Title *

Pulmonary toxicity of surface modified copper oxide nanoparticles

Abstract *

Copper oxide nanoparticles (CuO NPs) have various industrial applications e.g. in antimicrobial products and coatings in food packaging. Previously, we have shown that inhalation of CuO NPs lead to a dose-dependent pulmonary toxicity in rats. In this study, 10 nm CuO NPs were modified with either positively charged polyethylenimine (PEI) or negatively charged ascorbate coating (ASC). We hypothesized, based on in vitro study results using RAW264.7 cell macrophage-like cells, that ASC-coating could induce less pulmonary toxicity compared to PEI-coated CuO NPs. Rats were exposed nose-only to a fixed exposure concentration of ASC and PEI-coated CuO NP at 5 consecutive days. By varying the exposure duration, 3 hour-concentration equivalents of 0, 0.8, 2.3, 7.5 and 21.9 mg/m^3 for ASC and 0.6, 1.8, 6, and 17.3 mg/m^3 for PEI were generated. After exposure, on day 6, and on day 27, pulmonary toxicity markers in bronchoalveolar lavage fluid were analyzed and benchmark dose response analysis was performed. Lung histology revealed interstitial/alveolar inflammation and hypertrophy/hyperplasia of bronchioles/alveoli. BALF analysis supported the dose-dependent pulmonary inflammation and cellular damage. There were no differences ($P>0.05$) observed for lung damage and inflammatory markers between the two types of NPs, except for a potency difference. PEI-coated CuO induced bronchial hypertrophy at a lower dose compared to ASC-coated CuO NPs, whereas ASC-coated CuO NPs induced alveolar hypertrophy at a lower dose. This might be due to differences in deposition as a consequence of a difference in charge.

In conclusion, initially similar pulmonary responses were found for both surface modified CuO NPs in vivo with only minimal differences in the (toxic) potency between these NPs. In contrast to our hypothesis, the ascorbate coating does not protect against pulmonary toxicity.

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