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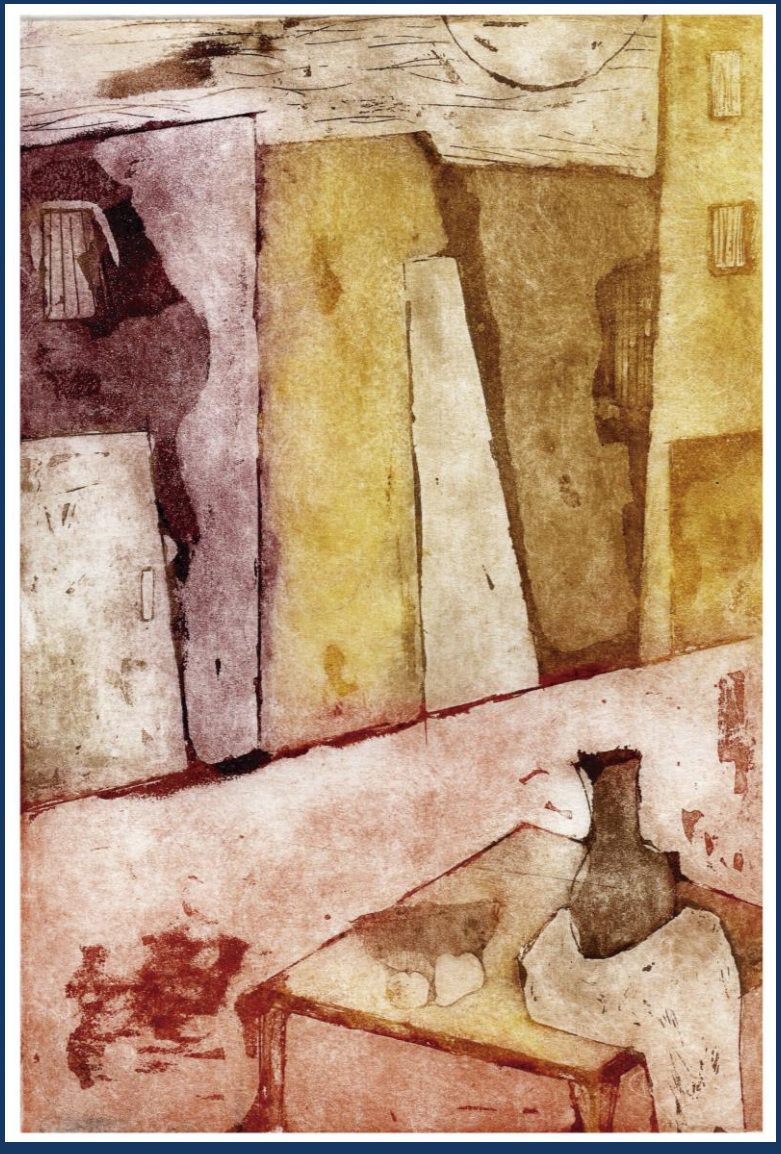

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La Tapa (Ver pág. 4)
Atardecer en la tarde
Antonella Ricagni

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REUNIÓN ANUAL DE SOCIEDADES DE BIOCIENCIA 2019

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Sociedad Argentina de Investigación Clínica (SAIC)

LI Reunión Anual de la
Asociación Argentina de Farmacología Experimental (SAFE)

XXI Reunión Anual de la
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XXXI Reunión Anual de la
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IX Reunión Anual de la
Asociación Argentina de Nanomedicinas
(NANOMED-ar)

VI Reunión Científica Regional de la Asociación Argentina de Ciencia y Tecnología de Animales de Laboratorio (AACyTAL)

con la participación de
The Histochemical Society

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biodegradables, bioadhesives and besides show a prolonged release, which makes as potentially useful for administration ocular. Latanoprost (LN) is an esterified prodrug that has a lipophilic nature, it reduces IOP through drainage of the aqueous humor. The principal goal was obtaining nanometric sized CUB through Top-down (TD) method and encapsulating LN for the treatment of glaucoma. TD approach was employed to prepare CUB of phytantriol in water with a solution of Pluronic®F127 as a stabilizer using ultrasonication. CUB were prepared at different concentrations of LN. The average particle size and zeta potential were measured using DLS. The CUB was characterized using small-angle X-ray scattering (SAXS) and isothermal titration calorimetry. The loading capacity was determined by HPLC. The in vitro release of LN from the CUB was studied using a dialysis method in cells coupled with LC/MS technique. To evaluate in vivo efficiency, the formulations were administered subconjuntival manner in normotensive rabbits. IOP and irritation were evaluated. The CUB had an average particle size of 200 nm with negative zeta potential values and it showed a good encapsulation efficiency of LN around 90 %. The SAXS studies revealed a double diamond Pn3m cubic structure for blank and LN-loaded CUB with a constant in the lattice parameter. The ITC assays showing a slight exothermic process of interaction between CUB and the drug. In vitro release essays exhibited a sustained release in the time at each concentration evaluated. In vivo essays showed an important reduction of IOP of about 20 % for 4 days without signal of significant irritation.

