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Faculdade de Ciências Farmacêuticas
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24th WEEK OF PHARMACEUTICAL SCIENCE AND TECHNOLOGY

School of Pharmaceutical Sciences
University of São Paulo

ABSTRACTS

September 27th to October 1st, 2021

São Paulo – Brazil

PREFACE

The 24th Week of Pharmaceutical Science and Technology (SFCT), an event organized by the research and the post-graduation committees of the FCF/USP, took place together with the 55th Pharmacy and Biochemistry University Week (SUPFAB) and with the 11th Annual Symposium of Pharmaceutical Sciences Research. The theme of the events was "Science as a Tool for Innovation" and explored the state of the art of drug innovation and the combat to fake news in science, as well as addressing all scientific aspects of the SARS CoV-2 pandemic. The Pharmacy and Biochemistry University Week (SUPFAB) is a pioneer annual event that was created in 1965 by the students of the academic center of pharmacy-biochemistry at the School of Pharmaceutical Sciences of University of São Paulo (FCF/USP). In 1995, the SUPFAB joined the Week of Pharmaceutical Science and Technology (SFCT). We have already established 26 years of fruitful partnership between students and professors that has brought excellent results so far.

This 2021 edition received over 700 atendeess registered in a 100% virtual event. The whole event addressed the latest technologies in the production of biopharmaceuticals using different technologies, including the development of serum against SARS-CoV-2, and in key areas of the pharmaceutical field. Moreover, several themes were addressed, always prioritizing science as the core of pharmaceutical performance. The pharmaceutical professional that works in the care of certain populations was valued, showing this facet in the mutual assistance of other health professionals, to try to mitigate the various ills and inequalities of the Brazilian population. Over the years, we could conciliate various themes of general interest to students from different levels of knowledge. Lectures and courses were addressed to include classic and fundamental themes of the pharmaceutical career to themes that are in the frontiers of knowledge. Students presented their scientific work in oral and scientific video sessions that brought a unique opportunity for learning and sharing information developed at USP. We would like to thank the dedication and commitment of all organizers, all students, employees, and staff of all divisions of the FCF/USP, which made this week possible. We also thank all the speakers who have shared their knowledge and experience with us.

Prof. Dr. João Paulo Fabi
President of the Scientific Committee

24th WEEK OF PHARMACEUTICAL SCIENCE AND TECHNOLOGY
SCHOOL OF PHARMACEUTICAL SCIENCES, UNIVERSITY OF SÃO PAULO

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11th ANNUAL RESEARCH SYMPOSIUM ON PHARMACEUTICAL SCIENCES

Science as a Tool for Innovation

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24th Week of Pharmaceutical Science and Technology
School of Pharmaceutical Sciences
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ABSTRACTS

FCF176-2021

DEVELOPMENT OF PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODEL TO ACCESS METOPROLOL SUCCINATE'S ABSORPTION FROM EXTENDED-RELEASE MINI-TABLETS

BRUNA WENYI CHUANG JOU[1] (IC); MARCELO DUTRA DUQUE[2]; MICHELE GEORGES ISSA[1] (PD); HUMBERTO GOMES FERRAZ[1]

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Introduction and Objectives: Physiologically-Based Pharmacokinetic (PBPK) modelling is used to predict drug absorption and distribution into tissues, contributing to understand the influence of *in vivo* drug release, driving the product development, mainly for extended release formulations. This study aimed to use the software GastroPlus® 9.8 and dissolution profile to predict the plasma concentration profile of extended-release metoprolol succinate mini-tablet (SCM).
Material and Methods: GastroPlus® 9.8, provided by Simulations Plus® was used to build a PBPK model to simulate and obtain data regarding the absorption profile of SCM. The used data were from literature and SCM's dissolution profiles came from previously research developed at DEINFAR-USP.
Results and Conclusions: The PBPK model was developed using literature data. It was validated using 50 and 100 mg oral solution's plasma concentration profile, followed by extended-release formulation's data, including the reference product. As all simulated profiles were similar to those reported in literature, they passed according to the success statistical criteria. Thus, the model accurately predicted the absorption of the SCM mini-tablets, which was compared with the reference product, showing high similarity. The PBPK model developed with *in silico* tool is able to predict *in vivo* absorption and shall help in the evaluation of formulation's potential, supporting the development of new formulations by optimizing the resources, increasing the rationality of the process.
Financing: FCF USP

FCF179-2021

ANTIOXIDANT EMULSIONS EFFICIENCY: EVALUATING EX VIVO LIPID PEROXIDATION

ANDRESSA COSTA DE OLIVEIRA (M), CLAUDINÉIA APARECIDA SALES DE OLIVEIRA PINTO (D), THAMIRES BATELLO FREIRE (M), ANDRÉ ROLIM BABY (PD), MARIA VALÉRIA ROBLES VELASCO (PD)

Department of Pharmacy, FCF/USP

Introduction and Objectives: Slow buildup of oxidative damage can contribute to cutaneous ageing and in the appearance of neoplasms and other diseases. This study's objective is to quantify the lipid peroxidation by the MDA-TBA adduct on the ex vivo stratum corneum and to evaluate the ascorbic acid (AA) influence when associated or not with the cafeic acid (CA) in cosmetic formulations.
Material and Methods: Two formulations were evaluated: F1: cosmetic base + AA 10.0% w/w e F2: cosmetic base + CA 0.2% w/w + AA 10.0% w/w. After approval of opinion Nº 3. 360,258 regulated by the CONEP/ Brasil, ex vivo assays were performed on 10 volunteers. The tape stripping method was used to remove stratum corneum (SC) from the volunteers forearms, using 4 tapes of Scotch MagicTM Tape. Posteriorly, the lipid peroxides were quantified by testing thiobarbituric acid reactive substances (TBARs), by HPLC.
Results and Conclusions: When the skin was radiated, had an increase on the lipid peroxidation ($9.4x10^{-3}$± 0.00 µM). F1 and F2 not radiated inhibited the quantity of TBARs formed, suggesting that the antioxidants protected the essential lipid biomolecules to prevent the skin aging control. The F1 and F2 irradiated tapes caused an increase in lipid peroxidation. The intensity of oxidative stress caused by the association CA + AA (F2), there was an increase of lipoperoxidation, ±100% when compared to the control, and ±130% when compared to F2 radiated. About the ultraviolet (UV) radiation, the antioxidant association didn't provide the necessary protection and neither prevented the lipoperoxidation skin, and it is recommended the use of photoprotect product (daytime); or to employ them at night.
Financing: CNPq

FCF180-2021

STUDIES OF ANTIOXIDANT ACTIVITY IN PHOTOPROTECTIVE FORMULATION USING BIOLOGICAL MEMBRANE OF SHED SNAKESKIN

THAMIRES BATELLO FREIRE (M), [1]ORLANDO RODRIGUES JÚNIOR (PD), CLAUDINÉIA APARECIDA SALES DE OLIVEIRA PINTO (PD), [2]CASSIANO CALOS ESCUDEIRO, ANDRESSA COSTA (M), ANDRÉ ROLIM BABY (PD), MARIA VALÉRIA ROBLES VELASCO (PD)

Pharmacy/ University of São Paulo; [1]Instituto de Pesquisas Energéticas e Nucleares; [2]Instituto de Pesquisa Clínica Integrada

Introduction and Objectives: Antioxidants of natural origin are used in medicines and cosmetics with several benefits, such as: photoprotective action, anti-aging, moisturizing and anti-pollutant. The anti-oxidative capacity of the human epidermis barrier is limited, so studies with the epidermis is essential. Shed snakeskin (SS) is composed by the stratum corneum and provides a human skin-like barrier This study evaluated the use of SS seedlings as an alternative for human or animal skin ex-vivo assays using Electron Paramagnetic Resonance spectroscopy (EPR) and Forster Resonance Energy Transfer (FRET).
Material and Methods: EPR, FRET and the percentual inhibition of the radical 2,2-diphenyl- 1-picrihydrazyl (DPPH•) were employed to evaluate the natural antioxidant substances (*Resveratrol/* RES 3.0 w/w and *Ferulic acid*/ FA 1.0 w/w) associated with organic sunscreens ingredients (*Ethylhexyl Methoxycinnamate/* EHMC 10.0%w/w and *Butyl Methoxydibenzoylmethano/* BMBM 5.0%w/w in a photoprotective emulsion (PB).
Results and Conclusions: RES and FA absorbed the energy emitted by EHMC, but not by BMBM in FRET, preventing the triplet state formation, favoring the photostability of this sunscreen. The observed antioxidant activity was higher for RES (97.0% inhibition of DPPH•) than for FA (91.0%) in PB. However, concentration of RES was higher than FA in PB. The SS + PB + FA association, with the lowest post-irradiation amount of free radicals, was the most effective, which corroborated the high percentage of radical inhibition *in vitro* and it was the better association with the photoprotective formulation.
Financial support: FAPESP; CAPES

FCF184-2021

EVALUATION OF PERUVIAN NATURAL COSMETIC SAMPLES

MARJORY BERNARDES FILETO (M)[1], MONICA GUADALUPE RETUERTO FIGUEROA[2], TÉRCIO ELYAN AZEVEDO MARTINS[1], CLAUDINEIA APARECIDA SALES O. PINTO[1], MARIA VALÉRIA ROBLES VELASCO[1].

[1]Department of Drugs and Medicines, FCF/USP, São Paulo. [2] Universidad Nacional Mayor de San Marcos, Peru.

Introduction and Objectives: In the last years, the cosmetic market has been adopting the trend of using vegetable ingredients in the form of extracts or advanced formulations, adding atributes, such as conditioning in the hair fiber. This work aims to evaluate the performance of walnut (Juglans regia), cat's claw (Uncaria tomentosa) and rosemary (Salvia rosmarinus) extracts on shine and combability of hair fiber.
Material and Methods: Samples: mixture of extracts: walnut, cat's claw and rosemary at: 1.5; 0.6; 0.3%w/v with the actions: antioxidant, anti-inflammatory, astringent and antiseptic. Vehicles- (F1) ethanol, glycerin, Cetearyl Alcohol /Sodium Cetearyl Sulfate (Lanette® N) and distilled water; (F2) ethanol, glycerin, propylene glycol and distilled water. Locks of dark brown and virgin hair (15cm) were washed and evaluated (combability/ Dia-stron® MTT 175 and shine/ Glossmeter®). Subsequently, it was treated with bleaching powder and hydrogen peroxide 40 vol, then F1 or F2 were applied and evaluated again.
Results and Conclusions: In the shine test, it showed a slight increase in brightness of the discolored locks comparing with virgin hair, with no level difference of F1 and F2. The combing test indicated that the applied F2 lock required more work to comb, indicating that the hair fiber got even dry, unlike the F1 required less force and better conditioning. The results indicated the chemical treatment damaged the hair cuticules and there were influence of vehicle and active ingredients of the extracts on the surface properties.
Financing: CNPq

FCF187-2021

ASSESSMENT OF POTENTIAL PROBIOTIC PROPERTIES OF ACID LACTIC BACTERIA ISOLATED FROM RAINBOW TROUT

SARA MARIANO FRANCO (IC), WELLISON AMORIM PEREIRA (D), ANNA CAROLINA MEIRELES PIAZENTIN (D), RODRIGO CARDOSO DE OLIVEIRA (PD), RICARDO PINHEIRO DE SOUZA OLIVEIRA.

Department of Biochemical and Pharmaceutical Technology, FCF/USP.

Introduction and Objectives: Introduction and Objectives: Probiotics are products based on bacteria or yeasts that exert positive effects on host health. In this study, the probiotic properties of acid lactic bacteria isolated from rainbow trout were evaluated and a species-level identification performed by MALDI-TOF.
Material and Methods: Material and Methods: 25g of rainbow trout (*Oncorhynchus mykiss*) excrement were homogenized and aliquots of ten-fold serial dilutions were seeded in MRS and M17 media. Plates were incubated (15, 25, 32 and 37º C) for up to 48 hours in anaerobic and aerobic conditions; A total of 300 CFU were isolated and characterized by biochemical tests and morphological analysis. Strains defined as Gram-positive, catalase negative with morphology corresponding to cocci and/or bacilli were selected MALDI-TOF identification. Finally, their antimicrobial properties were assessed by agar diffusion and BLIS (bacteriocin-like inhibitory substance) sensitivity tests against bioindicator strains.
Results and Conclusions: Results and Conclusions: The strains were identified as *Lactococcus lactis* and *Lactococcus garvieae*. *L. lactis* showed resistance at low pH and at high concentrations of bile salts. On the other hand, *L. garvieae* growth was inhibited after 1 hour of incubation at pH 3. BLIS of *L. lactis* showed good inhibitory effect against *L. monocytogenes* and *S. aureus*, while *L. garvieae* was effective against *L. monocytogenes*, *S. aureus* and *S. enterica*. In conclusion, both *Lactococcus* isolates could be considered as good probiotic candidates, particularly due to their antimicrobial effects against important pathogens.
Financing: FAPESP.

FCF189-2021

DEVELOPMENT AND EVALUATION OF FLUBENDAZOLE INHALABLE NANOPARTICLES FOR LUNG CANCER TREATMENT

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Introduction and Objectives: Lung cancer presents the highest number of diagnosis and mortality rates for cancer worldwide. Considering that chemotherapy represents an important role at all treatment stages of the disease, strategies that can improve availability of the drug and patient's quality of life are urgent. Believing that inhalatory route is a promising approach for repurposing drugs for lung cancer treatment, we explore the development of inhalable dry powder formulation of flubendazole.
Material and Methods: A nanosuspension of the current antihelmintic poorly soluble drug, flubendazole, was obtained through botton-up process, and the final dry powder formulation was obtained after spray drying. Fractional factorial design was applied to better understand spray drying process parameters and formulation optimization.
Results and Conclusions: Response surface design clarified the loading limitations, with maximum of 5% for previously established quality targets. Also, the optimized condition for 15% loading was feasible through addition of 20% l-leucine, leading to improved characteristics, with flubendazole particle size of 388.6 nm, median mass aerodynamic diameter of 2.9 μm, 50.3% FPF, emitted dose of 83.2% and triple of initial solubility. Research clarifying actual possibilities and limitations of nanoparticles and engineered nanocarriers are necessary to facilitate translation of bench studies to clinical trials.
Financing: Fapesp

FCF 190- 2021

COULD OXIDATIVE STRESS BIOMARKERS BE APPLIED TO IMPROVE RISK STRATIFICATION OF PATIENTS WITH CARDIOVASCULAR DISEASE?

