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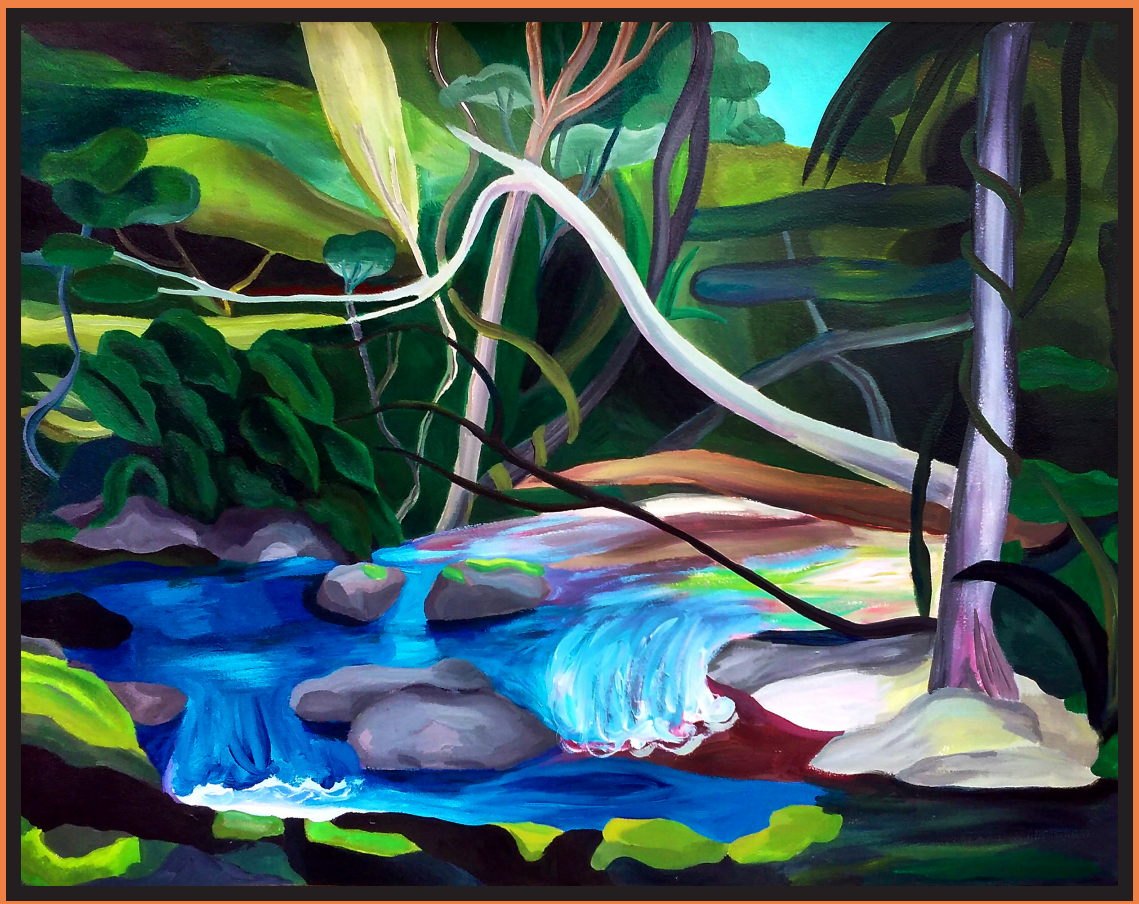

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REUNIÓN CONJUNTA SAIC SAB AAFE AACYTAL 2023

LXVIII REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE INVESTIGACIÓN CLÍNICA (SAIC)

XXV JORNADAS ANUALES DE LA SOCIEDAD ARGENTINA DE BIOLOGÍA (SAB)

LV REUNIÓN ANUAL DE LA ASOCIACIÓN ARGENTINA DE FARMACOLOGÍA EXPERIMENTAL (AAFE)

VIII REUNIÓN CIENTÍFICA REGIONAL DE LA ASOCIACIÓN ARGENTINA DE CIENCIA Y TECNOLOGÍA DE ANIMALES DE LABORATORIO (AACYTAL)

15-17 de noviembre de 2023
Hotel 13 de Julio – Mar del Plata

EDITORES RESPONSABLES
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Dra. Silvina Pérez Martínez
Dr. Ventura Simonovich
Dr. Gabriel Pinto

have occurred, in which the role of NABs in the development of the skin lesions has to be consider.

