A Surface Modification Platform on Eluting Medical Devices

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Statement of Purpose: A proprietary non-leaching betaine polymer modification was developed to tightly bind water molecules on a medical device surface and reduce platelet and bacterial attachment.[1] The long-term anti-thrombus and anti-infection platform technology was further explored to combine with agenteluting medical devices including orthopedic and cardiovascular devices. Surface chemistries were adapted to different substrate materials to provide a homogenous and functional modification.

Methods: Betaine monomers were applied to an orthopedic device (tibial nail, titanium alloy) and an eluting PICC (polyurethane). The surfaces of these devices were loaded with a model eluting agent (chlorhexidine or CHX) and modified with a betaine polymer. The protein adsorption was evaluated by methods previously reported.[1] A modified Centers for Disease Control and Prevention (mCDC) biofilm reactor was utilized for growing Escherichia coli with nutrient flow for a period of 24 hours followed by sonication and quantitative recovery (ASTM E2562–07). The performance of reducing microbial adhesion under a static condition was also evaluated. The test samples were first preconditioned in a 50% solution of serum in sterile water at 37°C for 18 hours to simulate the use of the device Samples were then immersed into culture medium with seeded bacteria or fungi, and incubated at 37°C. After 24 hours, samples were taken out and gently rinsed with PBS solution. The bacteria on the sample surface were removed by sonication, cultured on agar plates, and counted. The abrasion resistance stability of tibial nails was evaluated based on a described method.[2] Agent releasing from the substrate was measured by UV-Vis. The surface was characterized by ATR-FTIR, laser confocal microscope, contact angle, and SEM.

Results: Polybetaine-modified titanium samples were characterized for their surface chemistry and physical properties and found to have a homogenous surface modification. Through formulation optimization, controlled release of CHX was achieved for 8 weeks (Figure 1), as well as inhibition of the growth of both Gram-positive and Gram-negative organisms. Polybetaine-modified samples (with and without CHX) exhibited > 90% reduction in protein adherence relative to unmodified titanium substrates, indicating that the nonfouling properties are preserved throughout agent release. The polymeric modification system showed excellent mechanical integrity and strong adherence to the titanium substrate. Even after 4 weeks of CHX release in an aqueous solution at 37 °C, the shear strength of the polymer layers to the titanium substrate remained intact (> 10 MPa).

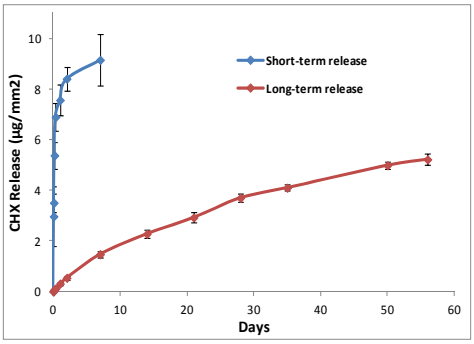

Figure 1. Controlled release of CHX from polybetaine-modified titanium.

A 4-log biofilm reduction was achieved on the modified external surface of a PICC shaft challenged with both gram positive and gram negative bacteria. Fibrinogen adsorption reduced 94 % compared with control catheter. The CHX can be released in a controlled profile by loading different amount of agent (Figure 2).

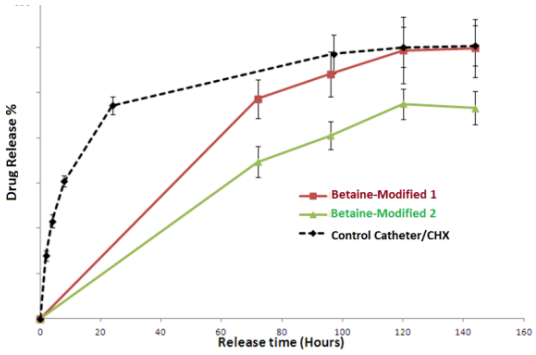

Figure 2. Controlled release of CHX from control and polybetaine-modified PICC catheter.

Conclusions: Betaine-modification is highly adaptable for many agent-eluting implantable devices including orthopedic devices and cardiovascular catheters. For different substrate, homogenous betaine modifications may maintain a high resistance to bacteria attachment, protein adsorption, and platelet adhesion. The modification was proven to be applicable to eluting surfaces. Controlled release may be achieved while maintaining long-term protein resistant properties.

References:

1. R. Smith. Science Translational Medicine. 2012: 4(153):153ra132.
2. H. Wang. OTA Abstract 1265: 2012

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