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Dra. Mariana Maccioni
Dra. Paula Schaiquevich
Dra. Hebe Duran

order to evaluate the effects and mechanisms involved in extrahepatic tissues.

353. (593) **CHARACTERIZATION OF A GENETIC MURINE MODEL OF ACUTE INTERMITTENT PORPHYRIA. AN OVER TIME STUDY**

Marìa Del Carmen Martínez1,2, Johanna Romina Zuccoli1, Silvina Fernanda Ruspini1, Ana María Buzaleh1,2

Acute intermittent porphyria (AIP) is an inherited disease due to Porphobilinogen deaminase (PBG-D) deficiency. Mouse models of human Porphyrias are useful to investigate disease pathogenesis and to develop new therapies. AIP model is a knockout mouse with targeted disruption of PBG-D that exhibits the typical biochemical/neurological characteristics of human AIP. The aim was to evaluate heme metabolism, hepatic damage and oxidative parameters in a genetic AIP model compared to wild type strain (*C57BL/6*). The study was performed in liver and brain using three groups (males and females): Wild type, T1 (PBG-D activity 55% reduced) and AIP (PBG- D activity 70% reduced. T1 and AIP PBG-D activity was according to the model in liver; in brain it was also reduced (40-50%, $p<0.01$) without differences between both genotypes. As was expected, 5-Aminolevulinic acid synthetase activity, heme regulatory enzyme, was elevated in liver (T1: 140%, $p<0.01$; AIP: 45%, $p<0.05$) and brain (T1: 257%, AIP: 95%, $p<0.05$) in both genotypes. Heme oxygenase (HO), involved in heme catabolism, was 100% ($p<0.05$) higher than wild type in brain in both sexes and genotypes, being hepatic HO only induced in females (50-100%, $p<0.05$). HO alteration, GSH variation and Catalase reduction (140%, $p<0.05$) would indicate stress oxidative instauration. Glutathione S-Transferase, hepatic damage marker, varied depending on the genotype. Tryptophan pyrrolase activity, pool regulatory heme marker, was elevated in liver and brain (87-140%, $p<0.05$) of AIP female. Considering that aging is a significant risk factor for impaired tissue functions and chronic diseases, alterations in the measured parameters were evaluated throughout life, using animals 12-15 months old; no major variations were observed. In conclusion, the present study has demonstrated that the differences among wild type and genetic models were more striking in AIP genotype respect to T1 and age did not affect significantly the metabolisms analyzed.

NANOMEDICINA

354. (221) **AMORPHOUS SILICA NANOPARTICLES: NEW THERAPEUTIC APPROACH FOR DRUG DELIVERY IN TRIPLE NEGATIVE BREAST CANCER**

Ibarra Agustina [(1)], Rodríguez Álvarez Tamara [(2)], Alonso Eliana N. [(1)], Coló Georgina P[(1)], Clemente Valentina [(1)], Facchineti M. Marta [(1)], Curino Alejandro C. [(1)], Ferronato M. Julia [(1)], Agotegaray Mariela [(2)].