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Introduction and Objectives: Cardiovascular diseases involve dyslipidemia, inflammation and oxidative stress. Although the relation among these conditions is well stablished, only biomarkers associated to dyslipidemia and inflammation are current in the clinical practices for diagnosis and evaluation of the patient's treatment. Our hypothesis is that oxidative stress biomarkers could contribute to improve the current scores. The aim was investigate the association of oxidative stress, lipid profile and inflammatory biomarkers through the application of statistical multivariate tools and discuss the main limitations involved in the oxidative stress biomarkers. This information will be useful to discuss the clinical relevance and also for further inclusion of oxidative stress biomarkers as part of the scores to stratify cardiovascular risk.
Results and Conclusions: It was observed on improvement of all 7 biomarkers (Total Cholesterol; Triacylglycerol, High Density Lipoprotein cholesterol; Low Density Lipoprotein cholesterol; Total Antioxidant Capacity; Malondialdehyde and hsCReactive Protein) among the treatments. Based on dendrogram,Group II studies, showed the best association among the biomarkers and also observed a reduction of oxidized LDL-C. The relationship of lipid profile and oxidative stress was evident in our study and may contribute to discuss reference values and methodologies for oxidative stress biomarkers.
Financing: CAPES

FCF 192-2021

EFFECT OF SUPPLEMENTATION WITH RESVERATROL ON BIOMARKERS ASSOCIATED WITH ATHEROSCLEROSIS IN HUMANS

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Department of Food and Experimental Nutrition, FCF/USP [1]Department of Nutrition, FSP/USP [2]Department of Statistics, IME/SP

Introduction and Objectives: Previous studies have suggested the beneficial effects of resveratrol against cardiovascular disease (CVD). However, there are inconsistent results on cardiovascular-related biomarkers mainly because of variable dosage, intervention time and baseline characteristics of the population. This work aims to classify the studies that applied resveratrol to supplement humans according to the major biomarkers and identify which protocol characteristics would be associated with each result profile.
Material and Methods: Randomized clinical trials that assessed resveratrol effect on biomarkers related to atherosclerosis were searched in databases. We selected 12 biomarkers to compose the matrix, based on their clinical relevance and higher variation level. A total of 32 assays were obtained from these 27 studies. The net change (%) was calculated for each biomarker.
Results and Conclusions: In general, the resveratrol supplementation improved all biomarkers selected in our analysis. Applying multivariate analysis, the assays were classified into 3 clusters. Studies that composed Cluster II were characterized by a mean dose of 454.14 mg/day for 74.21 days and showed higher reduction of triglyceride concentration and blood pressure, while those composing Cluster III applied doses around 273.75 mg/day for about 175.33 days and showed the highest HDL increase. Interventions with resveratrol could be customized according to the patient condition, in terms of "dose/time of intervention". This information can be applied to combine resveratrol with drugs to reduce blood pressure or improve lipid profile in further clinical studies.
Financing: FAPESP

FCF193-2021

ADHESION PROFILE AND ANTIMICROBIAL POTENTIAL OF BACTERIOCIN-LIKE INHIBITORY SUBSTANCE (BLIS) PRODUCED BY *Lactococcus lactis*

WELLISON AMORIM PEREIRA (D), ANNA CAROLINA MEIRELES PIAZENTIN (D), RODRIGO CARDOSO DE OLIVEIRA (PD), RICARDO PINHEIRO DE SOUZA OLIVEIRA

Department of Biochemical and Pharmaceutical Technology, FCF/USP

Introduction and Objectives: *Lactococcus* spp. is one of the most used probiotics in aquaculture. In the present study, we assessed the antimicrobial potential (BLIS) of a *Lactococcus* strains and its ability to adhere to the cell lines Caco-2.
Material and Methods: Two *Lactococcus* strains were identified at species level by sequencing the 16S rRNA. Kinetic growth assay was used to assess the BLIS mode of action against important bioindicator bacterial strains, such as *Listeria monocytogenes*, *Staphylococcus aureus*, *Salmonella enterica* and *Salmonella typhimurium*. Furthermore, the ability of the *Lactococcus* strain (107 CFU/mL) to adhere to the Human Colon Adenocarcinoma Cells (Caco-2) were evaluated at 1, 2, and 4 hours of incubation in 24-well culture plates. The number of CFU/mL was determined by the ratio between the number of bacterial cells that remained attached to the monolayer and bacterial cells previously added.
Results and Conclusions: *Lactococcus* strains (B1 and B2) were identified as *L. lactis* (100% of similarity and query cover). Both strains produced BLIS with antimicrobial effect against *L. monocytogenes*. Compared to control, BLIS of both strains effectively affected *L. monocytogenes* cell growth, especially by an extension of the LAG phase. In the Caco-2 cells test, the percentage of adhesion after 1h was 77% (B1) and 93% (B2). After 2hs, B1 had 75% and B2 83%. After 4h, the adhesion was 72% (B1) and 70% (B2).
Financing: FAPESP, CAPES.

FCF194-2021

INVESTIGATION OF THE IMPACT OF EZR EXPRESSION ON THE CLINICAL OUTCOME AND BIOLOGICAL CHARACTERISTICS IN PANCREATIC ADENOCARCINOMA PATIENTS

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Department of Pharmacology, ICB/USP

Introduction and Objectives: The aim of this work is to investigate the impact of ezrin expression, a protein that link the cell membrane and actin cytoskeleton and act as oncogene, on survival outcomes, clinical characteristics, and biological functions in patients with pancreatic adenocarcinoma from the TCGA cohort.
Material and Methods: The clinical impact (overall survival, disease-free survival, and progression-free survival) of EZR expression was investigated in the TCGA pancreatic adenocarcinoma cohort (n=177) by the proportional hazards Cox regression model. To identify differentially expressed genes (DEG) the limma-voom Galaxy package was applied comparing low vs high EZR expression groups. Volcano plots computing DEG were constructed. Heatmap was constructed using Morpheus and represents the top DEG between low vs high EZR expression. DEG obtained from the Galaxy tool was used for Gene Ontology analysis and the top ten upregulated and downregulated biological and molecular processes were illustrated.
Results and Conclusions: In multivariate analysis, high EZR expression was identified as an independent risk factor for OS (HR=3.02; p=0.04) and PFS (HR=2.50; p=0.04) when analyzed with confounders: T, N, M staging, gender, age and race..In the GSEA analysis, 15 cellular and molecular events were found to be positively enriched in patients with pancreatic adenocarcinoma according to expression of EZR, which we highlight PI3K/AKT/mTOR signaling pathway, that is essential for cell growth and proliferation. Our study suggests that EZR may be a potential prognostic marker and molecular target in pancreatic adenocarcinoma.

FCF 195-2021

USE OF SPENT COFFEE GROUNDS AS ALTERNATIVE MEDIA FOR GROWTH AND PRODUCTION OF ANTIMICROBIAL COMPOUNDS BY *Enterococcus faecium*135

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Introduction and Objectives: Coffee is one of the most consumed beverages worldwide, the consumption and production increase each year, as well they residues, the spent coffee grounds (SCG) is one of the principal residues, this residue is known for being sources of cellulose, hemicellulose, and proteins, presenting potential to be used as alternative carbon sources. The study evaluated the capability of SCG to be used as alternative media to growth of *Enterococcus faecium* 135 and its ability to produce antimicrobial compounds.
Material and Methods: SCG was pre-treated with 100 mg H_2SO_4/g, 45 min, autoclaved at 140 ºC, after the hydrolysate had the pH adjusted to 6 with NaOH, and sterile filtered in a 0,22 µm cup. The phenolic compounds of the hydrolysate were reduced using a C- 18 silica column. The alternative medium was made using the same salts and protein sources presented in MRS commercial media, using the SCG detoxified hydrolysate as carbon source. The cultives were carried at 35 ºC, 100 rpm in an orbital shaker for 24 hours. After this period, it was evaluated the viability (CFU/mL), production of lactic acid and activity against *Listeria monocytogenes*.
Results and Conclusions: After the pre-treatment it was possible to recover 43.15 g/L of total sugars of SCG. The viability increased 1 log CFU/mL after 24 hours and had an activity against *L. monocytogenes* of 431 AU/mL, and a production of 8.26 g/L of acid lactic. Concluding, SCG showed as a good alternative carbon source, positively influencing in the growth, production of acid lactic and antimicrobial compounds.
Financing: CAPES, FAPESP, CNPq

FCF197-2021

DEFORMATION CHARACTERIZATION OF EXCIPIENTS BY USING A SINGLE PUNCH TABLET PRESS MACHINE

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Introduction and Objectives: Tablets are the most common dosage form due to their facility to be administered by the patients and because of their versatility to mass production of medicines. They can be produced by direct compression, dry and wet granulation of the materials. All these pathways are directly influenced by the properties of the materials and affects the final compression process. This study investigated the deformation behavior of the most used excipients in tablets formulation.
Materials and Methods: To support this study, cellulose microcrystalline of different grades (101 and 102Q), as well as anhydrous and monohydrated lactose were selected to be characterized. All materials are compressed under the same conditions, using a single punch tablet press machine. Through the machine sensors and using the Heckel analysis and plots, the materials were able to be classified by their intrinsic deformation behavior extension, into plastic, elastic, or brittle materials.
Results and Conclusions: The celluloses went through an extensive plastic deformation process, caused by crystals dislocation and their slip-planes. MC102Q has a lower yield pressure than 101Q, what causes a higher slope curve, so MC102Q undergo the plastic deformation in a relative lower compression pressure. In the other hand, the lactoses showed fragmentation deformation behavior, being brittle materials. The anhydrous was more brittle than the monohydrated lactose because its angular shapes, which are more susceptible to fractures, showing a higher Py (yield pressure). This study approach showed to be a promisor tool of formulation development, helping us to obtain a better product with quality at the end of the process.

FCF198-2021

USE OF X-RAY DIFFRACTION, PRINCIPAL COMPONENT ANALYSIS AND PAIR DISTRIBUTION FUNCTION IN THE STUDY OF STRUCTURE OF LUMEFANTRINE AMORPHOUS DISPERSIONS

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Introduction and Objectives: Differentiating between a nanocrystalline and amorphous systems can be difficult to achieve with conventional X-ray methods, especially when amorphous solid dispersions of drugs (ASD) are concerned.
Amorphous systems have great potential to improve bioavailability of poorly soluble drugs. In this study, the local structure of polymer based amorphous dispersions of Lumefantrine, an important antimalarial drug, was investigated by the combination of the Atomic Pair Distribution Function (PDF) method and Principal Component Analysis.
Material and Methods: ASD formulation samples of Lumefantrine and different pharmaceutical polymers (HPMC E3, E15, HPMCP 50, 55 and 55S) were prepared by spray drying and analyzed using high-energy synchrotron X-ray diffraction. The data was then treated using PDF methodology combined with PCA analysis.
Results and Conclusions: Amorphous Three-dimensional scatterplots of PC1, PC2, PC3 constructed from PDF analysis (Figure 1) indicated that it is possible to differentiate the spray-dried amorphous preparations of LMF. Similar mixtures regarding crystallinity and polymer type were grouped together, while significantly different mixtures ended up spread farther apart in the plot. For the first time, it was demonstrated that this approach is a useful tool to investigate the structure of amorphous polymeric preparations when paired with PDF, which would greatly assist in the development and improvement of future drug formulations.
Financing: FAPESP

FCF199-2021

NT157 REDUCES CLONOGENICITY AND INDUCES APOPTOSIS BY MULTITARGET EFFECTS ON ONCOGENIC SIGNALING PATHWAYS IN LUNG CANCER

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Introduction and Objectives: NT157 is a synthetic molecule that inhibits the IGF1R/IRS pathway, and has also shown inhibition effects in STAT3 in different tumour models. It has also been described that NT157 also affects JNK, p38 MAPK and AXL expression. Despite the relevance of those signaling pathways in lung cancer, until this date, there is no data on NT157 effects in lung cancer models. The current study aims to analyze the cellular and molecular effects of NT157 in lung cancer cells.
Materials and Methods: Colony formation assays were performed to assess the clonogenic ability of cells upon treatment with vehicle or NT157. Western blotting assays were performed to determine the effect of the drug on protein expression and activation. An apoptosis assay was performed by flow cytometry using annexin V/PI staining.
Results and Conclusions: The clonogenic ability decreased in a dose-dependent manner, and flow cytometry results indicate an increase in apoptotic cell populations when treated with NT157. Western blot assay revealed that NT157 reduces IRS1 and AXL expression, downregulates STAT3, AKT, and 4EBP1 phosphorylation, upregulates JNK, phospho-ERK, and induces PARP1 cleavage and γH2AX. In conclusion, the results indicate that the treatment with NT157 was effective in decreasing clonogenicity and increase in apoptosis in lung cancer cells, as well as was able to suppress multiple oncogenic signalling pathways.
Supported by: FAPESP, CAPES, and CNPq.

FCF200-2021

USING A FRAGMENT BASED STRATEGY TO IDENTIFY COMPOUNDS THAT INTERACT WITH *Mycobacterium tuberculosis*' MurB LIGASE.

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Introduction and objectives: New therapy strategies against tuberculosis are necessary and the enzymes from the cellular wall biosynthesis are interesting targets since they are involved in many pathogenic resistance mechanisms. Accordingly, this work targets MurB, an essential enzyme for peptidoglycan biosynthesis in *M. tuberculosis* (Mtb). In this work, we aim to identify fragment-like compounds that interact with Mtb MurB using a fragment library composed of about 600 compounds through biophysical techniques. We also expect to obtain the protein-ligand interaction using molecular docking strategies.
Materials and Methods: Mtb MurB has been obtained as a synthetic gene cloned in pET28a, expressed in LB media and purified using affinity and gel filtration chromatographies. Thermal shift assays (DSF) were performed and docking experiments simulations were effected using GOLD and Autodock Vina softwares.
Results and Conclusion: At the moment, Mtb MurB was successfully expressed, purified in a soluble fraction, and used in two Thermal Shift screening strategies, leading to 72 promising fragments. These molecules still need further confirmation through other biophysical techniques such as RMN, ITC or protein co-crystallization. Molecular docking simulation were performed with the 17 most promising compounds in order to predict the interaction with Mtb MurB, enabling the identification of 5 new lead molecules against this target and help in the discovery of new Mtb inhibitors.
Financing: FAPESP; CNPq

FCF201-2021

EVALUATION OF *Dunaliella salina* GROWTH AND CORRESPONDING β-CAROTENE PRODUCTION IN TUBULAR PHOTOBIOREACTOR

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Introduction and Objectives: The purpose of this study was to investigate the influence of different amounts of sodium nitrate (1N= 75 mg L^{-1}; 1.5N = 112.5 mg L^{-1}, and 3N = 225 mg L^{-1}) and phosphate monobasic dehydrate (1P = 5.65 mg L^{-1}, 1.5P = 8.47 mg L^{-1}, and 3P = 16.95 mg L^{-1}) on the growth of *D. salina* (green microalgae) and β-carotene (natural pigment and pro-vitamin A) biosynthesis, by semicontinuous process with different replenishment proportions (R = 20% and 80%). β-carotene have been thought to have anti-cancer activity.
Material and Methods: The cultivations were carried out in two stages. At first, it was carried out in tubular photobioreactor, with the aim of obtaining high cell concentration. In the second stage, cells removed from the photobioreactor (from startup batch process and up to three sequential cycles) were submitted to stress condition by simultaneous lack of nutrients and high pH, in Erlenmeyer flasks (carotenogenesis induced). β-carotene was quantified by High Performance Liquid Chromatography
Results and Conclusions: Best results of cell productivity were obtained by semicontinuous process. Maximum cell density (Xm) obtained was not dependent of R, but the best results were obtained when using medium 1.5N:1.5P instead of 1N:1P. The content of β-carotene in the cells, in general, was higher in cells grown in medium 1N:1P in comparison with medium 1.5N:1.5P. The cultivation of *D. salina* with media 3N:3P led to a long lag phase, followed by decrease in cell density and cell lysis. The use of a tubular photobioreactor contributed to successfully cultivate this microalga without contamination by protozoa.
Financing: CAPES

FCF202-2021

EVALUTION OF CORTEX DAMAGE IN CHEMICHAL TREATED HAIR

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Introduction and Objectives: The cortex is primarily responsible for the force properties in human hair. The traction properties are an index of the cortical damage. The objective of this research was to evaluate the tensile pro-perties of the virgin hair fibers, bleached, dyed light (TLC) and ultra light blonde (TUC).
Material and Methods: Material and Methods: Fifteen strands of each lock hair were randomly selected and measured by micrometer Mitutoyo ® in three different lengths. Its average value was used to calculate the cross-sectional area of hair fiber and each strand was taken to Dia-stron ® MTT 175 to perform the tensile rupture test. This was performed at 100mm/min and extension of 200%. The mean of the cross- sectional area with the breaking strength was used to calculate the tensile strength (gmf.mm²).
Results and Conclusions: The mean values of the tensile strength in the hair fiber were (gmf.mm²): Control (CT): 4,03E+07; discoloured (DD): 2,44E+07; dyed light blonde (TLC): 1,01E+07; dyed ultra light blonde (TUC): 9,46E+06. The strands dyed TLC and TUC showed statistically equal results, however, when compared to the control, showing a decrease of ±75% in their resistance hair fiber, demonstrating a lower force needed to break them. Concluding, the discoloration and dyeing process modified the hair fiber integrity, causing irreparable damage fiber due to severe oxidation process in the cortex, making the hair dehydrated, fragile and brittle, directly interfering with hair health.
Financing: FAPESP.

