THE OHIO STATE UNIVERSITY
BIOMEDICAL SCIENCES
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PhD Candidate

Toxicity of Food-Relevant Nanoparticles in Intestinal Epithelial Models

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1187 Graves Hall
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VITA

June 12, 1988 . . . . . . . . . . . . . . . . . . . . . . . . . . Born – McMurray, PA

May 2010 . . . . . . . . B.S. Biochemistry and Molecular Biology
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COMMITTEE MEMBERS

Dr. W. James Waldman

Dr. Estelle Cormet-Boyaka

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ABSTRACT

Nanoparticles are increasingly being incorporated into common consumer products, including in foods and food packaging, for their unique properties at the nanoscale. Food-grade silica and titanium dioxide are used as anti-caking and whitening agents, respectively, and these particle size distributions are composed of approximately one-third nanoparticles. Zinc oxide and silver nanoparticles can be used for their antimicrobial properties. However, little is known about the interactions of nanoparticles in the body upon ingestion. This study was performed to investigate the role of nanoparticle characteristics including surface chemistry, dissolution, and material type on toxicity to the intestinal epithelium.

Only mild acute toxicity of zinc oxide nanoparticles was observed after 24-hour treatment of intestinal epithelial C2BBe1 cells based on the results of toxicity assays measuring necrosis, apoptosis, membrane damage, and mitochondrial activity. Silica and titanium dioxide nanoparticles were not observed to be toxic although all nanoparticles were internalized by cells. In vitro digestion of nanoparticles in solutions representing the stomach and intestines prior to treatment of cells did not alter nanoparticle toxicity. Long-term repeated treatment of cells weekly for 24 hours with nanoparticles did not change nanoparticle cytotoxicity or the growth rate of the treated cell populations. Thus, silica, titanium dioxide, and zinc oxide nanoparticles were found to induce little toxicity in intestinal epithelial cells.

Fluorescent silica nanoparticles were synthesized as a model for silica used in foods that could be tracked in vitro and in vivo. To maintain an exterior of pure silica, a silica shell was hydrolyzed around a core particle of quantum dots or a fluorescent dye electrostatically associated with a commercial silica particle. The quantum dots used were optimized from a previously reported microwave quantum dot synthesis to a quantum yield of 40%. Characterization of the silica particles showed that the surface properties resembled pure silica. These particles were able to be
detected *in vitro* as well as *in vivo* after oral administration of nanoparticles to mice by gavage. After four daily administrations, nanoparticles were detected by fluorescence confocal microscopy in intestines as well as liver, kidney, spleen, lung, and brain. Thus, silica nanoparticles were able to traverse the intestinal epithelium. Further investigation is needed to determine nanoparticle accumulation and potential functional consequences throughout the body.

Silver nanoparticles were particularly toxic to proliferating (subconfluent) C2BBe1 cells plated at low density, inducing 15% necrosis and a 76% decrease in mitochondrial activity. Silver nanoparticle treatment induced oxidative stress in cells based on increased GSH/GSSG ratios. In addition, silver nanoparticles induced G2/M phase cell cycle arrest and inhibited cell proliferation at doses forty times lower than those at which silica, titanium dioxide, and zinc oxide nanoparticles had inhibitory effects. Silver nanoparticles subjected to *in vitro* digestion before cell exposure required higher doses to induce toxicity, likely due to slower dissolution because of greater surface species adsorption. Silver nanoparticles did not cause toxicity or oxidative stress in confluent (stationary) cells. Thus, upon ingestion, silver nanoparticles may be especially toxic to proliferating stem cells in intestinal crypts, particularly in disease states with a compromised epithelium.
RECENT ABSTRACTS AND PRESENTATION


McCracken C., Zane A., Knight D., Dutta P., and Waldman W.J. Minimal Toxicity of Food-Relevant Nanoparticles and Oxidative Stress-Mediated Inhibition of Cell Proliferation by Silver Nanoparticles. OSUWMC Research Day, Columbus, OH. April 2015. (Poster Presentation)

McCracken C. Inhibition of Intestinal Epithelial Cell Proliferation by Food-Relevant Nanoparticles. Edward F. Hayes Graduate Research Forum, Columbus, OH. February 2015. (Oral Presentation)

McCracken C., Zane A., Knight D., Dutta P., and Waldman W.J. Inhibition of Intestinal Epithelial Cell Proliferation by Food-Relevant Nanoparticles. Biomedical Sciences Graduate Program Annual Retreat, Columbus, OH. December 2014. (Oral Presentation)

McCracken C. Minimal *In Vitro* Toxicity of Food-Relevant Nanoparticles in an Intestinal Epithelial Model. Edward F. Hayes Graduate Research Forum, Columbus, OH. February 2014. (Oral Presentation)


AWARDS AND HONORS

The Ohio State University Fellowship (2010)

Edward F. Hayes Graduate Research Forum, Professional Biological Sciences Oral Presentations, 1st Place (2015)

FUTURE PLANS

I plan to pursue a postdoctoral fellowship relevant to intestinal health and spend my career working to improve the health of those who suffer from intestinal diseases.