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Dose and batch-dependent hepatobiliary toxicity of 10 nm silver nanoparticles after single intravenous administration in mice

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ABSTRACT

Silver nanoparticles (AgNPs) are widely used because of their antimicrobial properties in medical devices and in a variety of consumer products. The extensive use of AgNPs raises concerns about their potential toxicity, although it is still difficult to draw definite conclusions about their toxicity based on published data. Our preliminary studies performed to compare the effect of the AgNPs size (10-40-100 nm) on toxicity, demonstrated that the smallest AgNPs determine the most severe toxicological effects. In order to best investigate the impact of physicochemical characteristics of 10 nm AgNPs on toxicity, we compare three different batches of 10 nm AgNPs slightly different in size distribution (Batch A: 8.8±1.7 nm; Batch B: 9.4±1.7 nm; Batch C: 10.0±1.8 nm). Mice were intravenously treated with two doses (5 and 10 mg/kg) of the 3 AgNPs. 24 hours after the treatment, mice were euthanized and underwent complete necropsy. Tissues were collected for histopathological examination and total silver content was determined in tissues by inductively coupled plasma mass spectrometry (ICP-MS). All batches induced severe hepatobiliary lesions, i.e. marked hepatocellular necrosis and massive hemorrhage of the gall bladder. The toxicity was dose-dependent and interestingly, the toxic effects were more severe in mice treated with batches A and B that contained smaller AgNPs. Since the total silver mass concentration was similar, the observed batch-dependent toxicity suggest that even subtle differences in size may contribute to relevant changes in the toxicological outcomes, confirming the fundamental involvement of physicochemical features with respect to toxicity.

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