Abstract

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Comparative cytotoxicity of nanosilver in human liver HepG2 and colon Caco2 cells in culture.

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Abstract

The use of silver nanoparticles in food, food contact materials, dietary supplements and cosmetics has increased significantly owing to their antibacterial and antifungal properties. As a consequence, the need for validated rapid screening methods to assess their toxicity is necessary to ensure consumer safety. This study evaluated two widely used in vitro cell culture models, human liver HepG2 cells and human colon Caco2 cells, as tools for assessing the potential cytotoxicity of food- and cosmetic-related nanoparticles. The two cell culture models were utilized to compare the potential cytotoxicity of 20-nm silver. The average size of the silver nanoparticle determined by our transmission electron microscopy (TEM) analysis was 20.4 nm. The dynamic light scattering (DLS) analysis showed no large agglomeration of the silver nanoparticles. The concentration of the 20-nm silver solution determined by our inductively coupled plasma-mass spectrometry (ICP-MS) analysis was 0.962 mg ml(-1) . Our ICP-MS and TEM analysis demonstrated the uptake of 20-nm silver by both HepG2 and Caco2 cells. Cytotoxicity, determined by the Alamar Blue reduction assay, was evaluated in the nanosilver concentration range of 0.1 to 20 μg ml(-1) . Significant concentration-dependent cytotoxicity of the nanosilver in HepG2 cells was observed in the concentration range of 1 to 20 μg ml(-1) and at a higher concentration range of 10 to 20 μg ml(-1) in Caco2 cells compared with the vehicle control. A concentration-dependent decrease in dsDNA content was observed in both cell types exposed

to nanosilver but not controls, suggesting an increase in DNA damage. The DNA damage was observed in the concentration range of 1 to 20 μg ml(-1) . Nanosilver-exposed HepG2 and Caco2 cells showed no cellular oxidative stress, determined by the dichlorofluorescein assay, compared with the vehicle control in the concentration range used in this study. A concentration-dependent decrease in mitochondria membrane potential in both nanosilver exposed cell types suggested increased mitochondria injury compared with the vehicle control. The mitochondrial injury in HepG2 cells was significant in the concentration range of 1 to 20 μg ml(-1) , but in Caco2 cells it was significant at a higher concentration range of 10 to 20 μg ml(-1) . These results indicated that HepG2 cells were more sensitive to nanosilver exposure than Caco2 cells. It is generally believed that cellular oxidative stress induces cytotoxicity of nanoparticles. However, in this study we did not detect any nanosilver-induced oxidative stress in either cell type at the concentration range used in this study. Our results suggest that cellular oxidative stress did not play a major role in the observed cytotoxicity of nanosilver in HepG2 and Caco2 cells and that a different mechanism of nanosilver-induced mitochondrial injury leads to the cytotoxicity. The HepG2 and Caco2 cells used this study appear to be targets for silver nanoparticles. The results of this study suggest that the differences in the mechanisms of toxicity induced by nanosilver may be largely as a consequence of the type of cells used. This differential rather than universal response of different cell types exposed to nanoparticles may play an important role in the mechanism of their toxicity. In summary, the results of this study indicate that the widely used in vitro models, HepG2 and Caco2 cells in culture, are excellent systems for screening cytotoxicity of silver nanoparticles. These long established cell culture models and simple assays used in this study can provide useful toxicity and mechanistic information that can help to better inform safety assessments of food- and cosmetic-related silver nanoparticles.

KEYWORDS: Caco2 cells; HepG2 cells; cytotoxicity; mitochondrial injury; nanoparticles; nanosilver; oxidative stress; silver nanoparticles

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