help to determine whether the dietary phytochemicals can be given to humans daily as broad spectrum nutrient supplements to prevent different diseases. These studies will also aid in the design of more highly developed and effective prevention strategies, and treatment of CVDs and breast cancer involving dietary constituents.

1493 Amoebicidal Activity of Extracts of *Rhus trilobata* on *Entamoeba histolytica* Trophozoites

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In Mexico, intestinal amoebiasis morbidity is estimated in 5,000 cases per 100,000 people, being children the most affected. Metronidazole (MTZ) is considered the antiamoebic drug of election, being the most used for the treatment of luminal and extraluminal infection. Secondary adverse effects of long-time MTZ administration included cytotoxic and genotoxic effects as well as carcinogenic risk; in addition, amoebas might develop resistance to these drugs. The objective of this work was to evaluate the amoebicidal activity of the plant extract *Rhus trilobata* on *Entamoeba histolytica* trophozoites. With this purpose, steams and fruits extracts of *Rhus trilobata* were prepared by boiling in water (AE) or by maceration in 70% methanol. Solid phase separation using C18 columns and solvents of different polarity were used for separation of stems extracts. Viability tests of cells treated with the obtained fractions were performed using the WST-1 reagent; concentrations tested were 0, 2.5, 5 and 10 µg/mL of each extract. Results showed that crude AE, and both A2 and A4 fractions, had a significant decrease on trophozoites viability compared with control cells without treatment; the effect of A2 and A4 fractions at 10 µg/mL had no difference with MTZ IC50 (0.04 µg/mL). Methanol extract or their fractions had no significant effect on trophozoites viability at concentrations tested. Both extracts of fruits, aqueous and methanolic, decreased significantly the cell viability in a dose-response, by an IC50 of 17.13 y 17.17 µg/mL, respectively. These results demonstrated that *Rhus trilobata* extracts contain compounds that have an important amoebicidal effect. Additional studies are being conducted to elucidate the nature and mechanism of these active ingredients. (This work was partially supported by FOMIX CHIH-2010-C01-147532).

1494 General Composition and Antifungal Effect of Commercial Ethanolic Mexican Propolis on *Aspergillus flavus*

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Propolis is a natural resinous substance collected by bees and majorly used as beehive sealant. As the result of multi-chemical composition, propolis has many biological properties that can benefit human and animal health, such as its potential use to control fungal contamination in foods. In this research we determined the general composition and the *Aspergillus flavus* antifungal effects of 10 commercial ethanolic extracts collected in Mexico. Total resin, protein (Bradford assay) and polyphenol content (Folin-Ciocalteu reagent) were measured to evaluate propolis composition. *A. flavus* inhibition of radial growth assay was used to evaluate its antifungal effectiveness. Briefly, fungal buttons (0.5 mm diameter x 2 mm thick) of *A. flavus* culture were placed in the center of petri dishes prepared with propolis media (propolis 0, 0.5, 1, 2.5 and 5% in Sabouraud media) and placed on an incubator at 32 C for 5 days. Inhibition of growth was measured with a ruler and recorded in addition, spore suspensions at 5 day culture of all treatments was evaluated by using a Neubauer's chamber (haemocytometer) on tween media. Data was analyzed with parametric assays of Analysis of Variance (One-Way ANOVA), and the comparisons between the means were performed using the multiple comparison test of Tukey, with a significance level of 5% ($P \leq 0.05$). Results showed moderate variations of propolis composition. Ranges of resin content were 370-900 mg/mL, while protein and polyphenol ranges were 0-3.8 mg/mL and 90-2270µg/mL, respectively. Variations were also noted in antifungal effectiveness where inhibition of growth varied from 0.5, 1 % as the lowest effect and 2.5 %as the minimal effective concentration, in the spore count the 2.5 and 5% are the most effective concentration and 1% and lower concentration haven't differences with the 0% treatment. Clearly the effectiveness of propolis as antifungal can be influenced by its chemical composition. Funding: CONACYT-SNI 56078. Key words: propolis, *Aspergillus*, antimicotic.

