The Antithrombogenic Potential of a Polyhedral Oligomeric Silsesquioxane (POSS) Nanocomposite

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We have developed a nanocomposite using a silica nanocomposite polyhedral oligomeric silsesquioxane (POSS) and poly(carbonate−urea)urethane (PCU) for potential use in cardiovascular bypass grafts and the microvascular component of artificial capillary beds. In this study, we sought to compare its antithrombogenicity to that of conventional polymers used in vascular bypass grafts so as to improve upon current patency rates, particularly in the microvascular setting. Using atomic force microscopy (AFM) and transmission electron microscopy (TEM), surface topography and composition were studied, respectively. The ability of the nanocomposite surface to repel both proteins and platelets in vitro was assessed using thromboelastography (TEG), fibrinogen ELISA assays, antifactor Xa assays, scanning electron microscopy (SEM), and platelet adsorption tests. TEG analysis showed a significant decrease in clot strength (one-way ANOVA, $p < 0.001$) and increase in clot lysis (one-way ANOVA, $p < 0.0001$) on the nanocomposite when compared to both poly(tetrafluoroethylene) (PTFE) and PCU. ELISA assays indicate lower adsorption of fibrinogen to the nanocomposite compared to PTFE (one-way ANOVA, $p < 0.01$). Interestingly, increasing the concentration of POSS nanocages within these polymers was shown to proportionately inhibit factor X activity. Platelet adsorption at 120 min was also lower compared to PTFE and PCU (two-way ANOVA, $p < 0.05$). SEM images showed a "speckled" morphologic pattern with Cooper grades I platelet adsorption morphology on the nanocomposite compared to PTFE with grade IV morphology. On the basis of these results, we concluded that POSS nanocomposites possess greater thromboresistance than PTFE and PCU, making it an ideal material for the construction of both bypass grafts and microvessels.

Introduction

The ideal cardiovascular graft, whether a bypass graft or a microvessel, should have the ability to withstand high shear stresses, have similar bulk viscoelasticity to those of the native vessels they are anastomosed to, and, most importantly, possess thromboresistant properties. With decreasing vessel diameters at low-flow states,[1] the interplay between these factors is significantly amplified. While results with poly(tetrafluoroethylene) (PTFE) and poly(ethylene terephthalate) (Dacron) are satisfactory in larger vessels, patency is far lower in small-diameter grafts,[2] especially with Dacron, which has high platelet adsorption characteristics.[3] In the case of microvessels (<1 mm diameter), animal models using PTFE have shown a 20−25% patency rate in rat femoral vessels, while the control vein grafts in the experiment remained patent.[4] This is because these polymers adsorb significant amounts of fibrinogen[5] and activate thrombus formation on its lumen,[6] while the differential compliance at the anastomotic site causes the formation of intimal hyperplasia (IH).[7−9]

Therefore, autologous vein grafts remain the "gold standard" for both macro- and microvascular repairs[2] at low-flow states, as they are both compliant and nonthrombogenic. However, donor-site morbidity and the need for an additional surgery remain the drawbacks. To overcome this, there has been considerable work put into developing biological alternatives, particularly as small-diameter and microvascular grafts.[10] Their main advantages include non-thrombogenicity and optimal radial compliance, but growing them in vitro is lengthy with a high possibility of infection.[1,2,10,11] This has prompted other researchers to look into ready-made polymeric options which are bioactive or, in other words, mimic the biology of nature's vessels. While PTFE and Dacron have limitations, certain groups have turned to polyurethanes (PU), as they possess optimal physicomechanical properties and are resistant to flexural fatigue.[12] We have previously worked on a newer carbonate-based polyurethane, poly(carbonate−urea)urethane (PCU), which

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