2803 Exposure to Respirable Biodiesel/Diesel Blend (BD50) Exhaust Particulate Generates Pronounced Aberrations in Male Reproductive System

E. R. Kisin[1], N. Yanamala[1], M. T. Farcas[1], D. W. Gutkin[4], M. R. Shurin[4], V. E. Kagan[2], A. D. Bugarski[3] and A. A. Shvedova[1,5]. *[1]EAB, NIOSH, Morgantown, WV; [2]Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA; [3]Office of Mine Safety and Health Research, NIOSH, Pittsburgh, PA; [4]Pathology, UPMC, Pittsburgh, PA and [5]Physiology and Pharmacology, WVU, Morgantown, WV.*

Biodiesel (BD) is considered an environmentally friendly, renewable fuel produced from vegetable and seed oils, animal fats and/or waste oils. Blends of BD with conventional hydrocarbon-based petroleum diesel (PD) are most commonly distributed for use in the fuel marketplace. Exposure to particles found in diesel exhaust (DE) has been reported to cause respiratory disease, cardiovascular disease and lung cancer. The disruption of male reproductive function has also been observed after exposure to DE particulates. To address whether respirable BD influences the murine male reproductive system, we compared the adverse effects of BD50 and PD exhaust particulate in C57BL6 mice. We found that pulmonary exposure to BD50 particulate significantly altered sperm integrity including concentration, motility and morphological abnormalities during the time course of post exposure. Moreover, BD50 caused up-regulation of inflammatory cytokines, increase in testicular testosterone, and reduction of serum luteinizing hormone. Testicular histopathology revealed interstitial edema, clustering of the dystrophic seminiferous tubules with arrested spermatogenesis and the presence of degenerating spermatocytes. Additionally, we observed that exposure to inhalable BD50 particulate caused severe oxidative stress and DNA damage in male reproductive organs as compared to PD. Overall, these results demonstrate that exposure to respirable BD50 exhaust particulate, in comparison to PD, generates pronounced adverse effects on male reproductive function.

2804 Genotoxic Effects of Cobalt Nanoparticles *In Vivo*

Y. Mo[1], R. Wan[2], Y. Zhang[1], A. Gu[3], D. Tollerud[1] and Q. Zhang[1]. *[1]Department of Environmental and Occupational Health Sciences, University of Louisville, Louisville, KY; [2]Department of Pathology, Fujian Medical University, Fuzhou, China and [3]Institute of Toxicology, Nanjing Medical University, Nanjing, China.*

Our and other groups have demonstrated that exposure to cobalt nanoparticles (Nano-Co) caused oxidative stress and inflammation *in vitro* and *in vivo*, which have been shown to be strongly associated with genotoxic and carcinogenic effects. However, few studies have been reported on Nano-Co-induced genotoxic effects *in vivo*. Here, we propose that Nano-Co may have genotoxic effects due to its high capacity for causing oxidative stress and inflammation. Our results showed that exposure of mice to Nano-Co (50 µg/mouse) for one week resulted in extensive lung inflammation. Ki-67 and proliferating cell nuclear antigen (PCNA) were stained by immunohistochemical methods to determine cell proliferation. Our results showed that increased Ki-67 and PCNA staining was observed in bronchiolar epithelial cells and hyperplastic type II pneumocytes in mouse lungs exposed to Nano-Co for one week. After four months of treatment, extensive interstitial fibrosis and proliferation of interstitial cells with inflammatory cells infiltrating the alveolar septa were observed. In the thickened alveolar walls, bronchiolization of the alveoli was observed, which was characterized by replacement of alveolar epithelial cells with bronchiolar-type epithelium and sometimes micro-papillomatosis. A large number of macrophages lined the alveolar walls, and emphysematous changes appeared. Increased nuclear Ki-67 and PCNA positive immunostaining was also found in some bronchiolar epithelial cells and bronchiolized cells in lungs from mice treated with Nano-Co. Moreover, exposure of mice to Nano-Co for three and six months caused increased level of 8-OHdG in genomic DNA of mouse lung tissues. Our results suggest that exposure to Nano-Co resulted in oxidative stress and lung inflammation and cell proliferation. In addition, gpt delta transgenic mice were intratracheally instilled with Nano-Co for four months and the mutant frequency and mutation spectrum in gpt gene was determined. Our results showed that Nano-Co induced a much higher mutant frequency as compared to controls, and the most common mutation was G:C to T:A transversion, which may be explained by Nano-Co-induced formation of 8-OHdG. These findings have important implications for understanding the potential health effects of nanoparticle exposure.