0839 - METHOD OF PREPARATION AND CHEMICAL PHYSICAL CHARACTERIZATION OF NP-HSA LOADED WITH MELATONIN WITH POSSIBLE APPLICATION IN NEURODEGENERATIVE EYE DISEASES

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Abstract/Resumen: The development of ophthalmic formulations for the treatment of ocular pathologies, such as glaucoma, presents a challenge due to the low absorption and bioavailability of drugs in the ocular pathway. Transport systems based on human serum albumin nanoparticles (NP-HSA) represent an important strategy, since in addition to being an endogenous molecule, significant amounts of active ingredients can be incorporated into the particle. NP-HSA are of our interest to transport melatonin, an insoluble drug that has been described as an effective antioxidant in the retina with direct and indirect free radical scavenging activity. The objective of this work was design, formulate and characterize NP-HSA loaded with melatonin with possible application in eye diseases, such as glaucoma. The obtaining of NP-HSA was carried out by desolvation process. Different crosslinking agents (CA) such as Gantrez, polyethylene glycol 400, Eudragit S100 and hydroxypropylmethylcellulose-phtalate were tested, based on the existence of functional groups capable of interacting with NP-HSA, all of them non-toxic compounds and approved as excipients for pharmaceutical formulations. In addition, it was evaluated if the change in the sequence of CA addition in the formulation, produces changes in obtaining NP-HSA, in order to achieve greater stability, yield and encapsulation efficiency. Colloidal dispersions with a pH close to neutrality were obtained. Regardless of the CA used and the order in which it was added to the system, all NP-HSA presented a unique and uniform population with a particle size between 150-230 nm. The percentages of yield (75,9 %) and encapsulation efficiency (16,8 %), showed that the method of obtaining NP-HSA whose CA is Eudragit S100, was the most efficient, obtaining optimal and stable systems in time. These results will allow us to advance in a greater physicochemical characterization, as well as in in vitro release tests of Melatonin to evaluate its release over time.

0862 - MAGNETIC NANOCLAYS: INCORPORATION AND DIRECTED DELIVERY OF NAPROXEN

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CENTRO DE INVESTIGACIÓN Y TECNOLOGÍA QUÍMICA - CITEQ-CONICET-UTN

Abstract/Resumen: Layered double hydroxides (LDH) nanoclays have many applications as matrices in pharmaceutical fields as support for controlled release systems of drugs, vitamins, biomolecules, with potential applications orally or intravenously of modified release systems. Naproxen (Nap) is a nonsteroidal anti-inflammatory drug (NSAID) used to reduce pain involved in osteoarthritis, rheumatoid arthritis, bursitis, gout. This work reported studies of intercalation drug content and magnetic response. Nap has been incorporated by the direct method (coprecipitation) into nanoclays MgAl LDH-type material at pH 10 with molar ratio equal 2, and them was impregnated with magnetic nanoparticles of Fe_3O_4. By X-ray diffraction its possible observed the drug incorporation into nanoclay and the magnetic response was studied in a vibrating sample magnetometer (VSM) at room temperature, in order to obtain super paramagnetic materials. The amount of intercalated Nap was determined by UV-visible spectroscopy at 271 nm. The basal spacing recorded was 2.3 nm this value suggests the drug has been incorporated in the interlayer of the solids, since the interlayer distance for MgAl LDH is 0.76 nm. The new gallery heights indicate that the drugs have been stacked as monolayer particles perpendicular to the LDH plane. Drug content obtained was 65 %, which indicates that it was partially incorporated into nanoclays. This system presented super paramagnetic behavior at room temperature, a property desired for use in biomedicine. The modified nanoparticles obtained suggest that these materials have potential applications as directed release systems of Nap by magnetic fields use. This work provides significant in-sight into the important area of storage, transport, and delivery of anionic drug using MgAl-LDH as host solid.

