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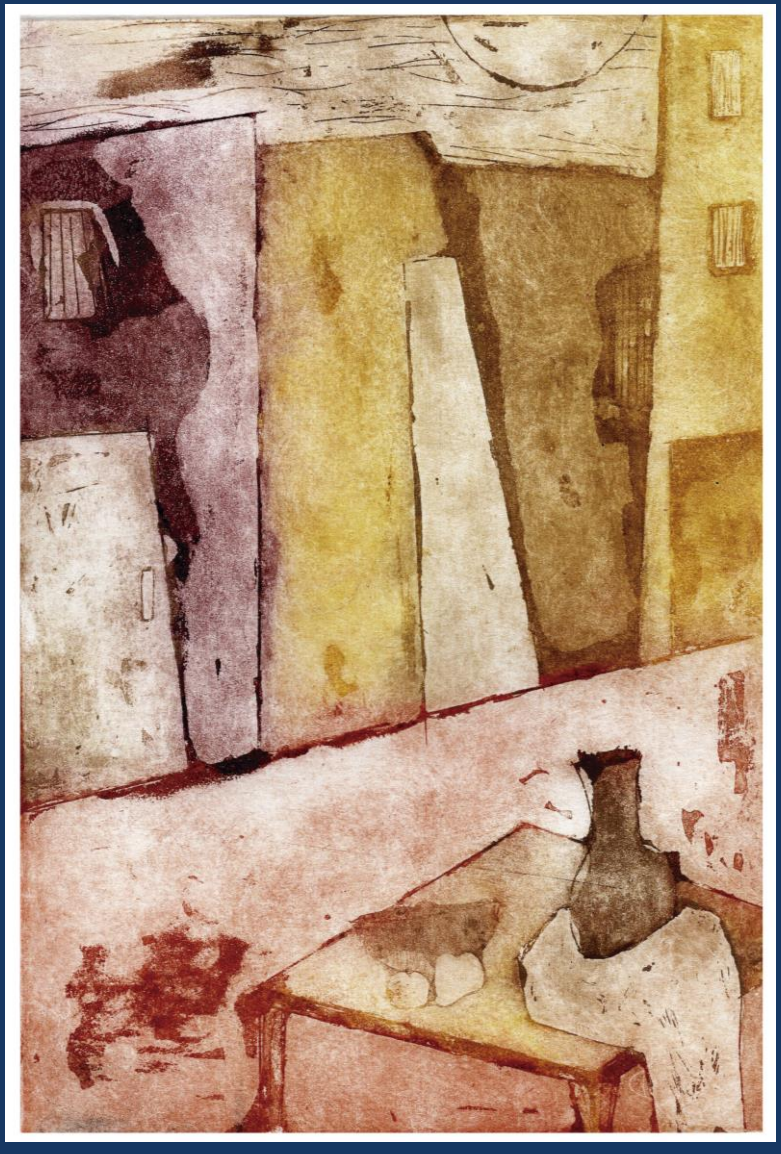

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proteins. Proteoral is a recombinant fusion protein of 92 kDa molecular weight produced by biotechnology manufacture. Proteoral has the intestinal absorption activity with the essential secretion signal located in the C-terminal with a number of glycine-rich tandem repeats in the consensus sequence responsible for the enhancing of transepithelial paracellular secretion efficiency in the intestine. The protein nanoparticle synthesis method starts from buffer solutions containing the Proteoral a therapeutic protein, a gastro-resistant polymer, and a stabilizing hydrophilic polymer. The protein nanoparticles, with an average size between 250 and 350 nm, are dispersed in an aqueous solution and they act as a vehicle carrying the therapeutic protein. In the oral administration, the protein nanoparticles are formulated using liquid vehicles or solid vehicles. We present the carrier Proteoral is a totally effective strategy in therapy of oral administration of Follicle-stimulating Hormone in an optimized oral formulation that transports the therapeutic protein and releases to the circulation system with biological activity by transepithelial paracellular passage.

