

Integrated Approach Toward Understanding the Toxicity of Inhaled Nanomaterials

Supporting/Contributing Agency: U.S. EPA (RD-83171701-0) and NIOSH (R01 OH009448)

It is becoming increasingly clear that an integrated approach that includes both inhalation toxicology studies and full characterization of nanomaterials is necessary for understanding inflammatory response as it relates to the physicochemical properties of nanomaterials (Pettibone, Elzey, and Grassian 2008). This EPA/NIOSH study investigated the pulmonary inflammatory response of mice following whole-body inhalation exposure to well-characterized copper and iron nanoparticles in acute and subacute studies (Pettibone et al. 2008). Characterization of these manufactured particles with XRD, TEM, and XPS showed a metallic core and an oxidized surface coating (as shown for iron in the Figure).

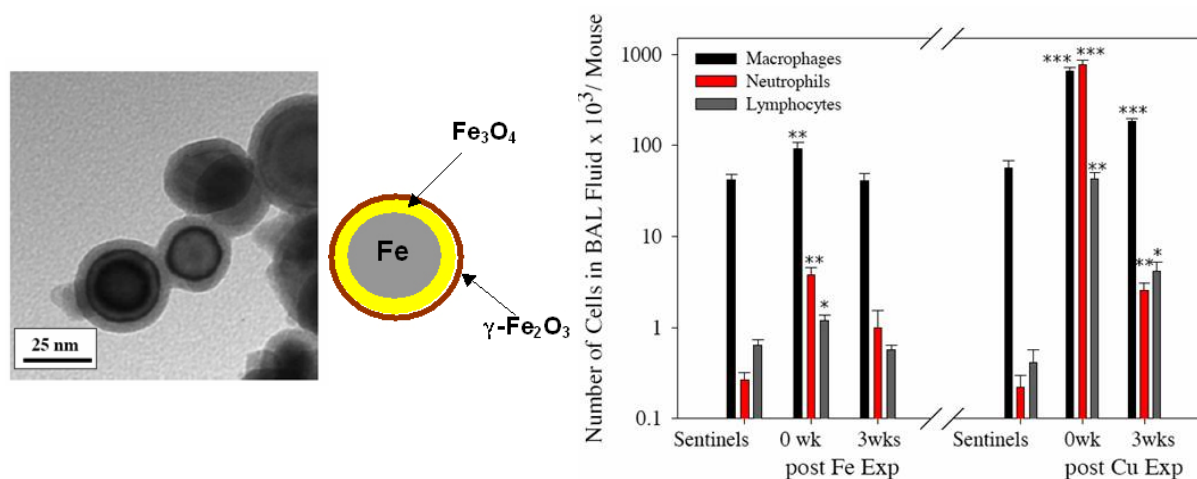


Figure. Caption.

Although no significant pathology was found following acute exposure, following sub-acute exposure, both iron- and copper-exposed mice showed increased inflammation compared to sentinels. Furthermore, copper nanoparticle-exposed mice had significantly higher inflammatory response immediately and three weeks post exposure. At biologically relevant pHs, *in vitro* dissolution studies showed a greater propensity of copper nanoparticles to dissolve in simulated biological fluids compared to iron. Dissolution leads to an increase in ion concentration with concomitant decrease in nanoparticle size.

The increased inflammatory response of copper in the mice model is proposed to be associated with the decrease in nanoparticle size and increased ion concentration produced from the dissolution of copper nanoparticles *in vivo*.

References/Publications

- Pettibone, J.M., A. Adamcakova-Dodd, P.S. Thorne, P.T. O'Shaughnessy, J.A. Weydert, and V.H. Grassian. 2008. Inflammatory response of mice following inhalation exposure to iron and copper nanoparticles. *Nanotoxicology* 2:189-204.
- Pettibone, J.M., S. Elzey, and V.H. Grassian. 2008. "An Integrated Approach Toward Understanding the Environmental Fate, Transport, Toxicity and Health Hazards of Nanomaterials." In V.H. Grassian, ed., *Nanoscience and nanotechnology: Environmental and health impacts*, pp. 43-68. Hoboken, NJ: John Wiley & Sons, Inc.