compared to sham-control (0.6 + 0.2 g vs. 0.7 + 0.1 g, respectively; $p < 0.05$). Due to decreased pup and placental mass, PE was significantly reduced in e-cig dams (3.7) versus 4.4 in sham-control. Sex ratio within pups was also calculated. There was a trend for fewer male pups to be born to e-cig dams, however at the time of submission the ratio was trending, but not significant (p=0.06). Interestingly, 4 of 6 e-cig dams exhibited signs of pyometra, a uterine infection noted by pus within the uterine body. Whereas pyometra was not observed in any sham-control dams. Future directions will include protein analysis of placental tissues. At this time, it appears that PG/VG exposure alone has adverse health effects on fetoplacental health. *Support: WV-CTSI NIH-U54 GM104942-05 (ECB), NIH-R01 ES015022 (TRN).*

3654 Mechanisms of Cell Injury following Pulmonary Exposure to Inhaled Molybdenum Trioxide Nanoparticles (MoO_3 NPs) in Golden Syrian Hamsters

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MoO_3 NPs are extensively used in biomedical, agricultural, and engineering industries due to their physical properties. With an increased use of MoO_3 NPs the risk of exposure leading to adverse health effects to the human population is heightened. The purpose of this study is to evaluate the possible mechanism of injury from pulmonary exposure to inhaled MoO_3 NPs in Golden Syrian Hamsters. Hamsters were exposed via a whole body exposure chamber and divided into four groups: a room air control group, a control group exposed to aerosolized H_2O for 4h/day for 8 days, a group exposed to 5mg/m^3 MoO_3 NPs for 4h/day for 8 days (5-NP), and a group exposed to 5-NP, but given a 1 week recovery period post exposure (5-REC). Lung tissue from the 5-NP and 5-REC groups had increased levels of Beclin-1 (1.4 and 1.8 fold, respectively with significance in the 5-REC group) and Cathepsin B (2.8 and 2.3 fold, respectively, with significance in the 5-NP group). LC3-I was decreased in both 5-NP and 5-REC (.85 and .79 fold, respectively) and LC3-II decreased in 5-NP (.78 fold) and increased in 5-REC (1.2 fold), data was not significant for LC3-I and II. The NLRP3 inflammasome biomarkers were increased in both 5-NP and 5-REC respectively: NLRP3 (2.5 and 3.6 fold, with significance in 5-REC), ASC (1.3 and 1.7 fold, no significance for both groups), and Caspase 1 (3.8 and 3.0 fold, with significance in the 5-NP group). Levels of inflammatory cytokines were increased in 5-NP and 5-REC: IL-1β (1.5 fold significance for both groups) and TNF-α (1.5 and 2.6 fold, respectively, with significance in the 5-REC group). Ultrastructure morphology of the lungs in the 5-NP and 5-REC group had particles internalized in the interstitial cells and formation of autolysosomes. Animals in both the 5-NP and 5-REC groups were able to initialize autophagy, but protein expression of LC3 was decreased; indicating interference in autophagosome formation. MoO_3 NPs exposure resulted in increased expression of Cathepsin B that activated the formation of the NLRP3 inflammasome and release of Caspase 1 in both 5-NP and 5-REC groups. Active Caspase 1 led to an increase of IL-1β in both 5-NP and 5-REC groups that led to cell death via pyroptosis. Internalization of MoO_3 NPs may further support cell damage and death induced by pyroptosis. Results from this study indicate that toxicity from inhalation exposure to MoO_3 NPs may be mediated by autophagy and pyroptosis.

3655 Lung Toxicity and Gene Expression Changes in Response to Multiwalled Carbon Nanotubes Exposure in Rats

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Carbon-based nanomaterials have many applications and, therefore, human exposure to them potentially resulting in adverse health effects should be anticipated. Determination of the molecular mechanisms underlying the toxicity induced by carbon nanotubes has merit in the prevention of the adverse health effects potentially resulting from their exposures. Currently, a rat toxicity model was employed to investigate the molecular mechanisms underlying the lung toxicity induced by exposure to multi-walled carbon nanotubes (MWCNT). Rats were exposed, by whole-body inhalation, to air or an aerosol containing MWCNT particles to result in cumulative doses (concentration x time) ranging from 22.5 to 180 (mg/m^3)•h over a three-day period. Toxicity and global gene expression profiles were determined in the rat lungs, 16-hours following the last exposure. MWCNT particles, associated with alveolar macrophages (AMs), were detected in the lungs of the exposed rats. Mild to moderate histological changes consisting of increased cellularity, thickening of the alveolar wall, alveolitis, fibrosis, and granuloma formation were detected in the rat lungs. Bronchoalveolar lavage (BAL) toxicity parameters such as lactate dehydrogenase activity, number of AMs and PMNs, oxidant production by phagocytes, and levels of multiple cytokines (IL-1β, IL-10, IL-13, IL-16, IL-18, MCP-1, MIP-2, and TNF-α) were significantly altered in response to inhalation exposure to MWCNT in the rats. Global gene expression profiling identified several significantly differentially expressed genes (fold change >1.5 and FDR p value <0.05) in the lungs of the MWCNT exposed rats, compared with the controls. Bioinformatics analysis of the gene expression data identified significant enrichment of several diseases/biological functions (for example, cancer, leukocyte migration, inflammatory response, mitosis, and cell movement of phagocytes) and canonical pathways (for example, kinetochore metaphase signaling pathway, granulocyte and agranulocyte adhesion and diapedesis, acute phase response, and LXR/RXR activation). The alterations in the lung toxicity parameters and gene expression changes exhibited a dose-response to the MWCNT exposure. Taken together, the data provided insights into the molecular mechanisms underlying the pulmonary toxicity induced by inhalation exposure of rats to MWCNT.

