ics present in PM. We evaluated the ultrastructural cytotoxicity effects by transmission electron microscopy (TEM) on J774A.1 macrophages (MQ) and A549 alveolar epithelium (AEC) cells exposed for 24 h to 50μg/cm2 of chemically characterized coarse and fine PM collected in Mexico City. Macrophages avidly phagocytized PM. Coarse PM were observed as dense fibrous bodies inside phagolisosomes; cytoplasmic organelle lysis, increase in filopodia and chromatin condensation were also evident. The exposure to fine PM showed agglomerates of particles in cytoplasmic lysosomes and vacuoles, mitochondria swelling and crest destruction, and condensed chromatin and membrane blebbing. AEC also internalized PM. Coarse particles were observed as solid dense aggregates within lysosomes, perturbation of cytoplasmic architecture, chromatin condensation and darkness of lamellar and dense bodies were also apparent. Exposure of AEC to fine PM showed aggregates of particles in lysosomes, presence of filamentous structures in the cytoplasm, mitochondrial swelling and chromatin condensation. TEM revealed a more dramatic organelle lysis and cytoplasmic perturbation from exposure to coarse than to fine PM, yet exposure to fine PM induced mitochondrial damage. Our results indicate that ultraestructural cytotoxic effects in MQ and AEC varied according to PM physicochemical properties despite of the cell type. These observations suggest that coarse and fine PM have a direct effect on organelle structure, particularly mitochondria and cytoskeleton, thus affecting metabolic energy generation and also promoting cell death, events that could contribute to adverse health effects.

510 PULMONARY HAZARD STUDY IN RATS WITH THREE FORMS OF ULTRA-FINE-TIO2 PARTICLE-TYPES: DIFFERENTIAL RESPONSES RELATED TO SURFACE PROPERTIES.

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The aim of this study was to assess lung toxicity in rats of newly developed, well characterized, ultrafine-TiO2 particles and compare them to TiO2 samples in two different size ranges. Groups of rats were intratracheally instilled with doses of 1 or 5 mg/kg of either two ultrafine rutile TiO2 particle-types (uf-1 or uf-2); rutile R-100 fine-TiO2 (F-1); 80/20 anatase/rutile P25 ultrafine-TiO2 (uf-3); or quartz particles. Phosphate-buffered saline (PBS) solution instilled rats served as vehicle controls. Following exposures, the lungs of PBS and particle-exposed rats were evaluated for bronchoalveolar lavage (BAL) fluid inflammatory markers, cell proliferation, and by histopathology at post-instillation time points of 24 hrs, 1 week, 1 month, and 3 months.
The range of lung inflammation/cytotoxicity/cell proliferation and histopathological responses was quartz > uf-3 > F-1 = uf-1 =uf-2. Exposures to quartz and to a lesser degree, uf-3 anatase/rutile TiO2 particles produced pulmonary inflammation, cytotoxicity and adverse lung tissue effects. In contrast, exposures to F-1 fine-TiO2 particles or to uf-1 /uf-2 ultrafine-TiO2 particle-types produced transient inflammation. We conclude that differences in responses to anatase/rutile uf-3 TiO2 particles vs. the rutile uf-1 and uf-2 TiO2 particles could be related to crystal structure, inherent pH of the particles, or chemical reactivity. Thus, based on these results, inhaled rutile ultrafine-TiO2 particles are expected to have a low risk potential for producing adverse pulmonary health effects. Finally, the results demonstrate that exposures to ultrafine-TiO2 particle-types can produce differential pulmonary effects, based upon their composition, and crystal structure. Thus, the lung toxicity of anatase/rutile uf-3 should not be viewed as representative for all ultrafine-TiO2 particle-types.

