better extraction of compounds and also the largest number of compounds with bioactive potential, possibly due to its non-polar characteristic.

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QUANTIFICATION OF GOBLET CELLS IN THE JEJUNUM OF ANIMALS CHEMICALLY INDUCED TO COLORECTAL CARCINOGENESIS ADMINISTERED WITH MICROENCAPSULATED QUERCETIN AND *Bifidobacterium animalis*

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Keywords: Antioxidant. Oxidative stress. Probiotic.

Introduction: According to the National Cancer Institute, the number of people with colorectal cancer (CRC) has increased every year, being one of the cancers with the highest incidence. CRC is a disease that affects the large intestine, and among the systemic consequences generated by cancer, we can highlight oxidative stress that causes cellular apoptosis and can affect the gastrointestinal tract. **Aim:** The aim of the study was the quantification of PAS^+ goblet cells of the jejunum of rats chemically induced to CRC administered with microencapsulated quercetin and *Bifidobacterium animals*. **Methods:** Thirty 50-day-old male Wistar rats randomly distributed in five groups with 6 animals each: control (C); colorectal cancer (CR); CR + quercetin (CQ), CR + probiotic (PC); CR + probiotic + quercetin (CQP); CR was chemically induced by DMH administration (40 mg / kg). The treated animals received microencapsulated 10 mg/kg quercetin and $5 \cdot 10^7$ UFC *Bifidobacterium animalis* daily by gavage. At the end of the experimental period of 112 days, the animals were euthanized and the jejunum was collected and intended for the standard histological technique (fixation, embedded in paraffin and cuts) and posterior staining with Periodic Acid Schiff (PAS). The quantification of the PAS^+ goblet cells was performed on the epithelium of 30 villi and 30 crypts per animal (180 crypt/villus units per group) in images captured with a 20X objective. The results were discovered through statistical analysis and the significance level was set at 5%. All procedures described were previously approved by CEUA (n°1126010419). **Results:** The results showed an increase of 5,5% in the number of PAS^+ goblet cells on the epithelium of villi in the animals of the CR group compared to the control ($p = 0.04$). The treated animals (CQ, CQP, and CP) on the other hand showed a reduction of 5,5%, 11% e 15%, respectively, in the number of PAS^+ goblet cells on the epithelium of villi compared to the CR group ($p < 0.03$). The number of PAS^+ goblet cells in the crypts did not show any significant changes between the studied groups. **Conclusion:** The development of CRC caused an increase in the number of goblet cells in the jejunum of the animals, a possible defense mechanism against the damage caused by the oxidative stress generated by the CRC. Both treatments, and especially quercetin alone, attenuated this raise demonstrating protective antioxidant effects on the mucosa and maintenance of the epithelium.

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THE EFFECTS OF PHARMACEUTIC ATTENTION IN THE SELF-CARE OF DIABETES MELLITUS SUFFERERS PARTICIPANTS FROM THE RESEARCH AT THE FARMÁCIA BÁSICA MUNICIPAL JEOVÁ RIBEIRO IN CASTRO-PR.

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Keywords: Pharmacotherapeutic monitoring. Diabetes Mellitus. Glucose. Participants.

Introduction: Diabetes Mellitus (DM) types 1 and 2 is a disease that occurs by glucose rate change due to by metabolic problems.Type 2 DM is on the rise in Brazil and most countries.The low acceptance to the therapeutic is a public health issue for users who attend at Farmácia Báscia Municial Jeová Ribeiro in Castro/PR. **Aim:** Identify problems of adherence to the treatment, promote control of DM and encourage reflection about procedure changes from other health professional. **Methods:** Clinical study developed at Farmácia Básica Municipal Jeovah Ribeiro, that provides service to the Brazilian Integrated Health System(SUS) DM holders patients, in the city. Participants are selected among the ones that make use of de insulin available at the city public pharmacy, with or without oral hypoglycemic, with ages above 40 years old, according to the inclusion and exclusion criteria. The population under study is of 65 participants.The selected ones were separated into 37 female participants and 28 male participants. The participants are invited to attend lectures with blood glucose test reading. After that, they are selected for a first appointment, and invited to sign the Informed Consent |Term (ICF)) to carry out the pharmacotherapeutic monitoring, exam solicitations, evaluation and caring plan.The evaluations are made every 3 months with laboratory exam solicitations for the evaluation. **Results:** From the total of 37 female participants, 23 are in pharmacotherapeutic following. Of the total of 28 male participants, 14 are in pharmacotherapeutic following. Preliminary results depend on analysis and reports. We have, at the moment, 11 research participants with HbAlc reduction. Among them, 5 participants with values of 1,4% to 1,7% HbAlc reduction in 4 women and 1,0% in 1 man, value reduction between 0,2% to 0,7% in 4 women and 0,1% and 0,3% in 2 men, respectively. These are partial results, due to its needs of more evaluations. **Conclusion:** Participants showed significant interest in to knowing more about their illnesses and feld stimulated to take part in the research. It was noted that the pharmaceutics fundamental role on a multiprofessional health team and there is hope for new reflections from other health professionals.