457. 362. **COMPARISON OF POLYPHENOL CONTENT IN ARBEQUINA AND BARNEA VARIETALS OF EXTRA VIRGIN OLIVE OILS FROM LA RIOJA**

Guzzonato Agostina [1,2], Nowakowski Federico[3], Ramirez Maria Rosana[1,2]

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Extra virgin olive oil (EVOO) is characterized by a maximum free acidity expressed in oleic acid of 0.8 g/100 g of oil. It mainly contains triglycerides, triterpenoids and polyphenols (PT). The PT content is related to oxidative stability, and the difference between the varietals is more than 45% of the PT. The PT found in the highest proportion are secoiridoids, oleuropein and ligustroside aglycones. During the olive oil extraction process, changes occur in the chemical structure of the secoiridoids of the fruit, giving rise to simpler forms such as hydroxytyrosol and tyrosol. From the perspective of human health, the importance of these compounds is due to their antioxidant capacity and the role they play in preventing degenerative diseases. The aim of this work was to determine the PT content in the EVOOs obtained from Barnea and Arbequina varietals produced in La Rioja. The extracts were analyzed by liquid chromatography with a UV detector, using syringic acid as an internal standard and tyrosol as an external standard. Conventional extraction method and calibration curves were performed. T- Student test was applied to determine the difference among the means ($P<0.05$). Significant differences were recorded between both EVOOs. Barnea varietal presented 248 mg/kg and the Arbequina varietal 268 mg/kg of PT. Regarding hydroxytyrosol, 1.8 mg/kg and 3.0 mg/kg respectively were detected. Taking these factors into account and considering that the same extraction and analysis method were applied, it can be seen that the EVOO extract of var. Arbequina from La Rioja presents a total phenol content, which is higher than that of the Barnea variety and, in turn, is within the range of values recorded for Arbequina oils of European origin. This shows that 20 grams of this oil provide the amount of PT recommended in the daily diet, and indicates that it can be an interesting raw material for the development of food supplements and/or natural cosmetics.

458. 375. **POTENTIAL OF COLOMBIAN AMAZON PLANT EXTRACTS BASED ON THE *IN VITRO* INHIBITION OF *GIARDIA LAMBLIA* TROPHOZOITES**

Joaquín Alejandro Tarruella[1], Juan Javier García-Bustos[2], Gabriel Luna Pizarro[3], Jorge Lautaro Caro[1], María Fernanda Salazar Zaffaroni[1], Brenda Casarsa[1], María Belén Joray[4], María Carolina Touz[3] and Jerónimo Laiolo[1,3]

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Giardiasis is a parasitic disease caused by the protozoan *Giardia lamblia* and is one of the main causes of diarrheal diseases worldwide resulting from the consumption of food and water contaminated with this parasite. Currently, exist eight genotypes (A-H) but only two of them—genotype A (including different strains like strain WB) and genotype B—have the capability to infect humans. The primary drugs used globally for treatment belong to the 5-nitroimidazole family, including metronidazole (MTZ) and tinidazole. However, a therapeutic failure rate of up to 20% has been observed, along with cross-resistance between different therapeutic agents. This study aimed to evaluate extracts of native plants from the Amazon region in Colombia with the primary goal of identifying new sources of active compounds capable of inhibiting the in vitro growth of *G. lamblia* trophozoites. In an initial stage, the giardicidal action of 17 extracts (at a concentration of 500 μg/mL) was analyzed on the WB/1267 strain. Those extracts demonstrating favorable biological activity underwent calculations to determine their median inhibitory concentration (IC_{50}). Among these, the extracts from *Astrocaryum chambira*, *Attalea butyracea*, and *Bactris gassipae* stood out, presenting IC_{50} values of 133.4±43.5 μg/mL, 93.1±31.6 μg/mL, and 332.1±62.9 μg/mL, respectively. A synergism test was also conducted using MTZ in combination with the extracts of interest. The IC_{50} of these extracts was computed for MTZ-resistant WB/1267 strains and GS/H7 (genotype B), encompassing both the original strains and MTZ-resistant strains. This study contributes to the potential expansion of treatment options for giardiasis by identifying novel plant extracts with promising inhibitory effects on *G. lamblia*. The findings hint at the possibility of developing alternative therapies to address the challenges posed by therapeutic resistance in combating this parasitic disease.

459. 408. **ANTI-INFLAMATORY PROPERTIES OF DEACYLCYNAROPICRIN FROM Cyclolepis genistoides**

Natalia Alza[1,2]; Teresa Pirker[3], Eva-Maria Pferschy-Wenzig[3]; Rudolf Bauer[3]; Gabriela Salvador[1,4]

