Antibacterial Sol-Gel Films on Implant Material with Tailored Controlled Release Properties

S Radin[1], J Parvizi[2], P Ducheyne[1], I Shapiro[2]
[1]University of Pennsylvania, Philadelphia 19104, [2]Thomas Jefferson University, Philadelphia, PA19107

Introduction: Prevention of infection in open fractures is challenging, especially when fracture fixation implants are used. For the treatment of fractures it is desirable to apply a thin antibacterial film on the osteosynthesis material. Room temperature processed silica sol-gels are novel, resorbable and biocompatible, controlled release materials (1-4). Vancomycin, a potent antibiotic used in treating osteomyelitis, can be released from sol-gel granules in active form (1,2). Recently, it was shown that a thin sol-gel film composed of several layers can be used for the controlled delivery of antibiotics (5). In this work, we study the mechanisms of controlled release from thin sol-gel films on Ti-alloy substrate.

Materials and Methods: Ti6Al4V plates (ELI, President TI), 0.5-mm thick, were cleaned and passivated prior to film deposition. Tetraethylorthosilane (TEOS), deionized (DI) water, ethanol (Eth), and 1N HCl (DI:HCl:TEOS molar ratio=5:0.01:1, Eth/TEOS volume ratio=2) were mixed to form a sol. Sols with nominal vancomycin concentration of 3, 5, 10, and 20 % (drug/SiO_2, % by weight) were prepared by adding corresponding amounts of vancomycin dissolved in water to the sol. Sol-gel fims composed of three layers were deposited by dip coating at a withdrawal speed of 100 mm/min. Each layer was air-dried prior to deposition of a next layer.

In vitro release and film stability were studied at 37^{0}C by using phosphate buffered saline (PBS, pH 7.4). The solutions were replenished daily. Vancomycin concentrations were measured spectrophotometrically at 280 nm. The film stability was determined by measuring the weight loss as a function of immersion time.

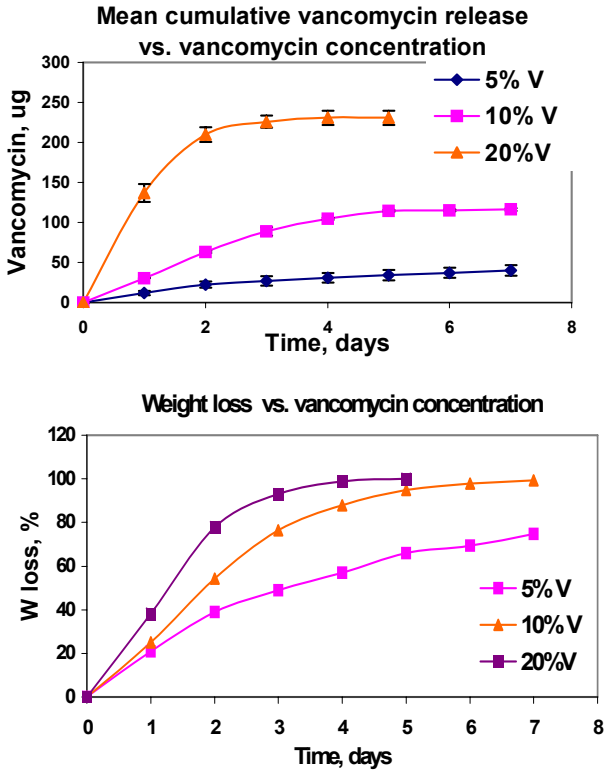
Results and Discussion: With increase of vancomycin concentration from 3% to 20%, the drug load in a 3-layer film was increased from 5 to 35 µg/cm^2. Vancomycin release and film stability data as a function of immersion time and vancomycin concentration are shown in Figures 1a and 1b, respectively. The data demonstrate time-dependent and load-dependent release of vancomycin from sol-gel films. The rates of release increased with the load. At larger concentrations (20%), fast release with 90% release of the original load by 2 days was observed. In contrast, films with lower concentrations (5%) showed a slower and steady release with a cumulative release of 56% after 7 days of immersion. As shown in Figure 1b, stability of these sol-gel films was also time-dependent and load dependent. A 100%-release of the original load corresponding to a 100%-weight loss and an increase in the dissolution rate (evaluated as the weight loss) with the drug load were observed. These observations suggest that film dissolution is the more prevalent mechanism controlling the release from these thin films. Thus, control of the drug release rates is possible through the modification of the film stability.

The data also demonstrate that at the various concentrations studied, the daily release of vancomycin (µg/ml) from the multi-layer films considerably exceeded the minimal inhibitory concentration (MIC) of vancomycin against Staphylococus aureus (1.5-3 µg/ml).

Conclusions: The *in vitro* data demonstrate that thin and resorbable, long-term controlled release sol-gel films can be applied to Ti alloy substrates and that film resorption is the main mechanism underlying the control of release.

This study suggests that the release rates and the film stability can be tailored to therapeutic needs by controlling film resorption rates. As such, silica sol-gel thin films can be used as a drug delivery system with potential clinical applications in prevention or treatment of periprosthetic infections.

Figure 1 a, b



References: (1) S Radin and P Ducheyne Kluwer 2004 p 59-74; (2) S Radin et al 2001 J Biomed Mater Res, 57:313-20; (3) Radin S et al. 2005 Biomaterials,26:1043-52; (4) Ahola M et al 2000 Int J Pharm, 195:219-27; (5) S Radin et al Proceed 47th SFB Mtg

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