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IN VIVO EXPERIMENTAL STUDIES AND ALOPECIA: MOLECULAR BIOLOGY ANALYSIS

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Keywords: hair growth, methodological parameters, plant extracts, animal model.

Introduction: Alopecia is a chronic multifactorial disease that significantly affects the psycho-emotional state of patients, reducing their social interactions and quality of life. Research on herbal compounds has increased in recent years, aiming the development of more effective and less toxic agents for the treatment of hair loss. **Aim:** This study aimed to map the molecular biology methods *in vivo* experimental studies on the use of plant species as a research model for the investigation of possible therapeutic options for the treatment of alopecia through a scoping review. **Methods:** The systematic search was performed in the electronic databases Medline, Scopus, Web of Science, and Scielo. Experimental *in vivo* studies used mice as animal model were included, which used molecular biology analysis to investigate plant species as a therapeutic option for hair growth. The survey was carried out in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), the Cochrane Handbook for Systematic Reviews of Interventions and the Joanna Briggs Institute methodology for scoping reviews. **Results:** Initially, 1021 studies were retrieved from the databases, 217 studies for full reading and 41 studies included for data extraction. Molecular biology methods identified in the studies were: immunohistochemical analysis, real-time polymerase chain reaction, western blot assay, and enzyme-linked immunosorbent assay. These analyzes evaluated the levels and expression of growth factors, proteins, and genes involved in the hair growth cycle. **Conclusion:** With the synthesis of the data, it was possible to identify the methodological aspects of the molecular biology analyzes used to investigate plant species in hair growth activity using animal models.

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THE USE OF *Cannabis sativa* IN COSMETIC PRODUCTS

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Keywords: Cannabidiol; Cannabis sativa; CBD-based cosmetics; CBD extraction;

Introduction: Cannabinoid compounds are substances extracted from *Cannabis sativa*, the cannabinoids of greatest scientific interest are cannabidiol (CBD) and tetrahydrocannabinol (THC). THC has a psychoactive effect, causing euphoria, increased appetite and short-term memory loss. In addition, it also has very important medicinal characteristics, such as analgesic, muscle relaxant, anti-inflammatory and in small concentrations associated with CBD, it can be used for the treatment of diseases such as epilepsy (CONSELHO, 2022). CBD is a cannabinoid found in large amounts in *C. sativa*, without psychoactive effects and its concentration is dependent on the culture, ranging from 0.03% to 29.6% of the plant. It is a compound identified as a potent therapeutic agent, with anti-inflammatory and neuroprotective effect, used in the treatment of epilepsy, anxiety, neurodegenerative diseases, multiple sclerosis and neuropathic pain (LIMA et al., 2021; CONSEIL, 2022). **Objective:** The objective of this work was to highlight studies on *C. sativa*-based cosmetics, find the possible mechanisms of action of *C. sativa*-based cosmetics and identify possible indications for the use of these products. **Methods:** A systematic review of the literature was performed. PubMed, Scielo and Google Scholar databases were used as research sources. Keywords used: Cannabidiol; *Cannabis sativa*; CBD-based cosmetics; CBD extraction; cannabinoids. Publications between 2000 and 2022 were considered. **Results:** The literature review showed 20 publications on the topic. The result found regarding the mechanism of action of *C. sativa*-based cosmetics was the proof that the endocannabinoid system is present in the skin, with signaling molecules called endocannabinoids, specific receptors and enzymes that synthesize and degrade endocannabinoids and transporters. Thus, it has been shown that these products act on skin homeostasis and are widely used as a barrier, especially in cases of skin disorders such as acne, itching and atopic dermatitis. **Conclusion:** The systematic review proved that there are good studies with the *C. sativa* species, but the incorporation of the species in cosmetic products is something new and that is constantly evolving. The need for the development of new studies in the area was proved, and mainly of quality policies for the incorporation of the products to the commerce.