511 EFFECTS OF CONCENTRATED AMBIENT ULTRA-FINE/FINE PARTICLES IN INSULIN-RESISTANT, OBESE RATS.

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We hypothesize that inhaled ambient ultrafine (UF) particles can induce oxidative stress-related injury of target cells in the cardiovascular system, thus providing a plausible mechanism for adverse effects observed in sensitive populations. We measured pulmonary and cardiovascular endpoints related to inflammation and oxidative stress in a diabetic rat model after exposure to concentrated UF/fine particle-containing aerosols. The Harvard ultrafine concentrated ambient particle system (HUCAPS) was used to generate the aerosols (particle number concentration ~0.05-1.3 x 10^6/cm^3; count median diameter ~75 nm) for acute exposures (4 hrs; 3 x 6 hrs). Obese, insulin-resistant homozygous male JCR:LA-cp rats (cp/cp; 13-15 months) as well as non-diabetic, lean heterozygous males (+/?; 5-13 months) were exposed to the HUCAP aerosols; controls were exposed to particle-filtered air. We collected blood, bronchoalveolar lavage fluid, and several tissues (lungs, heart, carotid arteries, aorta, liver, pancreas, spleen, kidneys, brain) after exposure. JCR cp/cp rats had slightly higher total lung lavage cell numbers, more blood leukocytes and leukocyte aggregates, and less glial fibrillary acidic protein in brain. These parameters were not consistently affected by HUCAP exposure. Although lavage neutrophils remained unchanged, there was a trend towards elevated protein, lactate dehydrogenase, and β-glucuronidase in HUCAP-exposed rats that was independent of genotype or exposure duration. After 3 days of exposure, the amplification of aortic mitochondrial DNA (12 kb) was significantly decreased in HUCAP-exposed cp/cp rats as compared to +/? rats and air-exposed controls. These results show that small oxidant stress-related changes occur after acute exposure to real-world particles in an animal model relevant to the study of UF particle effects in humans.

512 INFLUENCE OF ENDOTOXIN AND GLUCAN ON *IN VITRO* OXIDATIVE AND INFLAMMATORY POTENTIALS OF FINE AND COARSE PM FROM PAVED ROADS.

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Biological materials are known to contribute to the composition and toxicity of ambient particulate material (PM), but the nature and extent of contribution are largely unknown. Similarly, PM resuspended from paved road surfaces contributes to exposures, but the nature and toxicity of road dust is poorly documented. Dust was collected from active traffic surfaces at 55 sites in 6 U.S. regions using a non-contact vacuum method. Samples were sieved and aerosolized, and the PM2.5 and PM10-2.5 fractions were collected. Samples were analyzed chemically and for endotoxin, a lipopolysaccharide marker for gram negative bacteria (limulus amebocyte assay), and 1,3-β-D-glucan, a carbohydrate marker for fungi and some bacteria (glucatell lysate assay). Samples were tested in vitro for oxidative potential (oxidation products from incubation with linoleic acid) and for inflammatory potential (cytokines produced by incubation with human blood). Relationships between in vitro potency ranking and endotoxin and glucan contents were examined. Mean values for both endotoxin and glucan were similar for the two PM size fractions, but values varied considerably among individual samples. Overall, neither endotoxin nor glucan were strongly correlated with either oxidative or inflammatory potential, indicating that other chemical components drove those effects. However, both size fractions of dust collected at the perimeters of cattle feedlots in Kansas and Texas were among those having the greatest inflammatory potential, and also had by far the highest endotoxin contents (4x mean value for PM2.5, and 8x mean value for PM10-2.5).
Supported by the National Environmental Respiratory Center with funding from multiple government and non-government sponsors.

513 ASSOCIATIONS BETWEEN CHEMICAL COMPOSITION OF FINE PARTICULATE MATTER FROM SIX EUROPEAN CITIES AND INFLAMMATORY RESPONSES IN THE MOUSE LUNG.

