## Silver and Antimicrobial Effects

For decades, silver has been studied for its antimicrobial properties. One study demonstrated that, when exposed to silver ions, gram-negative *Escherichia coli* and grampositive *Staphylococcus aureus* both experienced cytoplasm membrane shrinkage or detachment from the cell wall.<sup>1</sup> Additionally, an electron-light region appeared in the center of the cells and silver ions were detected inside the cells, suggesting possible mechanisms by which silver ions attack bacteria and a general defense mechanism of the bacteria against the silver. Bacterial DNA lost its ability to replicate and the protein became inactivated after silver treatment.

Silver nanoparticles were found to be attached to the membrane and within the cells of several Gram-negative bacteria—*Escherichia coli*, *Vibrio cholera*, *Pseudomonas aeruginosa*, *Salmonella typhi*—after exposure, indicating that the nanoparticles are able to penetrate the bacteria.<sup>2</sup> This study also found that the bacteriocidal properties of silver were size-dependent, because the nanometers that directly interacted with the bacteria in this way were those that were 1 to 10 nanometers in diameter.

One study found that large doses of intravenously injected colloidal silver led to hemolysis; bone marrow hyperplasia; systemic concerns such as anorexia, weakness, weight loss, and anemia; and death in dogs.<sup>3</sup> Another study assessed the toxic effects of intravenously-administered silver nanoparticles ranging in size from 11 to 75 nm.<sup>4</sup> Researchers concluded that these silver nanoparticles, at a dose range of 97.64–132  $\mu$ g/kg, were safe and non-toxic to the experimental models.

Another study explored the biochemical and hematological effects of intravenous silver nanoparticle (10 nm) administration in rats.<sup>5</sup> There were no significant dose-related changes in the hematology and blood biochemical values with IV administration. Coagulation time in terms of the active partial thromboplastin time (APTT) and prothrombin time (PT) did not show any significant changes, when compared to the control group.

Some have reported that intravenous administration of silver nanoparticles leads to multiple organ toxicity. In one experimental model, mice were administered 25  $\mu$ g silver nanoparticles (10, 75, and 110 nm) or silver nitrate solution containing 2.5  $\mu$ g silver on day 1, 4 and 10.<sup>6</sup> Tissue samples of liver, kidney, and lung were collected on the day 7 after the last

injection. In these models, silver nanoparticles (but not silver nitrate) were taken up by vascular endothelial cells and induced intracellular reactive oxygen species. This was closely related to disruption of the integrity of endothelial layer, leading researchers to conclude that this silver nanoparticle-induced leakiness of endothelial cells could mediate peripheral inflammation in the liver, kidneys, and lungs through intravenous exposure. Researchers did, however, note that the severity of liver inflammation was greatest in mice injected with 75 and 110 nm particles of silver, suggesting that the severity of unwanted side effects increases with particle size.

Additional research demonstrated that nanoparticles with sizes <5.5 nm are rapidly and efficiently excreted through the urine, while 10–20 nm nanoparticles were trapped in the liver and eliminated in the feces,<sup>7</sup> further supporting the idea that the size of nanoparticles may significantly impact its effect on the body.

Clinical research regarding the intravenous use of silver is non-existent and experimental research is limited.

## Reference List

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