IDENTIFICATION AND QUANTIFICATION OF FATTY ACIDS OF *Pfaffia glomerata* STEMS CULTIVATED *EX VITRO* AND *IN VITRO*

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Keywords: ***Pfaffia glomerata*, fatty acids, direct esterification.**

Introduction: *Pfaffia glomerata* (Spreng.) Pedersen (Amaranthaceae, Brazilian ginseng) is a plant native to South America and is traditionally used in folk medicine. Brazilian ginseng extracts are mainly obtained from its roots while the aerial parts are discarded in the field as waste. However, there is a lack of studies on obtaining metabolites of interest, such as fatty acids in the aerial parts of this plant. Fatty acids are important in biosynthesis of specialized metabolites. **Aim:** The aim of the study was to identify and quantify fatty acids of stems from *P. glomerata in vitro* and *ex vitro* by Gas Chromatography coupled to Mass Spectrometry (GC-MS) and Gas Chromatography-Flame Ionization Detector (GC/FID). **Methods:** The analytical method of direct esterification of fatty acids was performed on stems cultivated *in vitro* (S-IV) and *ex vitro* (S-EV) of *P. glomerata*. A portion of 100.0 ± 1.0 mg of the samples were placed in 2.0 mL of NaOH (1.5 mol L^{-1}, in MeOH) and placed in an ultrasonic vat. After the reaction, 2.0 mL of H_2SO_4 (1.5 mol L^{-1}, in MeOH) were added and replaced in an ultrasonic vat, 1.0 mL of *n*-hexane was added and centrifuged at 2000 rpm for 5 min. The upper phase was collected and the *n*-hexane addition step repeated twice identified and quantified by GC-MS and GC/FID analysis, respectively. Fatty acid methyl esters were identified by comparison with mass spectra from the NIST 11.0 database (National Institute of Standards and Technology) and by FAME (Fatty Acid Methyl Esters) standards. **Results:** Fourteen fatty acids were identified in S-EV and S-IV, the absolute quantification by GC/FID showed a predominance of unsaturated fatty acids in S-EV and S-IV (231.45 and 289.24 μg 100 mg^{-1}, respectively) with emphasis on the important α-linolenic acid (C18:3n3, omega-3), polyunsaturated linoleic acid (C18:2n6c, omega-6), and γ-linolenic acid (C18:3n6) present in greater amounts in S-IV (3.10, 186.80 and 10.26 μg 100 mg^{-1}, respectively). Among the major saturated fatty acids, a higher amount of palmitic acid (C16:0) (161.65 μg 100 mg^{-1}) and stearic acid (C18:0 (34.29 μg 100 mg^{-1}) was quantified in S-IV. **Conclusion:** Direct esterification is a fast technique that reduces the amount of solvent and sample and with less environmental impact when compared to conventional methodologies. The stems of *P. glomerata* are an alternative source for obtaining unsaturated and saturated fatty acids, which have economic value and potential industrial application.

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EVALUATION OF EPRINOMECTIN RELEASE PROFILE FROM THERMORESPONSIVE BIOADHESIVE SYSTEMSFOR VETERINARY PURPOSES

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Keywords: drug delivery system, semi-solid, thermoresponsive systems, eprinomectin.