FCF203-2021

ROLE OF LEUKOTRIENES AND RAS IN MUSCLE AND LIVER FROM TYPE 1 DIABETIC MICE

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Introduction and Objectives: Type 1 Diabetes (T1D) is a disease associated with several physiological disorders. Increased renin-angiotensin system (RAS) components, deregulated autophagy, and the presence of leukotrienes (LTs) is linked to diabetogenesis. Therefore, we investigated the involvement of RAS and LTs in muscle and liver of mice with T1D.
Material and Methods: T1D were induced with streptozotocin (STZ) in 129sve mice and 129sve mice LTs KO ($5LO^{-/-}$) and to inhibit RAS, mice were treated with captopril (C). Plasma and mice tissues were used for further analysis. This study was approved by CEUA no. 08/2014 - book 03 - ICB/USP
Results and Conclusions: Plasma levels of non-esterified fatty acids (NEFA) from $5LO^{-/-}$ T1D mice treated with C was decreased together with decreased plasma levels of resistin and leptin, despite the treatment with C or the presence of LTs. In insulin tolerance test, T1D $5LO^{-/-}$ mice had better insulin sensitivity with treatment with C. In muscle, treatment with C increased RAS, insulin receptor (IR) and autophagy (A) markers. In liver, the treatment with C increased the expression of RAS and IR markers. Our results suggest that LTs contributes to the development of insulin resistance in T1D and a possible role of C in insulin sensitivity and activation of autophagy.
Financing: CAPES; CNPq; FAPESP

FCF204-2021

APPLICATION OF METHODS TO ESTIMATE THE CHEMICAL COMPOSITION OF DISHES CONSUMED IN BRAZIL

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Introduction and Objectives: Estimate the chemical composition of dishes consumed by the Brazilian population and make them available in the Nutrient Intake Evaluation Database (TBCA BD-AIN) and the computational tool, Nutri (Intelligent Solutions in Nutrition), under development.
Material and Methods: The study was carried out in three steps: (i) definition of the standard recipe for the dishes consumed by the Brazilian population; (ii) definition of the calculation estimation method; and (iii) classification of dishes. In the first step, a standard recipe was defined, commonly used by the Brazilian population, and cited in the National Dietary Intake Survey (POF/IBGE, 2020). In the second step, the methods to estimate the chemical composition of the dishes were defined: (i) direct method – the proportion of prepared ingredients; (ii) indirect method – from raw ingredients and application of factors (Giuntini et al., 2019). In the third step, the calculated dishes were classified for use in the computational tool.
Results and Conclusions: New foods were grouped into 3 categories: soft foods (524 sweet and savoury dishes), vegan foods (44 dishes), and vegetarian foods (9 dishes). To calculate the chemical composition of the dishes with texture change, the direct estimation method was used. The indirect method was used to calculate the chemical composition of the vegetarian and vegan dishes. All 5,227 foods were classified into 'food types' in the TBCA BD-AIN. In addition to the calculation of the significant number of dishes, including those with new characteristics, TBCA BD-AIN foods were classified according to the types of dishes. This classification of the food, combined with the data of chemical composition, will allow the computational tool under development to elaborate personalized menus.

FCF205-2021

ROLE OF HYPERGLYCEMIA AND INFLAMMATION IN BONE MARROW DERIVED MACROPHAGES IN TYPE 1 DIABETES

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Introduction and Objectives: Hyperglycemia damages the immune system, turning diabetic patients more susceptible to infections. This high susceptibility is caused, at least in part, due to an inadequate immune response. Thus, the aim of this study was to evaluate the influence of hyperglycemia in bone marrow derived macrophages (BMDM) from diabetic and non-diabetic animals, with lipopolysaccharide (LPS)-induced response.
Material and Methods: T1DM was induced by alloxan (60mg/kg, i.p) [CEUA/FCF/USP nº570/2018]. BMDM from diabetic (D-BMDM) and non-diabetic (ND-BMDM) C57BL/6 mice were used. Macrophages were maintained in culture medium with normal (5.5 mM) and high glucose (25 mM) concentration, stimulated or not with LPS (100 ng/mL) and Nigericin (20μM), at the times of 30 minutes, 2, 4, 6, and 24 hours. Cytokines were dosed by enzyme immunoassay (EIA) at all times.
Results and Conclusions: Alterations in the secretion of pro-inflammatory cytokines IL- 6, IL-1β and TNF-α were verified, where BMDM stimulated with LPS+Nigericin showed an increase in the secretion of these cytokines. D-BMDM showed a decreased after 2 hours in TNF-α secretion in normoglycemic and hyperglycemic medium with LPS+Nigericin stimulation, when compared to the control group. However, D-BMDM showed an increased in IL-1β secretion in normoglycemic and hyperglycemic medium with LPS+Nigericin stimulation at all times. Therefore, with our results we can suggest that hyperglycemia affects cytokines secretion, performing an important role in the inflammatory response of BMDM in diabetic mice, given that alterations on the secretion of these proteins may have an impact in the immune response against infections.
Financing: FAPESP, CNPq, CAPES

FCF206-2021

IMPACTO OF ALLOXAN AND STREPTOZOTOCIN ON IMMUNOLOGICAL PARAMETER OF T LYMPHOCYTES IN DIABETIC MICE INDUCED

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Introduction and Objectives: Alloxan (ALX) and streptozotocin (STZ) are amply used to induce type 1 diabetes (T1D) in animal models. This study aims to evaluate the differences in immune parameters of T lymphocytes caused by ALX and STZ in T1D induced mice.
Material and methods: T1D were induced in C57BL/6J mice by ALX or STZ and the animals were evaluated for: Hematological parameters; Immunological and morphological analyses in the thymus, spleen and pâncreas.
Results and conclusions: Both ALX and STZ induced a decrease in the blood leukocytes and lymphocytes, compared to control mice (CT). STZ mice show increase in neutrophils and reduction in lymphocytes percentage in bone marrow. The STZ mice showed a decrease of T lymphocytes in the thymus, and B lymphocyte in pancreas and spleen, and the ALX mice showed an increase in T and B cells only in thymus. Both diabetic groups showed morphological alterations in thymus and pancreas. Reduced *in vitro* activation of lymphocytes was found in STZ mice. Mice immunized with ovalbumin (OVA) showed a more intense antigen-specific paw edema response in the STZ mice. The effects of the ALX and STZ influenced lymphoid organ and their cell populations.
Financial: FAPESP, CNPq

FCF207-2021

LACTIC ACID BACTERIA FERMENTATION HYDROLYSES GLUTEN AND MAY DECREASE ITS IMMUNOREACTIVITY IN VITRO

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Introduction and Objectives: Nitrogen plays an important role for the metabolism of lactic acid bacteria (LAB). Several LAB species present an efficient proteolytic system able to produce enzymes that can hydrolyze food proteins involved in food allergy. Gluten is a protein complex that can trigger disorders like wheat allergy and celiac disease. This study investigated the effect of *Enterococcus* (E.) *faecalis* fermentation on the extension of gluten hydrolysis and on its immunoreactivity in vitro.
Material and Methods: Two gluten-proteolytic *Enterococcus faecalis* (EF004 and EF023), isolated from French foods, were used to ferment gluten broth. The extension of gluten hydrolysis after fermentation was evaluated by Reverse phase high performance liquid chromatography with UV and High-Resolution Accurate Mass Spectrometry detection. The immunoreactivity of the fermented samples was assessed by Western blot. For all analysis, an acidified gluten broth (pH 4) was used as negative control.
Results and Conclusions: Fermentation by *E. faecalis* 004 and 023 decreased the gluten content and released several different peptides with lower immunoreactivity to gluten specific polyclonal and monoclonal antibodies in vitro. Proteolytic LAB can be explored to decrease the immunoreactivity of food proteins, as gluten, by fermentation and rises as a potential tool to develop hypoallergenic foods or bio-therapeutic supplements.
Financing: FAPESP

FCF213-2021

EVALUATION OF THE PRESENCE OF TRANS AND SATURATED FATTY ACIDS IN STUFFED COOKIES AND WAFERS PRODUCED IN BRAZIL

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Introduction and Objectives: The consumption of trans fatty acids in food has been related to circulatory problems. The WHO in 2018, recommended its total elimination by the year 2023. Thus, in Brazil in 2019 the RDC 332 stated that as of January 1, 2023, the production of partially hydrogenated fat is prohibited. Currently, the legislation in force on trans fat is the RDC 54 from ANVISA. The objective of this study was to evaluate the levels of trans and saturated in stuffed cookies and wafers, evaluating the amount of trans and saturated fats present in these foods and comparing the results with the RDC 54.
Material and Methods: One hundred and three samples of stuffed cookies and wafers were analyzed. The methodology used to determine the fatty acids in the cookies was AOAC 996.06. Fatty acid composition was performed by GC1020 Shimadzu gas chromatograph. The results were expressed in g per 100 g of sample and g/portion.
Results and Conclusions: Sixty-three stuffed cookies and 40 wafers were analyzed, with trans fat contents of 0.03 to 5.21 g per 100 g and 0.03 and 8.54 g per 100 g in the stuffed cookies and wafers, respectively. Therefore, it was found that some brands of stuffed cookies and wafers still have large amounts of trans fat in their composition, causing health risks for the consumer. In relation to stuffed cookies and wafers with the absence of trans fat on the labels, the vast majority were not in accordance with RDC 54. Therefore, the urgent need for changes in current legislation and more frequent inspections by the competent bodies, and the prohibition of trans fatty acids, due to the harmful effects of consuming this type of fat on the health of the population.
Financing: CNPQ.

FCF217-2021

EFFECT OF L-ASPARAGINASE II FROM *E. coli* ON HUMAN MELANOMA CELLS

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Introduction and Objectives: Melanoma patients harboring BRAF mutation can be treated with MAPK inhibitors, e.g. Vemurafenib, but may exhibit drug resistance and increased tumor invasiveness in response. In treatment of solid tumors prone to metastasis, L-asparagine restriction has been shown to have pharmacological potential. An efficient strategy for depletion of this amino acid is treatment with the enzyme L-asparaginase (ASNase). The objectives of this work are to analyze the effect of ASNase and combinatory treatment of ASNase and Vemurafenib on viability and metastasis in human melanoma cells $BRAF^{V600E}$.
Material and Methods: asnB/pET-15b plasmid and *E. coli* BL21(DE3) were used to obtain ASNase. The enzyme was obtained by: induction of expression with IPTG and purification by chromatography. Evaluation of enzyme was perfomed by SDS-page and Nessler's reagent. *Mycoplasma* sp. detection was performed by PCR. The cell lines used were SK-MEL- 28 and SK-MEL-28 resistant to Vemurafenib. Analysis of the effect of treatment with ASNaseII and combinatorial treatment with ASNaseII and Vemurafenib after 72h on cell viability was performed by MTT assay.
Results and Conclusions: The ASNaseII half-maximal inhibitory concentration for the cell lines is around 0.20 UI/mL. Inclusion of ASNaseII in concentrations less than or equal to 0.2 IU/mL in Vemurafenib treatment protocols ranging from 1 to 6 µM does not significantly alter the number of metabolically viable cells of sensitive or resistant human melanoma cell lines. These results are interesting since little is known about the subject. Further on, effect on metastasis process will be analyzed.
Financing: CNPq; FAPESP

FCF218-2021

USE OF MICROREACTORS FOR DETERMINING KINETIC AND THERMODYNAMIC PARAMETERS IN THE SYNTHESIS OF AN LOBEGLITAZONE INTERMEDIATE

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Introduction and Objectives: It was determined the kinetic and thermodynamic parameters in the synthesis of 2-[[6-(4-methoxyphenoxy)pyrimidin-4-yl]methylamino]ethanol (2L), through the Arrhenius and Eyring model, using continuous flow microreactors. This compound is the second intermediate product of Lobeglitazone synthesis, used in the treatment of diabetes mellitus.
Material and Methods: Two solutions were prepared: (A) 4-chloro-6-(4-methoxyphenoxy)pyrimidine (1) in ethanol (B) 2-methylaminoethanol (2) in ethanol. Both solutions were fed into the microreactor at the appropriate flow rates. Mean residence times (t) 1 to 20 min and temperatures (T) 65 to 160°C were studied. Samples were collected for HPLC- UV analysis for quantification of the reactant 1 and calculation of half-life time ($t_{1/2}$), reaction rate constant (k), activation energy (Ea); enthalpy (ΔH), entropy (ΔS) and Gibbs free energy (ΔG) in the Transition State (TS).
Results and Conclusions: The $t_{1/2}$ values at 140 and 160°C (t = 8 min) suggests that the reaction is controlled by kinetics. The k value increases with temperature, T, being 14 times higher at 160°C than at 65°C ($k = 0.37x10^2$ and $7.15x10^{-1}$ M^2 s^{-1}, respectively). ΔG increased 18.5%, from 99.3 to 117.6 kJ mol^{-1}, with the increase of temperature from 65 to 160°C, respectively, suggesting that the increase of Gibbs free energy is directly related to the variation of TΔS values. Negative values of TΔS were obtained, suggesting that the entropy in the transition state (TS) is lower than that of the reagents, suggesting that the reaction of synthesis of (2L) is bimolecular and thermodynamically favorable.
Financing: FAPESP; CAPES

FCF220-2021

CHEMICAL CHARACTERIZATION OF Echium plantagineum SEED OIL OBTAINED BY THREE METHODS OF EXTRACTION

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Introduction and Objectives: Echium seeds oil has been considered an important non-GMO alternative to marine oils as a source of omega 3 fatty acids supplementation, due to its high proportion of stearidonic acid. The process applied to the seeds can affect the chemical, physical, functional and sensory characteristics of the extracted oil. Thus, we aimed to determine chemical and sensory parameters of the oil obtained from *Echium plantagenium* seeds submitted to three extraction procedures.
Material and Methods: Extraction procedures of *Echium* seeds- Hydraulic press: HYD; continuous screw press: PRESS; and solvent technique: SOLV. A blend of PRESS and SOLV samples was mixed only for the sensory analysis.
Results and Conclusions: The extraction method changed minor compounds such as gamma-tocopherol, campesterol, beta-sitosterol, phenolic compounds, beta-carotene and chlorophyll, changing the color of the samples. Some of these minor compounds were oxidized during the extraction procedure, mainly using hydraulic pressing. Our data showed that the type of extraction process changes the chemical composition of the echium oil, but these alterations did not reduce its nutritional quality or sensory acceptability. However, the oil obtained from screw press, followed or not by hexane extraction, showed higher concentration of phenolic compounds, improving the health attributes of the echium oil for human consumption.
Financing: FAPESP

FCF221-2021

IMPACT OF EXOGENOUS MEJA AND ETHYLENE ON PRIMARY AND SECONDARY METABOLISMS IN TOMATO (*Solanum lycopersicum* L. cv. Grape)

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Introduction and Objectives: The interaction of MeJA with phytohormones can promote the production of secondary metabolites with biological activity, which can result in many benefits to human health due to the antioxidant property. In this context, efforts to manipulate tomato by using postharvest hormonal treatment in order to improve metabolites levels that are important to plant growth and human nutrition have received considerable attention. The aim of this study was to show the impact of metabolic profile on quality and nutritional properties under exogenous ethylene and MeJA during fruit ripening.
Material and Methods: The treatments were performed using 100 ppm of gaseous ethylene and 100 ppm of MeJA during 24 h. Ethylene emission, fruit surface color and metabolomics analysis were measured at 4, 10, and 21 days after harvest, considering the untreated fruits as control group.
Results and Conclusions: Ethylene positively impacted sugars mainly fructose, sucrose and glucose during ripening; while MeJA increased organic acids (citric, succinic, malic, oxaloacetic and fumaric acids) and amino acids (glutamic acid, glutamine, GABA, aspartic acids, tryptophan and phenylalanine) at 10 DAH; and fatty acids at 4 DAH. Regarding secondary metabolites, accumulation of carotenoids levels (mostly lycopene) were induced by both hormonal treatments, at 10 and 21 DAH by MeJA and ethylene, respectively. Tocopherols and phytosterols were impacted positively by MeJA followed by ethylene at 10 DAH. Most of the metabolites changes contributed to the sensory and nutritional value of the fruits, proposing that the MeJA and ethylene can be applied as tools to improve the quality of the tomato.
Financing: FAPESP; CAPES

FCF222-2021

ASSESSMENT OF ACUTE TOXICITY OF CYANOBACTERIAL EXTRACTS USING THE BRINE SHRIMP (*Artemia salina*) LETHALITY ASSAY

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Introduction and Objectives: Cyanobacteria are considered a rich source of specialized metabolites with potential for pharmaceutical and biotechnological applications. Several natural products produced by these organisms display therapeutically relevant activities, such as antimicrobial, antiviral, anti-inflammatory, cytotoxic, and anticancer. To identify biologically active metabolites, acute toxicity assays are useful in the early detection of natural products with cytotoxic or potential anticancer activities. In this work, six extracts of different cyanobacterial strains in culture and three extracts from freshwater cyanobacterial blooms were obtained and evaluated for acute toxicity using the brine shrimp microcrustacean (*Artemia salina*) lethality assay.
Material and Methods: *Artemia salina* cysts were incubated in artificial seawater at 25°C for 24h under constant aeration. After hatching, 1 µL of DMSO solutions of cyanobacterial extracts in different concentrations were added to 99 µL of the seawater solution containing 10-15 nauplii. After 24 hours, deaths were recorded. Potassium dichromate was used as positive control and DMSO as negative control.
Results and Conclusions: Two of the nine tested extracts showed toxicity (LC50<1000 µg/mL). Their computed LC50 values were 415 µg/mL (cultured *Anagnostidinema amphibium*) and 383 µg/mL (field collection, assemble containing *Microcystis aeruginosa*), which classifies both as moderately toxic. These extracts will be subjected to bioassay-guided fractionation and dereplication for the identification of the bioactive compounds.
Financing: PUB-USP, FAPESP