0863 - LUMINESCENT SILICA- BASED NANOMATERIALS FOR BIOMEDICINE

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INBIOSUR, DEPTO DE BIOLOGÍA, BIOQUÍMICA Y FARMACIA, UNIVERSIDAD NACIONAL DEL SUR (UNS)-CONICET (1); INSTITUT PASTEUR MONTEVIDEO (2); INSTITUTO DE QUÍMICA DEL SUR INQUISUR UNS-CONICET (3)

Abstract/Resumen: Silicon dioxide (SiO_2), a material known as "silica" presents properties that make it a good candidate as a biomaterial: it has a very labile surface for functionalization, it is easy to synthesize and it is biocompatible. Calcination after synthesis of silica NPs yields luminescent nanomaterials. Fluorescent NPs themselves would offer enhanced functionality in terms of these properties with respect to conventional organic fluorophores. In this work, the influence of the synthesis method on the hydrodynamic diameter of silica fluorescent NPs was studied in order to obtain an optimal formulation as potential theranostic. Stöber process, involving tetraethylorthosilicate (TEOS) and 3-aminopropyltriethoxysilane (APTES), has been applied to obtain different formulations from increasing APTES initial concentration. After synthesis, the NPs were calcined at 450 °C. Characterization was performed by FTIR, TEM, DRX, fluorescence spectroscopy/microscopy and DLS to determine hydrodynamic diameter (Hd). NPs synthesized without APTES do not present fluorescent properties, while the APTES containing NPs are fluorescent. Increasing concentration of APTES induces larger NPs with low stability in physiological medium. The optimal synthesis condition resulted with a TEOS:APTES ratio of 1:0.1 rendering a Hd of 450 nm with polydispersion index near 0.20. This formulation is suitable for biomedical applications in terms

of Hd and stability as potential theranostic agent for multiple pathologies, including Chronic Lymphocytic Leukemia that is of our particular interest. CLL is the most common adult leukemia in Western countries and is defined by the accumulation of mature, CD5+ B lymphocytes in peripheral blood, bone marrow and secondary lymphoid organs. Despite important progress in treatment, relapse occurs and this leukemia remains incurable in many cases. New therapeutic approaches by innovative tools acting in synergism with the last therapies approved in CLL are desirable.

0980 - SOLID DISPERSIONS AS A PHARMACEUTICAL STRATEGY FOR CARRING BENZNIDAZOLE

José María BERMÚDEZ | Cintia Alejandra BRIONES NIEVA | Santiago Nicolás CAMPOS | Alicia Graciela CID | Elio Emilio GONZO | Analía Irma ROMERO | Mercedes VILLEGAS

INSTITUTO DE INVESTIGACIONES PARA LA INDUSTRIA QUÍMICA (UNIVERSIDAD NACIONAL DE SALTA – CONICET)

Abstract/Resumen: Solid dispersions (SD) are considered one of the most successful strategies for improving the dissolution of poorly soluble drugs. Benznidazole (BZL) is an antiparasitic agent with low water solubility, used as a first-line drug for the treatment against Chagas disease. The aim of this work was to evaluate the dissolution properties of BZL from SD based on Gelucire® and poloxamer. SD based on Gelucire® 44/14 (G4414) were prepared by a modification of the fusion method with 20, 40 and 50 % w/w BZL loads (DS G4414-20, DS G4414-40 and DS G4414-50, respectively). A SD using a mixture of G4414 and poloxamer 407 (P407) (1:1) with 40 % w/w BZL load was also prepared. SD morphology was compared with the corresponding physical mixture by scanning electronic microscopy (SEM), and the dissolution profiles were obtained at 37 °C using 0.1 N HCl as dissolution medium. The data were adjusted by the Lumped model, a mathematical model developed and validated by our research group, which allowed to calculate the initial dissolution rate (DRi), the time needed to dissolve 80 % of the drug (t80%) and the dissolution efficiency (DE). SEM revealed that drug crystals were not distinguished in the SD, whereas they were clearly present in the corresponding physical mixtures, confirming that the BZL was dispersed in an amorphous matrix. The data from the dissolution profiles were properly adjusted using the Lumped model (R^2 >0.89). Not only the DRi but also the amount of BZL dissolved were improved when formulated in a SD, and decreased along with an increase in the BZL load. The SD based on the mixture of G4414 and P407 showed the greater DRi (13.70 mg/min), which was 16 times higher than the DRi of the free drug. It can be concluded that the SD developed are promising to formulate an extemporaneous suspension of BZL with adequate biopharmaceutic properties, what would lead to better oral bioavailability in the treatment against Chagas disease.