Introduction: Eprinomectin is a semisynthetic derivative of the group of avermectins which displays great therapeutic efficiency against endo and ectoparasites. This is synthesized by using products of fermentation, such as avermectins B1, which is as mixtures of homologous B1a (>90%) and B1b (<10%). Its use is highlighted due to the safety approved for use for use in lactating animals. Polymers with bioadhesive characteristics, such as carbomers, and thermoresponsive properties, such as polaxamers, have been used to develop pharmaceutical systems for controlled drug release and to improve the bioavailability. The development of this thermoresponsive bioadhesive system is due to the need to keep the formulation in place (pour on) for a sufficient time so that its release and action is effective, safe and avoids falling and contaminating the soil. **Aim:** The evaluation of the *in vitro* release profile of eprinomectin from polymeric systems. **Methods:** Two polymeric systems containing eprinomectin were prepared. Formulation F1 was composed of eprinomectin 0.5% (w/w), isopropanol 15% (w/w), poloxamer 407, 17.5% (w/w), and Carbopol 934P®, 0.3% (w/w). Formulation F2 was composed of eprinomectin 0.5% (w/w), isopropanol 15% (w/w), poloxamer 407 17.5% (w/w) and Carbopol 974P® 0.3% (w/w). The *in vitro* release profile of eprinomectin was investigated using Franz vertical diffusion cells. The quantification of the released drug was evaluated at 30, 60, 120, 240, 360 and 480 min (n = 3). 1g of the formulation was directly added on the wall of Franz cell in direct contact with the release medium (50 ml of 5% Tween solution), maintained at 37 ºC under constant magnetic stirring. In the time intervals, 1.0 mL of the release medium was collected with replacing of dissolution medium. The collected samples were analyzed by HPLC using a validated method. **Results:** The *in vitro* release profile of eprinomectin showed the first detection of homologue B1a in both formulations at 60 min. At 480 min, 77.88% of eprinomectin B1a was released in F1, and 29.5% in F2. However, eprinomectin B1b was not detected in any of the formulations. Both systems displayed anomalous transport of release mechanism of B1a, leaded by Fickian diffusion and relaxation of polymer chains. The drug release was started at 60 min, showing a slow release profile; however, the release from F1 (77.80% ± 4.37) was faster and higher than from F2 (29.50% ± 1.21). **Conclusion:** The *in vitro* eprinomectin release from systems F1 and F2 was governed by anomalous transport, controlled by Fickian diffusion and polymer relaxation.

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USE OF CRUDE RECOMBINANT *BACILLUS SUBTILIS* WB800 CYCLOMALTODEXTRIN GLUCANTRANSFERASE ENZYME AND ALTERNATIVE MEDIUMS FOR THE PRODUCTION OF CYCLODEXTRINS

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Keywords: CGTase recombinate, cyclodextrin, alternative mediums.

Introduction: Cyclodextrins (CDs) have the ability to encapsulate numerous molecules and have applicability in several industrial areas, however, their production cost is high, and their yield is low, which limits their application. **Objective:** The present study evaluated the efficiency of using the enzyme cyclomaltodextrin glucantransferase (CGTase) from recombinant *Bacillus subtilis* WB800 without purification and alternative mediums for the production of CDs. **Methods**: For the production of recombinant *B. subtilis* CGTase, 2xYT medium (2) was used, which was supplemented with kanamycin (25 µg/mL) and incubated at 30 °C, at 100 rpm, for 5 days. The alternative mediums used were: medium for the production of CDs molecules (1) only with the addition of the enzyme (medium 1A) and only with the presence of the microorganism (medium 1B), and the 2xYT medium only with the addition of the enzyme (medium 2A) and only with the presence of the microorganism (medium 2B). The mediums were supplemented with kanamycin and added with corn starch and subsequently incubated at 30 °C, 100 rpm, for 5 days. 5 mL aliquots were collected every 24 h for chromatographic analysis. **Results:** All mediums evaluated showed considerable production of CDs, even without the enzyme going through the semi-purification and/or purification step. The time of 48 h was the one that showed the highest production of CDs, especially β-CD, with emphasis on the 2xYT medium, regardless of the presence of the microorganism or just the enzyme (13.26 and 15.06 mmol/L of β- CD, respectively). It was possible to observe that the concentration of β-CD started to decrease progressively, especially in the medium containing the microorganism (1A medium). This event may be related to the fact that the microorganism is producing other enzymes that act in the degradation of the recombinant CGTase or, still, due to the possibility of the microorganism consuming the DCs over time. **Conclusion:** Alternative mediums plus corn starch was an interesting strategy, especially for the production of β-CD, which is currently the most used and commercially available. In addition, the use of the enzyme without purification is a promising alternative, as it contributes to the reduction of costs and steps in the production of CDs and, consequently, can favor its industrial application.