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INFLUENCE OF *Lactobacillus acidophilus* LA5 ON THE COMPOSITION OF THE GUT MICROBIOTA USING AN IN VITRO GUT MICROBIOME MODEL

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Introduction and Objectives: The gut microbiota refers to the microorganisms that inhabit the intestinal tract and live-in symbiosis with the host. A microbiota in dysbiosis can induce inflammation in different parts of the human body. Therefore, the use of probiotics can help in modulating the microbiota in dysbiosis. The aim of this study was to verify the impact of *Lactobacillus acidophilus* - LA5 on the intestinal microbial composition of adults (40-50 years) using the Simulator of Human Intestinal Microbial Ecosystem (SHIME®).
Material and Methods: The experimental period in the SHIME® was 6 weeks. After 7 and 14 days of colonic fermentation, the gut microbiota (16S rRNA gene sequencing) and metabolites (Short Chain Fat Acids) were analyzed. Statistical analyses were performed using ANOVA and Tukey's multiple comparison test as well as bioinformatics analysis for microbiota diversity.
Results and conclusions: The effect of La5 on the microbiota composition occurred during the 14 days of treatment, as an increase in the abundance of Bacteriodetes and a decrease in Firmicutes. Analysis of the relative abundance of the main families showed a change during the treatment, through an increase ($p<0.05$) of the families Veillonellaceae and Bacteriodaceae and a decrease ($p<0.05$) of Ruminococcaceae. There was a significant increase of some genera such as *Bacteroides* and *Mitsuokella* and a decrease of *Achromobacter* and *Catabacter*. Megasphaera spp. stimulated with the La-5 treatment has been reported to produce gut metabolites and recognized to contribute to increased anti-inflammatory and immune responses. Finally, this study showed a positive and promising result of La-5 treatment in increasing gut homeostasis.
This work was carried out with the support of CAPES-Funding Code 001 and FAPESP

FCF226-2021

BIOLOGICAL EFFECTS OF SULFATED POLYSACCHARIDES ON CANCER CELL

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Introduction and Objectives: Cancer is one of worldwide main cause of death, with more than 10 million people in 2020. The search for compounds with anticancer activities as adjuvant treatment for chemotherapy is continuous. Studies have indicated anticancer effects of sulfated polysaccharides found in foods, and some of these polysaccharides show structure similarities to heparin or chondroitin sulfate, which can inhibit the protein midkine. The midkine is a growth factor which the high expression is associated with the proliferation and survival of tumors and could be a target to be explored in cancer treatment. The aim of this study is to evaluate the biological effects of commercial sulfated polysaccharides from different seaweeds in culture of cancer cell that express midkine.
Material and Methods: For an initial screening, cancer cells were analyzed for midkine expression by western blotting. After the selection of midkine$^{+/+}$ cells, the effects of food sulfated polysaccharides, fucoidan, and carrageenans kappa, iota and lambda, on cell viability were evaluated.
Results and Conclusions: Midkine$^{+/+}$ HepG2 cells (hepatocarcinoma) were treated with samples. It was observed a decreased on HepG2 viability for all of sulfated polysaccharides evaluated, mainly on 1000 and 2000 µg/mL concentrations and after 72h of incubation. The decrease of cell viability was higher using lambda carrageenan and fucoidan. With the follow up of investigation of biological effects on HepG2, we expect to identify food sulfated polysaccharides with anticancer effects in *in vitro* assays and the possible interaction with midkine, which can be used as chemotherapy adjuvant or dietary supplements.
Financing: CNPq, FAPESP

FCF227-2021

ENDOTOXIN TEST VALIDATION BASED ON RECOMBINANT FACTOR C FOR NORMAL SALINE INJECTION

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Introduction and Objectives: Endotoxin contamination is a threat to the safety of pharmaceuticals products, especially parenteral drugs. Any sterile and/or pyrogen-free pharmaceutical product requires regulatory specifications to ensure patient safety. This study covers the first part of a validation investigation of an endotoxin quantitation commercial kit based on recombinant factor C (rFC - Endozyme II® Go) for large volume parenteral solutions.
Material and Methods: The samples were spiked with endotoxin solutions between 0.0005 and 10 EU/mL and tested by the rFC kit to evaluate precision, accuracy, detection and quantification limits, linearity, and robustness. We assayed each of the six points at least five times.
Results and Conclusions: The relative standard deviation (RSD) for precision testing ranged from 1.9 to 8.3 %. The recovery accuracy values of endotoxin were between 61 % and 125 % for the range from 0.005 to 10 EU/mL. There was 8.0 % of invalid data along with the study: 4.6 % related to sample/PPC recovery and 3.4 % related to sample/PPC RSD. The results demonstrated that the rFC method allows endotoxin quantification with accuracy, precision, specificity, and linearity for the range of 0.005 and 10 EU/mL for parenteral use of saline.
Financing: FAPESP

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WORKING DILUTION DETERMINATION OF ANTIBOTHROPIC AND ANTI- TETANUS HYPERIMMUNE SERUM FOR ENDOTOXIN TEST BY RECOMBINANT FACTOR C

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Introduction and Objectives: The recombinant factor C (rFC) method is an option for endotoxin test in products that have complex matrices and that currently suffer interference when tested by the LAL method, such as hyperimmune sera. The objective of this work was to determine the working dilution of antibothropic and anti-tetanus hyperimmune serums that presents recovery values between 50 and 200% for the positive product control (PPC), to be used in a validation study of the rFC endotoxin determination assay.
Material and Methods: Antibotropic and anti-tetanus hyperimmune serums were tested undiluted, 1:10 dilution (v/v), and 1:100 dilution (v/v), in non- pyrogenic water. The three solutions of each serum were transferred individually to twenty wells of EndoLISA® microtiter plate, five replicates of sample and PPC were tested in duplicate, according to the kit manufacturer's guidelines. The PPCs were spiked, additionally, with 5 EU/mL of control standard endotoxin.
Results and Conclusions: The average recovery values of endotoxin for antibotropic and anti-tetanus serum were, respectively, 26.8%/1.2% (undiluted), 69.8%/56.6% (dilution 1:10) and 99.2%/103.4% (dilution 1:100). The results demonstrated that the rFC method allows the PPCs recovery from 50-200% for the 1:10 and 1:100 dilutions. The undiluted samples were considered to contain interfering factors preventing the use of the tested endotoxin kit. The results indicate that under the evaluated conditions, the reagent has the potential to be used for serum endotoxin determination in a validation study.
Financing: FAPESP

FCF229-2021

FLOW SYNTHESIS OF 2-((6-(4-METHOXYPHENOXY)PYRIMIDIN-4-YL)AMINO)ETHANOL

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Introduction and Objectives: The present study aimed to synthesize the 2-((6-(4- methoxyphenoxy)pyrimidin-4-yl)amino)ethanol in capillary micro reactor by replacing the usual reactant 2- methylaminoethanol by 2-aminoethanol. This product is the second intermediate of a drug analogous to the Lobeglitazone (Duvie®), a glitazone used in the treatment of type 2 diabetes mellitus.
Material and Methods: To study the synthesis in flow in capillary micro reactor, the reaction procedure was adapted from the batch process and the reactants solutions were fed separately to the microreactor. The use solvents in temperatures above the normal boiling points is of one of the advantages of Micro reactor Technology (MRT). It was tested the temperatures 65, 78, 100, 120, 140, 160 °C, mean residence
times of 1, 2, 4, 8, 12, 16 and 20 min using ethanol as a green solvent. The product yield and reactant conversion were calculated through analysis of reactant and product concentration determined by HPLC- UV.
Results and Conclusions: It was verified that the use of micro reactor benefited the reaction with the possibility of increasing the temperature above the normal boiling point. At 65 °C, the product yield was 6.1%; 78 °C, 11% and at 100 °C, 30%. However, for temperatures of 120, 140 and 160 °C, the yield was substantially high, 52, 70 and 85%, respectively, demonstrating the feasibility of the MRT, by achieving extreme reactional conditions with safety and maximizing the product formation. In sequence to this work, the flow synthesis will be compared with the batch process, comparing the parameters production, productivity, intensification rates and number of equivalent micro reactors.
Financing: FAPESP, CAPES

FCF230-2021

BIOLOGICAL EFFECTS OF PECTINS EXTRACTED FROM DIFFERENT TYPES OF FRUIT ON THE TREATMENT OF INTESTINE CANCER CELLS

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Introduction and Objectives: Pectins are soluble dietary fibers that may exhibit antitumor activity by interacting with the protein GAL-3 and by other apoptosis- inducing mechanisms. The project aims to establish the relationship between the chemical compositions and structures of modified and unmodified chayote, papaya and passion fruit polysaccharides with likely beneficial effects of their consumption on health.
Material and Methods: Previously extracted pectin samples, followed 3 paths: 1) Extraction with water giving the water-soluble fraction (WSF). 2) Extraction with water and subsequent chemical modification (WSF EM). 3) Modification and then extraction with water (WSF ME). The chemical modification of the pectins was done by methodology Staples; Rolke (2013). The fractions were analyzed by HPSEC and by HPAEC to determine the molecular weight and sugar composition. Hemagglutination, according to Ogawa et al. (1995) and Gong et al. (1999), for affinity analysis with GAL-3. Colorimetric Assay of Cell Viability by MTT Reduction. Flow cytometry for cell cycle analysis (BD Cycletest Plus DNA) and apoptosis (PE Annexin V Apoptosis Detection KIT). Analysis of gene expression by qPCR according to MIQE.
Results and Conclusions: The chemical modification of pectins improved the biological activity. Pectins decreased cell viability by multiple mechanisms. Cell cycle arrest (GOG1-S), induction of late apoptosis and alteration in the expression of genes related to apoptosis, regulation, migration, differentiation, and cell proliferation were observed. These findings increase the possibilities of the emergence of new types of food supplements that can be used as inducers of apoptosis by multiple mechanisms.
Funding: CAPES; CNPQ; FAPESP.

FCF232-2021

A PUBLIC COHORT OF MELANOMA PATIENTS EXPLORING REDOX- RELATED PROTEINS: HARNESSING THERAPEUTIC BENEFITS

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Introduction and Objectives: Melanoma is the most aggressive type of skin cancer and despite the available therapies, minimum residual disease is still refractory. ROS/RNS play a dual role in melanoma and redox proteins modulate the disease by controlling ROS/RNS levels from initiation to metastasis and resistance. These proteins could act as biomarkers and targets. So, antioxidant blockade could be exploited for therapeutic benefits. We analyzed information obtained from a public cohort of melanoma patients about the expression of redox-related proteins during the disease stages.
Material and Methods: Micro-array data containing samples from 18 common nevi, 11 dysplastic, 8 radial phase growth, 15 vertical phase growth and 5 melanoma metastases was used (GEO- GSE12391). The statistical analysis was ANOVA followed by Tukey post hoc test.
Results and Conclusions: NOS2, SOD1, GPX1, NOX2, NOX4, PRX1, PRX4, PRX5 and PXDN are increased in vertical growth phase, while SOD3, CAT, GSTT1, NOX1, PRX2 and PRX6 are decreased. NOS2, GSR, NOX2, NOX4, PRX3, PRX4 and PRX6 are increased in metastasis, while SOD3, CAT, GLRX, GSTP1, GSTT1, TXN, PRX1, PRX2 and PRX5 are decreased. It evidences that different isoforms of the same protein could play opposite roles and the same isoform could be increased or decreased depending on the stage of the disease. We believe that by understanding redox homeostasis in melanoma drug resistance we would open up a new hunting ground for targets in the development of combined therapy, avoiding non-specific therapies.
Financing: FAPESP, CNPq, CAPES.

FCF233-2021

THERMAL MODIFICATION OF PASSION FRUIT PECTIN DECREASED THE VIABILITY OF HUMAN COLON CANCER CELLS

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Introduction and objectives: Dietary fiber is known as one major beneficial food component for human health, including anticancer potential. Pectin is a soluble fiber and is commonly found in vegetable sources. Structurally modified pectin has had their anti- carcinogenic effect suggested and studied through diverse mechanisms, such as cell cycle restoration or interruption, proliferation pathways and Galectin-3 inhibition and immune modulation. An important candidate for modified pectin source is the yellow passion fruit (*Passiflora edulis f. flavicarpa*), which is majorly composed of homogalacturonan chains. The aim of the present study is to test a thermic treatment for pectin extraction, characterize the obtained matrix and analyze potential biologic effects in cell culture of colon cancer cells.
Material and methods: The commercially obtained fruits were peeled, the mesocarp extracted, dried and crushed. The flour was purified with four different methods and submitted to two different periods of thermal treatment (120 ºC), 30 and 60 minutes (P1 and P2, respectively). The monosaccharide composition, molecular size and yield were obtained, and HCT-116 cells were treated with the samples.
Results and discussion: All samples were majorly composed of galacturonic acid (>96%). The total cell wall related yields were influenced by exposition period. P2 had higher yield in two different samples (81.6 x 53.9 % and 65.6 x 54.6 % against P1). As expected, P2 had lower molecular weights compared to P1, between 74 and 95 kDa in comparison to >670 kDa. The HCT-116 cells were treated with the modified pectins at a 0.2% final concentration, and showed a decrease in viability compared to control, demonstrating new bioactive compounds were formed.
Financing: CNPq; FAPESP

FCF234-2021

DEVELOPMENT OF BOARD GAMES FOR DISCIPLINES IN HIGHER EDUCATION

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Introduction and Objectives: The use of games and differentiated activities for didactic purposes is an alternative to the usual teaching and learning model, very centered on the teacher's figure. The implementation of games in academia, provides a different perspective and ways of reasoning different from those used in traditional teaching methods. The adoption of games as a teaching methodology demonstrates several advantages, such as encouraging healthy competition and interdisciplinarity. Besides, they promote a collective exchange of experience and work with various behavioral skills, such as the exercise of reasoning, motivation, teamwork and interpersonal relationships. Therefore, it is desired to promote a distinct and dynamic teaching methodology in which the student has active participation with the inclusion of games developed by the Farmagamers group. The idea is, moreover, to offer a more playful and fun approach, deviating a bit from the traditional model.
Material and Methods: Other existing games were used for research purposes; later, characteristics that would best meet the objective were selected. In this way, boards, cards and other elements were fit, perfecting the games developed by the group. The method consists of applying them in the classroom and observing student adherence and retention of concepts.
Results and Conclusions: The game FarmaHistory was applied in the classroom in 2019, which had a very positive response and broad student's participation. The methodology was identified by students as a good teaching tool. Therefore, it is expected to be able to apply the other games developed by the group in person and broadly in the future.
Financing: Programa Unificado de Bolsas

FCF235-2021

MAIN CLINICAL VARIABLES FOR THE COVID-19 PATIENTS' MANAGEMENT AT THE COMPREHENSIVE HEALTH CARE IN BRAZIL: SYSTEMATIC REVIEW PROTOCOL

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Introduction and Objectives: The epidemiological reach of COVID-19 has aroused concern around the world. Understanding the influencing factors of the disease can reduce the burden on health systems and negative economic impacts. The objective is to understand and relate the variables that have been associated with the clinical management of the disease.
Material and Methods: The systematic review protocol followed Cochrane guidelines, progressing through the stages of search, selection, extraction, compilation, analysis and results. Pooled standardized mean differences and 95% confidence intervals will be calculated. The risk of bias of observational studies will be assessed using Downs and Black instrument.
Results and Conclusions: To represent the search strategy, three PRISMA flowcharts were created for the levels of health care. Data from the included studies are being extracted and their quality is being assessed. Consent between authors was analyzed using Kappa coefficient (0.70). The protocol of this review intends to investigate subgroups at each level of health care, including confounding factors: analyzing the difference in groups between the variables age and sex, for example. This protocol showed a robust method to conduct systematic reviews to identify clinical variables associated with COVID-19.
Financing: FAPEMIG

FCF240-2021

RATIO BETWEEN CITRUS FLAVANONES-PHASE II METABOLITES AND THEIR GUT-DERIVED PHENOLIC ACIDS DETERMINE THE RESPONSE IN CARDIOMETABOLIC BIOMARKERS

