Improvement of Interfacial Adhesion by ATRP and Stereocomplex for Drug-Eluting Stents

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Introduction: Bare metal stent (BMS) was used in coronary artery disease but often elicits inflammation, thrombosis, and even restenosis. To avoid this problem, a drug-eluting stent (DES) has been developed and found effective in reducing restenosis. However, DES on which polymer coated layer still suffers from delamination or cracking that can cause a hazardous to health. These phenomena are happened because of the weak attraction between the metal surface and the polymer layer. Therefore, the interfacial adhesion has attracted attention of many researchers. Choi *et al*, have been reported an improvement in the interfacial adhesion using direct surface initiated ring-opening polymerization (SI-ROP) of L-lactide.[1] We introduced a new nanocoupling and stereocomplex concept by "grafting from" method. Poly(L-lactide) (PLLA) was grafted from the hydroxyl groups of poly(2-hydroxyethyl methacrylate) (PHEMA)-grafted Cobalt-chrome (CC) and it was coated with PDLLA.

Materials and Methods: Cobalt-chrome (CC) plate (1 × 1 cm^2) was obtained from HanKook Vacuum Metallurgy (Korea). Poly(D,L-lactide) (PDLLA; 75:25, MW: 110,000) was purchased from Boehringer Ingelheim (Germany). All the chemicals were used without further purification. Prior to the piranha treatment, CC specimens were polished, cleaned in ethanol and dried by argon gas. The piranha treated CC was silanized by 2-bromo-2-methyl-N-(3-(trimethoxysilyl)propyl)propan amide (BTP Am) that initiate atom transfer radical polymerization (ATRP) of 2-hydroxyethyl methacrylate (HEMA). The hydroxyl groups of the PHEMA formed initiate the ring opening polymerization (ROP) of the L-Lactide at 100 ^oC for three days. Sirolimus-in-PDLLA matrix was ultrasonically coated to the control and the modified samples. The modification steps were characterized by ATR-FTIR, XPS, water contact angle, and atomic force microscopy (AFM). The thickness of ultrasonically PDLLA film was determined from the cross-sectional scanning electron microscopy (SEM) image. The drug release profile was studied for 42 days under physiological conditions.

Results and Discussion: The piranha solution was used to activate the surface *via* hydroxyl group formation that can be used for silanization process. The silanized CC are used as initiator for ATRP reaction of the HEMA monomers. To avoid the cytotoxicity of the bromine molecules, the specimens were reacted with sodium azide and then reduced to give amino group. Both the amino and the PHEMA hydroxyl groups on the surface were used for ROP of L-lactide in the presence of appropriate catalyst ($Sn(Oct)_2$). The modification steps were characterized by ATR-FTIR (Fig. 1). The peaks at 1745, 2930, and 2960 cm^{-1} were attributed to carbonyl of ester groups and C-H stretching in PLLA. The thickness of the coated layer was 2.59 µm as determined by SEM. Meanwhile, PDLLA was ultrasonically coated on the PLLA grafted-CC substrate; we suggest nanocoupling and stereocomplex formed through the interface between the coated PDLLA) and the grafted PLLA. The effect of nanocoupling and stereocomplex was confirmed from the drug release of unmodified and modified specimens under physiological conditions as illustrated in Figure 2. It was observed that the unmodified-CC coated with a polymer layer was detached after 35 days as a result of the instability of this layer. On the other hand, the PLLA grafted-CC samples showed stability with control drug release. Therefore, this result demonstrates that nanocoupling and stereocomplex can be effective increasing the adhesive strength between polymer coating and metal substrate.

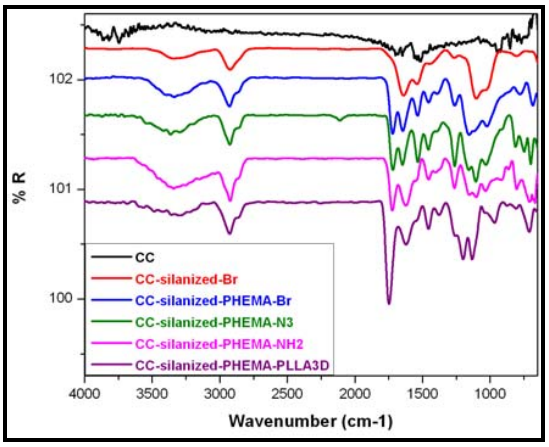

Fig. 1. ATR-FTIR spectra of the Co-Cr control and modification steps.

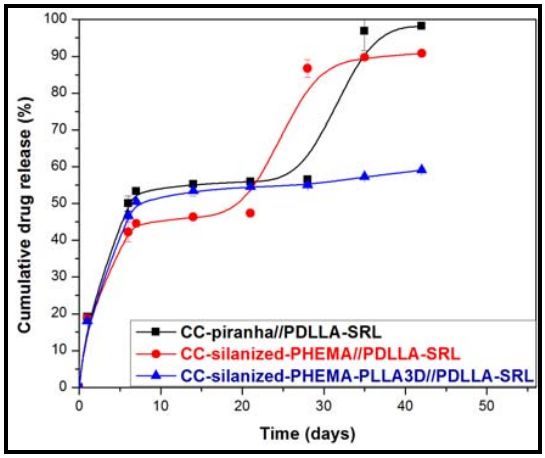

Fig. 2. Sirolimus release profile of different specimens.

Summary: PLLA-grafted CC by ATRP was stereocomplex-nanocoupled successfully with PDLLA that increase the interfacial adhesion of polymer coating that can be applied to many biomedical applications including DES.

References:

1. J. Choi, *et al.*, *Langmuir*, 27, 14232 (2011).