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Triple Negative Breast Cancer(TNBC) is a heterogeneous group of tumors with difficult clinical management. Nanotechnology represents a strategy to improve current therapies. The aim of this work is to develop amorphous silica nanoparticles(SiNPs) as carriers for drugs involved in TNBC. Synthesis, physicochemical characterization and evaluation on the viability of TNBC cell lines of two SiNPs formulations were performed: amino-functionalized SiNPs($Si@NH_2$) and SiNPs modified with folic acid(FA) (Si@FA). Modified Stöber process was applied to obtain $Si@NH_2$. FA was covalently linked (Si@FA). Characterization was performed by FTIR and DLS to determine hydrodynamic diameter(Hd). Viability assays by crystal violet staining were performed in human MDA-MB-231, murine 4T1 TNBC cell lines and in non-malignant murine breast HC11 cells (10 - 500 µg/mL SiNPs, 24 h). Reactive oxygen species (ROS) generation was determined by DCDCDHF assay in MDA-MB-231 cells (500 μg/mL SiNPs). A pilot in vivo assay was conducted in mice to evaluate SiNPs acute toxicity: 30 mg/kg of $Si@NH_2$, Si@FA or control were administered weekly for 1 month. FTIR spectra confirmed functionalization with NH_2 and FA; Hd resulted as 643.7 nm and 600.0 nm respectively. Si@FA displayed a significant reduction of the viability of MDA-MB-231 and 4T1 TNBC cells. $Si@NH_2$ decreased 4T1 cell viability ($p<0.001$) although no effect was found for MDA-MB-231 cells at any of the concentrations tested. Both NPs increased ROS production with respect to control (Si@FA: $p<0.001$; $Si@NH_2$: $p<0.01$) and between them ($p<0.001$). Regarding to HC11 cells, NPs had no effect on viability. The observation of the internal organs of the animals showed no macroscopic alterations; no changes in hematocrit, behavior and body weight were observed. Altogether, these results suggest that Si@FA could be a promising nanotechnology for TNBC treatment. Further studies are in course to evaluate their effects in combination with conventional drugs.

355. (225) **LIPOSOMAL ASCORBIC ACID - PHYSICOCHEMICAL CHARACTERIZATION**

María Belén Sierra

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Objective: Physicochemical characterization of pure sunflower lecithin liposomes and sunflower lecithin liposomes combined with cholesterol, and ascorbic acid, by means of Z-potential, particle size, conductivity, density and ultrasound velocity measurements dependence with temperature. This work is meant as a preliminary screening for the development of improved delivery and bioavailability of vitamin C systems.

Materials and methods: Phosphatidylcholine from sunflower (H100), Cholesterol (Chol) and ascorbic acid (AA). H100, H100-Chol, H100-AA and H100-Chol-AA liposomes were prepared. *Zeta potential (ZP), size and conductivity* measurement of liposomes was determined with a Zetasizer Nano ZS90 equipment. Anton-Paar DSA 5000 was used to get continuous and automatically, densities (ρ) and sound velocities (u).

Results: ZP curves as a function of temperature showed that the most negative surface charge was that of the H100 Chol system, with positive surface charges for the others. H100 and H100-Chol conductivities were the lowest measured and were found to be very close to each other. H100 AA y H100 Chol AA systems had the highest conductivities. Particle size was 150 nm for H100 Chol AA liposomes, 200 nm for H100 AA liposomes and 250 nm for H100 and H100 Chol and remained constant. The lower specific volume of H100-Chol-AA liposomes in comparison with H100 membranes may be indicative of a more compact lipid bilayer structure for the former. Specific compressibility values for H100 Chol AA and H100 were similar.

Conclusions: Ascorbic acid encapsulated in sunflower phosphatidylcholine liposomes shows well-organized morphology, uniform particle size, which might lead to an improved bioavailability. It could result to be a good alternative to protect and transport vitamin C in the body.

356. (243) **CHARACTERIZATION AND IN VITRO EFFECTS OF GERANIOL-LOADED PECTIN MODIFIED NANOSTRUCTURED LIPID CARRIERS ON LUNG CANCER CELLS**

Lung cancer is the first cause of cancer-related deaths in the world. Many of the current therapies are still inefficient and/or present highly toxic undesirable side effects. The aim of the present work was the design of biocompatible and non-toxic hybrid pectin (P) nanostructured lipid carriers (NLC) containing geraniol (GOH), a monoterpene with antitumor activity, as a novel platform for the bioactive delivery of anticancer drugs.

Nanoparticles (NPs) were prepared by hot homogenization/ultrasonication method. Different pectin formulations were prepared by modifying their amount (0.1 and 0.5%, w/v) in the formulation and/or metoxilation degree -Low (LMP, 33%) and high (HMP, 74%). Ten different formulations were prepared: NLC/GOH, NLC/LMP0.1/GOH, NLC/LMP0.5/GOH, NLC/HMP0.1/GOH, NLC/HMP0.5/GOH, and their respective counterparts without GOH. NPs were characterized