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Introduction and Objective: A large heterogeneity in biological response after orange juice intervention is observed and partly due to the large inter-individual variation in their bioavailability. This work aimed to identifiy subjects responsive to orange juice consumption according to citrus flavanones-phase II metabolites and gut-derived phenolic acids.
Material and Methods: In a single-arm study, volunteers consumed orange juice for 60 days. Anthropometric parameters and blood were collected before and after the intervention. The 24- hour urine was collected after single dose of orange juice.
Results and Conclusions: a high variation was observed in biochemical parameters and anthropometric variables after daily intake of orange juice. Sex, age, and BMI were not determinant for the observed variation in cardiometabolic biomarkers. Gut-derived phenolic acids were the major compounds recovered in 24-hour urine, and less amount of flavanone-phase II metabolites. Large inter-individual variation was observed in the excretion of the total metabolites, and volunteers were divided in three subset according to the phenolic acids and phase II metabolites ratio in high, medium and low ratio. Volunteers belonging to subset that present an intermediate ratio showed a significant reduction in total cholesterol, HDL and blood pressure. In conclusion, citrus flavanones metabolites seems to be able to improve cardiometabolic biomarkers, and phase II metabolites where important for this effect.
Financing: FAPESP; CNPq

FCF241-2021

OCCURRENCE AND GEOGRAPHIC DISTRIBUTION OF TOXIC CYANOBACTERIA SPECIES IN BRAZIL

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Introduction and Objectives: Brazilian water supplies are commonly affected by cyanobacteria blooms, which are mostly toxic. Monitoring cyanotoxins in Brazilian reservoirs is an extensive public health and sanitary concern, and it is required to know the distribution and biodiversity of these toxins. This study consists of collecting data about the occurrence of Brazilian episodes with the presence of toxic cyanobacteria.
Material and Methods: Data collection considered published scientific studies using the Scielo Brazil database and the following search criteria: keywords *toxic cyanobacteria* "or" *cyanotoxins* "or" *cianotoxinas* "or" *cianobactéria tóxica* "or" *cyanoHAB*. In addition, the Web of Science database with keywords *cyanotoxins* "or" *toxic Cyanobacteria* "or" *cyanoHAB* "and" *Brazil* for research and the CAPES periodic portal to access the select articles were also used.
Results and Conclusions: To date, data collection included 42 papers, but only 23 are specifically related to the toxin tested (by bioassay, HPLC, ELISA, MALDI-TOF, and MS) with the cyanobacteria species, while the others were reviews or PCR analyses that did not confirm the toxin or correlated the toxin with the cyanobacteria. Most records of toxic species found in Brazil were from reservoirs (93%), where the main species were planktonic (94%), and they were noticed in ten Brazilian states (BA, CE, PA, PB, PR, PE, RN, RS, SC, and SP). Regarding the toxins found, 42% were saxitoxins, 29% were microcystins, 18% were cylindrospermopsins, 7% were unknown to the author, 2% were anatoxin-a and, 1% was guanitoxin. Toxic cyanobacteria species occurring in Brazil were represented by 19 genera: 58% of the order Nostocales, 21% of Chroococcales, 17% of Oscillatoriales, and 4% Synechococcales.
Financing: CAPES

FCF242-2021

VOLUNTEERS WERE STRATIFIED ACCORDING TO CITRUS FLAVANONES-PHASE II METABOLISM PROFILE AFTER SINGLE DOSE OF 'PERA' AND 'MORO' ORANGE JUICES

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Introduction and Objective: The citrus flavanones are bioavailable, but a large interindividual variation on their absorption and metabolism was observed. We assessed the main determinants underlying interindividual differences in the metabolism of citrus flavanones.
Material and Methods: In a randomized cross-over study, non-obese and obese women ingested a single dose of 'Pera' and 'Moro' orange juices. Citrus flavanones phase II metabolites were measured in 24-hour urine.
Results and Conclusion: A large inter-individual variation in the excretion of phase II metabolites was observed, but not correlated with anthropometric variables, age, and biochemical parameters. Subjects were stratified according to the amount of the metabolites excreted, reflecting the gut metabolism. Furthermore, taking a new approach considering the phase II metabolism, the oPLS-DA evidenced two subsets of subjects based on the metabolite excretion profile named 'Excretion Profile A' and 'Excretion Profile B'. The 'excretion profile A' presents a low biotransformation rate of hesperetin and naringenin monoglucuronides to the respective diglucuronide, while the 'profile B' presented a higher excretion rate. In this case, the polymorphism on UGT enzyme may be responsible for this variation. These findings, together with biological response, may contribute to the identification of responsive groups to orange juice consumption, thus providing a more specific nutritional approach.
Financing: FAPESP; CNPq

FCF243-2021

ORANGE JUICE CONSUMPTION MODULATES GUT MICROBIOTA AND IMPROVES OXIDATIVE STRESS AND INFLAMMATORY MARKERS IN OBESE INDIVIDUALS WITH INSULIN RESISTANCE

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Introduction and Objectives: Orange juice presents flavanones that have been associated with reducing risk of obesity-associated diseases. We evaluated the effects of two variety orange juices on oxidative stress, inflammatory response, and gut microbiota in obese individuals with insulin resistance.
Material and Methods: In a randomized cross-over study, volunteers consumed 'Pera' (POJ) and 'Moro' orange juices (MOJ) for 15 days. Blood, urine, and fecal samples were collected before and after the intervention.
Results and Conclusions: Daily consumption of orange juice significantly reduced the total and HDL-cholesterol, beyond the urinary 8-OHdG and the plasmatic MCP-1 levels. Furthermore, several other parameters were also altered. Multivariate analyzes evidenced the effect of orange juice consumption, mainly due to the modulation of inflammatory response and oxidative stress related parameters. Volunteers with different obesity classes had their gut microbiota affected in different ways. Nevertheless, both juices affected the microbiota in a similar way, with POJ providing more accentuated changes than MOJ. Firmicutes/Bacteriodetes ratio changed after interventions, indicating that the obesity-associated gut microbiota dysbiosis was also affected by orange juice. Bifidobacterium and other genera correlated with health and disease markers had their relative abundance altered by juice consumption. In conclusion, regular consumption of orange juice seems to be able to reduce oxidative stress and the inflammatory response, in addition to modulating the gut microbiota.
Financing: FAPESP

FCF244-2021

STABILITY STUDY OF A RECOMBINANT PROTEIN BASED ON *Plasmodium vivax* CS PROTEIN CANDIDATE FOR MALARIA VACCINE

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Introduction and Objective: Our research group aims to develop a recombinant vaccine based on *P. vivax* Circumsporozoite Protein (PvCSP). Recently, we demonstrated that a formulation containing the yPvCSP-AllCT chimeric protein induced high long-term antibody titers as well as a protective effect in immunized mice, indicating great potential to future phase I clinical trials. Based on these results, it has become necessary to evaluate the stability of the vaccine formulation, as this type of study is essential during the developmental stages of a product. Thus, our objective is the expression and purification of the yPvCSP-AllCT chimeric protein, and the evaluation of the stability of the formulation at three different storage temperatures and in two different pharmaceutical forms, liquid and lyophilized.
Materials and Methods: The recombinant protein was expressed from *Pichia pastoris* yeast and was purified by FPLC. The stability and integrity of the recombinant protein was evaluated over 180 days, through tests such SDS-PAGE, Western Blot, circular dichroism, SEC and DLS.
Results and Conclusions: The recombinant protein, in a liquid formulation, proved to be stable for 180 days only when it was stored at -20°C. In a lyophilized formulation, the protein remained without signs of degradation during 6 months when stored at -20°C and 5°C, but appears to be aggregated, but this result did not impair the recognition of the protein by antibodies, as shown by the W. Blot assay. The presented results demonstrate that the vaccine formulation remained stable in some of tested conditions. Considering the difficulty in maintaining the cold chain in the locals where malaria is an endemic disease, our data is promising.
Financing: FAPESP

FCF246-2021

FUNCTIONALITY OF THE HUMORAL RESPONSE INDUCED BY THE SARS-COV-2 VIRUS INFECTION IN ASYMPTOMATIC VERSUS SYMPTOMATIC INDIVIDUALS

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Introduction: Antibodies specific to the SARS-CoV2 nucleoprotein (NP) and spike proteins have been detected in the human plasma, on average, after 10 days and later of the viral exposure. However, only spike-specific antibodies have been associated with neutralizing capacity. On the other hand, it remains elusive how important other functional aspects of anti-SARS-CoV2 antibodies are, such as their ability to activate the complement system or elicit monocyte-mediated phagocytosis. Thus, the objective of this study is to compare the functionality of the SARS- CoV2-specific humoral response found in asymptomatics versus symptomatics to Covid-19.
Materials and Methods: After running a rapid test for the presence of anti-SARSCoV2 IgM through immunochromatography in 1,006 employees of the Brazilian Revenue Service from the metropolitan area of São Paulo city, 191 individuals that were positive accepted to participate in our study. Whereas 167 of 191 reported to be asymptomatic until that blood drawing, the 24 remaining individuals informed to be previously symptomatic. Then, we used an ELISA to detect NP-specific IgG titers and confirm their previous viral exposure. Also, we have attempted to express the full-length or a partial spike sequence protein in IPTG-treated *E. coli* and set up an ELISA for the detection of spike-specific IgG.
Results: We ran a NP-specific ELISA with plasma samples from 191 individuals, and identified 58 responders and 133 non-responders. Among the responders, 51 (87.93%) were asymptomatics and 7 (12.07%) symptomatics, corresponding respectively to 31.14% and 29.17% of each group. Also, the reactivity index of responders followed a similar distribution pattern in both groups. Regarding the spike protein, we detected a positive expression of a partial sequence only in the bacterial pellet.
Conclusion: The rapid test used for IgM does not necessarily indicate that the patient would already have anti-viral IgG.

FCF248-2021

A GREEN DISPERSIVE LIQUID-LIQUID MICROEXTRACTION FOR QUANTITATIVE ANALYSIS OF SYNTHETIC CATHINONES IN POSTMORTEM BLOOD

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Introduction and Objectives: Synthetic cathinones (SC) are a new type of substances synthesized to illicit endeavors, mimicking the psychoactive effects of traditional stimulants. These new chemicals pose a threat to public health, as little is known of their toxicological properties and they are not detected by conventional analytical methods, thus the development of new ones applicable to SC is of high importance. With that in mind, the aim of the present work is to develop and validate a quantitative analytical method for SC in blood applying the principles of Green Analytical Chemistry (GAC)
Material and Methods: A dispersive liquid-liquid microextraction (DLLME) was developed and a UPLC-MS/MS was employed for all analyses. Ethical Committee approval nº 46404121.8.3001.0067.
Results and Conclusions: Our data shows similar efficiency of methanol (MeOH) and acetonitrile (ACN) for protein precipitation on analyte extraction; however, a trend of higher analyte recovery was observed with ACN. Next, considering SC are found at low concentrations in blood and the use of low sample volumes was intended to fit GAC principles, DLLME as a technique with great analyte recovery was chosen; however, hazardous solvents are commonly employed. Ethyl acetate is a greener alternative to chlorinated solvents and no works have been published so far using it in DLLME. Thus, a comparison between the extraction of SC using chloroform and ethyl acetate was performed and equivalent or even higher analyte recovery was observed when using the latter. We demonstrated for the first time that ethyl acetate is suited to replace chloroform in DLLME, while efficiency and sensitivity using low volume samples is improved; thus, the method is fit for validation
Financing: CNPq; CAPES/INSPEQT

FCF249-2021

THE INFLUENCE OF ETHYLENE ON PAPAYA PULP SOFTENING: A SYSTEM BIOLOGY APPROACH

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Introduction and Objectives: Papaya fast pulp softening is coordinated by ethylene-induced increase of the expression of pectinases. RNA-seq analysis of ethylene-treated and non-treated papayas enabled a wide transcriptome overview to elucidate the role of ethylene during ripening at the gene expression level.
Material and Methods: Unripe papaya fruits were kept for 12 hours in an ethylene-saturated closed system. Samples were taken before treatment, 12 hours and 24 hours after treatment (including control ones). Ethylene emission, peel and pulp firmness and peel color were measured. Total RNA was extracted from frozen samples and sequenced in Illumina HiSeq2500 after library synthesis. Data was processed and submitted to analyses of differential expression, enrichment and co-expression. RT-PCR and meta-analysis with mined papaya transcriptomes were carried out to confirm the mRNA expression profiles and to attribute gene function using a system biology approach.
Results and Conclusion: Ethylene treatment triggered ripening as observed in phenotypic parameters and in the higher numbers of DEG in comparisons between control and treated samples. The identified transcription factors were related to ethylene response and a set of genes from PG, rhamnogalacturonate lyases, galactanases, and XTH were up-regulated, while most of the PL and PME genes were down-regulated. Modular analysis revealed high, inverse correlation between ethylene and other physiological measures, as well as hub genes related to aroma enhancement and carotenoid pathways. Genes related to cell wall disassembling were deeply interconnected in a co-expression network, emphasizing the centrality of PG.
Financing: FAPESP; CNPq

FCF252-2021

EFFECTS OF PAPAYA (*Carica papaya*) PECTINS ON COLON CANCER SPHEROID FORMATION USING A TRIDIMENSIONAL CO-CULTURE MODEL

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Introduction and objectives: The effects of unripe and ripe papaya pectins and modified citrus pectin (MCP) were tested on the formation of colorectal cancer spheroids using a tridimensional co-culture model
Methods: Colon cancer cell lines HT29 and HCT116 were co-cultured with normal mouse fibroblasts NIH3T3. Cancer cells were labeled with tracer DiI (red) and fibroblasts were labeled with tracer DiO (green) before the spheroid formation. Ripe and unripe pectins at 0.2% and MCP at 1% (m/v) were added to media during the formation with 3 different cell proportions for 24h, 48h and 72h.
Results and conclusions: The best proportion of cancer cells and fibroblasts were 3:1 for homogenous spheroid formation. Ripe papaya pectin had no effect on any spheroid formation. MCP at 1% inhibited the formation of all spheroids at 24h. Unripe papaya pectin at 0.2% inhibited the formation of spheroids with only cancer cells at all time points and the spheroid with the proportion 3:1 of cancer cells to fibroblasts. Normal fibroblasts spheroids and spheroids with the proportion 1:3 and 1:1 of cancer cells to fibroblasts were not affected by unripe papaya pectins. These results indicate a cancer-specific effect of unripe papaya pectin on the formation of tridimensional spheroids.
Financing: FAPESP

FCF253-2021

NUTRITIONAL AND PHYTOCHEMICAL PROFILE OF MAMA CADELA (*Brosimum gaudichaudii*) FROM BRAZILIAN CERRADO

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Introduction and Objectives: Mama-cadela (*Brosimum gaudichaudii*) is a native fruit from the Brazilian Cerrado biome, which has an orange-yellow coloring, a sweet flavor and may be consumed in natura. Overall, it can be considered as a good source of dietary fiber and bioactive compounds as others fruits from Cerrado biome, such as pequi, jenipapo and jatobá, for example. The objective is to analyze the nutritional composition and phytochemical compounds of mama-cadela from Brazilian Cerrado.
Material and Methods: Liquid chromatography (LC) coupled to mass spectrometry (MS) and AOAC methods.
Results and Conclusions: Mama-cadela supplied: 69.69% moisture, 3.25% proteins, 2.03% fats, 0.45% ash, 18.02% "available" carbohydrates (by difference), 1.23% soluble dietary fiber (DF), 5.71% insoluble DF, 6.94% total DF, 1021,17mg/100g (mg%) soluble sugars (glucose, fructose and sucrose), 1546.11mg% organic acids (malic acid, citric acid and tartaric acid), 18.21mg% carotenoids and 74.04mg% phenolic compounds. The characterization of flavonoids and phenolic acids showed the following compounds: 3-O-caffeoylquinic acid (chlorogenic acid), 4-O- caffeoylquinic acid, hesperidin, quercetin-4'-O-glucoside e quercetin-3-O-glucuronide. As conclusion, mama-cadela provided good nutritional quality, highlighting the total DF and bioactive compounds (carotenoids and phenolics).
Financing: FAPEMIG; FAPESP

FCF255-2021

BIOGENIC COMPOUNDS FROM TRADITIONAL FERMENTED FOODS ARE ABLE TO RELIEVE FATIGUE

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Introduction: Exercise-induced fatigue is reflected in the inability or difficulty in motor activities, resulting from a synergistic effect of peripheral and central mechanisms. Generally involves symptoms like weariness and gastrointestinal discomforts. Traditional fermented products (e.g., kombucha, water kefir, and milk kefir) have been widely consumed over the decades to alleviate those symptoms. The consumption of Tibicos, milk-kefir, and kombucha, a symbiotic community of LAB, AAB, and yeasts, had shown positive effects to alleviate the fatigue symptoms.
Objectives: Evidence of the possible mechanisms for interventions in fatigue with the consumption of traditional fermented products.
Material and Methods: 85 papers from database Science Direct, PubMedCentral, and Google Scholar, published in the last ten years with the MeSH terms "Randomized placebo clinical trials", "Fatigue", "Tibico", "Kombucha", "Kefir", "Water-Kefir" were selected and compared.
Results: IL-6 and IL-1 have recently been discussed as one of the main factors in exercise-induced fatigue. The biogenic compounds formed through the fermentation result in a profile variety, rich in vitamins, short- chain fatty acids, and components antioxidants. Athletes, recreational runners, and cyclists had positive interventions with rich polyphenols beverages and some strains in separate clinical trials, acting in the oxidative status and intestinal permeability, respectively, and as a modulator of cytolytic. Conclusions: Changes in the immune profile and energy metabolism occur depending on exercise intensity, substrate, and initial colony used, possibly providing an anti- fatigue effect.