ADVANCES ON BIO-NANOMATERIALS BASED ON SILICA AND MAGNETIC TARGETING

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Conventional treatments for various pathologies currently find limitations related to the low bioavailability of drugs used in the blank site and the adverse effects associated with them. Nanotechnology allows us to create platforms with biocompatible materials for anchoring drugs and biomolecules that can target the specific organ or tissue. Silica nanomaterials provide a versatile surface, added to the fact that from the implementation of specific synthesis methods, self-luminescent materials can be achieved. Thus, it is possible the conjugation in a same material of high value theranostic properties for applications not only in biomedicine but also in the field of research to elucidate the mechanisms by which nanomaterials enter the cell and are metabolized. Another tool for addressing nanomaterials to specific sites in the body is the development magnetic nanoparticles. They consist of an iron oxide core with superparamagnetic properties coated with biocompatible materials that allow the incorporation of drugs. The application of an external magnetic field allows to concentrate the nanoparticles at the desired site. The main pathologies to which we apply this nanotechnology in our laboratory are based on inflammatory, tumor and bone disease. We have developed various platforms of silica and magnetic nanoparticles evaluating the effect of biocompatible coatings and their physicochemical properties. We perform studies on biocompatibility in vitro on vascular and bone cells and on in vivo invertebrate models such as C. elegans as well as on murine mammalian models, achieving magnetic in vivo targeting to bone system in mice. In this way, the great applicability of these nanosystems in the biomedical field is demonstrated in order to improve the conventional therapies of different pathologies with great social impact.

Short talks of Nanomedicine selected posters:

0669 - STUDY OF ROUTES OF ADMINISTRATION OF ALBUMIN NANOPARTICLES FOR THE TREATMENT OF RETINAL PATHOLOGIES

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Abstract/Resumen: Retinal pathologies are treated with therapeutic agents that are administered invasively and periodically. Nanoparticles (NPs) could be a new way of performing therapies directed to the retina. the aim of this study was to evaluate different routes of administration of NPs to reach the retina and to analyze the response of the retinal pigment epithelium (RPE) to the presence of NPs. We evaluated NPs of 20 and 100 nm in diameter of human albumin associated with a quantum dot. We inoculated the 20 nm NPs through intravitreal (IV), subconjunctival (SCj), and suprachoroidal (SC) injections and the NPs of 100 nm only through SCj injections. The distribution was observed at 3 and 24 hours after the inoculation in wholemounts of retinas and choroids in a fluorescence microscope. In addition, the RPE cell line, ARPE-19, was incubated with NPs for 3 and 24 h, and were observed under fluorescence microscopy. In the IV inoculations, the NPs were detected mainly in the retina and vitreous humor, both at 3 and 24 h. After 24h, we observed inflammatory cells containing NPs. The SC inoculations showed NPs in the choroid and in the retina mainly in regions associated with blood vessels (after 3 h), persisting in inflammatory cells after 24 h. In SCj inoculations, NPs of both 20 and 100 nm were detected in the choroid (after 3 and 24 h) and in the RPE (after 24 h). In the ARPE-19 cells, we observed presence of NPs in the cytoplasm and also in the extracellular matrix, mainly after 24 h of incubation, for both NPs. We concluded that NPs compose of protein showed high biocompatibility, since we did not observed aggregation in none of the tissues analyzed. From the *in vitro* studies we can infer that the ARPE-19 cells could endocyte the NPs. From the *in vivo* studies the most promising route of administration would be the SCj, because of the NPs reach the target tissues being less invasive than the others studied.

0082 - NANOFILMS OF ADSORBED THYMOL FORMED ON TITANIUM SURFACES FOR BIOMEDICAL APPLICATIONS. ANTIMICROBIAL ACTIVITY AND BIOCOMPATIBILITY

