Short Communication

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The Pharmacological Effects of Silver Nanoparticles Functionalized with Eptifibatide on Platelets and Endothelial Cells

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Abstract

Purpose: In the search for new drug delivery platforms for cardiovascular diseases and coating of medical devices, we synthesized eptifibatide-functionalized silver nanoparticles (AgNPs-EPI) and examined the pharmacological activity of AgNPs-EPI on platelets and endothelial cells in vitro and ex vivo.

Methods: Spherical AgNPs linked to eptifibatide were synthesized and characterized. Cytotoxicity was measured in microvascular endothelial cells (HMEC-1), platelets and red blood cells. Platelet mitochondrial respiration was measured using the Oxygraph-2k, a high-resolution modular respirometry system. The effect of AgNPs-EPI on the aggregation of washed platelets was measured by light aggregometry and the ex vivo occlusion time was determined using a reference laboratory method. The surface amount of platelet receptors such as P-selectin and GPIIb/IIIa was measured. The influence of AgNPS-EPI on blood coagulation science was assessed. Finally, the effect of AgNPs-EPI on endothelial cells was measured by the levels of 6-keto-PGF1alpha, tPa, cGMP and vWF.

Results: We describe the synthesis of AgNPs using eptifibatide as the stabilizing ligand. The molecules of this drug are directly bonded to the surface of the nanoparticles. The synthesized AgNPs-EPI did not affect the viability of platelets, endothelial cells and erythrocytes. Preincubation of platelets with AgNPs-EPI protected by mitochondrial oxidative phosphorylation capacity. AgNPs-EPI inhibited aggregation-induced P-selectin expression and GPIIb/IIIa conformational changes in platelets. AgNPs-EPI caused prolongation of the occlusion time in the presence of collagen/ADP and collagen/adrenaline. AgNPs-EPI regulated levels of 6-keto-PGF1alpha, tPa, vWf and cGMP produced in thrombin stimulated HMEC-1 cells.

Conclusion: AgNPs-EPI show anti-aggregatory activity at concentrations lower than those required by the free drug acting via regulation of platelet aggregation, blood coagulation, and endothelial cell activity. Our results provide proof-of-principle evidence that AgNPs may be used as an effective delivery platform for antiplatelet drugs.

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Biography

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