Удружење токсиколога Србије
Serbian Society of Toxicology

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INTERNATIONAL UNION OF TOXICOLOGY

10th Congress of Toxicology in Developing Countries (CTDC10)

12th Congress of the Serbian Society of Toxicology (12th SCT)

BOOK OF ABSTRACTS

Metropol Palace Hotel
April 18-21, 2018
Belgrade, Serbia

Belgrade, 2018

10th Congress of Toxicology in Developing Countries (CTDC10)
12th Congress of the Serbian Society of Toxicology (12th SCT)

Book of Abstracts

Publisher
Serbian Society of Toxicology
Vojvode Stepe 450, 11000 Beograd
E-mail: vevodi@pharmacy.bg.ac.rs

Editor
Vesna Matović

Editorial Assistant
Stefan Mandić-Rajčević

Design and Prepress
Atelje, Beograd
www.atelje.rs

Printed by
Dosije studio, Beograd
www.dosije.rs

Publishing Year
2018.

Circulation
350

ISBN 978-86-917867-1-7

(6 mg/Kg body weight) through intraperitoneal injection for a period of two weeks (5 days/week) from PND 15 to PND28. To study the protective effect of nutrient metal mixture, pups were administered calcium (Ca), iron (Fe) and zinc (Zn) in combination as 0.02% by a single gavage together with Mn injection. The results showed mitochondrial succinate dehydrogenase (SDH), lactate dehydrogenase (LDH), and isocitrate dehydrogenase (ICDH) activities decreased in cortex and cerebellum at PND 28, PND 60 and 3 months age group rats following exposure to Mn. Most notably, Mn exposure decreased the activities of thyoredoxin reductase (TrxR), aconitase (Acon), superoxide dismutase (SOD), and catalase (CAT) while the MDA levels increased in the cortex, and cerebellum of selected age groups of rats. *In silico* findings revealed that aconitate hydratase in complex with modified control cluster (S4F3Mn) influences the Acon activity in the presence of the substrate. Mn-exposed rats exhibited deficits in total locomotor activity and grip strength in rats. However, supplementation of the nutrient metal mixture containing Ca, Fe and Zn reversed the effects of Mn on energy metabolism, oxidative damage of mitochondria and motor behaviour of the rats. In conclusion, our findings demonstrate that exposure to Mn during the development of brain greatly increased the mitochondrial dysfunction, subsequently, associated with motor coordination deficits in rats. Furthermore our results suggest that application of nutrient metal mixture may potentially be beneficial in treating Mn- neurotoxicity.

Supported by Science and Engineering Research Board (DST, Govt. of India), File No. YSS/2015/000289.

Keywords: oxidative damage, *in silico* studies, aconitase, manganese, motor functions

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NANOMATERIALS

The Removal of Ni^{2+} and Cd^{2+} -ions onto Synthetic Mineral Based Composite Functionalized by Polyethylenimine

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This study presents the synthesis of porous cordierite-based ceramics and its surface activation by polyethylenimine/nano-CeO_2 for the heavy metal removal. The synthesis was carried out by the addition of following powders: MgO, Al_2O_3, and SiO_2 in 2:2:5 molar ratios, respectively. The oxide(s) mixture was further processed in two sequential stages: i) ball milled in the ethanol for 40 minutes and palletized under the pressure of 3 t/cm^2, as a pre-sintering process, and ii) the pallets were further sintered for 2h in the air atmosphere at 1350 °C, under a heating rate of 20 °C/min. The sintered mineral composite was crashed and sieved, and mixed with 20 wt % of nanocellulose, as a pore forming agent. Nanocellulose mixture was pressed into pallets under 5 t/cm^2 and sintered at 700 °C, under a heating rate of 5 °C/min. The obtained synthetic cordierite was further tested as the adsorbent activated by polyethylenimine/nano-CeO_2 for the removal of Ni^{2+} and Cd^{2+} -ions. The adsorption isotherms, kinetics models, and thermodynamic parameters were also analyzed, manifesting that the adsorption is a spontaneous and endothermic process. The phase composition of the pristine and activated cordierite was analyzed by the X-ray diffraction method (XRD), Fourier transformation infrared (FTIR) spectroscopy and scanning electron microscopy (SEM). This work has shed light on the mechanism of heavy metals removal from the

aquatic medium using the novel hybrid (nano)synthesized material.