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Abstract/Resumen: Titanium (Ti) and its alloys are widely used in the construction of permanent orthopedic and cardiovascular

implants. However, one of the most frequent causes of failures are bacterial infections by Staphylococcus aureus. This is aggravated by the abusive use of antibiotics that generate microbial resistance to conventional therapies. As a consequence, new antimicrobial nanotechnologies (AMN) emerge as promising alternatives to prevent prosthetic infections. The aim of this work was to evaluate the antimicrobial effect of an innovative AMN: thymol (TOH, phenolic phytocompound) nanofilms adsorbed on Ti (NPTOH-Ti) against S. aureus. The biocompatibility was also determined using preosteoblast cells (MC3T3-E1). To that end, 1 cm diameter grade 2 Ti discs were used and TOH was adsorbed onto their surface by 2 h immersion in 0.1 M TOH acid solution. NPTOH-Ti was detected by infrared spectroscopy (FTIR-ATR). The antibiofilm activity of NPTOH-Ti and Ti (control) was determined by immersing the metal discs in a suspension of S. aureus (10^8 bacteria/ml) for 3 h. Subsequently, the number of bacteria adhered on the discs was caunted after sonication by colony forming unit (CFU). In addition, Live/Dead (Invitrogen) staining was used to determine if the adhered bacteria were alive or dead. Finally, biocompatibility of NPTOH-Ti and Ti was assessed by staining the preosteoblast cells with acridine orange. The results showed that NPTOH-Ti has effective anti-biofilm properties. On the one hand, viable bacteria were not observed by the plating count method and Live/Dead staining exhibited only dead (red) bacteria on the surface. On the other hand, control Ti revealed 4 ± 0.5 $x10^5$ adhered bacteria that were mostly (95 %) alive (green). In addition, NPTOH-Ti and Ti showed similar cell adhesion and growth (107 ± 12 and 100 ± 16 % respectively; $p>0.05$). It was concluded that NPTOH-Ti are biocompatible and have anti-biofilm properties which make them promising to prevent prosthetic infections.

SAFE SYMPOSIUM I

STRATEGIES TO IMPROVE ANTIMICROBIAL DRUG BIOAVAILABILITY

Chairs: María Celina Elissondo / Hector Alejandro Serra

THE CHALLENGE OF IMPROVING ANTIMICROBIAL THERAPY WITH CURRENTLY AVAILABLE DRUGS

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Nowadays antimicrobial resistance (ATMR) is a global health crisis. At the current rate of emergence and spread of ATMR, annual loss of life is expected to reach 10 million deaths by 2050 with a very high economic cost. Combating ATMR requires a multifaceted approach that facilitates sustainable and equitable use of antimicrobials (ATM), thwarts the spread of infectious disease, preserves existing ATM therapies and fosters innovation of new therapies and diagnostic tools. A critical component of the ATMR solution is the development of novel ATM drugs to cover the diminishing effectiveness of existing ATM that are relied on every day for essential clinical care. However, due to a variety of inherent market failures, the present business model for ATM has not adequately responded to the growing demand for innovation. First, the success rates of moving an ATM through the different clinical phases suggests that of the ~ 39 drugs in development, only 13 will translate into a market. Second, most new ATM do not have the novel mechanisms of action or novelty in chemical matter targeting well validated targets, which are necessary to significantly ensure effectiveness against resistant pathogens. Numerous of the products in the pipeline are redevelopments or combinations of existing ATM. In third place, many of these drugs do not target the highest priority ATM resistant pathogens. Therefore, scientific and clinical advancements in ATM development are inherently challenging, particularly relative to other therapeutic fields. For this reason, our research group is choosing to focus development efforts on alternatives such as the preparing and characterizing supramolecular systems and new nanomaterials for the treatment of infectious diseases.

USE OF CYCLODEXTRINS TO IMPROVE THE BIOAVAILABILITY OF ANTIMICROBIAL DRUGS

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For many years, researchers have worked with supramolecular structures involving binary inclusion complexes with cyclodextrins (CDs). CDs are cyclic oligosaccharides used for the improvement of water-solubility, stability and bioavailability of drugs. More recently, the formation of multicomponent complexes with CD (i.e. the inclusion of a third auxiliary substance) has become more frequent due to of the versatility and further synergistic optimization possibilities that can be reached. In this context, an interesting approach in which we have been working is the development of drug delivery systems containing an ATM drug in combination with CDs and auxiliary substances with recognized antibiofilm properties. The structural and energetic features driving the inclusion of guest molecules within the CD cavity is a complex phenomenon, involving a dynamic network of intermolecular interactions and solvent effects, among other. Consequently, in order to form efficient multicomponent inclusion systems, it is necessary to identify