

Optimal conjugation of catechol group onto hyaluronic acid in coronary stent substrate coating for the prevention of restenosis

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Abstract

Although endovascular stenting has been used as an interventional therapy to treat cardio- and cerebro-vascular diseases, it is associated with recurrent vascular diseases following stent thrombosis and in-stent restenosis. In this study, a metallic stent was coated with dopamine-conjugated hyaluronic acid with different ratios of catechol group to improve hemocompatibility and re-endothelialization. Especially, we were interested in how much amount of catechol group is appropriate for the above-mentioned purposes. Therefore, a series of dopamine-conjugated hyaluronic acid conjugates with different ratios of catechol group were synthesized via a carbodiimide coupling reaction. Dopamine-conjugated hyaluronic acid conjugates were characterized with ¹H-nuclear magnetic resonance and Fourier transform infrared spectroscopy, and the amount of catechol group in dopamine-conjugated hyaluronic acid was measured by ultraviolet spectrometer. Co-Cr substrates were polished and coated with various dopamine-conjugated hyaluronic acid conjugates under pH8.5. Dopamine-conjugated hyaluronic acid amounts on the substrate were quantified by micro-bicinchoninic acid assay. Surface characteristics of dopamine-conjugated hyaluronic-acid-coated Co-Cr were evaluated by water contact angle, scanning electron microscopy, and atomic force microscopy. The hemocompatibility of the surface-modified substrates was assessed by protein adsorption and platelet adhesion tests. Adhesion and activation of platelets were confirmed with scanning electron microscopy and lactate dehydrogenase assay. Human umbilical vein endothelial cells were cultured on the substrates, and the viability, adhesion, and proliferation were investigated through cell counting kit-8 assay and fluorescent images. Obtained results demonstrated that optimal amounts of catechol group (100 μmol) in the dopamine-conjugated hyaluronic acid existed in terms of various properties such as hemocompatibility and cellular responses.

Keywords

Vascular stent, hyaluronic acid, dopamine, thrombosis, restenosis

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