3656 The Protective Role of Quercetin on Silver Nanoparticles-Induced Hepatotoxicity in Sprague-Dawley Rats

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Silver nanoparticles (Ag-NPs) are among the most commercially used nanomaterial globally. Due to their strong antibacterial properties, Ag-NPs can be found in many consumer products, as well as applications for life sciences. Due to its extensive usage it can cause adverse biological effects, leading to great concern about the human health and environment. The current study aims to confirm the hepatotoxicity induced by silver nanoparticles (Ag-NPs) and to assess the possible role of quercetin (Qur) against hepatotoxicity caused by Ag-NPs. Twenty five healthy male Sprague-Dawley rats were divided into three groups. First group of rats were control group (distill water), in the second group Ag-NPs was administered orally to the rats at the dose of 100 mg/Kg and the third group was administered with 100 mg/Kg Ag-NPs along with 100 µl of Qur for five consecutive days. The role of Qur antioxidant against toxicity of Ag-NPs was determined by measuring certain serum liver enzymes (alanine and aspartate aminotransferases, gamma-glutamy transferases, alkaline phopshatases) and biomarkers of oxidative stress malondialdehdye (MDA) and reduced glutathione (GST) in the liver tissues of the rats. Samples were collected 24 hrs after the last treatment following standard protocols. There was a significant increase in the level of serum liver enzymes (ALT, AST, ALP, GGT) and MDA in the Ag-NPs exposed rats relative to control rats; whereas, on the contrary, reduced glutathione was considerably decreased in the Ag-NPs exposed rats compared to the control rats. Co-administration of Qur to AgNPs (100 mg/Kg) exposed rats produced significant changes in the biochemical parameters compared to Ag-NPs exposed rats. There was a decrease in the level of liver enzymes and oxidative stress biomarkers and increase in reduced glutathione in the Qur +Ag-NPs group. This may indicate that Qur antioxidant might have acted as a protective agent against the liver dysfunction caused by hepatotoxcity of Ag-NPs.

3657 Chronic Exposure to the Food Additive Silicon Dioxide (E551) at a Human-Relevant Dose Blocks Induction of Oral Tolerance to Dietary Antigens

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Food-grade SiO_2 (E551 in EU), composed of aggregated nanoparticles (NPs), is used as an anticaking and antifoaming agent in powdered foods, with chronic dietary exposure in humans (0.8-74 mg/kg/day). Because SiO_2-NP models block induction of oral tolerance (OT, an immune mechanism for food antigen acceptance), the current study in mice aimed at evaluating whether chronic exposure to E551 at a human-relevant dose, added to a solid food matrix or in liquid suspension, alters the establishment of OT towards a food antigen model. Mice were daily treated for 60 days without (controls) or with E551 (10mg/kg BW/day) in water suspension (gastric gavage) or incorporated into food pellets (solid matrix). Food intake was controlled. At day 41, mice were orally exposed to the dietary antigen ovalbumin (OVA) (20mg/mouse; OVA-tolerized mice) or PBS vehicle for 3 days. All mice were subsequently immunized by subcutaneous injection of OVA (100µg/mouse) on day 48. Blood was collected 1 week after for anti-OVA IgG serum titers to evaluate OT induction *in ova*-tolerized mice exposed or not to E551. In all groups, to further assess OT to food antigens, mice were *de novo* challenged by oral OVA (25µg/mouse) for 5 days before sacrifice. Isolated immune cells from mesenteric lymph nodes (MLN) were activated by PMA/ionomycin to assess pro- (IFNγ) and anti-inflammatory (IL-10, TGFβ) cytokine secretion measured by ELISA. Fecal lipocalin (Lcn)-2 level was used as a global marker of gut inflammation. In control mice, OVA tolerance protocol (oral OVA) lowered by 87% circulating anti-OVA IgG levels ($p<0.0001$) compared to oral PBS group, showing normal OT induction to OVA. In contrast, anti-OVA IgG titers did not decrease *in ova*-tolerized mice chronically exposed to E551 regardless of the vehicle, showing blockade of OT to food antigens. *in ova*-tolerized mice exposed to E551 through food pellets, *de novo* oral challenge with OVA increased ($p<0.05$) fecal Lcn-2 levels (+131%) and IFNγ (+139%) production by MLN cells, together with a drop ($p<0.05$) of TGFβ (-46%) and IL10 (-46%) compared to OVA-tolerized controls, demonstrating gut inflammation. These results showed that chronic E551 exposure at a human dietary level in solid or liquid matrix impairs OT to dietary antigens, and promotes intestinal inflammation supporting food intolerance.

SOT 61ST ANNUAL MEETING & TOXEXPO • SAN DIEGO, CA MARCH 27–31, 2022

The Toxicologist

Supplement to *Toxicological Sciences*

SOT | Society of Toxicology

Toxicological Sciences
The Official Journal of the Society of Toxicology
www.academic.oup.com/toxsci

OXFORD UNIVERSITY PRESS

ISSN 1096-6080 Volume 186, Issue S1 March 2022

Publication Date: March 23, 2022