THE INFLUENCE OF COPOLYMER COMPOSITION AND COATING METHOD ON DRUG RELEASE FROM BIODEGRADABLE SURFACE LAYER

KATARZYNA JELONEK[1]*, JOANNA JAWORSKA[1], PIOTR DOBRZYŃSKI[1], JANUSZ KASPERCZYK[1,2], MAŁGORZATA PASTUSIAK[1], MICHAŁ SOBOTA[1]

[1] CENTRE OF POLYMER AND CARBON MATERIALS, POLISH ACADEMY OF SCIENCES, CURIE-SKLODOWSKA 34 ST., ZABRZE, POLAND
[2] SCHOOL OF PHARMACY WITH THE DIVISION OF LABORATORY MEDICINE IN SOSNOWIEC, MEDICAL UNIVERSITY OF SILESIA, KATOWICE, POLAND, CHAIR AND DEPARTMENT OF BIOPHARMACY, JEDNOŚCI 8, SOSNOWIEC, POLAND
*E-MAIL: KATARZYNA.JELONEK@CMPW-PAN.EDU.PL

[ENGINEERING OF BIOMATERIALS 138 (2016) 54]

Introduction

The development of drug eluting stents (DES) has significantly decreased the restenosis rate [1]. However, many studies have shown that the side effects of DES still remain, e.g., inflammation, late thrombosis, and late restenosis. These side effects are caused by the DES's lack of capacity for adjusting the drug dose, drug effectiveness, and release behavior according to the disease condition of the treated blood vessel [2]. Therefore, for DES, it is essential to control the dose and the release behavior of the drug. The ideal DES should have a slow and controlled drug release, with release kinetics in which the antiproliferative drug can be quickly released initially in the first week, but the total release time should be maintained for at least a month after the DES implantation [3]. There are many factors that influence the drug release from DES, such as the polymer, drug, coating methods, drug storage, elution direction, coating thickness, pore size in the coating, and release conditions as well as the influence of the hemodynamics after the implantation [4]. In this study, biodegradable drug-eluting polymer coating layer is developed. This surface layer is intended to cover biodegradable stents. The influence of copolymer composition and coating method on release rate of sirolimus has been analyzed.

Materials and Methods

Drug – eluting coating layer has been obtained from poly(lactide-co-trimethylene carbonate) (PLA/TMC) and sirolimus by air brushing and dip coating method. The morphology of coatings was observed by SEM. *In vitro* drug release study was conducted at 37°C in release media consisting of 0.9% sodium chloride, 0.05% Brij 35, and 0.0003% BHT dissolved in purified water. Quantification of sirolimus was performed at the wavelength of 287 nm using a high performance liquid chromatography (HPLC) system equipped with a reverse phase C-18 column maintained at 40°C. The mobile phase consisting of methanol and 0,1% formic acid (85:15 v/v) was delivered at a flow rate of 1ml/min.

Results and Discussion

The drug release rate has become one of the important criteria for the evaluation of drug-eluting stents. The selection of the drugs and the carriers as well as the drug coating preparation process can reduce or negate the potential disadvantages of DES. In the study we analyzed the influence of several factors on release of sirolimus e.g. copolymer composition, amount of drug, coating method and concentration of drug-polymer solution used for dip coating procedure. Observations of the surface obtained by dip coating method showed that PLA/TMC forms homogenously distributed, smooth layer (FIG. 1A) with even thickness.

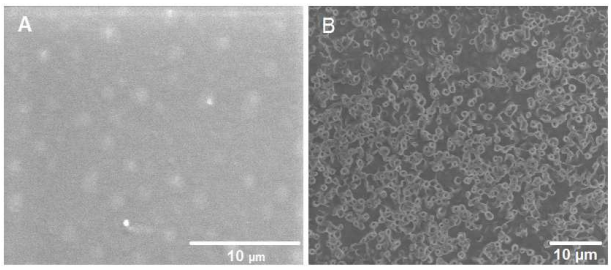

FIG. 1. SEM micrograph of PLA/TMC drug eluting layer before (A) and after 13 weeks of degradation (B).

For a biodegradable polymer, the hydrolytic cleavage of the polymer chains leads to the degradation or erosion of the matrix, which usually controls the release of drug [5]. In fact, the surface became porous during degradation (FIG. 1B), which facilitated drug release. Most of sirolimus was released until 13 weeks of degradation. The drug release and polymer erosion should be simultaneous; hence, there are not drug remnants in the tissue after hydrolytic degradation of the polymer [6].

Conclusions

The biodegradable drug eluting coating layer was developed. Regular and even release process make them a promising solution for medical applications.

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".

References

[1] D.M. Sun, Y.M. Zheng, T.Y. Yin, C.J. Tang, Q.S. Yu, G.X. Wang, Coronary drug-eluting stents: From design optimization to newer strategies, J Biomed Mater Res A, 102 (2014) 1625-1640.
[2] K. Park, Dual drug-eluting stent, Journal of Controlled Release, 159 (2012) 1-1.
[3] T. Liu, Y. Liu, Y. Chen, S.H. Liu, M.F. Maitz, X. Wang, K. Zhang, J. Wang, Y. Wang, J.Y. Chen, N. Huang, Immobilization of heparin/poly-L-lysine nanoparticles on dopamine-coated surface to create a heparin density gradient for selective direction of platelet and vascular cells behavior, Acta Biomater, 10 (2014) 1940-1954.
[4] T.Z. Hu, J.L. Yang, K. Cui, Q. Rao, T.Y. Yin, L.L. Tan, Y. Zhang, Z.G. Li, G.X. Wang, Controlled Slow-Release Drug-Eluting Stents for the Prevention of Coronary Restenosis: Recent Progress and Future Prospects, Acs Appl Mater Inter, 7 (2015) 11695-11712.
[5] E.M.M. del Valle, M.A. Galan, R.G. Carbonell, Drug Delivery Technologies: The Way Forward in the New Decade, Ind Eng Chem Res, 48 (2009) 2475-2486.
[6] J. Han, P.I. Lelkes, Drug-Eluting Vascular Grafts, in: J.A. Domb, W. Khan (Eds.) Focal Controlled Drug Delivery, Springer US, Boston, MA, 2014, pp. 405-427.