Antibiotic release from HA-coated porous metal structures under static and dynamic conditions

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Introduction: Orthopedic devices made with porous Ti6Al4V metal structures have historically demonstrated excellent biocompatibility. Their high surface area also provides potential for their use in drug delivery applications[1]. Previous work has demonstrated that a hydroxyapatite (HA) coating can facilitate controlled release of antibiotics from porous metal discs[2]. In this study the antibiotic release from HA-coated porous metal discs has been analyzed in static and dynamic conditions *in-vitro*. A combination of rifampin and minocycline was chosen because they are highly effective in preventing bacterial colonization of staphylococci strains that are a leading cause of infection[3].

Methods: Four porous Ti6Al4V metal discs were coated with HA using an electrodeposition process (37°C, pH 6.4). Both HA-coated and uncoated (control) discs were soaked in 10mL of methanol solution of rifampin and minocycline of concentration 40mg/mL for 30 minutes, then oven-dried at 40°C. Under static conditions separate sets of identical discs were soaked in 100mL PBS for 1, 4, 8, 24, 48, 120, 192, and 336h. All the samples were incubated in parallel under identical conditions. In the dynamic study, one set of discs were soaked in 25mL PBS solution, which was replenished at each of the abovementioned time points. All PBS solutions from both static and dynamic systems were analyzed using Ultra-High Performance Liquid Chromatography to determine the elution percentage of each antibiotic over time. After 7 days in static conditions, a zone of inhibition study was conducted to determine the antibacterial efficacy of the antibiotics present in the discs against *S. aureus*.

Results: After 14 days, degradation of minocycline was considerably higher in the static process compared to the dynamic process (Fig 1). On a 48h timescale, in either of the elution conditions, the HA-coating decreased the release of minocycline by 58 ± 12% and rifampin by 25 ± 7%. For either antibiotic, dynamic conditions increased antibiotic elution by 2.01 ± 0.32 times for HA-coated discs and by 1.44 ± 0.24 times for the control. Finally, microbiology testing showed that, even after 7 days, the antibiotics remaining on the discs were still bioactive (Fig 2).

Conclusion: HA-coated porous metal structures provided a more controlled antibiotic release over a 48h timescale, and also showed potential to reduce minocycline degradation and improve antibiotic efficacy over 14 days.

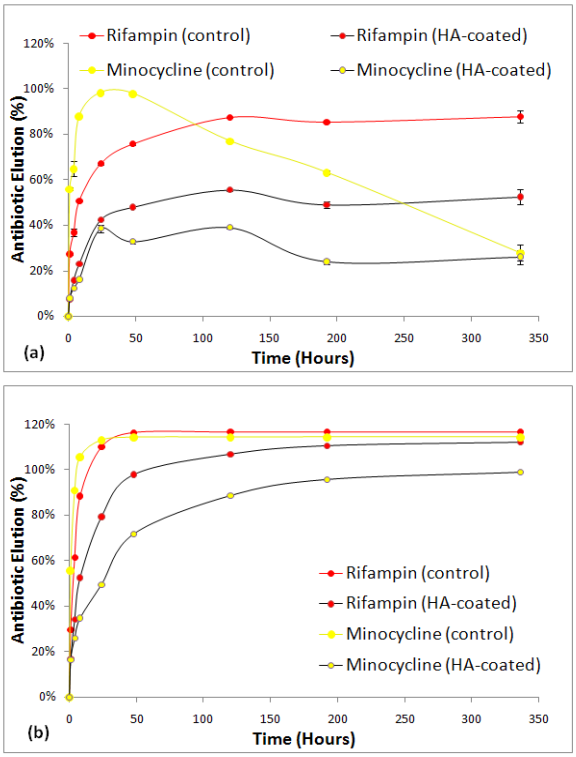

Fig 1 – Antibiotic elution from HA-coated and uncoated porous metal discs under (a) static and (b) dynamic conditions.

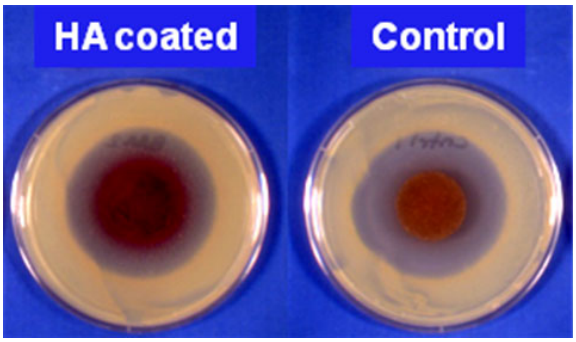

Fig 2 – Zone of inhibition from porous metal discs after 7 days in a static environment.

Ref: [1] Moojen et al. J Orthop Res 27:710-716, 2009.
[2] Bagadia et al., Poster at Society for Biomaterials, 2010.
[3] Raad et al. Antimicrob Agents Chemother 39(11) 2397-400, 1995.