FCF256-2021

MILD TOXICITY OF SILVER/SILVER CARBONATE NANOPARTICLES: EXPOSURE TIME AND ROUTE DEPENDENT EFFECTS ASSESSED WITH THE CHORIOALLANTOIC MEMBRANE OF CHICKEN EMBRYO MODEL

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Introduction and Objectives: Bioassay-based Technologies are helpful in the safety evaluation of medical and pharmaceutical products for human and animal health. The in vivo model of chorioallantoic membrane of chicken embryos (CAM) is convenient for the risk assessment of bioactive materials with mild toxicity, when analytical methods with high sensibility are required. This work was designed to evaluate the effects of silver/silver carbonate nanoparticles after 10 days of incubation, after a single exposure (E0-E10). Previous data on E0-E6 and E0-E8 were suggestive of mild toxicity.
Material and Methods: A single exposure to silver/silver carbonate nanoparticles provided by ADP Soluções® was performed at E0. Embryo size and weight were assessed at 10 days of incubation (E10). Results were compared to those observed on E0-E6, E0-E8, E4-E10, E6-E10 and E6-E10. Egg shell surface and albumin injection routes were tested. CAM images were obtained with a HP G2410 Scanjet scanner. Digital images were processed, vessel densities and membrane areas were measured. CAM growth and complexity were analysed as previously described. (OJALA et al., Lecture Notes in Computer Science, 1842: 404, 2002)
Results and Conclusions: Development interruptions and lethality were not induced by silver/silver carbonate nanoparticles at E0-E10. Effects upon development of the tissues of viable embryos could be related to the route and time of exposure. No effects were detectable at E6. The CAM growth and complexity were reduced after injection of nanoparticles, egg shell was partially protective. Observed effects were more pronounced at E10 than at E8.
Financing: CNPq PIBITI; FAPESP PIPE; ADP Soluções

FCF257-2021

COLOR AND BRIGHT ALTERATIONS OF HAIR FIBER AFTER CHEMICAL DAMAGE

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Introduction and Objectives: The color of hair is importante to evaluate the integrity of the cuticles and the pigments present (melanin and artificial) in the cortex, and the brightness about the light reflexion of the cuticles. The objective of this work was to evaluate the damage by chemical processes in the hair fiber through the analysis of brightness and color in wavy hair.
Material and Methods: Eighteen locks of virgin dark brown (wavy) hair were used, in six groups, pre-treated with standardized washing. Subsequently, the chemical treatment: bleaching, dyeing (light blonde and ultra light blonde) and smoothing (ammonium thioglycolate and guanidine hydroxide) were performed. These locks were compared using gloss (Samba Hair®) with Luster and Color changes with the CIELAB* system and color analysis (Chroma Meter CR-400® colorimeter).
Results and Conclusions: Strands treated with straighteners had no color change, but after application of thioglycolate they presented smoother and softer sensory characteristics compared to guanidine. The brightness intensity of the locks treated with guanidine were statistically equal to that of the control (27u.a.), but with thioglycolate was higher (37u.a.). The smoothed locks had no color change, but the dyed ones did, because the solubilization of the yellow pigments in the color of the formulation components and lower reflectance of the lighter shades. In discolored and dyed locks, the value of Luster has been reduced, locks dyed with ultra light blonde had Luster = 1.73 a.u. It was possible to conclude that the lighter the hair shaft luminosity, the lower the shine and the greater the wear.
Financing: FAPESP

FCF258-2021 FCF258-2021

SYNTHESIS OF A LOBEGLITAZONE ANALOGOUS AND ITS INTERMEDIATES IN BATCH PROCESS

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Introduction and Objectives: The present study aimed to synthesize a molecule analogous to the drug Lobeglitazone (Duvie®), which is used in the treatment of type 2 diabetes mellitus, called Lobeglitazone- b, synthesized by replacing the reagent 2-methylaminoethanol by 2-aminoethanol in the synthesis from one of its intermediates.
Material and Methods: To study the synthesis of Lobeglitazone-b, analogous to the drug Lobeglitazone, 5 reaction steps were adapted in a batch reactor, followed by purifications, carried out by work-ups, chromatographic columns and recrystallizations. Subsequently, the product characterization was made through UHPLC-MS analyzes and the determination of the reaction yields was performed by HPLC-UV.
Results and Conclusions: The new molecule had been identified before as one of the Lobeglitazone metabolites, that is, Lobeglitazone being bio transformed into other molecules, however, it had not yet been synthesized. In this work, the molecule of interest was synthesized and identified, demonstrating the feasibility of the proposed route, with the finding that this route is promising for the synthesis of the new product in batch. It was verified that for the synthesis of intermediate 1 the reaction yield was 91%, for intermediate 2, 69%, and for intermediate 3, 12%. However, for intermediate 4 and product 5 (Lobeglitazone-b), only the characterization by UHPLC-MS was performed at the time. In sequence to this work, it will be developed analytical methods for the quantification of intermediate 4 and product 5.
Financing: FAPESP, CAPES

FCF260-2021

DEFINED VERSUS COMPLEX GROWTH MEDIA FOR PHOTOLYASE PRODUCTION IN RECOMBINANT *Escherichia coli*

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Introduction and Objectives: Recombinant proteins are of great relevance due to their therapeutic potential. Commercialization of these potential medicines implies in the need of industrial scale production and a rigid batch-to-batch control. Growth medium is the substrate necessary for an organism's growth and protein production. Thus, the choice of an adequate growth medium can drastically affect production yield. This work refers to the comparative study of a complex (Luria-Bertani) and a chemically-defined medium in *E. coli* BL21 (DE3) culture to produce photolyase, an enzyme with pharmaceutic and cosmetic potential since it repairs UV damage to DNA, responsible for photolesion and skin related conditions.
Material and Methods: Recombinant *E. coli* BL21 (DE3) expressing photolyase was cultivated in both media and the cultivation and kinetic parameters determined, namely specific growth rate (μx), total biomass concentration (Xmax) and biomass productivity (Px). The intracellular photolyase was extracted and purified by affinity chromatography in AKTA FPLC.
Results and Conclusions: Cultures in complex media exhibited higher μx (1.008 h^{-1}), lower Xmax (1.99 $g \cdot L^{-1}$) and Px (0.39 $g \cdot L^{-1} \cdot h^{-1}$). Cultures in defined media presented lower μx (0.668 h^{-1}), but reached superior Xmax (3.614 $g \cdot L^{-1}$) and Px (0.51 $g \cdot L^{-1} \cdot h^{-1}$). A clear band corresponding to photolyase was observed by SDS-PAGE, confirming protein expression. Results demonstrated the advantage of photolyase production in defined media culture, due to its reproductivity and the capacity of attaining higher biomass concentration.
Financing: State of São Paulo Research Foundation (FAPESP); National Council for Scientific and Technological Development (CNPq).

FCF261-2021

QUALITATIVE SCREENING FOR ADULTERANTS IN WEIGHT-LOSS SUPPLEMENTS HIGHLY CONSUMED DURING THE SARS-CoV-2 PANDEMIC

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Introduction and Objectives: The demand for natural prescription-free slimming products, which promise quick and healthy results, increased during SARS-CoV-2 quarantine. However, reports of adverse events related to this type of product point to a possible presence of controlled use substances in the capsules. This study aimed to evaluate the composition of some slimming supplements to investigate the presence of adulterants.
Material and Methods: The increase in the search for these products in the period before and after the beginning of quarantine was evaluated employing the Google Trends tool, using keywords related to weight loss with natural products. The slimming capsules were purchased online and labeled alphabetically. The qualitative screening for controlled substances was performed by X-ray diffraction, applying the Rietveld refinement between the calculated diffractograms and those available in the *Cambridge Structural Database®*.
Results and Conclusions: Qualitative analysis evidenced the presence of crystalline phase's sibutramine (anorectic), hydrochlorothiazide (diuretic) and potassium hydrochloride (electrolyte regulator) in capsules A and B. Rietveld refinement proves that approximately 45% of the crystalline phase corresponds to the anorectic, 40% to the diuretic and 15% to the electrolyte regulator in both samples, popularly known for reducing body mass. However, as these active ingredients are not stated in the capsules composition, consumers are at serious risk of developing liver and heart diseases. Therefore, it is necessary to alert the population about the dangers related to such adulterated supplements and withdraw them from the market.

FCF272-2021

EVALUATION OF D-LIMONENE SUPPLEMENTATION ON POSTPRANDIAL GLYCEMIA IN A REMOTE CLINICAL STUDY

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Introduction and Objectives: D-limonene is a monoterpene with beneficial health properties including anti-inflammatory, hypoglycaemic and lipid-lowering effects. The aim of this study was to evaluate the effect of D-limonene supplementation on the postprandial glycemic response in a remotely-conducted clinical study.
Material and Methods: This study was approved by the Research Ethics Committee (CAEE 37850720.0.0000.0067). Forty-two individuals aged 18-70 years of both genders were supplemented with 2 g/day of D-limonene capsules or placebo (canola oil) for two weeks. Before and after the supplementation, participants were subjected to a dietary challenge consisting of 75g glucose, 70ml canola oil, 20g casein diluted in water. Capillary blood glucose levels were monitored for 3 hours after dietary challenge.
Results and Conclusions: Postprandial blood glucose reaches Cmax within 60 minutes, increasing in average 30% from baseline. After 90 minutes, glycemia starts decreasing and at t=180 minutes, it was still 20% higher than in the fasting state. The supplementation with D- Limonene did not affect the postprandial glycemic response. Preliminary results indicate that the D-limonene-induced improvement in the glycemic response (observed in some volunteers) is negatively correlated with initial AUC of glycaemia. This remotely conducted clinical study has demonstrated to be a feasible alternative as research protocol adapted to the needs imposed by COVID-19 pandemic.
Financing: CAPES, Food Research Center (FoRC).

FCF274-2021

ASSESSMENT OF IN VITRO DISSOLUTION OF DESVENLAFAXINE SUCCINATE EXTENDED-RELEASE TABLETS AVAILABLE IN THE BRAZILIAN PHARMACEUTICAL MARKET

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Introduction and Objectives: Among the drug delivery technologies, matrix systems for extended-release (ER) tablets are an interesting option to prolong drug effect, and improve the treatment patient compliance, beside its easily scale up process. Desvenlafaxine (DVL) is an antidepressant drug available as ER tablets that was approved by the FDA in 2008. In this product, the drug delivery is controlled by a hydrophilic matrix, making the dissolution profile essential, which must follow specific release kinetics. However, there are only a few studies around it, and there is a lack of information from the dissolution profile of commercial formulations. This study aims to compare the dissolution profiles of different DVL ER tablets available in the brazilian market.
Material and Methods: The dissolution profile of the DVL reference product and three of its generic versions were obtained using the FDA's dissolution method, which consisted of a 24h test in a basket at 100 rpm and 900 mL of NaCl 0.9%. The statistical analysis was conducted using the software Minitab®.
Results and Conclusions: When the comparison was based on the difference and similarity factors, f1 and f2, all dissolution profiles of the generic formulations were equivalent to the reference product. However, the plot of dissolution profiles showed that one of the generics had a slightly faster release, which was confirmed by statistical analysis of the dissolution efficiencies. Comparing the characteristics of the tablets, it was possible to link this difference to the tablet size, showing that the modulation of the DVL release can be related to the thickness of the gel layer formed during the dissolution.

FCF275-2021

OBTENTION OF A PLURONIC LECITHIN ORGANOGEL (PLO) INJECTABLE FORMULATION CONTAINING MELOXICAM FOR VETERINARY USE

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Introduction and Objectives: Pluronic and lecithin organogels (PLO) consist of dispersions where organic particles are interpenetrated by a liquid (dispersed phase), where the thickening agent, usually a solid or semi-solid, appears in smaller quantities and has the function of immobilizing the dispersed phase in a three- dimensional (3D) elastic or viscoelastic network. It has potential use in several areas of both human and veterinary application, especially, in long-acting injectable products (LAIs) as they allow the administration of drugs that can not be ingested. This study aimed to obtain a pluronic and lecithin organogel injectable antiinflammatory formulation for veterinary use.
Material and Methods: Soy lecithin, isopropyl myristate, Pluronic® F-127, medium- chain triglycerides, cholesterol, and meloxicam were used in the formulations and the adequate amounts of each component to form the organogel were established with the aid of a pseudo ternary phase diagram obtained through the XLSTAT 2020 software. Ten formulations were produced and evaluated by the potential of formation of the three-dimensional matrix. The most promising were tested for viscosity, thermo-reversibility, XRD, and spreadability.
Results and Conclusions: The apply of phase diagram enabled the adequate formulation composition to form the three-dimensional matrix. It was also possible to observe the stability of the organogel system even with thermoreversibility being constantly tested, as well as its ability to easily transport drugs with very low solubility, such as meloxicam. The selected injectable organogel system proved to be a safe and promising carrier of drugs for a long-acting antiinflammatory veterinary treatments.
Financing: CAPES.