1495 Compounds and Fractions from *Oxyanthus speciosus* Showed Good *In Vitro* Antimycobacterial Activity and Low Cytotoxicity Profile

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Tuberculosis, a disease caused by *Mycobacterium tuberculosis* has re-emerged at an alarming rate, becoming a global concern due to the upsurge of HIV/AIDS and resistant strains, remains a threat to the health of human. TB was reported to cause 1.4 million mortality of the world's population in 2012 and an estimated 8.7 million death. The incidence, prevalence and mortality rates of TB have reduced in the Western world but still remain alarming in Asia and Africa. The upsurge of resistance strains has rendered the available drugs ineffective. The use of medicinal plants is an alternative to the use of synthetic drugs as a curative agent for infectious disease, arousing the interest of researchers investigating substitutes to modern medicine. The acetone extract, fractions and 2 compounds from *Oxyanthus speciosus* DC. were screened for their anti-mycobacterial activity against 3 non-pathogenic mycobacteria namely: *Mycobacterium aurum*, *Mycobacterium fortuitum* and *Mycobacterium smegmatis* and a pathogenic mycobacteria: *Mycobacterium tuberculosis* (8104) using a microdilution assay. Bioautography was used to determine the presence of antimycobacterial compounds of the plant extracts and fractions. Cytotoxicity was determined using the tetrazolium-based colorimetric cellular assay (MTT) against C3A human liver cells and Vero kidney cell. The selectivity index (SI) values of the extracts were calculated. The extract had a significant activity against the 4 tested organisms with a minimum inhibitory concentration (MIC) values ranging from 60 - 170 µg/ml. Two fractions out of 11 had significant activity against *M. smegmatis* with MIC value of 39µg/ml. Compound 1 showed a moderate activity against all the tested mycobacteria strains with MIC values ranging from 12.5 - 50 µg/ml. The acetone leaf extracts of *O. speciosus*, and 4 fractions had relatively low cytotoxicity with LC50 value ranging from 0.160 - 0.383 mg/ml against C3A human liver cells. Compound 1 showed no cytotoxicity against Vero kidney cell even at the highest concentration (200 µg/ml) while compound 2 had an LC50 value of 33.77 µg/ml. The crude extract and all the fractions had selectivity index (SI) values (LC50/MIC) ranging from 0.03-3.27. Compound 1 had the best SI values ranging from 4-16. The promising activity of compound 1 *in vitro* suggests its potential as an anti-TB drug candidate.

1496 Nano-Scaled Cerium Oxide Induces Platelet Activation *In Vivo*

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Nano-scaled cerium oxide (nCeO2) is used in a variety of applications, including use as a fuel additive, catalyst, and polishing agent, yet potential adverse health effects associated with nCeO2 exposure remain incompletely understood. *In vivo* studies using a rat model have shown that inhaled nCeO2 can deposit in deep lung tissues and induce fibrosis; however, little is known about other potential cardiovascular disorders (CVD) associated with nCeO2 exposure. Similarly, blood-based biomarkers to predict risk of nCeO2-induced disease remain limited. To address these knowledge gaps, rats were intratracheally instilled with 3.5 mg/kg nCeO2 and plasma samples were analyzed 28 days after treatment to identify potential biomarkers of such nCeO2 -induced disorders. Plasma samples revealed increased levels of pro-inflammatory mediators such as IL-1β and IL-6, as well as the pro-fibrogenic mediator TGFβ1 in response to nCeO2. Platelets are one of the main sources of circulating TGFβ1, and these small (3-5 µm), anucleate cells are known to contribute to numerous inflammatory disorders and CVD following activation and subsequent degranulation. Thus, we hypothesized that platelets are activated in response to nCeO2 treatment. Consistently, we found that platelets isolated from nCeO2-treated rats released significantly more TGFβ1 than those isolated from control animals, indicating degranulation of these cells and suggesting that platelets may be contributing to nCeO2-induced fibrosis and CVD. Interestingly, an amorphous silica-coated nCeO2 (amsCeO2) induced levels of TGFβ1 from platelets

