Silver nanoparticles as potential antiplatelet, antibacterial and hemocompatibile agents

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Abstract
Background: Among metal nanoparticles, silver nanoparticles (AgNPs) are emerging as an attractive tool for many nanomedical applications. We hypothesized that AgNPs, a known antimicrobial agent, can be used as blood-compatible, "ideal material'' in medical devices or as a drug delivery system. Therefore, the aim of the current study was to investigate if functionalized AgNPs affect platelet function and platelets as well as endothelial cell and red blood cells viability *in vitro*. Methods: AgNPs, functionalized with reduced glutathione (GSH), polyethylene glycol (PEG) and lipoic acid (LA) were synthesized. Quartz crystal microbalance with dissipation was used to measure the effect of AgNPs on platelet aggregation. Platelet aggregation was measured by changes in frequency and dissipation, and the presence of platelets on the sensor surface was confirmed and imaged by phase contrast microscopy. Flow cytometry was used to detect surface abundance of platelet receptors. Lactate dehydrogenase test was used to assess the potential cytotoxicity of AgNPs on human blood platelets, endothelial cells, and red blood cells. Commercially available ELISA tests were used to measure the levels of thromboxane B2 and metalloproteinases (MMP-1, MMP-2) released by platelets as markers of platelet activation. Antimicrobial activity was assessed by the minimal inhibitory concentrations (MIC). Results: 2 nm AgNPs-GSH, 3.7 nm AgNPs-PEG both at 50 and 100 µg/mL, and 2.5 nm AgNPs-LA at 100 µg/mL reduced platelet aggregation, inhibited collagen-mediated increase in total P-selectin and GPIIb/IIIa, TXB2 formation, MMP-1, and MMP-2 release. The tested AgNPs concentrations were not cytotoxic as they did not affect, platelet, red blood cell or endothelial cell viability. Conclusion: All tested functionalized AgNPs inhibited platelet aggregation at nontoxic concentrations. AgNPs have antimicrobial properties against pathogens commonly associated with the placement of the biomaterial into the vessel. Therefore, functionalized AgNPs can be used as an antiplatelet agent or in design and manufacturing of blood-facing medical devices, such as vascular grafts, stents, heart valves, and catheters.
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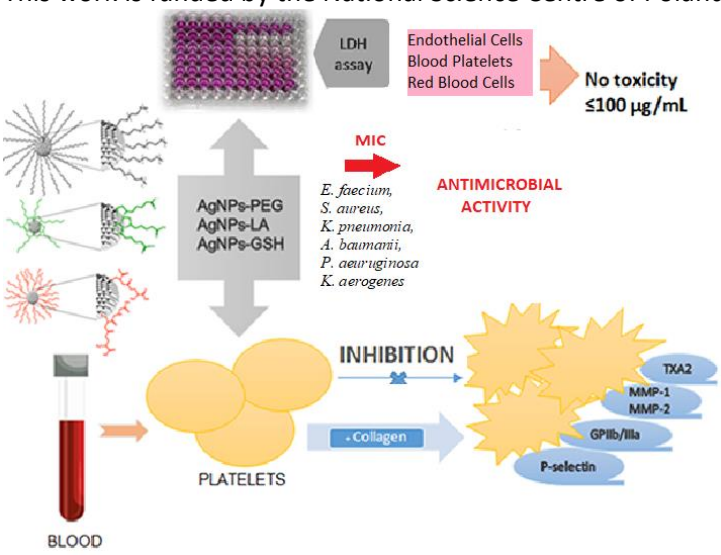

Figure 1. Antiplatelets and antimicrobial properties of hemocompatible AgNPs.