2778 Nanosafety Assessment of TiO2 Nanoparticle-Embedded Cosmeceutical Nanotoxicity on Human Skin and Lung Cells

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The toxicity and the exact subcellular localization of various nanocosmeceuticals need to be critically evaluated before their applications for phototherapy for skin cancer and UV protection. Although many nanomaterials have already been reported to penetrate the cell membrane, and enter the cells, the mechanisms involved in these processes and the exact intracellular identification of nanomaterials or chemically modified nanocosmeceuticals has not been determined. As the surface chemistry plays a key role in interactions of the nanoparticles (NPs) with the cell membrane, it is essential to understand the effect of the surface modifications (which change the size, surface charge, and surface energy of nanomaterials) on their interaction with cells. The effect of the TiO2 nanoparticles modified with palmitoleic, palmitic, stearic and oleic acids [cosmeceutical (CM)-NPs] on human skin fibroblast and lung adenocarcinoma cells was investigated and compared with bare TiO2 nanoparticles (B-NPs) in order to assess the safety of the nanomaterials. Cell toxicity, internalization and intracellular localization of these NPs were measured using NP-exposed cells by a variety of techniques, including electron spectroscopy imaging-transmission electron (ESI-TEM) analysis. Our experiments revealed that both B-NPs and CM-NPs entered the cells after 24 h of exposure. Agglomerates of B-NPs as well as individual B-NPs were observed in large quantities inside human skin and lung cells. Our results demonstrated that the TiO2 nanoparticles modified with fatty acids appeared to be less toxic than B-NPs in both human skin and lung cells.

2779 Evaluating the Cytotoxic Effects of Cellulose Nanocrystals (CNCs) Using Autobioluminescent Yeast and Human Cells

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Cellulose nanocrystals (CNCs) are widely used in different industries including pharmaceutical and cosmetic production due to their adept physical and biological properties. Because CNCs are becoming a more prevalent material and have a high potential of being redistributed in the environment, it is important to understand their toxic potentials in biological systems, including organisms of various trophic levels. This study evaluated the cytotoxic effects of CNCs in the lower eukaryotic organism Saccharomyces cerevisiae and human embryonic kidney (HEK293) cells using autobioluminescent yeast and human cell reporters, respectively. The S. cerevisiae and HEK293 reporter cells were engineered to express a synthetic bacterial luciferase operon (luxCDABE) that self-generates all the required substrates for bioluminescent production. As a result, these reporter cells allow for continuous monitoring of the same cell population throughout the period of toxicant exposure, providing a facile means for tracking the temporal dynamics of toxic effects on living cells. When exposed to CNCs at concentrations ranging from 0.001 g/L to 1 g/L, both the yeast and human cells reported time and dose-dependent effects. Exposure to CNCs at 0.001 g/L and 1 g/L reduced bioluminescent output in S. cerevisiae by 5% and 10% compared to untreated control cells 8 hours post-treatment, respectively, and further decreased the signal by 25% and 70% 12 hours post-treatment, respectively. In HEK293 cells, treatment with CNCs at 1 g/L initialized a significant decrease (by 23%) in metabolic activity at 2 days post-treatment, and the bioluminescent output continued to decline to less than 10% compared to untreated controls at 7 days post-treatment. CNCs at 0.001 g/L did not result in significant changes in metabolic activity throughout the entire period of exposure. These results demonstrate the cytotoxic potential for elevated concentrations of CNCs in varying biological systems.

2780 Hydroxyl Radical Generation and Cytotoxicity of Zinc Nanoparticles in RAW 264.7 Cells

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Handling nanoparticles presents novel hazards to human health, especially when used commercially before possible toxic effects may be evaluated. Zinc nanoparticle use is expanding and exposures are possible during the manufacture of concrete, rubber, food products, sunscreen, and paint. The toxicity of zinc nanoparticles has been investigated but little is known regarding zinc nanowires, a material with properties that make it ideal for solar cells and electronics. In this study, zinc metal nanoparticles (MNP), zinc oxide nanoparticles (NP), zinc oxide micron particles (MP), and zinc oxide nanowires (NW) were comparatively investigated. Potential toxic effects due to inhalation exposures were studied using RAW 264.7 mouse macrophage cells. Shape, diameter, and percentage of zinc in the sample were also characterized. A CellTiter-fluor assay was used to determine cell viability and a CytoTox assay was used to determine lactate dehydrogenase (LDH) release following 4 h and 24 h exposures for three different particle doses (10, 25, and 50 µg/ml) to assess cytotoxicity of the various particles. Electron Paramagnetic Resonance (EPR) was used to determine free radical production in both acellular and cellular experiments. There was a trend towards decreased viability at 4 h with the highest dose and at 24 h with the middle dose, but changes were only significant at 24 h with 50µg/ml for all particle types. LDH levels in cell culture media were significantly increased with MNP treatment at 50µg/ml for 4 h. After 24 h, all particles at 25 and 50 µg/ml caused significant LDH release. EPR results indicated that MNP stimulated significantly greater hydroxyl radical (·OH) production than NP, MP, and NW upon reaction with H2O2 and in the presence of RAW cells. Our results demonstrate that while MNP stimulated the most ·OH production, all of the zinc particles decreased cell viability, suggesting multiple mechanisms for zinc nanoparticle cytotoxicity.

2781 ZnO Nanoparticle Ingestion Alters Intestinal Epithelial Function

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Zinc oxide nanoparticles (ZnO NPs) are used to make cans of sulfur producing foods, which provides a risk for ZnO NP ingestion. Canned foods were analyzed for Zn content with ICP-MS and TEM. These results showed that a serving of canned food contains approximately 1.4x10^15 NPs per meal. Doses used for experiments were determined by dividing this amount by the surface area of the small intestine or the surface area of the jejunum for a low (7.12x10^8 particles/cm2) and high dose (1.78x10^9 particles/cm2), respectively, and an intermediate dose (1x10^9 particles/cm2) was also investigated. 10 nm particles (Mellorium Technologies, Inc.) were characterized using dynamic light scattering (DLS) and nanoparticle tracking analysis (NTA). An *in vitro* model of the GI tract containing Caco-2 and HT29-MTX cell line co-cultures and a simulated digestion was used for ZnO NP exposure studies. Characterization of the ZnO nanoparticles with TEM showed that placing the particles in cell medium resulted in smaller aggregates (90-93 nm) than in water (300-450nm), DLS and NTA showed aggregate sizes of 130 and 178 nm in water, respectively. *In vitro* digestion was shown to partially dissolve the NPs. For nanoparticle exposure experiments, the three doses were used for both acute (4 hours) and chronic (5 days) time periods. After exposure to ZnO NPs, iron, zinc and copper cell uptake and transport were measured by adding stable isotopes (58Fe, 63Cu, and 67Zn) to the digest and cell medium, collecting the medium, and analyzing the isotope content with ICP-MS. Glucose transport was modeled using the fluorescent glucose analog 2-NBDG. Cell viability was measured with a MTT assay, oxidative stress was measured using CellROX® (Life Technologies) reagent, nutrient transporter gene expression was determined using RT-PCR, and tight junction functionality was assessed using transepithelial resistance and immunocytochemistry for the tight junction protein occludin. Following both acute and chronic exposure, cell viability decreased, which may be the result of the Zn2+ ions that dissolve in the cell medium or digest. ZnO NP exposure increased ROS formation and decreased nutrient transport and uptake and occludin expression in the intestinal epithelial cells as well as influenced in the expression of transporter genes, suggesting that ZnO ingestion may result in significant metabolic effects.

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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.

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.

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