consistent with those isolated from saline-treated animals, demonstrating that "safety-by-design" strategies for preparing engineered nanomaterials may prove useful in ameliorating some of the harmful effects of nCeO2. Collectively, these results shed light on possible biomarkers for nCeO2-incuded disease and highlight a potential role for platelets in such diseases. Disclaimer: The findings and conclusions in this abstract are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

1497 Animal Inhalation Exposure to Nanomaterials: Design, Conduct, and Data Interpretation

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With the dramatic growth of nanotechnology, there are concerns about potential health risks of these man-made nanoparticles in workplaces. These particles possess a large specific surface area which can enhance their reactivity on cellular surfaces as well as small size that allows translocation across cellular barriers once deposited in the lungs. Toxicological studies have been conducted by using laboratory animals exposed to aerosols containing nanoparticles via inhalation. The design of an adequate animal exposure is based on human equivalent dose in an occupational environment. However, physical properties of airborne nanoparticles in an exposure chamber are sometimes difficult to determine because their size and concentration may be different from those of particles in the bulk material due to aggregation. In addition, particle loss onto chamber surfaces due to diffusion and electrostatic charges affects the uniformity in the chamber. It is thus important to investigate the dispersion property and aerodynamic behavior of test nanomaterials prior to conducting the exposures. In this study, three nanomaterials, titanium dioxide (TiO2), carbon nanotubes (CNT), and cerium oxide, were respectively selected to mimic real-life aerosols with a diverse range of particle morphologies. They were used to demonstrate that different nanomaterials may require different exposure designs. Results indicated that, not only different generation (e.g., powder dispersion, liquid nebulization, *in situ* flame reaction) and characterization (e.g., microscopic counting, gravimetric analysis, real-time monitoring) methods should be selected to complement the diverse physical characteristics of the particles, but analysis in terms of exposure metric (count, surface area, or mass) and dose relevancy (e.g., metric, target, and response) should be carefully dealt with depending on the biological endpoints of the studies. For example, an acoustic vibration setup with a gravimetric tool was adequate for fibrous CNT exposure, while a magic-finger activation system with a number-based monitoring device was suitable for spherical TiO2 exposure. In summary, the information provided here will help researchers effectively design and conduct animal inhalation exposure studies that yield useful toxicological data of nanomaterials.

1498 A Framework for the Derivation of a Health-Based Occupational Exposure Limit for Silver Nanoparticles

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With the increased production and widespread commercial use of silver nanoparticles (AgNPs), human and environmental exposures to AgNPs are inevitably increasing. In particular, persons manufacturing and handling AgNPs and AgNP containing products are at risk of exposure, potentially resulting in health hazards. While silver dusts, consisting of micro-sized particles and soluble compounds already have established occupational exposure limits (OELs), silver nanoparticles exhibit different physicochemical properties from bulk materials and an additional OEL may be needed. Our framework integrates toxicological and exposure data newly available for AgNPs to determine potential health risk to workers and to derive an OEL. Our approach considers toxicokinetic factors and is adjusted for silver dosimetry and clearance. Our proposed OEL for AgNPs is based on a dosimetrically adjusted benchmark concentration (BMC) calculated from subchronic rat inhalation toxicity assessments, and estimated human equivalent concentration (HEC). It is anticipated that our recommended level will protect workers from potential health hazards, including lung, liver, and skin damage. This work was done in collaboration with the NCNHIR Consortium and supported by NIH/NIEHS grants U19ES019545, P30ES07033 and RD835.

