Biodegradable, Antibacterial Coatings for Orthopaedic and Dental/Craniofacial Implants

*Norowski, PA; *Noel, SP; **Courtney, HS; * Yuan, YL; *Richelsoph, K;** Ong, JL; *Bumgardner, JD; *Haggard, WO
*University of Memphis, Memphis, TN; ** University of Tennessee-Health Science Center, Memphis, TN.

Statement of Purpose:

2.6 million people in the United States receive orthopaedic implants annually. Approximately 4% of these implants must be removed due to bacterial infection acquired during implantation[1]. An innovative method of treatment for infection could reduce the number of implants removed due to infection. Localized delivery of antibiotics appears to be an efficient treatment approach[2]. This study evaluated the in vitro release of gentamicin from chitosan coated o titanium. Chitosan was used due to its good bone compatibility and function as a drug delivery vehicle[3,4].

Methods:

Chitosan or gentamicin-loaded chitosan coatings were covalently bonded to commercially pure titanium coupons via silane-glutaraldehyde molecules[4]. Specimens were solution cast in 87.4% (Vanson, WA) or 78% (Agratech, MS) deacetylated chitosan, dissolved in a 1 wt % solution of acetic acid. The antibiotic-loaded coatings contained 36 wt % gentamicin. Controls did not contain gentamicin. Elution testing was performed to determine the amount of antibiotic in solution at 6, 12, 24, and 72 hrs. The coated coupons were placed in 40 mL of phosphate buffered saline and agitated in a 37 ^{o} C water bath. Solutions were sampled and renewed at each time point. The gentamicin concentrations were then measured using a fluorescence polarization immunoassay technique (TDxFLx, Abbot Labs, IL). A bacterial zone of inhibition (ZOI) study was also conducted to assess the antibacterial activity of the coatings. Tests were conducted with *staphylococcus epidermitis* and *staphylococcus aureus*.

Results / Discussion:

Results showed very rapid initial release of gentamicin. After 24 hours, gentamicin release was less than 1 μg/mL/cm^2 for both degrees of deacetylation (DDA). However, there were differences in the rate of gentamicin release from the two types of chitosan used. The 78% DDA chitosan released higher concentrations of drug at the 6, 12, and 24 hour time points. The 87.4% DDA chitosan provided a slightly slower elution rate, and released higher concentrations than the 78% DDA after 3 days (Figure 1).

For the prevention of implant infection, the initial "burst" of eluted drug in the beginning is desirable. These concentrations of eluted gentamicin will prevent any bacterial colonization that might be present post-implantation. Additionally, the presence of chitosan in the wound site may stimulate the wound healing process[3], and provide an osteoconductive surface for bone-metal ingrowth[4].

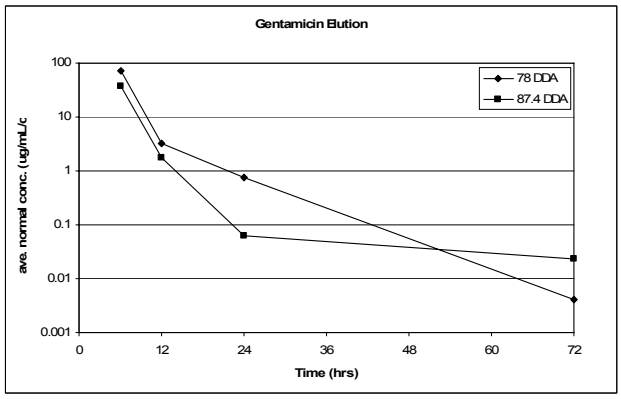

Figure 1 - Elution profile of Gentamicin loaded coatings.

The zone of inhibition study demonstrated the antibacterial activity of the antibiotic-loaded coatings. For these coatings, the zone of inhibition for *staphylococcus epidermitis* extended 14.4 mm from the edge of the Ti coupon. No detectable zone of inhibition for the chitosan-only coated coupon and Ti control was seen in comparison gentamicin loaded coatings (Figure 2). Chitosan controls do exhibit an inherent antibacterial activity[3], which is more prominent for *staphylococcus aureus* cultures. In general, the ZOI for the 78% DDA chitosan and chitosan-gentamicin coating extended farther than those for the 87.4% DDA chitosan.

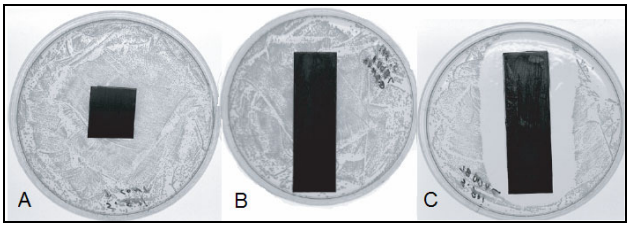

Figure 2 – *Staphylococcus epidermitis* ZOI: A) Ti control; B) Ti coated with 78% DDA chitosan; C) Titanium coated with chitosan-gentamicin composite

Conclusions:

Based on these results, antibiotic-loaded chitosan demonstrates the potential to serve as a suitable coating for orthopaedic and dental/craniofacial implants. Elution tests revealed rapid drug release profiles for both chitosan materials tested, with the 78% DDA chitosan having the more rapid release of gentamicin. Future work includes mechanical testing to quantify the adhesion of the coating at the metal-coating interface. There is also a need to test the effects that crosslinking would have on the drug release profile.

References:

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3. Di Martino, A. *Biomaterials* 2005; 26, 5983-5990.
4. Bumgardner, JD. *J. Biomater. Sci. Polymer Edn*, 2003;14(5), 423-438.