0981 - ANPHOTERICINE B RELEASE FROM POLYMERIC FILMS. MODELING AND PHARMACEUTICAL PARAMETERS DETERMINATION

José M BERMÚDEZ | Cintia Alejandra BRIONES NIEVA | Alicia G CID | Elio E GONZO | Florencia PISTÁN | Analia I ROMERO | Mercedes VILLEGAS

INSTITUTO DE INVESTIGACIONES PARA LA INDUSTRIA QUÍMICA (UNIVERSIDAD NACIONAL DE SALTA – CONICET)

Abstract/Resumen: Leishmaniasis is a "neglected" endemic disease and is a priority public health problem for Salta and Argentina. Treatment currently available in our country is very painful and invasive. Particularly for cutaneous leishmaniasis, there is no topical/local treatment that meets the activity, safety and cost requirements. For this reason, polymeric films with an appropriate drug load are proposed as alternative systems. Two polymers were selected, one of natural origin, sodium alginate (SA), and one synthetic, carbomer (CB). Amphotericin B (AnB) was used as a specific drug for the leishmaniasis treatment. The films were prepared with different drug concentrations using only SA or a combination of SA and CB. The cross section of the films was observed by scanning electron microscopy (SEM) and the in-vitro release assays were performed at 37 °C. The release profiles were analyzed and adjusted using the Lumped model developed and validated by our research group. Pharmaceutical interest parameters were calculated: t80% is the time required to reach 80 % dissolution of the total drug available, the dissolution efficiency is defined as the area under the dissolution profile up to a certain time, and the average dissolution time provides information about the ability of the polymer platform to delay the drug release. SEM images showed that films loaded with AnB maintained a dense structure and the drug was evenly distributed throughout the thickness of the film. AnB release profiles revealed that the CB incorporation caused a marked increase in the initial release rate, with a burst drug release in a short period of time, effect that is not suitable for systems that must modulate the drug release. Pharmaceutical relevance parameters were calculated and compared. It was determined that the SA films were able to modulate the drug release rate and presented optimal values of the parameters, in particular the film loaded with the highest percentage of AnB.

Toxicología / Toxicology III

Chairs: Florencia Chiappini | Sandra Ferreira

0139 - IMBALANCE IN HOMEOSTASIS RAT PLACENTA EXPOSED TO CADMIUM (G20). EFFECTS OF SOY PROTEIN AS A PROTEIN SOURCE

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Abstract/Resumen: Autophagy and apoptosis are two crucial and interconnected processes in the placenta that are often influenced by oxidative stress. Alteration between the protective and destructive mechanisms of autophagy and apoptosis seems to be associated to pregnancy-related disorders. In addition, Cd can pass through the placenta and accumulates in fetal tissues, so that rat fetal toxicity is caused by placental or maternal Cd-induced dysfunction, not by a Cd direct effect on fetuses. On the other way, soy protein is becoming increasingly important in the human diet. Isoflavones (genistein) could cause hypertrophy in endometrium and alter reproductive function in different species. To evaluate the possible protective role of soy protein consumption compared to the mechanisms by which Cd exerts its toxicity, 4 lots of female Wistar rats were used: 2 lots received casein (Cas) and 2 lots soybean (Soy) as protein source. Within each group, 1 lot received regular water (Co) and the other, 15 ppm of Cd in the drinking water. We determined TBARS, CAT and GPx activity, and nitrite concentration. RT-PCR was performed using the following primers: MT I; MT II; Nrf-2; NOX-2, SOD-2 and CAT. In Soy-Cd group Nrf-2, SOD and MT I expression increased ($p<0.05$, $p<0.01$, $p<0.001$). While mRNA NOX-2 and MT II expression decreased ($p<0.01$; $p<0.01$; $p<0.00$, respectively). Bcl-2 positive immunostaining increased in both intoxicated groups ($p<0.001$; $p<0.01$), while PCNA increased ($p<0.001$), compared to control group. Caspase-3 immunohistochemical stain decreased in Soy-Cd group ($p<0.001$). Oxidative stress and placentation are closely interrelated. We demonstrated the presence of oxidative and nitrosative stress in placental tissue. This situation may lead to an imbalance in the placental process and result in early