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A new dextran-graft-polybutylmethacrylate copolymer coated on 316L metallic stents enhances endothelial cell coverage

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ABSTRACT

Amphiphilic copolymers based on the copolymerization of hydrophilic and hydrophobic moieties offer versatility in various biomedical material applications. Here, a new biocompatible copolymer of dextran-graft-polybutylmethacrylate is synthesized for the coating of metallic endovascular stents. Coating of metallic surfaces is performed and analyzed by X-ray photoelectron spectroscopy, attenuated total reflection Fourier transform infrared spectroscopy, contact angle measurement, atomic force microscopy and scanning electron microscopy before and after deformation corresponding to stent deployment by a balloon catheter. In the conditions described here, the resulting coating is smooth and uniform with neither cracks nor detachment after stent expansion. Interestingly, surfaces coated with the copolymer greatly improve in vitro adhesion and growth of endothelial cells. This copolymer provides new opportunities for implanted biomaterials.

1. Introduction

Coronary stent implantation has become a common practice in cardiovascular surgery. However, restenosis remains by far the main complication of this technique. Indeed, the endothelium injury resulting from stenting triggers the migration and proliferation of smooth muscle cells (SMCs) that could lead to in-stent thrombosis and vessel occlusion [1]. The main strategy to avoid thrombus formation is to favor re-endothelialization of the arterial vessel after implantation and to limit SMC proliferation.

Metallic surfaces are not suitable for endothelial cell coverage and they generally induce the adhesion of platelets that stimulate the proliferation of SMCs and lead to restenosis. Surface treatments have been proven effective to modify the biological response [2]. For instance, metallic surface roughness can be decreased by electropolishing [3] to reduce platelet adhesion [4,5] and to avoid inflammation process. In addition, numerous studies refer to the stents covered by a polymeric layer for improving stents in coronary arteries [6,7]. This second strategy allowed for a combination of chemical modification, drug release, and roughness reduction of the stent surface. In this context, coating metallic stents by polymeric biocompatible materials has already been described and several polymers were examined, such as polyurethane, poly(ethylene terephthalate), polyorganophosphazene, poly(L-lactic acid), and polydimethylsiloxane [8]. These coatings build up a layer that protects the surrounding tissues against the corrosion products of metallic stents [9,10] while preserving metal mechanical properties. As cell adhesion also depends on surface wettability [11,12], this parameter can be controlled by varying the nature and the composition of the polymeric material [13,14].

Among biocompatible polymeric materials, both methacrylate polymers and polysaccharides such as dextran have been widely studied. Previous works demonstrated the non-toxicity of dextran, which was developed as a blood expander and biocompatible hydrogel [15,16]. On the other hand, polymethacrylates are also currently used in pharmaceutical or biomedical applications. Poly(*n*-butyl methacrylate) is a particularly interesting methacrylate polymer due to its mechanical properties. It has already demonstrated its efficiency as a biocompatible component for drug eluting stents [17,18]. In a previous work, we have prepared films made of copolymers with different dextran/n-butyl methacrylate ratios and thus various hydrophilic/hydrophobic properties of the resulting copolymers [19]. It has been established that copolymers made of 89% PBMA and 11% dextran promote endothelial cell growth. These films were also elastic and interesting to evaluate as stent coatings to improve the metallic backbone properties.

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