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Chronic inflammation is considered a common pathological mechanism in many diseases including cancer, heart disease, diabetes, arthritis, and neurodegenerative disorders. Combating inflammation with plants and natural compounds is thought to be a strategy for replacing current therapy that causes severe side effects. The aim of our work was to study the anti- inflammatory properties of bioactive constituents from the aqueous extract of Cyclolepis genistoides D. Don (Asteraceae). This plant has been used in folk medicine in northern and central Argentina for bone pain (analgesic properties) and as a diuretic in kidney diseases. The metabolite analysis of the aqueous extract by LC-HRMS revealed the presence of coumarins (isofraxidin, fraxetin), phenolic compounds (caffeoylquinic acids and their sulfate derivatives, luteolin and its glucuronide, luteolin-7-sulfate) and two sesquiterpene lactones, deacylcynaropicrin (DACP) and its 11,13-dihydro derivative (DH-DACP). In our lab, we previously demonstrated the ability of C. genistoides and DACP to modulate the transcription factor NFμB by blocking its nuclear translocation. To gain more insight in the anti-inflammatory potential, the pharmacological activity was also evaluated in other inflammation-related cellular in vitro models. We found that DACP (20 μM) inhibited not only NFμB1 but also COX-2 gene expression in PMA-differentiated and LPS-stimulated THP-1 cells. In addition, nitric oxide production was inhibited by DACP in microglial BV-2 cells exposed to LPS and IFN-γ (IC50 = 10.4 +/- 0.7 μM). However, DH-DACP (20 μM) had no effect on the studied pro-inflammatory pathways. The difference in pharmacological properties of both sesquiterpene lactones could be explained by the Michael acceptor moiety present in the DACP structure. Taken together, we hypothesize that DACP could be a lead compound for the development of anti-inflammatory agents due to its ability to inhibit NFκB pathway.

460. 453. **ISOLATION AND CHARACTERIZATION OF AN ABIETANE DITERPENE FROM COLEUS NEOCHILUS WITH POTENT ANTIPROLIFERATIVE ACTIVITY ON A HUMAN BREAST CANCER CELL LINE**

Carla Luciana Mayora Justel[1,2], Tamara Valladares[1], Valeria Cavallaro[3,4], Ana Paula Murray[3,4], Isabel Alicia Lüthy[5], María del Carmen Esandi[1,2], Ariana Bruzzone[1], Natalia Alza[1,4]

[1]Instituto de Investigaciones Bioquímicas Bahía Blanca-CONICET, [2]Departamento de Biología Bioquímica y Farmacia - UNS, [3]INQUISUR-CONICET

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Coleus spp. have diverse ethnobotanical applications, with their most prevalent use being attributed to their medicinal properties. We have previously described the antiproliferative effect of the ethanolic extract from *C. neochilus* (also known as "boldo rastrero") on different human breast cancer cell lines. The present study is focused on the extraction and isolation of compounds responsible for this effect. The ethanol extract (BRET) was subjected to solvent-solvent extraction, yielding four different sub-extracts: hexane (BRHX), chloroform (BRCL), ethyl acetate (BRAE), and methanol-water (BRAM). Remarkably, incubation with BRAE (50 µg/ml) was more effective in reducing the viability of human breast cancer cell line MCF-7 than the other fractions (BRET: 23%, BRHX: 29%, BRCL: 52%, BRAE: 68%, and BRAM: 10% reduction; $p<0.05$) as determined by MTT assays. Given these results, BRAE was subjected to further fractionation. A column chromatography using silica gel and mixtures of dichloromethane and methanol as mobile phase rendered eleven fractions, among which seven demonstrated a significant reduction in cell viability (50 µg/ml, $p<0.05$). Notably, fractions 6 (F6) and 7 (F7) exhibited an even greater reduction in cell viability compared to BRAE (BRAE: 74%, F6: 80%, F7: 98%, reduction; $p<0.05$). Subsequently, a second separation was conducted on F7 using the same chromatographic conditions. This led to the isolation of an abietane diterpene identified by 1D and 2D NMR experiments as 7α,12β,17-triacetoxy-6β,19-dihydroxy-13β,16-spirocicloabiet-8-ene-11,14-dione. This diterpenoid showed a significant reduction in MCF-7 cell viability (25 µg/mL: 96%, 10 µg/mL: 26% reduction; $p<0.05$). Therefore, this metabolite could be responsible, at least in part, for the antiproliferative activity of *C. neochilus*. To our knowledge, this compound has been isolated for the first time from *C. neochilus* and this is the first report of its antiproliferative effect on breast cancer cells.

461. 548. **QUALITY BY DESIGN IN THE DEVELOPMENT OF AN ORAL SELF-NANOEMULSIFYING SYSTEM FOR PAIN TREATMENT**

Karem Alejandra Arrigoni-Rodriguez[1], Laura Carolina Luciani-Giacobbe[1], María Eugenia Olivera[1*]
[1]*Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba y Unidad de Investigación y Desarrollo en Tecnología Farmacéutica, CONICET-UNC. Haya de la Torre y Medina Allende, Córdoba, Argentina. CP: X5000HUA.*

