PEGylated Terpolymers with Non-Fouling Properties

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Statement of Purpose: The function of many blood contacting biomedical devices is undermined by thrombus which results from spontaneous adsorption of proteins to the biomaterial surface followed by the subsequent attachment of cells. In previous work we have discussed the design of a biostable metharcylic terpolymer with tunable mechanical properties [1, 2]. Furthermore, we have electrospun the polymer into highly relevant tissue scaffolds and biofunctionalized the polymer with peptide ligands specific to human blood outgrowth endothelial cells (HBOECs) and human umbilical vein endothelial cells (HUVECs) [3-6]. In this phase of the research we wish to covalently incorporate chemical motifs which impart non-fouling properties to the polymer material to undermine the protein adsorption and cell adhesion steps necessary for thrombus formation. Poly(ethylene glycol) (PEG) is the chemical structure incorporated into the polymer due to its well documented non-fouling character.

Methods: Terpolymer was produced through free radical copolymerization of hexyl methacrylate (HMA), methyl methacrylate (MMA), and poly(ethylene glycol) methacrylate (PEGMA). The interfacial properties of the polymer were modulated through control of the concentration of PEGMA incorporated into the polymer chains. Materials containing 0 to 25 mol % PEGMA have been synthesized. The polymer was characterized through NMR, GPC, water adsorption, static contact angle measurements, and cell adhesion studies.

Results: The composition of the polymer was analyzed through NMR analysis as shown in Figure 1. The composition of the polymer tracks closely with the composition of the monomer feed illustrating the ease with which the PEG content can be tailored. For the remainder of the document, terpolymers will be referred to by the mole percent of monomers used in the feed.

Feed composition (mol % HMA/MMA/PEGMA)	Polymer composition (mol % HMA/MMA/PEGMA)
20/80/0	22/78/0
20/78/2	22/76/3
20/75/5	22/72/6
20/73/7	22/70/8
20/70/10	22/66/11
20/65/15	22/63/15
20/60/20	21/59/20
20/55/25	20/56/25

Figure 1: Terpolymer composition vs. feed compsotion.

Static contact angle analysis was used to analyze how the hydrophilicity of the interface changed with increasing PEG concentration as shown in Figure 2. As expected, the polymer interface becomes more hydrophilic as the concentration of PEG increases as observed by a decrease in the contact angle.

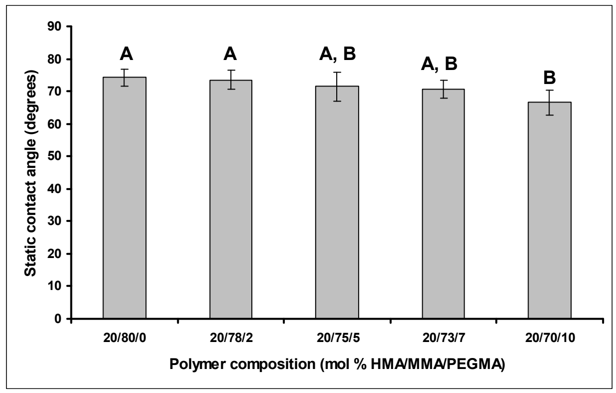

Figure 2: Contact angle vs. composition. Averages linked by the same letter are not significantly different.

Materials containing 10 mol % PEGMA were effective at resisting the cellular attachment of various cell lines under static culture conditions.

Conclusions: A terpolymer containing poly(ethylene glycol) non-fouling pendant groups has been synthesized. The concentration of PEGMA in the polymer can be modulated through control of the monomer feed composition. Furthermore, as the concentration of PEGMA in the polymer increases, the material interface becomes more hydrophilic as indicated by a decrease in the static water contact angle. The increased hydrophilicity of the material results in a surface possessing non-fouling character as indicated by resistance to cellular adhesion.

References:

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