EFFECT OF VASCULAR SCAFFOLD COMPOSITION ON RELEASE OF SIROLIMUS

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[ENGINEERING OF BIOMATERIALS 148 (2018) 30]

Introduction

Bioresorbable vascular scaffolds (BRS) have been designed to provide mechanical support against acute recoil to treat arterial restenosis and to overcome the complications of metallic drug-eluting stents (DES) e.g. vascular inflammation, hypersensitivity reactions and incidence of thrombosis [1,2]. Many studies have shown that the side effects of DES and BRS still remain, e.g. inflammation, late thrombosis, and late restenosis. The lack of capacity for adjusting the drug dose and inadequate release behavior are one of the main reasons of these side effects [3]. Therefore, the drug release rate has become one of the important criteria for the evaluation of drug-eluting stents. The objective of this study was to develop degradable sirolimus-eluting polymer coatings applicable to bioresorbable polymer-based scaffolds. Moreover, a detailed analysis of sirolimus release and degradation of scaffolds has been conducted. So far, mainly polymeric coatings of metallic stents have been studied in regard to explain drug release mechanisms.

Materials and Methods

Two kinds of scaffolds models obtained by microinjection molding from poly(lactide-co-glycolide-co-trimethylene carbonate) (length 16 mm; Ø 6 mm) were coated by dip coating method with sirolimus eluting layer composed of poly(L-lactide-co-trimethylene carbonate) (poly(L-lactide-co-TMC); PLLA/TMC). *In vitro* degradation and drug release study was conducted for 180 days at 37°C in modified sodium chloride (0.9%). Scaffolds explanted from pigs were used for evaluation of *in vivo* degradation and drug release. Quantification of sirolimus was performed at the wavelength of 287 nm using a high performance liquid chromatography (HPLC). The BRS were characterized before and after degradation. Changes in the polymer composition were monitored on the basis of ^{1}H NMR spectroscopy. The molar mass and molar mass distribution of the polymer were determined by gel permeation chromatography (GPC). Morphology of scaffolds was observed by means of polarizing microscopy and scanning electron microscopy (SEM).

Results and Discussion

Two kinds of scaffolds obtained from poly(lactide-co-glycolide-co-TMC) with lower and higher lactide content (scaffold 1 and scaffold 2, respectively) were coated with solution composed of poly(lactide-co-TMC) and sirolimus. The surface of scaffolds with drug-eluting layer of ≈ 2.7 µm thickness (FIG. 1C) was smoother than uncoated scaffold (FIG. 1A), but had numerous, tiny cavities (FIG. 1B).

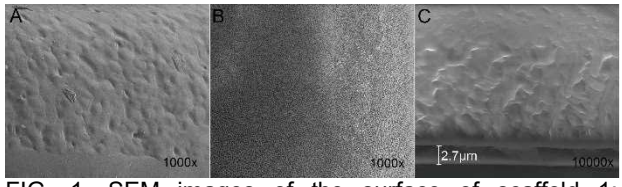

FIG. 1. SEM images of the surface of scaffold 1: uncoated (A), coated (B) and coated cross-section (C).

The developed coatings showed controlled release of antiproliferative agent with elimination of burst effect (FIG. 2). However, differences in degradation and drug release profile from two kinds of scaffolds were observed. Scaffold 2 composed of polymer with higher lactide content showed slower and bi-phasic, erosion-controlled release of sirolimus. On the contrary, sirolimus release from scaffold 1 composed of polymer with lower content of lactide was mainly controlled by diffusion.

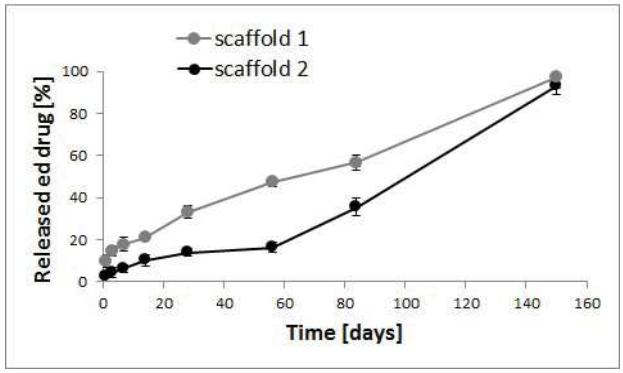

FIG. 2. In vitro release of sirolimus from scaffolds (S.D. shown as error bars, n = 3).

Conclusions

The biodegradable coatings of vascular scaffolds providing regular release of sirolimus were developed. The study demonstrated that characteristics of scaffold and its degradation is a crucial factor that must be considered in development of bioresorbable vascular scaffolds with controlled release of antiproliferative agent.

Acknowledgments

This study was conducted in the frame of project of The National Centre for Research and Development No. PBS3/A9/38/2015 "Obtaining of self-expanding, polymeric and biodegradable, drug-eluting vascular stents".

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