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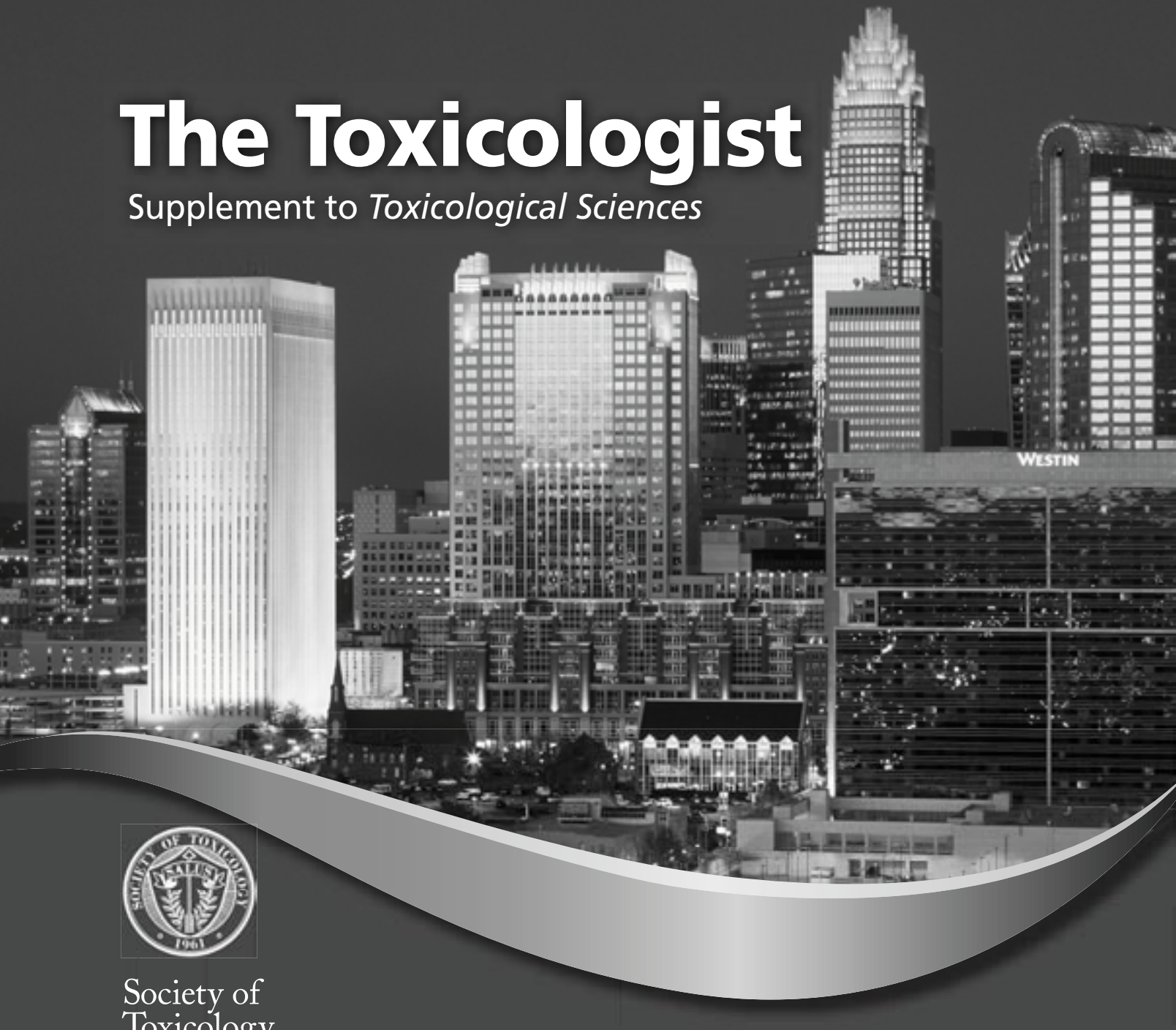
Inflammation is regarded as an important mechanism in associations between urban air fine particulate concentrations and mortality and morbidity among cardiorespiratory patients. We investigated the association of fine particulate ($PM_{2.5-0.2}$) chemical composition with inflammatory responses in the mouse lung. The $PM_{2.5-0.2}$ samples were collected using an optimized high volume cascade impactor during selected seasons in six European cities. Ions (IC), water-soluble elements (ICP-MS) and PAH-compounds (GCMS-SIM) were analyzed from these samples. Healthy C57BL/6J mice were intratracheally instilled a single dose (10 mg/kg) of the $PM_{2.5-0.2}$ samples. At 4, 12 and 24 hours after the exposure, the lungs were lavaged and the bronchoalveolar lavage fluid (BALF) was assayed for indicators of inflammation and tissue damage: cell number, total protein and cytokines (TNF-α, IL-6 and KC). The responses at the most feasible time-point for each parameter were analyzed for Spearman (ρ) correlation with the measured chemical constituents. All the measured inflammatory responses correlated strongly with each other. Significant positive correlations (ρ=0.83-1.0) of the inflammatory responses were measured with dicarboxylic acids, Ca_2^+, Ni and V. Significant negative correlations (ρ=-0.83 to -1.0) were found with NO_3^-, NH_4^+, K^+, As, and total and genotoxic PAH compounds. In conclusion, the present results suggest that fine particles originating from different sources may have differential effects on the respiratory tract.

The Toxicologist

Supplement to *Toxicological Sciences*



Society of Toxicology

46th Annual Meeting and ToxExpo™

Charlotte, North Carolina

An Official Journal of the Society of Toxicology

www.toxsci.oxfordjournals.org

OXFORD UNIVERSITY PRESS

ISSN 1096-6080
Volume 96, Number 1, March 2007

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster discussion, workshop, and poster sessions of the 46th Annual Meeting of the Society of Toxicology, held at the Charlotte Convention Center, Charlotte, March 25–29, 2007.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 449.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 480.

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