BIORESORBABLE VASCULAR SCAFFOLDS - EFFECT OF COATING PARAMETERS ON MORPHOLOGY AND DOSE OF ANTIRESTENOTIC DRUG

KATARZYNA JELONEK[1]*, JOANNA JAWORSKA[1]*, MONIKA MUSIAŁ-KULIK[1]*, MATEUSZ STOJKO[1], MICHAŁ SOBOTA[1], JAKUB WŁODARCZYK[1], MAŁGORZATA PASTUSIAK[1], JANUSZ SZEWCZENKO[2], KAROLINA GOLDSZTAJN[2], PIOTR DOBRZYŃSKI[1], JANUSZ KASPERCZYK[1]

[1] CENTRE OF POLYMER AND CARBON MATERIALS, POLISH ACADEMY OF SCIENCES, CURIE-SKLODOWSKA 34 ST., ZABRZE, POLAND
[2] DEPARTMENT OF BIOMATERIALS AND MEDICAL DEVICES ENGINEERING, FACULTY OF BIOMEDICAL ENGINEERING, SILESIAN UNIVERSITY OF TECHNOLOGY, 41-800 ZABRZE, POLAND
*E-MAIL: KJELONEK@CMPW-PAN.EDU.PL, JJAWORSKA@CMPW-PAN.EDU.PL, MMUSIAL@CMPW-PAN.EDU.PL

[ENGINEERING OF BIOMATERIALS 163 (2021) 81]

Introduction

Coronary artery disease (CAD) is the leading global cause of death, accounting for more than 9 million deaths per year according to World Health Organization estimates in 2016 [1]. Implantation of drug eluting stents (DES) has become the standard of care for patients undergoing percutaneous coronary intervention (PCI) [2]. Moreover, novel fully bioresorbable vascular scaffolds (BRS) have been designed to overcome the complications of metallic drug eluting stents (DES), e.g. vascular inflammation, hypersensitivity reactions and incidence of thrombosis [3]. However, the design of BRS continues to evolve with the intention to further improve short- and long-term outcomes. The scaffolds should restore luminal patency, but they can also act as a local delivery device for therapeutic agents. The use of biodegradable drug-eluting coatings are therefore being widely explored. The objective of this study was to develop degradable sirolimus-eluting polymer coatings applicable to bioresorbable polymer-based scaffolds by ultrasonic coating system and to identify parameters that may be used for tailoring the drug dose.

Materials and Methods

Cardiovascular scaffolds obtained by microinjection molding from poly(lactide-co-glycolide-co-trimethylene carbonate) (TMC) (Ø 5.4 mm) were used for coating study. The scaffolds were coated with sirolimus eluting layer composed of poly(L-lactide-co-trimethylene carbonate) (poly(L-lactide-co-TMC) (PLLA/TMC) by ultrasonic method using ExactaCoat (Sono-Tek) ExactaCoat (Sono-Tek) equipped with nozzle with Impact Ultrasonic Spray Shaping. Factors influencing the properties of coating layer were compared, e.g. concentration of polymer solution (1.0 % and 2.5 %), number of layers (3, 5 and 7) and type of nozzle (60 kHz and 120 kHz). The scaffolds were characterized for drug dose and morphology. Quantification of sirolimus in coating layer was performed at the wavelength of 287 nm using a high performance liquid chromatography (HPLC; LaChrom Elite®VWR/Hitachi, Tokyo, Japan). Morphology of scaffolds was observed by means of scanning electron microscopy (SEM; FEI Company, Quanta 250 FEG) and optical microscope (KEYENCE, VHX 7000).

Results and Discussion

The surface of bioreborbable cardiovascular scaffolds was modified by biodegradable polymer containing antirestenotic drug using ultrasonic coating system. The ultrasonic method enabled to form smooth coating, well-integrated with scaffold (FIGs. 1, 2). The amount of drug increased significantly in coating layer produced from 2.5 % polymer solution compared to 1.0% polymer. The coatings composed of 3 layers obtained from 1.0% polymer solution contained about 50 µg of sirolimus. Drug content increased to about 100 µg in 5 layers and to 140 µg in 7 layers. The coatings obtained from 2.5% polymer solution contained about 170 µg, 300 µg and 400 µg of sirolimus in 3, 5 and 7 layers, respectively.

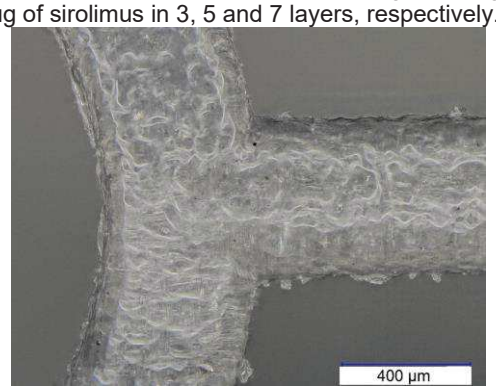

FIG. 1. Optical microscope image of the part of scaffold obtained from PLGA/oTMC coated with 7 layers of PLLA/TMC (1.0 %) and sirolimus using 60 kHz nozzle.

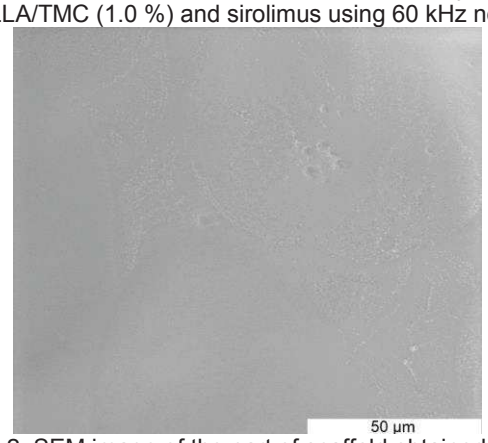

FIG. 2. SEM image of the part of scaffold obtained from PLGA/oTMC coated with 7 layers of PLLA/TMC (1.0 %) and sirolimus using 60 kHz nozzle.

Conclusions

Sirolimus-containing PLLA/TMC coating was developed for application by ultrasonic coating system. The drug content may be modified by number of layers and concentration of polymer solution.

Acknowledgments

This study was conducted in the frame of project of The National Centre for Research and Development No. POIR.04.01.02-00-0105/17 – MICROINJSTENT "The technology for developing and obtaining the next generation of vascular stents through microinjection".
The Authors thank to Keyence for providing a VHX-7000 digital microscope for imaging of the scaffolds.

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