2805 Effects of Different Sizes of Silver Nanoparticles on *Gammarus fossarum* (Crustacea, Amphipoda): Link Between Physiological and Behavioural Responses

A. C. Gutleb[3], K. Mehennaoui[3], A. Georgantzopoulou[2,3], S. Cambier[3], G. Maël[4], J. Andreï[4], V. Felten[4], T. Serchi[3], S. Contal[3], J. Ziebel[3], C. Guignard[3], Y. Balachandran[1], S. Pain-Devin[4] and L. Giambérini[4]. *[1]Bharathiar University, Coimbatore, India; [2]NIVA, Oslo, Norway; [3]ERIN, Luxembourg Institute of Science and Technoogy, Esch-sur-Alzette, Luxembourg and [4]LIEC, University Lorraine, Metz, France.*

Despite the growing number of studies on the toxicity of AgNPs, their mechanisms of action in aquatic organisms are still poorly understood. The aim of this study was to investigate the toxic effects of different sizes of "conventionally synthesized" (AgNPs 20 and 200 nm) and "green synthesized" (making use of plant extracts avoiding solvents and other hazardous chemicals) (AgNPs 23 and 27 nm) particles on survival, physiological and behaviour responses of *Gammarus fossarum*. A first experiment aimed at determining the toxicity of AgNPs and Ag+, and to compare the sensitivity of two different populations of *Gammarus fossarum*. The first set of animals (Gf1) was collected at La Maix (Eastern France) and the second one (Gf2) was collected at the Schwaarzbaach (Colmar-Berg, Luxembourg). After sexing, males were kept and following a ten-day acclimatization period, animals were exposed during 72h to Ag+, AgNPs 23nm (1 - 8 µg.L-1), AgNPs 27 nm (1 - 100 µg.L-1), AgNPs 20 and AgNPs 200 nm (10 -1000 µg.L-1). The results showed that Ag+ (LC50Gf 1 = 3.9 µg.L-1, LC50Gf 2 = 2,3 µg.L-1) was the most toxic form of silver for both populations, followed by AgNPs 23 nm (LC50Gf 1 = 7.7 µg.L-1, LC50Gf 2 = 4.9 µg.L-1), AgNPs 27 nm (LC50Gf 1 > 100 µg.L-1, LC50Gf 2 = 5.5 µg.L-1) and AgNPs 20 nm (LC50Gf 1 = 835 µg.L-1, LC50Gf 2 > 1000 µg.L-1). Gf2 appeared to be the most sensitive population and was selected for the second experiment. Exposure to the highest concentration of Ag+ and AgNPs 23 nm (3 µg.L-1) led to a significant decrease in survival rates of Gf2. The sub-lethal investigations showed that Ag+ at 1 and 3 µg.L-1 and AgNPs 23 nm at 3 µg.L-1 significantly ($P<0.05$) decreased osmoregulation and locomotor activity. AgNPs 20 nm and AgNPs 27 nm had no effects on any of the studied responses. In addition to highlighting the potential of *G. fossarum* as a model organism in nanotoxicology, this study illustrates that AgNPs act at very low concentrations and their toxicity may be dependent on their physico-chemical properties.