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CHARACTERIZATION OF THE PHARMACOTHERAPY FOR DIABETES MELLITUS TREATMENT IN PATIENTS ASSISTED BY THE PHARMACEUTICAL CARE SERVICE

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Keywords: Pharmacotherapy Analysis, Pharmaceutical Care, Polypharmacy, Diabetes Mellitus

Introduction: Pharmaceutical assistance has gone through variations in its form of action from the transformations of the health system, with expansion of the attributions of the pharmacist, who started to provide clinical practices of co-responsibility with the care and integration with the team, defined as pharmaceutical care. This context of multiprofessional health care is amplified due to aging process of the population and the increase of chronic-degenerative diseases, such as Diabetes Mellitus (DM). **Aim:** To characterize the pharmacological therapy used by patients with diabetes mellitus. **Methods:** Partial data were obtained from a single-arm longitudinal clinical study developed by a working group in seven municipalities in the state of Paraná during the implementation of a pharmaceutical care service for patients with type 2 diabetes mellitus, diagnosed for at least 6 months, treated in the municipal primary care, aged between 40 and 85 years, using oral or injectable antidiabetic agents, and with a HBA1C level equal to or higher than 7% or postprandial glycemia >180mg/dL. **Results:** Seventeen patients participated in the study, with a mean age of 60 years (41-75 years), 11 were men (64.7%). Regarding drug treatment, 88.2% of patients used oral antidiabetic agents (OADs) and 94.1% used insulin. Two patients (11.8%) used only insulin, 5.9% (n=1) only OADs and 82.3% (n=14) associated insulin and OADs. Among insulin users, 14 patients (87.5%) used only slow-acting insulin (NPH). All users of OAD used metformin and 26.7% (n=4) associated more than one OAD. Of these, one patient used two OADs, two patients associated insulin + two OADs and one patient associated insulin + three OADs. There was also one patient on insulin + metformin + GLP-1 receptor agonist due to the presence of microalbuminuria. The OADs used were from the biguanide class (metformin), SGLT2 inhibitors (dapaglifozin and empaglifozin) and sulfonylureas (glibenclamide and gliclazide). All patients used other medications in addition to those used for treating diabetes mellitus. On average, the amount of medications used was seven, ranging from three to 13 medications. **Conclusion:** Patients with diabetes mellitus mostly have other associated health problems, therefore polypharmacy is recurrent, making it essential the pharmacotherapeutic monitoring by trained professionals who contribute to greater adherence to treatment, empowerment over their health, and reduction of risks inherent in the pharmacological treatment (adverse drug reactions, drug interactions), aiming exclusively at improving their clinical condition and greater survival.

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THE IMPACT OF SOCIAL DISTANCING ON PATIENTS' MENTAL HEALTH DURING THE COVID-19 PANDEMIC

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Keywords: Keywords: Pandemic; COVID-19; Social distancing; Mental health.

Introduction: Since the beginning of the Covid-19 pandemic, social distancing has beenproposed by international health bodies as a fundamental controlling. In Brazil it was implemented by local governments. Despite its effectiveness in curbing the virus, social distancing could have an additional deleterious impact on peoples' mental health, particularly those with pre-existing conditions. **Objective:** This study aimed to explore the experiences and perceptions of patients of a public primary health care setting in a small municipality in the interior of Paraná about the impact caused by social distancingexperienced during the pandemic. **Methods:** Semi-structured interviews with patients. The interviews were recorded and transcribed verbatim. The transcripts were then thematically analyzed. This study was approved by the Research Ethics Committee (approval no. 4,064,706/2020). **Results:** A total of 19 patients were interviewed. It was evident that the pandemic caused feelings of fear, loss, worriness, low self-esteem, emotional and mental health problems such as anxiety. Participants reported fear of the pandemic, mainly because it was something unknown and frightening, intensified by the spread of fake news. Social distancing in some cases intensified mental health problems due to isolation and lack of social interaction, especially with friends and family. Patients who participated in this research sought non-pharmacological measures to treat the psychological symptoms, in addition to the use of psychoactive medicines. **Conclusion:** The restriction measures and social distancing caused changes in the patients' lives, impacting their mental health. Despite not having a national lockdown, the regional closures caused and impact on the individuals' mental health. More studies are needed to investigate whether the perception of these patients' mental health has returned to pre- pandemic levels, since all measures of social restriction have already been revoked.

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