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Toxicological Interactions of Silver Nanoparticles and Non-Essential Metals in Human Hepatocarcinoma Cell Line

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Abstract : Synergetic and antagonistic effects of drugs are well-known concerns in pharmacological assessments of dose and toxicity. Similar approach should be used in assessing cellular uptake and cytotoxicity of nanoparticles. Since nanoparticles are released into the aquatic environment they may interact with existing xenobiotics. Here we used biochemical assays and quantitative proteomics to assess the cytotoxicity of silver nanoparticles (AgNP) when human hepatoma HepG2 cells were co-exposed to 2 nm AgNP together with either Cd2+ or Hg2+ ions. Time-course experiments (2h, 4h, and 24h) were conducted to assess the first response to the exposure studies. The general trend was that a synergetic toxicological response was observed in cells exposed to both AgNP and Cd2+ or Hg2+, with AgNP and Cd2+ being more toxic. This was observed by a significant increase in the ROS and superoxide level of >35% in the case of AgNP+Cd2+ compared to the sum of responses of AgNP and Cd2+, individually. Metabolic activity and viability also dropped more for AgNP+Cd2+ (>10%) than for AgNP and Cd2+ combined. We used inductively coupled plasma mass spectrometry to investigate if AgNP facilitates larger influx of toxic metal ions into HepG2 cells. Only Hg2+ ions was found to be more efficiently engulfed as the concentration of Hg2+ was found 2.8 times larger compared to exposure experiments with only Hg2+. This effect was not observed for Cd2+. We now continue with deep proteomics studies to obtain wider details on the mechanism of the toxicity related to AgNP, Cd2+, and AgNP+Cd2+, respectively.

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