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**POROUS SILICA NANOPARTICLES LOADED WITH NORFLOXACIN**

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The effect of raw magnetic mesoporous silica nanoparticles ($MMSiO_2$) and 4.97% Norfloxacin-loaded $MMSiO_2$ (NFX-$MMSiO_2$) was tested on an *E.coli* bacterial growth to evaluate inhibitory activity. $MMSiO_2$, with a core ($Fe_3O_4$)-shell type structure, were prepared by a modification of the Stöber method. The average size, surface area and isoelectric point was 125 nm, 471 $m^2g^{-1}$ and 2.4, respectively. A suitable range of concentrations of NFX-$MMSiO_2$ [16 $\mu$g/mL, 8 $\mu$g/mL, 4 $\mu$g/mL, 2 $\mu$g/mL] was seeking to the minimum inhibitory concentrations known by NFX. Microdilution inhibitory assay was conducted for of $MMSiO_2$, NFX-$MMSiO_2$ and NFX. The samples were incubated for 18h at physiologic temperature of 37°C and absorbances were measured in a Multiskan GO VWR Co Microplate Spectrophotometer, Thermo Scientific. The results were standardized subtracting the absorbances of the vehicle and data were statistically analyzed.
The evidence suggested differences in the inhibitory activities depending on NFX-$MMSiO_2$ concentrations when compared to NFX. At low doses, the major prevalence of growth decrease was observed for NFX-$MMSiO_2$ in comparison to the same doses of the antibiotic, whereas at higher concentrations of NFX-$MMSiO_2$ the effect decreased in comparison to free NFX. There was exposed a decline in the inhibitory growth activity of NFX according to its minimum inhibitory concentration (MIC) in contrast to $MMSiO_2$ which activity remained constant. It was also observed that $MMSiO_2$ did not present a direct effect on the bacteria. However, these NPs could have enhanced the antibiotic effect at lower doses. This fact may be due to the outcome of iron from the NPs and to changes in the ionic force of growing medium.
Results demonstrate that loading NFX into $MMSiO_2$ would be a strategy to target the drug to specific sites in the organism under the influence of an external magnetic field, at low concentration to ensure a better performance in comparison to free NFX.

**361.** (297) **VALIDATION OF A SCALABLE METHOD USING CHROMATOGRAPHY TO ISOLATE ENGINEERED EXTRACELLULAR VESICLES CARRING IGF1 DERIVED FROM HUMAN UMBILICAL CORD PERIVASCULAR CELLS FOR THE TREATMENT OF EXPERIMENTAL LIVER FIBROSIS**

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Introduction: Extracellular vesicles (EVs) derived from human umbilical cord perivascular cells (HUCPVC) over-expressing IGF1 mediates therapeutic effect on liver fibrosis in mice. We aimed to validate these results using EVs isolated by affinity chromatography, a scalable method.
Methods: HUCPVC were infected with adenoviruses codifying for human IGF1 (AdIGF1) or green fluorescence protein (AdGFP). Viability was determined by MTT assay. IGF1, TNF-$\alpha$, and CD63 levels were determined by ELISA. EVs were isolated from HUCPVC supernatants by anion exchange chromatography and characterized by electron microscopy. Expression of pro-fibrogenic genes (Col1A2 and $\alpha$SMA) on hepatic stellate cells (LX2) were determined by qPCR. Antifibrotic effect of EVs was determined in BALB/c mice with liver fibrosis (thioacetamide for 8 weeks). The treatments were administered on week 6 (Groups: Saline, EVs-AdIGFI or EVs-AdGFP, 3 doses, 15 $\mu$g/dose/mice every 5 days).
Results: First, we found that HUCPVC infected with 2.5 to 30 MOI showed over-expression of IGF1, keep cell viability and exert an anti-inflammatory capacity on J774 macrophages revealed by decreased TNF-α expression ($p<0.0001$ vs LPS). HUCPVC-derived EVs isolated by chromatography showed typically size, shape, and CD63 expression. Increased IGF1 levels were observed on lysed-dialyzed EVs-AdIGFI indicating its loading on EVs ($p<0.001$). Pro-fibrogenic genes expression was reduced in LX2 cells after treatment with IGF1-loaded EVs ($p<0,01$ vs. DMEM). *In vivo* treatment with EVs-AdIGF1 resulted in a further amelioration of liver fibrosis when compared to saline group ($p<0,001$).
Conclusion: Our results showed that EVs-AdIGF1 isolated by a chromatographic scalable method carry IGF1 and keeps anti-fibrotic activity. This data provides a novel approach of nanomedicine to generate therapeutic tools for the treatment of iver fibrosis.

**362.** (332) **DEVELOPMENT AND CHARACTERIZATION OF SOLUPLUS® NANOMICELLES ASSOCIATED TO SPECIFIC IgG AS AN INNOVATIVE STRATEGY FOR THE DETECTION AND NEUTRALIZATION OF SHIGA TOXIN TYPE 2**

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Shiga toxin type 2 (Stx2) is the main virulence factor of Shiga toxin producing *Escherichia coli* and is responsible for triggering Hemolytic Uremic Syndrome (HUS). We aimed to develop and characterize polymeric nanomicelles (PN) with the amphiphilic polymer Soluplus® coupled to anti-Stx2 IgG in order to introduce innovative proposals for the detection of Stx2 and treatment of HUS. PN of Soluplus® were formulated in PBS and coupled with IgG anti Stx2 from hyperimmune (PN-IgG-Stx2) or control bovine colostrum (PN-IgG-Ctrl). The hydrodynamic size of PN, PN-IgG-Stx2 and PN-IgG-Ctrl was evaluated by Dynamic Light Scattering. Morphology of PN or PN-IgG-Stx2 was analyzed by Transmission Electron Microscopy (TEM). The PN toxicity was evaluated on both Vero and Human Glomerular Endothelial cells (HGEC) and cell viability was determined by neutral red uptake. After coupling PN with IgG, Stx2 neutralization capacity of PN-IgG-Stx2 or PN-IgG-Ctrl was evaluated on Vero and HGEC cells and the percentage of cell viability was analyzed. The hydrodynamic size of the PN of Soluplus® and IgG-Stx2 showed an average diameter of 70.2 ± 1.5 nm and 40.9 ± 2 nm, respectively. When both components were coupled, a single peak with a similar hydrodynamic size of the PN was observed (70.4 ± 0.2 nm). TEM analysis revealed circular particles with a diameter corresponding to 100 nm either in PN and PN-IgG-Stx2 particles. PN-IgG-Stx2 were able to neutralize Stx2 on Vero and HGEC cells in a dose dependent manner. When comparing the neutralization capacity of Stx2 by IgG-Stx2 *vs* PN-IgG-Stx2 a significant improvement in the cell viability of Vero and HGEC was observed with the PN-IgG-Stx2 ($p<0.001$). The association between anti-Stx2 IgG from bovine colostrum and Soluplus® PN was optimized and characterized. Encouraging results of antibody functionality coupled with PN were registered. These results may open the perspective of the design of new nanoplatforms for neutralization and/or detection of Stx2.

**363.** (358) **ANTIOXIDANT NATURAL COMPOUNDS ADSORBED ON SILICA NANOPARTICLES**

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