Surface Modification of Stent Material Using Self-Assembled Monolayers for Sustained Delivery of Paclitaxel

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Introduction: Polymer-based platforms in drug-eluting stents (DES) cause adverse reactions in patients [1]. Hence, the development of a polymer-free drug delivery platform may have significant impact on reducing adverse reactions to DES. In this study, the use of a polymer-free platform, self-assembled monolayers (SAMs), is explored for delivering an anti-proliferative drug (paclitaxel – PAT) in clinically relevant doses (25 – 200 μg/cm^2) from an ultra-thin stent strut material (Co-Cr alloy).

Materials and Methods: Carboxylic acid (–COOH) terminated phosphonic acid SAMs were coated on Co-Cr alloy (L605 grade) surfaces. Three different doses (25, 100, and 200 μg/cm^2 – range of doses used in commercially available polymer-based DES) of PAT were deposited on SAMs coated surfaces by a microdrop deposition method as previously described [2]. PAT deposited SAMs coated Co-Cr surfaces are referred to here as SAM–PAT. Control experiments were carried out to coat PAT directly on Co-Cr alloy surfaces with no SAMs modification. PAT deposited control Co-Cr surfaces are referred to here as Ctrl–PAT. SAM–PAT and Ctrl–PAT specimens were thoroughly characterized using scanning electron microscopy (SEM), atomic force microscopy (AFM), Fourier transform infrared spectroscopy (FTIR), and X-ray photoelectron spectroscopy (XPS) for studying the morphology, distribution, and attachment of PAT on Co-Cr alloy surfaces. For drug elution studies, SAM–PAT and Ctrl–PAT specimens were immersed in phosphate-buffered saline/Tween-20 (PBS/T-20) solution for up to 35 days. PBS/T-20 samples were collected at 1, 3, 5, 7, 14, 21, 28, and 35 days and analyzed for the amount of drug released using high performance liquid chromatography.

Results/Discussion: SEM images showed the presence of high dense needle shaped PAT crystals on SAM–PAT (Fig 1a) while low dense PAT crystals were observed on Ctrl–PAT (Fig 1b). In addition to crystal deposits, PAT formed molecular coatings in powder-like morphology on both SAM–PAT and Ctrl–PAT surfaces (Fig 2 – AFM phase images). The FTIR spectra of SAM–PAT and Ctrl–PAT showed strong absorption bands for C=O stretches of ester, ketone, and amide groups at 1729 cm^{-1}, 1700 cm^{-1}, and 1639 cm^{-1}, respectively. The peaks for the finger print regions of PAT were observed at 1242 cm^{-1}, 1072 cm^{-1}, and 707 cm^{-1} (Fig 3). The XPS C 1s spectra of SAM–PAT and Ctrl–PAT were deconvoluted into four components: the peaks at 285 eV, 286.4 eV, 288.7 eV, and 290.5 eV were assigned to the carbon atoms in hydrocarbon, ether, ester, and aromatic rings of PAT, respectively. Thus, XPS and FTIR showed the successful coating of PAT on SAMs coated and ctrl Co-Cr surfaces. *In vitro* drug release studies showed that PAT was sustained released from SAMs coated Co-Cr surfaces for up to 35 days while burst release was observed from control Co-Cr surfaces within 1 to 3 days (Fig 4).

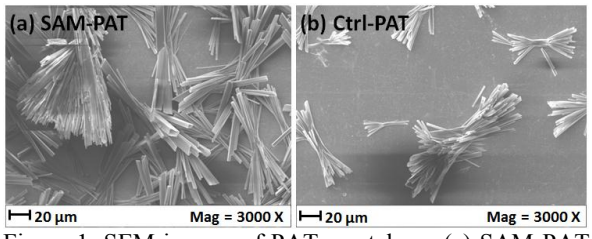

Figure 1. SEM images of PAT crystals on (a) SAM-PAT (b) Ctrl-PAT.

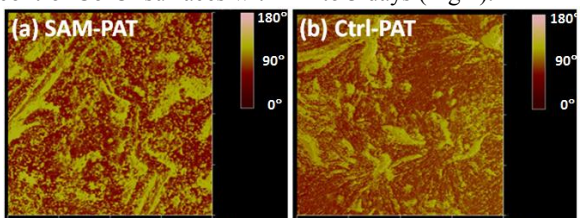

Figure 2. AFM tapping mode phase images of PAT molecular coatings on (a) SAM-PAT (b) Ctrl-PAT.

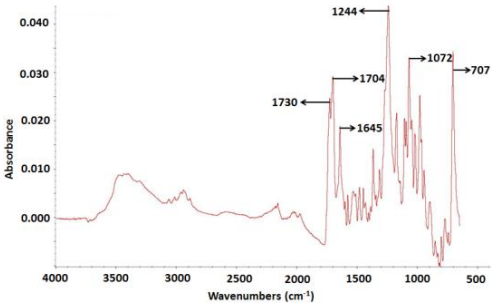

Figure 3. FTIR spectrum of SAM-PAT.

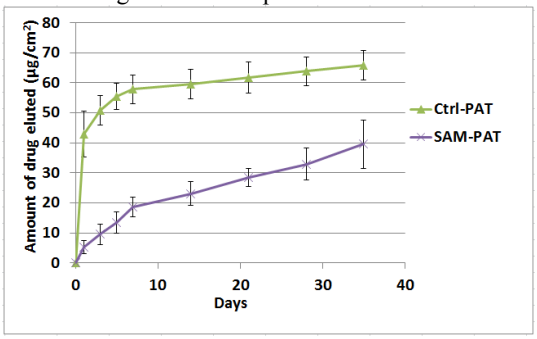

Figure 4. *In vitro* drug release profiles of SAM-PAT and Ctrl-PAT for 100 μg/cm^2 drug dose.

Similar release profiles were observed for 25 μg/cm^2 and 200 μg/cm^2 drug doses as well.

Conclusions: SAMs platform provided sustained release of PAT in clinically relevant doses from Co-Cr alloy surfaces. Thus, this study demonstrated the potential for an effective polymer-free platform to deliver drugs from coronary stents.

References: (1) Mani G *et al*. Biomaterials 2007, 28, 1689 (2) Mani G *et al*. Biomaterials 2010, 31, 5372

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