1499 Effects of CdSe/ZnS Quantum Dots on Reactive Oxygen Species and Respiratory Burst in Peripheral Blood Leukocytes Taken from Gclm Wild-type, Heterozygous and Null Mice

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CdSe/ZnS quantum dot (QD) nanoparticle exposure is associated with the production of reactive oxygen species (ROS), possibly as a consequence of compromised mitochondrial respiration, or activation of NADPH oxidases (NOX), either of which can result in enhanced superoxide anion radical (O2-.) levels. Neutrophils and monocytes are known to produce O2-. after stimulation with bacterial and fungal components, or with phorbol ester (PMA), which involves activation of a NOX-dependent respiratory burst. It is unknown what effect QDs have on ROS levels and NOX activation in peripheral blood leukocytes, and whether this is influenced by glutathione (GSH), which is dependent on glutamate cysteine ligase modifier subunit (Gclm) expression. In this study we evaluated the effects of QDs on ROS levels under basal and PMA-stimulated conditions in peripheral blood leukocytes from Gclm wild-type (WT), heterozygous (Het) and null (KO) mice. Leukocytes were incubated with QDs for 3 hr at increasing concentrations (0.25 nM - 5 nM), and basal and PMA-stimulated ROS levels in leukocyte subsets were measured using DCFDA fluorescence and flow cytometry. At low level exposure, QDs caused an increase in baseline ROS levels in blood neutrophils (but not monocytes) from Gclm KO and WT mice, but at higher QD concentrations (above 1 nM) there was depression of this effect. QDs caused inhibition of PMA stimulated NOX activity in neutrophils taken from Gclm WT and KO mice (but not Het mice). There was no appreciable effect of QDs on NAD(P)H levels, as indicated by UV light-induced blue autofluorescence. These data suggest that QD-mediated increases in ROS levels, with simultaneous inhibition of NOX activity may result in compromised neutrophil function and innate immunity, especially in cases of GSH deficiency. Support: NIEHS grants U19ES019545, P30ES007033, T32ES015459, T32AG000057.

1500 Different Surface Coatings on IONP Project Differential Proteomic Patterns of Protein Corona

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Protein corona (PC) has been proposed as the main biological entity of cell interaction that could define the toxicological response to Fe3O4 nanoparticles (IONP). Coating of IONP with polyethilenglycol (PEG) and polyvinylpyrrolidone (PVP), is a widely accepted strategy to avoid excessive protein binding and undesirable uptake. Previously we demonstrated that IONP coated with PEG induced complement activation and proinflammatory response in a rodent model i.v. administrated. This study aimed to identify the protein profile of the PC on IONP with different surface coatings. Blood plasma was employed as a source of proteins in order to form a hard PC on IONP bare (IONP-b), coated with PVP (IONP-PVP) and PEG (IONP-PEG). After PC formation, proteins were desorbed from IONP, resolved in a SDS-PAGE and identified by LC-MS-MS. Protein analysis was performed using Gene Ontology tools. In total, 409 proteins were identified adsorbed to IONP-b, 497 on IONP-PVP and 434 on IONP-PEG. A set of 263 proteins was found to be shared by all three IONP and account for 64%, 52% and 60% of IONP-b, PVP and PEG of total coronas, respectively. Proteins involved in response to an external stimulus, lipid transport, coagulation and complement system were mainly adsorbed to IONP-b. IONP-PVP showed less number of proteins involved in lipid transport but more proteins related to coagulation compared to IONP-b. Meanwhile PEG coating adsorbed less proteins associated to lipid transport and coagulation, and more related to the immune response compared to IONP-b. These results suggest that only a small particular set of proteins surrounding the IONP-PEG could impair homeostasis and be involved in inducing a pro-inflammatory response and complement activation *in vivo*. These findings could be used to perform selective protein targeting coatings to be used to avoid triggering of adverse effects to IONP.

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 55th Annual Meeting of the Society of Toxicology, held at the New Orleans Ernest N. Morial Convention Center, March 13–17, 2016.

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The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 629.

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- CE Continuing Education Courses
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- HH Historical Highlights Sessions
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