FCF277-2021

COMPATIBILITY STUDY OF CIPROFIBRATE WITH EXCIPIENTS BY DSC

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Introduction and Objectives: Drug-excipient compatibility studies are an important step in medicines development and Differential Scanning Calorimetry (DSC) can be used for this purpose. It provides data such as melting temperature (Tonset) and enthalpy (dHf), which are used as parameters for the study. When an excipient is compatible with the drug, the thermal curves obtained from binary mixtures are the sum of the results from pure components, preserving the Tonset and dHf values of the drug. Changes in the mixture result indicate interactions between the components, that should be investigated by complementary techniques. The aim of this work was to study the compatibility of ciprofibrate (CF), a lipid-lowering drug, with excipients magnesium stearate (MS) and anhydrous dibasic calcium phosphate (CP) by DSC.
Material and Methods: Samples of pure CF, each pure excipient and 1:1 w/w binary mixtures between CF and each excipient were analyzed (n=3) using DSC7020 equipment (SII Nano Technology, Japan). Samples were placed in hermetic aluminum crucibles and heated from 30°C to 135°C with heating rate of 10°C/min under nitrogen flow at 50 mL/min.
Results and Conclusions: DSC curve from CF showed an endothermic melting peak at Tonset= 114.3±0.4ºC with dHf= 123±5 J/g. Mixture with CP presented an endothermic peak at Tonset= 113.9±0.1°C with dHfus= 115±12 J/g. These values correspond to CF melting peak, it means that the drug was preserved in the mixture and there was no incompatibility between CF and CP. The result from mixture with and MS showed a peak at Tonset= 56.62±0.6°C, with dHfus= 217.83±26 J/g, that was not present in the curves from pure components, while CF melting peak was not found. Therefore, there was some interaction between CF and MS, which should be investigated.
Financing: Fipfarma

FCF279-2021

D-LIMONENE MODULATE FECAL BILE ACID PROFILE IN C57/BL6 MICE

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Introduction and Objectives: D-limonene (DL) is a monoterpene mostly found in citric fruits, known for its antimicrobial properties. Among many functions, the gut microbiota participates in the metabolism of bile acids (BA). These molecules are involved in the digestion of dietary lipids and in the regulation of energy metabolism. The hypothesis of this study is that given its antimicrobial properties, DL could modulate the composition of the intestinal microbiome impacting on the metabolism of BA.
Material and Methods: The study was approved by CEUA-FCF under the protocol #576. During 6 weeks, male C57/Bl6 mice were fed either normolipidic (NL) or high-fat (HL) diets supplemented with 0, 0.1 and 0.8% of DL. Samples of feces from the 5th week of treatment were used for BA quantitative analysis using high-resolution mass spectrometry.
Results and Conclusions: Feces from mice that received normolipidic diet had a higher content of Ω-muricholic acid compared to the feces from mice fed with the high-fat diet, regardless of DL treatment ($p<0.05$). The treatment with DL increased the fecal content of BA conjugated with taurine. Particularly, a-muricholic, Ω-muricholic and cholic acids were different comparing NL to HL 0.1% ($p<0.05$). The group HL 0.1% had lower weight gain compared to the other HL groups, suggesting that DL can modulate gut microbiota composition and energy metabolism. Further studies are underway to confirm this hypothesis.
Financing: FAPESP

FCF280-2021

IN SILICO INTERACTIONS OF LONG NON-CODING RNAs ASSOCIATED WITH PROSTATIC CANCER AND mRNA TARGETS

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Introduction and Objectives: Long non-coding RNAs (lncRNAs) are involved in the epigenetic mechanism of tumorigenesis and metastasis of prostatic cancer. This in silico study was proposed to assess interactions between prostatic cancer-related lncRNAs and their mRNA targets.
Material and Methods: The LncRNAs DRAIC, PCA3, PCAT1 and PCAT29 and the target mRNAs BRCA2, PRUNE2 and AR were selected from previous studies and were used to construct LncRNAs and mRNAs co-expression networks that were constructed using the MetaCore software (Clarivate Analytics, London, UK).
Results and Conclusions: The networks showed a direct inhibition of PCAT1 on tumor suppressor BRCA2 and interactions with miRNAs, transcription factors and the immunophilin FKBP5. PCA3 showed a direct inhibition on PRUNE2 (synonym BMCC1) and also interactions with miRNAs. Androgen receptor (AR) directly inhibits the expression of lncRNAs DRAIC, PCAT29 and PCA3, contributing to cancer progression. In conclusion, lncRNAs PCA3 and PCAT1 regulate negatively BRCA2 and PRUNE2, whereas DRAIC, PCAT29 and PCA3 are negatively regulated by AR, in peripheral blood of prostatic cancer patients.
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EFFECTS OF D-LIMONENE ON FATTY ACID ß-OXIDATION IN THE ADIPOSE TISSUE OF DIET-INDUCED OBESE MICE

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Introduction and Objectives: D-limonene is a monoterpene commonly found in citrus with lipid-lowering effects. This study aims at investigating the effect of D-limonene on fatty acid ß-oxidation in white adipose tissue.
Material and Methods: This study was approved by CEUA FCF, protocol #576. 11-week-old male mice (C57/Bl16 were induced to obesity by feeding a high-fat diet (HL). D-limonene was supplemented in the diet at concentrations of 0.1% and 0.8% (HL0.1 and HL0.8 groups, respectively) for 6 weeks. During the experimental period, body weight and food intake were monitored. After euthanasia, blood and tissues including liver, skeletal muscle and adipose tissue (epididymal, retroperitoneal, inguinal and brown) were sampled. The gene expression of enzymes involved in both energy and lipid metabolism such as UCP1 and PPARa were analyzed by real-time PCR in the epididymal adipose tissue.
Results and Conclusions: D-limonene-supplemented animals (HL0.1) showed an increase in UCP1 ($p < 0.05$) and PPARa ($p < 0.01$) gene expressions when compared to the HL group without supplementation. These findings suggest that D-limonene may have a lipid-lowering effect by activating key fatty acid ß- oxidation pathways in white adipose tissue in an obesity condition. These are preliminary data and further studies are being carried out to better assess the effects of D-limonene on lipid metabolism.
Financing: This work was funded by the FAPESP (2018/19189-0), CAPES (88887.486139)

FCF283-2021

EFFECTS OF D-LIMONENE IN THE LIVER BILE ACIDS PROFILE IN C57/BL6 MICE

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Introduction and Objectives: Bile acids (BA) can modulate intermediate metabolism, stimulating ß-oxidation of fatty acids and inhibiting gluconeogenesis. BA are synthetized in the liver and further metabolized by the gut microbiota into secondary BA. D-limonene (DL) is the main monoterpene of orange essential oil with antibiotic activity that could modulate gut microbiota and impact BA profile. The aim of this study was to evaluate the effects of DL on hepatic BA profile in mice.
Material and Methods: Male C57/Bl6 mice were distributed in 6 groups, fed either with a normolipidic (NL) or a high-fat diet (HF). After one week of acclimatization, mice were additionally divided in groups receiving diet supplemented with DL at 0, 0.1 and 0.8% for 6 weeks. Hepatic BA were quantified by high-resolution mass spectrometry. CEUA: 576.
Results and Conclusions: The HF group showed nearly 60% higher concentrations of ß-muricholic acid compared to the NL groups ($p<0,006$) and the supplementation with DL promoted a dose- dependent reduction of BA concentrations in the liver. In addition, the HF group treated with 0.1% DL showed nearly 45% higher hepatic concentration of Ω-muricholic acid compared to other HF groups ($p<0,04$). A similar result was observed for body weight gain, indicating a possible relation with Ω-muricholic acid. As Ω-muricholic acid is synthesized from ß-muricholic acid by the intestinal microbiota, we can assume that intestinal microbiota is being modified by the DL supplementation. Further studies are underway to investigate this hypothesis.
Financing: FAPESP; CNPQ

FCF-285-2021

IDENTIFICATION OF D-LIMONENE METABOLITES IN MICE URINE AFTER A CHRONIC INTAKE

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Introduction and Objectives: Chronic studies investigating health effects of bioactive compounds demonstrate that in many cases, products of the metabolization of the given compound are responsible for the reported biological effects. The identification of metabolites of bioactive phytochemicals is crucial to understanding their health effects. The aim of this work was to identify D-limonene metabolites in urine after chronic intake.
Material and Methods: Six male C57/Bl6 mice were fed a chemically defined diet supplemented with 0.8% of D-limonene for 6 weeks. Urine samples were collected before and at the end of the supplementation period. D-limonene metabolites were identified using high-resolution mass spectrometry. The identification was confirmed by mass spectra taking into account exact mass, isotopic pattern, MS/MS fragmentation and literature data. This study was approved by the CEUA (protocol 576).
Results and Conclusions: Five metabolites of D-limonene were identified in urine, corresponding to phase I and II metabolites. D-limonene undergoes hydroxylation followed by glucuronidation process, in which at least 3 different isomers were detected [327.1458; 327.1454; 327.1458]. Limonene can also be dihydroxylated and glucuronidated [345.1558]. Hydroxylated metabolites of limonene can be oxidized to carboxylic acid (perillic acid) followed by glucuronidation [341.1243]. All exact mass values showed an error of less than 1 ppm in relation to theoretical mass. The identification of metabolites allows the elucidation of dose dependent metabolism of D-limonene and identification of putative active molecules.
Financing: CNPq, FAPESP

FCF288-2021

MAPPING THE PRODUCTION CHAIN OF ARTISANAL CHEESES OF SÃO PAULO STATE.

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Introduction and objectives: São Paulo state's gaining reach in artisanal cheese's market. However, little is known about its production chain. This work aims to characterize São Paulo's artisanal cheese production chain, which may help create programs and strategies to help producers and consumers of these products.
Material and Methods: An online questionnaire was applied to cheese producers from the state of SP through the *Associação Paulista de Queijo Artesanal* and the *Rede de Pesquisa em Queijos Artesanais*, including topics about the dairy farm and cheese making process. Results were analyzed by descriptive statistics (relative frequencies, mean and standard deviation), using Minitab 20 software.
Results and Conclusions: 34 responses were collected, mostly from male participants aged 26-55 years (38%), located in São José dos Campos and Sorocaba (53%), which have been working as cheesemakers for about 1-3 years, with an impact of 25% of cheese sales on their income. The dairy farm's data showed that 70.6% are part of Associations, 44% are registered in the inspection service (IS), mostly at the municipal level (67%), and 92% of those without inspection would like to register. Products' diversity data showed that the most common are ripened and fresh (38%), followed by moldy and half- cured cheeses (24%), with a mean of 7 (±5) types of cheese per farm. In the cheese making process, cow's milk (76%), milked in the farm (82%) and slow pasteurized (42%) are the most common raw materials. 54% ripe their cheeses, but only 17% do it for minimum of 60 days, as required by Brazilian legislation. Therefore, owing to this diversity, it's important that new public policies programs be tailored according to the states' innovative production chain.
Financing: CNPq; FAPESP; CAPES.

FCF289-2021

METABOLIC ADAPTATIONS TO A MEAL AS A SOURCE OF INFORMATION TO IDENTIFY METABOTYPES AMONG POSTMENOPAUSAL WOMEN

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Introduction and Objectives: The characterization of postprandial responses provides novel information about phenotypical traits that can be used to identify metabotypes, fostering the development of personalised nutrition. This study aimed at evaluating serum concentrations of cholesterol, triacylglycerols and glucose in postmenopausal women after a dietary challenge.
Material and Methods: The study was approved by the Research Ethics Committee (CAEE 15438019.7.0000.0067). So far, five volunteers with a mean age of 59.6 y.o. were subjected to a dietary challenge consisting in the intake of a chemically defined meal (75g of glucose, 60g of canola oil and 20g of casein) . Blood samples were collected for 7 hours (at 0, 15, 30, 60, 90, 120, 180, 240, 300, 360 and 420 minutes). Serum cholesterol, triacylglycerols and glucose concentrations were measured using enzymatic kits.
Results and Conclusions: No significant differences were observed for serum cholesterol (p=0.531), triacylglycerol (p=0.245) and glucose (p=0.406) concentrations among the evaluated times. Despite the lack of statistical significance due to the low number of subjects, it was possible to identify that the peak of glucose occurred after 30 minutes, for total cholesterol after 2 hours, and for triacylglycerol after 5 hours. These are preliminary data and other volunteers have been recruited for this clinical trial (aim is N=40) which will contribute to a better understanding of the metabolic changes that take place in the postprandial period.
Financing: FAPESP; Food Research Center (FoRC).

FCF290-2021

DEVELOPMENT OF A METHOD BASED ON GREEN ANALYTICAL CHEMISTRY TO DETECT THE ACTIVE COMPONENTS OF AYAHUASCA IN HAIR

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Introduction and Objectives: Ayahuasca (AYA) is a beverage originated in South America and it is obtained by the fermentation of two plants: the leaf of *P. viridis* and the vine of *B. caapi*, which contains dimethyltryptamine (DMT) and β-carbolines (harmine, harmaline and tetrahydro-harmine), respectively. Due to its hallucinogenic effect, DMT is abused under different circumstances. In addition, the administration of AYA tea for the treatment of psychiatric disorders, such as depression and anxiety, has been widely studied. In this context, hair has been proposed as a valuable matrix for the evaluation of chronic exposure. The aim of this project is to develop an analytical method for the quantitation of AYA alkaloids in hair using techniques based on green analytical chemistry.
Material and Methods: Hair samples were digested with NaOH 0.5M and 1M for 3h and 24h. Analytes were extracted using liquid- phase microextraction and analyzed with UPLC-MS/MS. Ethical Committee approval n°66093117.1.0000.0067.
Results and Conclusions: First, hair must be digested in order to release the substancess for analysis. This process might greatly degrade the alkaloids present on samples; thus, the stability of such metabolites after digestion was evaluated. Our results showed that NaOH 1M at 40°C for 3h was the best condition to preserve the integrity of the analytes during digestion. We have achieved a procedure able to recover AYA metabolites from hair, which are found at extremely low concentrations; thus, the method is fit for validation. Noteworthy, there are no published methods for detecting the main AYA alkaloids in hair, especially β-carbolines.
Financing: CAPES PROEX

FCF291-2021

EFFECTS OF D-LIMONENE ON THE EXPRESSION OF GENES INVOLVED IN BILE ACID METABOLISM IN C57/BL6 MICE

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Introduction and Objectives: D-limonene is a monoterpene found in citrus fruits. Due to its antimicrobial effects, it is likely that it can modulate intestinal microbiota composition and bile acid metabolism. The effects of D-limonene on the expression of genes involved in bile acid metabolism in C57/Bl6 mice were investigated.
Material and Methods: Male mice (C57/Bl6) were distributed into eight groups fed either a high-fat or a normolipidc diet. After one week, both groups received D-limonene supplementation in the diet at 0, 0.1 and 0.8%. mRNA was extracted from liver samples using the RNeasy mini kit (Qiagen) and the expression of genes involved in bile acid synthesis and transport was assessed using RT-PCR. The analysed genes were CYP7A1 and SLC10A1 with HPRT1 serving as housekeeping.
Results and Conclusions: D-limonene had no effects on the expression of the genes analysed, but the high-fat diet-fed groups displayed an increase in the expression of CYP7A1 and a decrease in SLC10A1 expression. Considering that CYP7A1 is the rate-limiting enzyme in the biosynthesis of BA and that SLC10A1 is involved in their hepatic uptake, the observed effects seem to be compensatory. Further analyses to clarify this relationship are underway.
Financing: FAPESP; PUB, USP

FCF292-2021

DEVELOPMENT OF AN ANALYTICAL METHOD BASED IN QUECHERS EMPLOYING HUMAN UMBILICAL CORD TISSUE FOR THE EVALUATION OF MATERNAL FETAL EXPOSURE TO COCAINE

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Introduction and Objectives: The use of cocaine (COC) during pregnancy has deleterious effects on both the pregnant woman and the child, in addition to obstetric complications. Thus, the umbilical cord tissue (UCT) has been seen as an alternative sample. QuEChERS consists of extracting with partitioning and clean-up by a dispersive-solid, which makes it ideal for tissues. The aims is to develop and validate a method for determining COC and its metabolites (Anhydroecgonine methyl ester (AEME), ecgonine methyl ester (EME), benzoylecgonine (BZE) and cocaethylene (CE)) in human UCT through QuEChERS extraction and gas chromatography coupled to mass spectrometry.
Material and Methods: In UCT (1g) with deuterated of COC, BZE and EME were added 3mL of 0.1 M phosphate buffer (pH 6) for incubation at 120°C/30 min. The mixture with 3ml of dichloromethane: isopropanol: ammonium hydroxide (12:3:0.3) was used as solvent extraction and 25mg of PSA for clean-up. After drying, 35µL of PFP and PFPA were added for derivatization and dried under nitrogen flow at 70°C/10 min. The extract was reconstituted with ethyl acetate (50µL) and 1µL was injected in GC-MS.
Results and Conclusions: The extraction was able to detect AEME, EME, COC and CE. Therefore, this method needs an optimization, as not all analytes were extracted. Thus, cut the UCT into small threads, testing different incubation times and temperatures can improve homogenization and analytes availability for extraction. Adding salts to promote salting out and solvent volumes can improve extraction. It is necessary to test different buffers and extraction solvents. QuEChERS is promising for the determination of cocaine and its metabolites in UCT.
Financing: CNPq

FCF293-2021

CHARACTERIZATION OF IBUPROFEN SOFT GELATIN CAPSULES IMPURITIES AFTER FORCED DEGRADATION BY LC-MS-QTOF

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Introduction and Objectives: Physical and chemical interactions between excipients and the drugs can occur, affecting the stability and bioavailability of the drugs, and, consequently, their therapeutic efficacy and safety. The aim of this work was to develop a method that is capable of characterizing ibuprofen soft gelatin capsules impurities by LC-MS-QTOF after basic, acidic, oxidation, photolytic, metal ions, thermal, humidity degradation.
Material and Methods: The LC-MS-QTOF with electrospray ionization (ESI) analyses were developed using Shimadzu Prominence® and MicroTOF QII with Poroshell HPH-C18 150 × 4.6 mm, 4 µm, column at 25 °C, mobile phase constituted by 0.1% formic acid and acetonitrile in gradient at a flow rate of 0.2 $mL.min^{-1}$, 220 nm. This was performed in both negative and positive modes. Scan mode with an interval of *m/z* 50 to 800 with capillary voltage 4000 V for positive and 3500V for negative mode and flow rate of drying gas at 6.0 L.min-1, temperature of the drying gas at 200 °C and nebulizer at 35.0 psi for both. When performed MS/MS in positive mode, the range was changed from *m/z* 50 to 1200, three precursor ions were selected.
Results and Conclusions: In total, eight unknown impurities were found. The peaks identified and characterized were RRt 0.49, RRt 0.75, and RRt 0.95, above 0.17%, corresponding to the identification threshold. Impurities originated from the interaction of ibuprofen with excipients: esterification with PEG, with sorbitol/sorbitan, and with glycerol by- products, which has not yet been reported in the literature. The developed method can be used in several pharmaceutical areas.

