Functional macromolecules for simple surface modification of a biodegradable magnesium alloy to reduce thrombogenicity and improve corrosion resistance

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Statement of Purpose: Mg alloys represent a promising class of materials to serve as biodegradable scaffolds for a variety of tissue applications. In the cardiovascular area, degradable metallic stents could offer strength in the acute period followed by degradation after lumen stabilization. The lack of a permanent device in treated arteries would be clinically attractive. For candidate alloys one would desire a slower early corrosion rate, preserving mechanical strength, as well as low thrombogenicity, when the risk for thrombotic occlusion is particularly high. To achieve this behavior without altering the bulk properties of the alloy, we have developed and characterized siloxane functionalized phosphorylcholine (PC) and sulfobetaine (SB) macromolecules that can covalently react with Mg alloy oxide surfaces for the acute reduction of corrosion and platelet adhesion.

Methods: Siloxane functionalized PC or SB macromolecules (PCSSi or SBSSi) (**Fig. 1**) were synthesized by a thiol-ene radical photopolymerization technique [1] with 3-mercapto-propyl trimethoxysilane and 2-methacryloyloxyethyl-phosphorylcholine (PC) or *N*-(3-sulfopropyl)-*N*-(methacryloxyethyl)-*N*, *N*-dimethylammonium betaine (SB) monomers. The chemical structure of PCSSi and SBSSi were confirmed by ^{1}H-NMR and the synthesized macromolecules were reacted with Mg alloy (AZ31) surfaces by an anhydrous surface deposition method. Acute blood compatibility was assessed in vitro after fresh ovine blood contact under rocking conditions. The surfaces contacted with ovine blood were observed by scanning electron microscopy (SEM) and activated platelets in the bulk phase were quantified by flow cytometric assay using Annexin V binding [2]. Surface corrosion properties of modified and control unmodified surfaces were evaluated with electrochemical corrosion analysis.

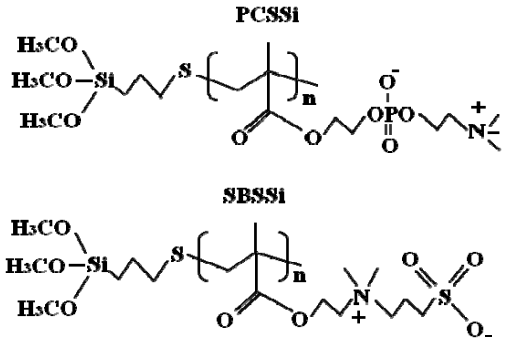

Figure 1. Structure of surface-modifying macromolecules

Results: Functional PC or SB macromolecule-modified surfaces (AZ31-PCSSi or AZ31-SBSSi) exhibited markedly decreased platelet adhesion (80% or 83% reduction, respectively) versus control Mg surfaces (AZ31) after 1 h ovine heparinized blood contact ($p<0.01$). The % activated bulk phase platelets quantified by Annexin V binding was also decreased in blood contacted with AZ31-PCSSi (3.7%) and AZ31-SBSSi (2.4%), compared to the AZ31 control (6.5%) ($p<0.05$). The corrosion current densities (I_{corr}) acquired from the potentiodynamic polarization curves on AZ31-PCSSi (4.82×10^{-9} A/cm^2) and AZ31-SBSSi (6.78×10^{-8} A/cm^2) surfaces were markedly lower than for the AZ31 control (1.93×10^{-5} A/cm^2) ($p<0.01$) which had a pitting corrosion point (E_{pit}: -1.32V) (**Fig. 2**). The coating resistance (R_{coat}) on AZ31-PCSSi (2.92×10^5 ohms) and AZ31-SBSSi (4.02×10^5 ohms) surfaces was also much higher than for AZ31 control surfaces (8.07×10^3 ohms) ($p<0.01$).

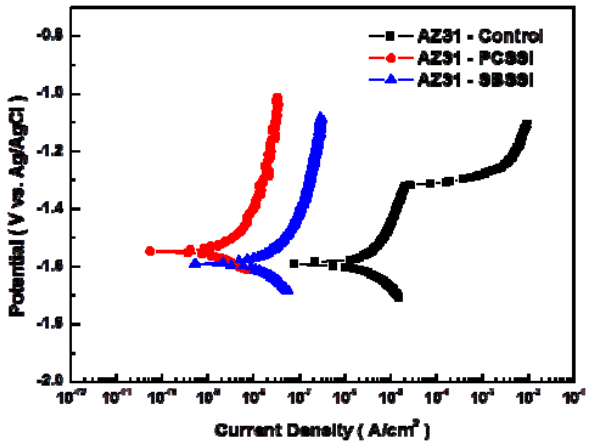

Figure 2. Potentiodynamic polarization curves of AZ31 control, AZ31-PCSSi and AZ31-SBSSi in a simulated body fluid.

Conclusions: Surface modification of a Mg alloy (AZ31) using siloxane functional PC or SB macromolecules effectively reduced acute thrombotic deposition as well as platelet activation in the bulk phase of the blood. Electrochemical corrosion testing showed markedly increased corrosion resistance on the modified Mg alloy surfaces. While further extended in vitro studies and in vivo evaluations are required, the developed molecules show promise in acutely reducing both the corrosion and thrombotic processes, which would be attractive for degradable metal stent modification.

References:

[1] Hoyle CE, *J Polym Sci* 2004;42:5301.
[2] Ye SH, *Colloid Surface B* 2010;79:357.

Acknowledgement: This research was supported by the NSF Engineering Research Center for Revolutionizing Metallic Biomaterials (Award #0812348).