Nanosized Therapeutic Self Assembled Monolayers (T-SAMs) on 316L Stainless Steel

Anil Mahapatro,[†] David M. Johnson,[‡] Devang N. Patel,[§]
Marc D. Feldman,[†§] Arturo A. Ayon,[†] and C.Mauli Agrawal*[†]

College of Engineering[†] and Department of Chemistry[‡], The University of Texas at San Antonio, San Antonio, TX&
Department of Cardiology[§], The University of Texas Health Science Center at San Antonio, San Antonio, Texas 78229

Introduction: In-Stent restenosis and therefore the need for repeat procedures, limits the long term benefit of coronary stents.[1] Various strategies have been attempted, but the most successful to date has been polymer coated drug eluting stents. Although fairly successful, this strategy still suffers from drawbacks such as polymer fracture during stent expansion, and an inflammatory reaction to the polymer, which could contribute to restenosis.[2] Thus, there is a need to develop alternate stent based drug delivery strategies. Attachment of therapeutic drugs to functional self assembled monolayers (SAMs) after their assembly on 316L stainless steel SS (currently used in coronary stents) could possibly serve as a localized drug delivery system, which, if used in coronary stents, could reduce arterial restenosis while minimizing or eliminating some of the problems with current technologies mentioned above.

Materials and Methods: 316L SS sample plates (20mm x 20mm x 2mm, ESPI Corp. Inc, Ashland,) were polished (final roughness 0.2 ± 0.1 µm), cleaned chemically (ultrasonicated for 10 min each in 70 % ethanol, acetone and 40 % nitric acid) and subjected to glow discharge gas plasma (GDGP) treatment (Harrick Scientific, NJ) for 3 min in an oxygen environment under reduced pressure (15 psi). The plates were then immediately dipped in amphiphile solutions (10 mM ethanolic solution) for 48hr of 11-Mercapto-1-undecanol (-OH SAM) to form functional SAMs, which were then used as precursors to attach ibuprofen (used as a model) on steel via lipase catalysis (60° C for 5 hr, in toluene). These samples were then characterized using X-ray photoelectron spectroscopy (XPS), fourier transform infrared spectroscopy (FTIR) and contact angle measurements

Results and Discussion: Gas plasma treatment was used to improve surface hydrophilicity and activate surface for deposition. Ibuprofen was selected for surface modification because it has a COOH functional group that could be attached to the -OH functional SAM on 316L SS. This drug was selected to demonstrate proof of concept; however similar reactions could be easily extended to other esterification reactions on SAMs. The drug attachment to the functional SAM was characterized via FTIR (Figure 1a). After the surface modification of -OH SAMs via lipase catalysis, we can see the presence of the C=O stretching bands at 1745 cm^{-1} which was absent in the FTIR spectra of -OH SAMs. The C=O band should only evolve after the esterification of the carboxylic moiety of the drug (ibuprofen) with the OH terminal SAM. XPS analysis was carried out to further characterize drug attachment. Figure 1b shows the C (1s) region for the -OH SAM before and after surface modification. The spectrum of the hydroxyl thiol SAM exhibits a slightly asymmetric photoelectron peak centered at 284.7 ev, which is characteristic of the carbon 'C' in the internal units of the methylene chain ($CH_2\underline{C}H_2CH_2$).[3,4] After lipase catalysis with ibuprofen we see a photoelectron peak evolving at 288.5 ev which arises from the 'C' (C=O) in carboxylic acid.[4] This would evolve only after the esterification of ibuprofen with the OH SAM.

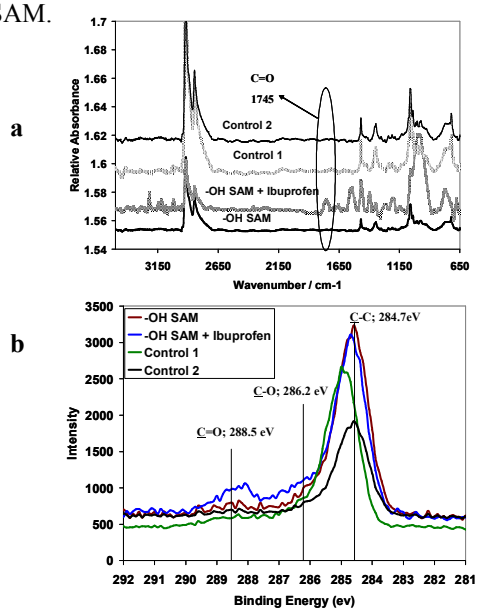

Figure 1. -OH terminated SAM on 316L before and after drug attachment. (a) FTIR spectra (b) XPS spectra; C (1s) region; [Control 1: with drug and without biocatalyst, Control 2: with biocatalyst but without drug]

Control reactions (Figure 1a and Figure 1b) gave spectra similar to that of the –OH SAM only, which strongly suggests that the surface modification has taken place due to lipase catalysis and suggests non existence or negligible non specific adsorption of the lipase and/or drug to the metal surface.

Conclusions: Therapeautic moieties can be attached directly to 316L SAMs which could be potentially used for localized arterial drug delivery. We expect this technology to assist in development of advanced drug delivery from metal implants.

References:

(1) Abizaid, A. *Circulation* **2001**, *104*, 533-8.
(2) Van der Giessen, W. J. *Circulation* **1996**, *94*, 1690-7.
(3) Palegrosdemange, C. *J Amer. Chem. Soc.***1991**, *113*, 12-20.
(4) Bain, C. D. *J Amer. Chem. Soc.***1989**, *111*, 321-335.