Anti-fouling Medical Coatings Prepared with Amphiphilic PEG-Silanes

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Statement of Purpose: Implanted blood-contacting polymeric medical devices are highly susceptible to thrombosis (i.e. clotting) which leads to diminished performance, device failure or embolic complications. Silicones and other hydrophobic polymers are widely used to prepare implantable blood-contacting medical devices including hemodialysis catheters, pacemaker components, heart valve leaflets, vascular prostheses and stent coatings. Unfortunately, their hydrophobic surfaces lead to significant adsorption of plasma proteins which initiates subsequent thrombus (clot) formation.[1] In contrast to silicones, polyethylene glycol (PEG) exhibits exceptional protein resistance. In this work, we sought to enhance the chain mobility of PEG molecules introduced into silicone in order to reduce protein adsorption. Conventional PEG-silanes consist of a PEG segment separated from the reactive group by a short alkane spacer [e.g. propyl as for $(RO)_3Si\text{-}(CH2)_3\text{-}(CH_2CH_2O)_n\text{-}OCH_3$)] which may limit the PEG chain mobility. We have prepared novel linear PEG-silanes with siloxane tethers and PEG segments of varying lengths (**Figure 1**). Thus, they are amphiphilic, a feature which is also associated with reduced protein adhesion. Linear PEG-silanes were used to form bulk-crosslinked silicone coatings as well as surface-grafted coatings and their resistance to protein and whole blood adhesion measured.

Methods: *Synthesis of Linear Amphiphilic PEG-Silanes.* The synthesis of linear amphiphilic PEG-silanes has been previously reported[1] and likewise used to prepare an extended series of analogous PEG-silane amphiphiles with varying siloxane tether (m) and PEG (n) segment lengths. *Preparation of Bulk-Crosslinked Coatings.* Selected PEG-silanes were each combined with silanol (Si-OH)-terminated PDMS (M_n = 3000 g/mol) in 2:3 molar ratio and cured at 150 °C oven for 24 h.[1] *Preparation of Silica-Filled Bulk-Crosslinked Coatings.* An acetoxy-cure silicone containing 20 wt% silica (MED-1137, Nusil) was dissolved in hexane (1:3 wt:wt) and selected PEG-silanes each added at 0, 1, 5, 10, 15 and 20 wt% based on solid weight of MED-1137. The resulting solution (1.5 mL) was cast onto a microscope slide and cured at RT (5 hrs) and under vacuum (12 hr). *Preparation of Surface-Grafted Coatings onto a Model Substrate.* Selected PEG-silanes were grafted onto an oxidized silicon wafer using toluene-based grafting solutions of varying molarity.[3] *Preparation of Surface-Grafted Coatings onto a Silica-Filled Silicone Surface.* Silica-filled silicone coatings were prepared via the aforementioned protocol (i.e. 0 wt% PEG-silane). Briefly, after subjecting to air plasma (1 min), the coatings were exposed to a grafting solution of selected PEG-silanes (e.g. 0.05 M in toluene, 0.8 mL, 2 hr). *Characterization.*

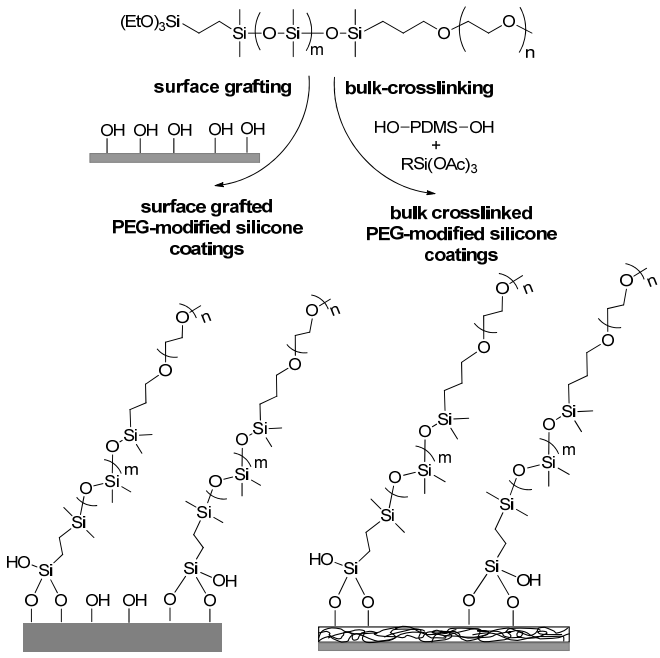

Figure 1. Preparation of coatings using amphiphilic PEG-silanes.

Static Adsorption of Proteins. The adhesion of Alexa Fluor 555 dye conjugate of bovine serum albumin (AF-555 BSA; MW = 66 kDa) and Alexa Fluor 546 dye conjugate of human fibrinogen (AF-546 HF; MW = 340 kDa) onto surfaces was studied by fluorescence microscopy (0.1 mg/mL in PBS; 3 hr exposure). Adsorption of Whole Blood. Fresh pig blood was exposed to the surface under static (1 hr) and flow conditions using a parallel-plate flow chamber (0.825 mL/min; wall shear stress = 60 dyne/cm2; 15 and 30 min).

Conclusions: On a stable silicon surface, the grafted PEG-silane concentration remains constant (i.e. no reconstruction). Increasing the length of the siloxane tether generally reduced adhesion. Bulk-crosslinked silicone coatings (with and without silica filler) prepared with PEG-silanes also generally showed reduced adhesion of protein and whole blood as the length of the siloxane tether was increased. Similarly analyses of coatings prepared with PEG-silanes having variable PEO segment lengths will also be presented.

References:

1. Murthy, R. Biomacromolecules 2007: 8, 3244.
2. Hawkins, M.L. J. Mater. Chem. 2012:22, 19540.
3. Murthy, R. Biomaterials 2009: 30, 2433.