

## Inhalation of environmentally relevant uraninite micro-particulates

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Uranium contamination is a threat to global health and the environment. Sources of uranium contamination include mining sites, weapons testing, or discharges of uranium from the nuclear industry (accidental or illicit). Uranium released into the environment can enter the human body via ingestion or inhalation, and its toxicity has been widely studied. However, most of these studies were conducted using soluble uranyl and not particulate U; the different chemical and physical properties associated with these phases of U might affect their toxicity. To assess the risk of inhaled U particles, there is a need to investigate their fate once they enter the lungs. This is especially true for particles smaller than 5 microns (<PM<sub>5</sub>), which can penetrate the lungs into the alveolar and interact with local cells such as lung macrophages via phagocytosis. In our study, we investigated the dissolution, chemical alteration and toxicity of an environmentally relevant particle, uraninite (UO<sub>2</sub>). To determine its dissolution behaviour, we examined UO<sub>2</sub> in two different systems: simulated lung fluid (SLF) and artificial lysosomal fluid (ALF). The SLF system represents the interstitial lung fluids, and the particles in this system were reacted for 180 days. The ALF system represents the macrophage's phagolysosome, and the particles in this system were reacted for 30 days. Samples were taken at different intervals for dissolved U. It was found that the UO<sub>2</sub> particles had low solubility in the SLF system while higher solubility in the ALF system. After reaction, the remaining particles were collected for characterization using electron microscopy and a range of synchrotron nano-focused spectroscopies. The main objective was to determine if there is any alteration of the particles' surface. UO<sub>2</sub> in SLF for 180 days showed significant dissolution and co-precipitation of a uranyl phosphate phase based on XRF, XRD, and XANES. However, UO<sub>2</sub> was heavily altered in ALF. Additionally, *in vitro* exposure of these particles (12 – 120 µg/mL) in RAW264.7 mouse lung macrophages and Mlg2908 mouse lung fibroblasts over 48 hours have shown both dose and time dependent toxicity. These data highlight the importance of studying radioactive particle behaviour in the pulmonary system.