2806 Evaluation of the Adjuvant Effects of Transcutaneously Exposed Silver Nanoparticles with Different Size in Mouse Model

Y.-M. Cho[3], Y. Mizuta[3], T. Toyoda[3], J.-i. Akagi[3], T. Hirata[1,3], R. Adachi[3], Y. Kimura[3], T. Nishimaki-Mogami[3] and K. Ogawa[3]. *[1]Department of Pharmacology, School of Pharmacy, Showa University, Tokyo, Japan; [2]Division of Biochemistry, National Institute of Health Sciences, Tokyo, Japan and [3]Division of Pathology, National Institute of Health Sciences, Tokyo, Japan.*

Silver nanoparticles (AgNPs) are, largely due to their antimicrobial properties, the most commonly used in consumer products such as cosmetics, clothing, household products, room sprays and even in food products. Although a human exposure via dermal as well as oral routes has been rapidly increased by large amount of manufacture and utilization, there are few reports on the immunotoxicity of transcutaneously exposed AgNPs. We investigated immunological and histopathological changes of mice transcutaneously sensitized with AgNPs. Citrate coated AgNPs of different primary sized (10, 60 and 100 nm in diameter) at a dose of 49 µg in 2 mM citrate buffer (vehicle) with 100 µg ovalbumin (OVA) was applied in skin patches to the left flanks of 8-week old BALB/c female mice 3 days a week for 4 weeks, and then an immune response was evoked with 1 or 5 mg of OVA given via i.p. or i.g. routes, respectively, and rectal temperatures, scores of anaphylactic responses, plasma histamine levels and histopathological changes were determined. In the OVA + AgNPs groups evocated via i.p. injection, increased IgG1 and IgE levels after sensitization and decreased rectal temperature, with augmented anaphylaxis scores and plasma histamine concentrations after evocation were noted, Ki67-positive germinal center in lymph nodes being observed more frequently than in the vehicle group. In the OVA + AgNPs groups evocated via i.g. injection, increased IgG1 and IgE levels were observed. In the both groups, no significant differences in any parameters between OVA and OVA + AgNPs groups were observed. Although this model is useful for evaluation of sensitization and anaphylaxis reaction, transdermalexposure to AgNPs is not sufficient to activate key immune pathways necessary for sensitizing mice for immediate hypersensitivity reactions in the present model.

The Toxicologist

Supplement to *Toxicological Sciences*

55th Annual Meeting and ToxExpo™

SOT

New Orleans, Louisiana

March 13–17, 2016

OXFORD
UNIVERSITY PRESS

ISSN 1096-6080
Volume 150, Issue 1
March 2016

www.toxsci.oxfordjournals.org

The Official Journal of the Society of Toxicology

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science and Increasing the Impact of Toxicology

www.toxicology.org

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.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 603.

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

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence. Author names which are underlined in the author block indicate the author is a member of the Society of Toxicology. For example, J. Smith.

Scientific Session Types:

- CE Continuing Education Courses
- EC Education-Career Development Sessions
- FS Featured Sessions
- HH Historical Highlights Sessions
- IS Informational Sessions
- PL Platform Sessions
- PS Poster Sessions
- RI Regional Interest Sessions
- R Roundtable Sessions
- S Symposium Sessions
- W Workshop Sessions

The 2016 SOT Mobile Event App and Online Planner

The Mobile Event App and Online Planner are available via the SOT website and app marketplaces. These mobile tools enable you, the attendee, to engage with organizers, exhibitors, and each other, and to manage your time and maximize your experience during the Annual Meeting. You also can access some ePosters electronically via the Mobile Event App until May 11, 2016.

To cite a 2016 SOT Annual Meeting Abstract, please format as follows: *The Toxicologist*, Supplement to *Toxicological Sciences*, 150 (1), Abstract #__, 2016, Title, First Author.

Copies of *The Toxicologist* are available at $40 each plus shipping ($15 shipping & handling in the USA and $50 for overseas shipments) from:

Society of Toxicology
1821 Michael Faraday Drive, Suite 300 • Reston, VA 20190

www.toxicology.org