Controlled drug release from hydroxyapatite-coated porous metal structure

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Introduction: Porous Ti6Al4V metal structures have been used in orthopedic applications for their excellent biocompatibility. Moreover, owing to their high surface area, animal studies have demonstrated use of porous metal structures for antibiotic delivery applications[1]. However, one associated drawback is the burst release of antibiotics from the metal surface at the implantation site. In this study, the effect of solution-deposited Hydroxyapatite (HA) coating on providing a controlled drug release from the porous metal structure was investigated. Minocycline and Rifampin combination was chosen because they provide synergistic activity against gram positive and gram negative bacteria that cause infection at the site of joint prostheses[2].

Methods: Six porous Ti6Al4V were coated with HA using an electrodeposition process (37°C, pH 6.4). The antibiotic coating solution of concentration 40mg/ml was made by mixing Rifampin and Minocycline powders in methanol. Each HA-coated disc was soaked in 10mL of antibiotic solution for 30 min and then oven dried at 40°C. The discs were first soaked in 100mL of PBS for 1h, and then transferred directly from PBS to 10mL of methanol to extract any remaining antibiotic overnight. The PBS solutions and the methanol solutions were analyzed in a Waters High Performance Liquid Chromatography system using a 60:40 potassium phosphate: acetonitrile mobile phase at a 1.15 mL/min flow rate. The experiment was repeated for 4, 12, 24, 48 and 96h. For each time point, the control group consisted of similar porous metal discs not coated with HA. FTIR (Continuum, Thermo Nicolet) was also conducted to determine the effect of HA coating on the conformation of adsorbed antibiotic.

Results: Figure 1 shows the SEM image of the HA coating deposited on the porous metal. The HA coating provides a high surface area which provides for enhanced interaction between HA coating and antibiotic molecules. As a result, HA-coated porous metal exhibited controlled release of drug molecules over the 4 day period as noted by 45% of minocycline and rifampin eluted from the HA-coated metal compared to 85-95 % of the drug eluted from uncoated porous metal (Fig. 2). FTIR analysis indicated that interaction with HA did not modify the conformation of the adsorbed antibiotic molecules.

Conclusion: HA-coated porous metal structures can provide controlled drug release.

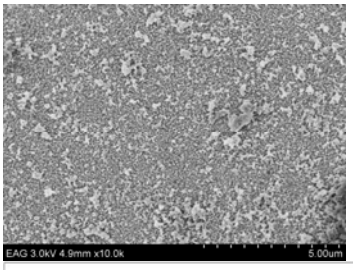

Fig.1: SEM image of HA coating on porous metal.

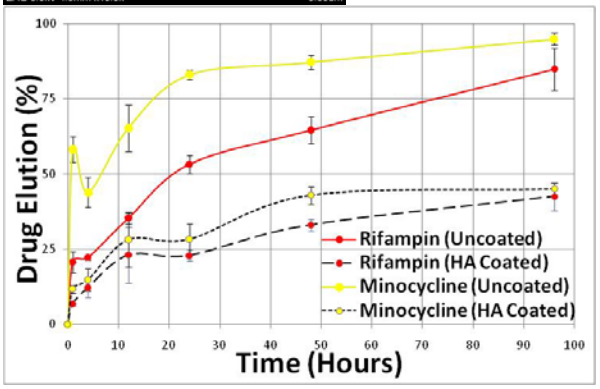

Fig.2: Antibiotic release from HA coated porous metal structure.

Ref: **[1]** Moojen et al. J Orthop Res 27:710-716, 2009. **[2]** Raad et al. Antimicrob Agents Chemother 39(11)2397-400, 1995.