A novel oral pharmaceutical composition of morphine (MOR) and omega-3 fatty acids (O3) generated a synergistic analgesic effect and reduced adverse events associated with MOR in a murine model (patent P-20120100854). Considering that a self-nanoemulsifying drug delivery system (SNEDDS) could enhance the oral absorption of O3, this study aimed to optimize a MOR-O3-loaded SNEDDS composition, maximizing the loading capacity of the oil phase. First, the limits of each component in the blank SNEDDS were explored using pseudo-ternary phase diagrams to then optimize them by means of a D-Optimal design, using ethanol, propylene glycol (Pg), kolliphor (K), and the oily phase (krill oil, AK) as independent variables. The key responses measured were polydispersity index (PDI) and mean droplet size (nm). Mathematical models were used to establish correlations between variables and responses, and a desirability function was applied to determine the optimal formulation (PDI ≤ 0.2 and smaller size). After optimization, component limits were adjusted for MOR-O3 loaded SNEDDS, which were evaluated similarly to blank SNEDDS, using Pg, K, and the oily phase: AK + MOR-O3 as independent variables. The predictive capability of the design space was confirmed with two independent optimized formulations, comparing obtained and predicted responses. Both the PDI and droplet size of blank SNEDDS and MOR-O3-loaded SNEDDS fitted significant mathematical models, defining design spaces. The most desirable blank SNEDDS formulation contained 28% Pg, 50% K, and 22% AK while the one loaded with MOR-O3 contained 33% Pg, 45% K, and 22% of oily phase, being transparent and of low flow with a droplet size of (15 ± 8) nm and PDI of 0.17 ± 0.05. In addition, it allowed the loading of MOR in the oily phase used in previous preclinical studies. In conclusion, this study offers a robust and predictive approach for developing MOR-O3 loaded SNEDDS suitable for future pain treatment applications.

P5-PHARMACOLOGY

FRIDAY 17TH NOVEMBER 9:00 - 10:30
CHAIRS: NATALIA ALZA
HUGO HECTOR ORTEGA
SILVINA ALVAREZ

462. 95. **NEUROPROTECTIVE ACTIVITY OF *N*-SUBTITUTED TRITERPENIC AZINES SYNTHETYZED FROM LUPEOL**

Florencia A. Musso[1,2], Natalia P. Alza[2,3], Gabriela A. Salvador[3,4], María Belén Faraoni[1,2]
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Currently, Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease, and its prevalence has doubled in the past 25 years. The main hallmark of PD is the progressive loss of dopaminergic neurons in the *substantia nigra*, which led to the typical motor symptoms. Despite decades of intensive efforts in finding a cure for PD, treatments alleviate symptoms through restoring dopamine deficiency or surgery. Our aim was to test the potential neuroprotection of a series of triterpenic azines in a cellular model of PD using the neurotoxic 6-hydroxydopamine (6-OHDA). Firstly, a semisynthetic approach was used to obtain a series of azines (C=N-N=C), interesting molecules for their biological properties. From the natural triterpene lupeol isolated from the plant *Chuquiraga erinacea*, we prepared 30-oxolupeol by allylic oxidation, being this latter the template for azine synthesis. Combining 30-oxolupeol different aromatic hydrazones led to 16 azines through a microwave-assisted method, with good yield. Secondly, the neuroprotective activity of these compounds was evaluated *in vitro*. Neuroblastoma cells IMR-32 were exposed to non-cytotoxic concentrations of azines in the presence of 6-OHDA (25 μM), and cell viability was determined by the MTT assay. Variable efficiency in neuroprotection was observed between azine derivatives. Whereby all of them showed some degree of restoration of cell viability at 50 μM, only three compounds displayed strong defense against 6-OHDA neurotoxicity at 10 μM, reestablishing control levels. The more active azines have the structural features of being *N*-substituted with a *para*-metoxy or *meta*-metoxy benzene at position 31, or with a furane ring. To conclude, these azines obtained from 30-oxolupeol are potential neuroprotective agents against 6-OHDA neurotoxicity and could be an inspiration for the development of new drugs for PD treatment.

463. 107. **EFFECT OF *Ligaria cuneifolia* INFUSION ("Argentine mistletoe") ON THE LIPID PROFILE AND ERYTHROCYTE AGGREGATION KINETICS IN DYSLIPIDEMIC PATIENTS**

Perez M[1], Ferrero M[1], Dobrecky C[5], Urli L[1], Balmaceda F[1], De Vuono D[4], Wagner M[5], Leiva R[3], Carnovale C[2], Luquita A[1]
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Ligaria cuneifolia (Lc), popularly known as "*Creole mistletoe*" is a hemiparasitic plant whose infusion is used in folk medicine to improve blood fluidity and decrease plasma cholesterol levels. Objectives: to analyze the effect of *Lc* infusion on plasma cholesterol levels (Cho), triglycerides and erythrocyte aggregation in patients with Cho>200mg/dl. Methods: blood samples were collected for basal determinations (C) from eight patients aged 50±15 years old (male)