Keywords: synthesis, surface coating, nanomaterial, toxic metals, adsorption.

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Oleic Acid Double Coated Iron Oxide Nanoparticles as New Relevant Biocompatible Nanoparticles with a Particular Mechanism of Activity

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Iron oxide nanoparticles have gained an increased interest in recent years due to their unique features, like: superparamagnetism, biocompatibility and stability in aqueous solutions. However, a lack of knowledge concerning the toxicity associated to their administration confines their use. This study was aimed to offer relevant information about the cytotoxicity induced by oleic acid double coated magnetic iron oxide nanoparticles (MIONPs) to a panel of healthy (keratinocytes, fibroblasts) and tumor (human and murine melanoma, lung carcinoma and breast carcinoma) cell lines. The MIONPs were obtained by combustion method followed by coating with a double layer of oleic acid. The physico-chemical properties of the biocompatible colloidal suspension were evaluated by means of suitable techniques, such as: optic microscopy (TEM and SEM), magnetic measurements (VSM) and dynamic light scattering (DLS). The cytotoxicity was detected with colorimetric cell-viability bioassays like MTT and Alamar blue. The dimensions of the coated MIONPs were in the range of 30 nm, size considered non-toxic for *in vivo* administration. The nanoparticles exerted a significant cytotoxic effect on all the tumor cell lines even at low concentrations (10 μM), whereas in the case of healthy cells the viability was affected only at the highest concentration tested (50 μM). The MIONPs induced a different kind of cell death, a particular enucleation process that was not described for other types of nanoparticles. These results show that MIONPs displayed a high stability in aqueous solutions (mandatory criteria for *in vivo* administration), and anticancer properties, making them suitable as nanoplatforms for chemotherapeutic agents.

This work was supported by a grant of Minister of Research and Innovation, CNCS - UEFISCDI, project number PN-III-P4-ID-PCE-2016-0765, within PNCDI III.

Keywords: magnetic iron oxide nanoparticles, oleic acid, cytotoxicity, melanoma, breast carcinoma

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Effects of Silver Nanoparticles on Neurodevelopment Using C57BL/6 and A/J Primary 3D Organotypic Mouse Midbrain Cultures

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Many consumer, commercial, and medical products have been increasingly using silver nanoparticles (AgNPs) for their antimicrobial properties. Observations of silver in adult and fetal brain following *in vivo* AgNPs exposures have also led to concerns about the potential of AgNPs as neurotoxicants. In this study, we investigated effects of gold-cored AgNPs of differing sizes and coatings (20nm AgCitrate, 110nm AgCitrate, and 110nm AgPVP) on neurodevelopment across two mouse strains using our 3D organotypic embryonic midbrain micromass cultures. Primary cells from gestational day (GD) 11 C57BL/6 or GD 12 A/J mouse embryos were used. After 24-hour AgNP exposures at three different time points of development (days *in vitro* (DIV) 7, 15, and 22), cytotoxicity was assessed by both nominal and dosimetric dose. Dosimetry of silver and gold was evaluated in cultures, where gold acted as a tracer for uptake of intact gold-cored AgNPs and silver as a tracer for dissolved particles. Results by nominal and dosimetric dose demonstrated significantly increased cell death in a dose-dependent manner at DIV 15 and 22, which represents differentiation stages of neurodevelopment in both strains. When assessed by dosimetric dose, cultures were more sensitive to smaller particles in both strains despite less uptake of Ag. The extent of AgNP dissolution in the micromass cultures across

CIP- Каталогизација у публикацији
Народна библиотека Србије

615.9(048)

CONGRESS of Toxicology in Developing Countries (10 ; 2018 ; Beograd)
Book of Abstracts / 10th Congress of Toxicology in Developing Countries (CTDC10) [and] 12th Congress of the Serbian Society of Toxicology (12th SCT), April 18-21, 2018, Belgrade, Serbia ; [editor Vesna Matović]. - Beograd : Serbian Society of Toxicology, 2018 (Beograd : Dosije studio). - 184 str. ; 30 cm

Na vrhu nasl. str.: IUTOX International Union of Toxicology. - Tekst štampan dvostubačno. - Tiraž 350. - Registar.

ISBN 978-86-917867-1-7

1. Udruženje toksikologa Srbije. Kongres (12 ; 2018 ; Beograd)

a) Токсикологија - Апстракти

COBISS.SR-ID 261499916