FCF294-2021

TOXIC EFFECTS OF CIGARETTE SMOKE AND HEAT-NOT-BURN TOBACCO VAPOR EXPOSURES ON EXPERIMENTAL ARTHRITIS

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Introduction and Objectives: Tobacco combustion exposure worsens rheumatoid arthritis (RA). Non-combustible tobacco devices, as heat-not-burn tobacco (HNBT), are emerging as harm reduction to smokers by releasing nicotine and lower combustible tobacco products. Nevertheless, their toxicity remains unclear. Hence, we here investigated the impacts of the tobacco combustible product (cigarette smoke; CS) or HNBT exposures on antigen-induced arthritis (AIA) in C57BL/6 mice.
Material and Methods: Animals were exposed to air, HNBT vapor, or CS during 1 hour/twice a day, under the Health Canada Intense (HCI) smoking regime, between days 14 to 20 after the first immunization. At day 21, 16h after last exposures, mice were i.a. challenged and the AIA effects were evaluated 24h later.
Results and Conclusions: CS- or HNBT- exposed mice presented equivalent blood nicotine levels. CS exposure worsened articular symptoms, pulmonary inflammation, and expression of lung and liver metallothioneins. Nevertheless, CS or HNBT exposures reduced lymphoid organs' cellularity. In vitro exposure to CS, HNBT or nicotine reduced mice splenocyte proliferation and IL-2 secretion, partially mediated by the activation of nicotine/a7nAchR pathway. Associated, data demonstrated the toxic mechanisms of CS or HNBT inhalation at HCI regime on RA, and highlight that further data are fundamental to assure the toxicity of tobacco products on the immune system during specific challenges.
Financing: FAPESP

FCF297-2021

IN SILICO ANALYSIS OF CIRCULATING LONG NON-CODING RNAs RELATED TO CHOLESTEROL HOMEOSTASIS

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Introduction and Objectives: Long non-coding RNAs (lncRNAs) have been implicated in the pathophysiological mechanisms of dyslipidemias and cardiovascular diseases (CVD). However, only a small group of lncRNAs has been functionally characterized until now. This *in silico* study was designed to predict the interactions of lncRNAs involved in cholesterol homeostasis with their target molecules.
Material and Methods: A PubMed (https://pubmed.ncbi.nlm.nih.gov/) was performed to select studies on circulating lncRNAs previously associated with cholesterol homeostasis. Interaction networks between the selected lncRNAs and their targets were built using MetaCore software (Clarivate Analytics, London, UK) and R script package.
Results and Conclusions: The lncRNAs TUG1, LncARSR, ZFAS1, HULC and MALAT1 were selected. The *in silico* analysis revealed their influence on cholesterol efflux (CHROME, TUG1 and ZFAS1), accumulation (H19, MALAT1 and LncARSR), biosynthesis (LncARSR and HULC) and metabolism (LASER and APOA4-AS). Results of network interactions showed that expression of H19, ZFAS1 and HULC is downregulated by miR-196a-5p, miR-486-5p and miR-133b-3p, respectively. Also, expression of TUG1 is downregulated by miR-34a-5p, while expression of miR-34a-5p is downregulated by LncARSR and MALAT1. In conclusion, miR-196a-5p, miR-486-5p and miR-133b-3p regulate negatively the lncRNAs H19, ZFAS1 and HULC, while LncARSR and MALAT1 regulate negatively the miR-34a-5p.
Financing: CAPES; FAPESP

FCF 298-2021

DELETERIOUS VARIANTS IN ABCC1 AND CYP3A5 ARE ASSOCIATED WITH INCREASED RESPONSE TO STATINS AND ADVERSE EVENTS IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

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Introduction and Objectives: Statin response is variable among individuals, possibly due to genetic variants. This study explored the influence pharmacogenetic variants on therapy response and statin-related adverse events (SRAE) in Brazilian patients with familial hypercholesterolemia (FH).
Material and Methods: Unrelated patients clinically diagnosed with FH, aged ³18 years, and on statin treatment were recruited. Laboratory and clinical information were collected from medical records. Exon-targeted gene sequencing was used to identify variants in genes related to FH and pharmacokinetics (PK) of statins. A prediction framework analysis was used to explore the functional impact of variants in PK-related genes.
Results and Conclusion: Of the 113 patients included, 34 carried an FH-associated variant. In 23 PK genes, 56 variants were predicted as deleterious (functionality prediction score - FPS>0.5). *ABCC1* rs45511401 (c.2012G>T) (FPS=0.8) was associated with high low-density lipoprotein cholesterol (LDL-c) reduction on statin treatment (adjusted $p<0.05$) and c.2012T allele increased by 18.1% LDL-c reduction ($p=0.016$, adjusted $p=0.090$). *CYP3A5*3* (rs776746) (FPS=1.0) was associated with high risk of SRAE ($p=0.015$, adjusted $p=0.064$). In conclusion, *ABCC1* c.2012T enhances statin response and *CYP3A5*3* increases the risk of SRAE in FH patients.
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FCF300-2021

IDENTIFICATION OF APOB VARIANTS USING NGS IN PATIENTS WITH FAMILIAL HYPERCHOLESTEROLEMIA

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Introduction and Objectives: Familial hypercholesterolemia (FH) is a hereditary disease characterized by high plasma low-density lipoprotein cholesterol and total cholesterol, increasing the risk of premature cardiovascular diseases. The molecular diagnosis is mainly attributed to variants in LDLR, APOB, PCSK9 and LDLRAP1 genes. The aim of this study is use next generation sequencing and bioinformatics tools searching variants pathogenicity in the APOB gene from a sample of the Brazilian population.
Material and Methods: FH patients (n=210) were sequenced in a panel enriched with the exonic regions of the APOB gene on the MiSeq platform (Illumina). Variants suggestive of pathogenicity were analyzed in silico using ANOVAR functional prediction tools and the data were classified according to the American College of Medical Genetics and Genomics (ACMG).
Results and Conclusions: A total of 55 variants were identified including 43 missenses, 2 splicing, 5 InDel, and 5 in regulatory regions (3'UTR and 5'UTR). 33 knows variants were identified and classified as benign and likely benign, 17 classified as variant of uncertain significance, and 1 classified as variant pathogenic or likely pathogenic according to ACMG for FH. In addition to providing the first description of 4 variants in the literature. These results provide the direction for in vitro biological functional studies to confirm involvement in the phenotypic manifestation.
Financing: FAPESP; CNPQ; CAPES

FCF303-2021

N-ACETYLCYSTEINE (NAC) ATTENUATES PHENOTYPES REGULATED BY QUORUM SENSING IN *Pseudomonas aeruginosa*

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Introduction and Objectives: The expression of many virulence genes in bacteria is regulated by quorum sensing (QS), and there is a growing interest in finding QS inhibitors (QSIs). *N*-acetylcysteine (NAC) is already used as a treatment of respiratory tract infections, with antibacterial properties, being able to interfere on biofilm formation and disruption. Nonetheless, little is known if NAC influences QS mediated bacterial communication. The aim of this work was to evaluate the effect of NAC as QSI in *Pseudomonas aeruginosa* PAO1.
Material and Methods: Evaluation of QSI was measured by green fluorescent protein (GFP) expression of monitor strains *P. aeruginosa lasB-gfp* and *rhlA-gfp*. Pyocyanin levels were quantified in chloroform-extracted cultures at 520 nm. Rhamnolipids were quantified adjusting the pH of the culture supernatant to 2 with HCl and measuring at 570 nm. Molecular docking was performed between seven LasR structures of *P. aeruginosa* with NAC, *N*-(3-oxododecanoyl)-L-homoserine lactone (3-oxo-C12-HSL) and (Z-)-4- bromo-5-(bromomethylene)-2(5H)-furanone (furanone C30) in CLC Drug Discovery Workbench 4.0 Software.
Results and Conclusions: The GFP signal is turned down in the presence of QSI, and NAC at 1000, 500, 250 and 125 μM was capable of inhibiting GFP expression for *lasB- gfp* and *rhlA-gfp* ($p < 0.05$). Pyocyanin and rhamnolipids production decreased ($p < 0.05$) 34 and 37% in the presence of NAC at 125 μM, respectively. NAC had a better binding score than the QSI furanone C30, suggesting it has potential to bind to LasR protein. Overall, NAC showed promising anti-QS activities in *P. aeruginosa* PAO1 that support its application in anti-virulence strategies.
Financing: CAPES; CNPq.

FCF304-2021

RATIONAL DEVELOPMENT OF DAPSONE NANOCRYSTALS

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Introduction and Objectives: Dapsone (DAP) is a synthetic derivative of diamino-sulfone and has dual main therapeutic activities: antimicrobial and anti-inflammatory. Although the extensive potential therapeutic indications, as a class II drug according to the biopharmaceutical classification system, its low aqueous solubility may impair its bioavailability. Nanotechnology represents a viable alternative to overcome solubility impairment. Nanocrystals represent a successful drug delivery system, with several products already on the market. A rational development through Design of experiments (DoE) was used to develop optimized dapsone nanocrystals.
Material and Methods: The nanosuspension was prepared using small-scale wet bead milling, according to Romero, Keck e Müller (2016). A surface response design was carried out using Minitab® 18 (Minitab Inc., State College, PA, US) software.
Results and Conclusions: The optimal parameters and the suitable stabilizer agent were established by Box–Behnken, resulting in nanocrystals with z-average of 200-250 nm (measured by dynamic light scattering), a remarkable 200-time reduction compared to the DAP raw material (56.7 µm). Furthermore, the distribution of particle size was monomodal, with Polydispersity Index lower than 0.2. Even after undergoing size reduction and lyophilization, the crystalline state of the drug substance was maintained. The nanosuspension presented stability against precipitation during four months of storage (30ºC and 65% relative humidity. Finally, the saturation solubility study of nanocrystals showed an improvement of
3.8 compared to DAP raw material in water. The rational approach enables the optimization of DAP nanosuspension. This innovative formulation allows a reduction of the administered dose, adverse effects, and therapy's cost without affecting efficacy. In summary, it might result in increased compliance among patients.
Financing: CAPES

FCF306-2021

EFFECT OF NATURAL COMPOUNDS IN *Salmonella* sp. BIOFILM FORMATION

BEATRIZ XIMENA VALENCIA QUECÁN (D), UELINTON MANOEL PINTO (PD)

Faculty of Pharmaceutical Sciences, University of São Paulo, Brazil

Introduction and Objectives: One cause of contamination in food industry can be attributed to biofilms which persist in food processing equipment. Natural Biocides may be an interesting approach to inhibit biofilm formation (BF). This study evaluated the effect of curcumin, naringenin, quercetin, baicalein, resveratrol, cinnamaldehyde, phytol, farnesol, vanillic acid, rosmarinic acid and eugenol on *Salmonella* sp. BF.
Material and Methods: A biofilm producing strain of *Salmonella* sp. was selected. Crystal violet method (CV) was used for biofilm quantification and compound's screening compared with growth control, and minimum inhibitory concentration (MIC) and growth curves of each compound were determined using micro dilution method, testing concentrations based on the literature. The five compounds with the best inhibitory effect using fixed concentrations of 50 and 500 µg/mL were chosen for additional tests, and then compared using a fixed concentration of 50 µM. The compound with the best inhibitory effect was selected for future studies.
Results and Conclusions: *Salmonella enterica* serovar Montevideo was the best biofilmforming strain among 28 tested serotypes. The MICs were determined, and sub-MIC concentrations were used to determine its effect on BF. The five compounds with inhibitory effect were quercetin, naringenin, eugenol, farnesol, resveratrol and cinnamaldehyde. However, cinnamaldehyde had the best inhibitory effect on BF in a concentration of 50 µM without affecting microbial growth. The results showed that cinnamaldehyde has an inhibitory effect on *Salmonella* Montevideo BF. More experiments will be carried out to test cinnamaldehyde effect alone and combined with commonly used biocides on biofilm morphology.
Financing: CAPES; CNPq

FCF307-2021

MIXER TORQUE RHEOMETER AS A TOOL FOR OBTAINING QUINOA GRANULES USING CHIA MUCILAGE AS A BINDER

ROSANA PEREIRA DA SILVA (PG), JEFFERSON GAZIRO (IC), WILY EDGARDO ALAYO MENDOZA (IC), FANNY JUDHIT VEREAU REYES (IC), ALANA SOUSA SILVA (IC) and HUMBERTO GOMES FERRAZ (PD)

Department of Pharmacy, FCF/USP

Introduction and Objectives: Quinoa *(Chenopodium quinoa Willd.)* is a gluten-free grain, widely cultivated in South America, especially in the Andes region, while chia *(Salvia hispanica)* is a seed rich in proteins, originally from Central America. Quinoa and chia grains are rich in dietary fiber, but chia is capable of forming viscous mucilage when in contact with water and can be exploited in the development of food, nutraceutical, and pharmaceutical formulations. Thus, the objective of this work was to study the feasibility of using chia as a binder for the production of quinoa granules, obtaining a preparation with high fiber content.
Material and Methods: The chia was purchased in powder form and the quinoa grains went through a grinding process. Subsequently, a Mixer Torque Rheometer (MTR) was used to study the granulation point and to control the parameters provided for in the tests, the Caleva Process Solutions Ltd software coupled to the MTR was used. A fractional experimental design was elaborated to evaluate the influence of the amounts of quinoa, thinner (microcrystalline cellulose), and chia binder in the granule formulations.
Results and Conclusions: It was possible to obtain a granulation point for each experiment without requiring an excessive volume of water. The highest torques were those with concentrations of 2.78, 20.0 and 23.08% of chia mixed in 30.77, 53.33 and 55.55% of quinoa, respectively and 23.0 to 46.0% of microcrystalline cellulose. Statistical analysis showed that chia contributed to a smaller volume of water, and the concentration of microcrystalline cellulose was able to influence the torque and volume of water needed to reach the granulation point. We concluded that chia was able to act efficiently as a binder for the production of quinoa granules, in order to produce tablets with high fiber content.

FCF308-2021

EXPLOITING KOMBUCHA'S YEAST METABOLISM ON BACTERIA STRESS RESISTANCE

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Departamento de Tecnologia Bioquímico-Farmacêutica FCF/USP

Introduction and Objectives: Traditional fermented foods have a wide variety of microorganisms, especially those from ingredients and the environment. This category is recognized as safe and has important long-term microbial stability—the complex interactions between different species justify this phenomenon. This work evaluated the probiotic bacteria viability during aerobic stress conditions associated with different yeast strains co-cultures.
Material and Methods: Ten different yeast isolates from kombucha were identified (MALDI-TOF) and co-cultured with Bifidobacterium animalis subsp. lactis HN019 on aerobic condition. Yeast isolates were inoculated ($1x10^6$ CFU/mL) in co-culture with $1x10^9$ CFU/mL of the bacteria in RCM and maintained at 37°C for 15 days in aerobic stress condition. After incubation period, the bacteria were recovered on RCA with cycloheximide on anaerobic conditions, and colony count was performed.
Results and Conclusions: We observed that of the 10 isolates, 3 of them were effective to maintain the bacterial viability after the incubation time, in which *Rhodotorula mucilaginosa* and *Pichia membranifaciens* provided the bacteria viability maintenance in 10^8 CFU/mL, while a third isolate, still unidentified, maintained the bacteria viability in 10^7 CFU/mL. However, the probiotic bacteria growing alone decreases 3 log CFU/mL on the same conditions. *Bifidobacterium* spp. usually suffer limitations in the presence of oxygen because they produce hydrogen peroxide to recover NAD+. These data suggest that such interactions can be used as a biotechnological tool, where yeasts can benefit the survival of bacteria through several mechanisms, such as increasing the antioxidant potential of the environment, enabling their survival even in aerobic conditions.
Financing: CAPES

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Examples:

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Janiszewski M, Lopes LR, Carmo AO, Pedro MA, Brandes RP, Santos CXC, et al. Regulation of NAD(P)H oxidase by associated protein disulfide isomerase in vascular smooth muscle cells. J Biol Chem. 2005 (in press).

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