Effects of Coating Methods and Solvents on the Deposition of Paclitaxel on Self-Assembled Monolayers Coated Stents

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Statement of Purpose: Some polymers used in stents to deliver drugs cause adverse reactions in patients.[1] Hence, the research in this area is currently focused on either developing more biocompatible polymer platforms or a totally polymer-free platform to deliver drugs from stents. Self-assembled monolayers (SAMs) belong to the category of polymer-free drug delivery platform. The use of SAMs to deliver drugs from 2D metal surfaces has been demonstrated.[2] This study is focused on coating an anti-proliferative drug (paclitaxel – PAT) on SAMs coated 3D cobalt-chromium (Co-Cr) alloy stents. The effect of different coating methods such as dip coating (DC), spray coating (SC), and centrifugal force coating (CFC) on the nature (morphology, uniformity, and distribution) of PAT deposited on SAMs coated stents was investigated. Also, the effect of different solvents such as ethanol (ETOH) and a mixture of ETOH and dimethyl sulfoxide (DMSO) (3:1, v/v) on the nature of PAT coating on SAMs coated stents was investigated.

Methods: A carboxylic acid terminated phosphonic acid SAM was coated on chemically cleaned Co-Cr alloy stents as previously described.[2] A solution of PAT (soln-1) in ETOH was prepared at a concentration of 4 mg/mL. Another solution of PAT (soln-2) was prepared in a mixture of ETOH and DMSO (3:1 ratio) at a concentration of 4 mg/mL. The two different solutions of PAT were used for coating the stents by the following three methods: (a) DC – stents were dipped in soln-1 or soln-2 for 1h, and then removed from the solution and air dried for 2h; (b) SC – stents were spray coated with soln-1 or soln-2 using the following parameters: flow rate 0.02 mL/min, focusing gas pressure 0.5 psi, rotation rate 70 rpm, horizontal translation speed 0.1 in/sec, followed by drying in N_2 and air; (c) CFC – stents were placed in a microcentrifuge tube with 1.2µL of soln-1 or soln-2 and centrifuged at 500 rpm for 8 min, and then removed from the solution and dried in air for 2h. All the stents coated with PAT by different methods and solvents described above were characterized using scanning electron microscopy (SEM).

Results: The SEM images of control (chemically cleaned) and all PAT deposited SAMs coated stents are provided in Fig 1. Fig 1A and B show the images of control stents. The surfaces appear smooth with no surface defects. When ethanol was used as a sole solvent (soln-1), the stents prepared by all the three different methods (DC, SC, and CFC) showed non-uniform drug coating. The needle shaped PAT crystals were sporadically present on the dip coated stent surface using soln-1 (Fig 1C). The spray coated stent using soln-1 (Fig 1E) had PAT crystals randomly present over the entire stent surface. Also, the drug coating had webbing between the stent struts. For the stents coated by CFC with soln-1 (Fig 1G), the drug coating was not uniform with areas of high drug concentration and areas of low to none drug concentration were present on the stent. On the contrary, the stents coated with soln-2 showed a uniform drug coating irrespective of the coating methods. The stent coated by DP with soln-2 (Fig 1D) had a uniform coating of small needle shaped PAT crystals distributed evenly over the entire stent surface. Similar results were also observed for the stents coated using the soln-2 by CFC (Fig 1H). The stent coated by SC with soln-2 (Fig 1G) showed a thin film morphology of PAT that uniformly covered the entire stent surface.

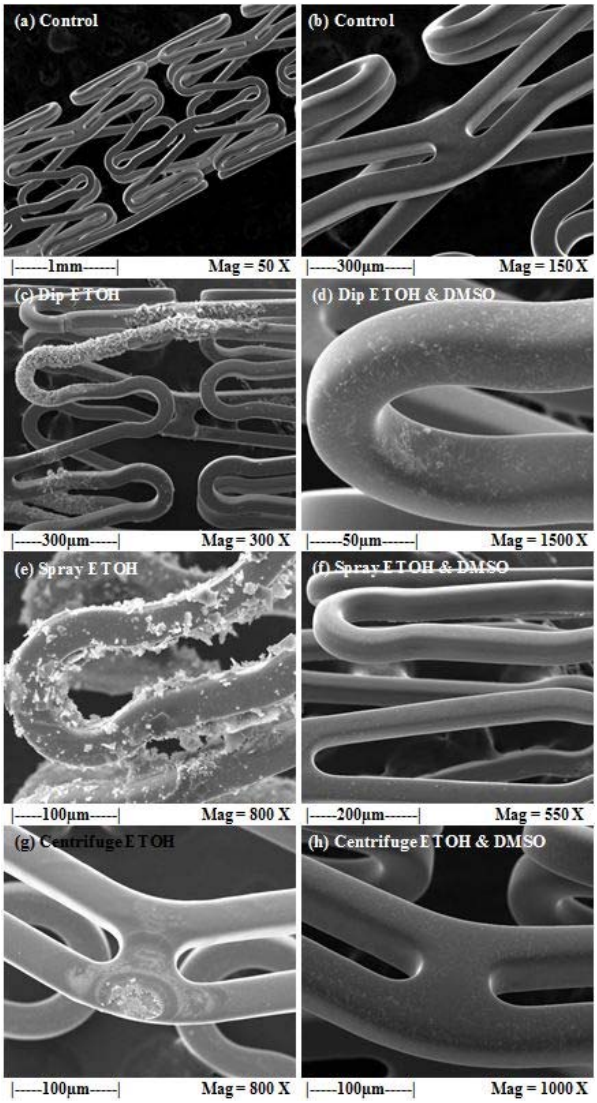

Fig 1. SEM images of control and PAT coated stents

Conclusions: This study demonstrated that a mixture of ETOH and DMSO (3:1 ratio) is a suitable solvent for obtaining a uniform drug coating on SAMs coated stents irrespective of the coating methods applied.

References: (1) Virmani R. Circulation 2004; 109: 701-705; (2) Mani G. Biointerphases 2011, 6, 33-42.

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