Blood Compatibility of Poly(ethylene glycol)-methacrylate /Acrylic acid Copolymer Coated Surfaces

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Statement of Purpose

A variety of medical devices is applied in contact with blood clinically, therefore it is essential to understand the interactions of blood with the implanted biomaterial surfaces which are closely related to the thrombus and embolus formation.[1] Poly(ethylene glycol) and its derivatives, with attractive water-soluble properties, preventing plasma protein adsorption, platelet adhesion, and thrombus formation by the steric repulsion mechanism were investigated extensively in literature.[2] Poly(ethylene glycol) methacrylate (PEGMA) /acrylic acid and PEGMA/dimethacrylate (PEG/DMA) hydrogels were used for drug delivery with a controlled drug releasing rate.[3-4] Furthermore, Nho et al showed that by radiation grafting PEGMA onto cellulose films followed by the incorporation of heparin, hemodialysis membrane presented excellent platelet resistance.[5] In this study, PEGMA was copolymerized with acrylic acid followed by crosslinking to modify the surface of tissue culture polystyrene (TCPS). The synthesized Az-conjugated copolymer was identified by various analytical methods include Fourier-transform Infrared (FTIR), nuclear magnetic resonance and gel permeation chromatography (GPC). The surface resistant property was examined by the platelet adhesion tests on the surfaces modified with crosslinked PEGMA/AA copolymers.

Methods

4,4'-azobis(4-cyanovaleric acid), acrylic acid (AA), poly(ethylene glycol) methacrylate, azidoaniline (Az), and *N*-Ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide (EDC), were from Sigma and used for polymer syntheses. The copolymerization of acrylic acid and PEGMA was initiated by 4,4'-azobis(4-cyanovaleric acid). The Az was then conjugated to PEGMA/AA copolymer via EDC. For the surface modification, the Az-conjugated copolymer of 1 mg/mL was added to TCPS 96-well plate with various volumes (50μL and 100μL) and crosslinked by UV exposure prior the platelet adhesion analyses based on the literature.[6] The platelet suspension was adjusted to 5×10^7 platelets/mL with platelet suspension buffer (PSB), and were added to the wells to adhere for 1 hr at 37°C (100 μL/well). The number of adhered platelets was determined by measuring the lactate dehydrogenase (LDH) activity.

Results and Discussion

The synthesized PEGMA/AA copolymer was firstly evaluated by FTIR. The disappearance of the C=C binding at 1600-1680 (cm^{-1}) indicated that the copolymerization was proceed (Figure 1). In addition, the number average molecular weight measured by GPC was about 10,000 (g/mol). The results demonstrated that the copolymer was successfully synthesized.

Moreover, the synthesized copolymer exhibited excellent anti-platelet adhesion effects (Figure 2). Compared with the TCPS surfaces which adhered more than 2.7×10^5 platelets/cm^2, the Az-PEGMA/AA coated surfaces showed a significant reduction for the number of adhered platelets depending on the volume of Az-conjugated copolymer. As demonstrated by (a) and (b) in Figure 2, the increase of copolymer volume, from 50 μL to 100 μL, effectively reduced the number of platelets to 4×10^4 and 7×10^3, respectively. This result illustrated that the Az-conjugated PEGMA/AA copolymer had an excellent capability to resist platelets adhesion on the surface. Furthermore, the more quantity of Az-PEGMA/AA would increase the resistance to platelets adhesion.

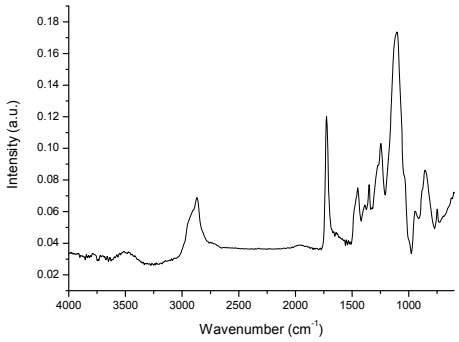

Figure 1. FTIR spectrum of PEGMA/AA copolymer.

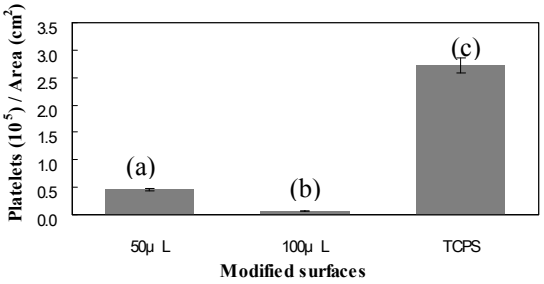

Figure 2. Platelet adhesion on Az-PEGMA/AA coated TCPS with different volume: 50μL (a), 100μL (b) and the control TCPS surface (c).

Conclusions

The Az-conjugated PEGMA/AA copolymer showed excellent platelet resistance which provides potential applications in developing novel blood compatible materials for tissue engineering scaffolds and for implants. The effects of experimental parameters such as added volume of copolymer will be further investigated by the physical-chemical analyses on the fabricated films to correlate the properties of copolymer to the platelet adhesion.

References

1. Chandran K, Burg K, Shalaby S. Soft Tissue Replacements. In: Bronzino JD, editor. Boca Raton,. FL: CRC Press, 1995.
2. Mao C, Qiu Y, et al. Adv. Colloid Interface Sci. 2004;110(1-2):5-17
3. Park S.E., Nho Y.C.,et al. Radiat. Phys. Chem 2004; 69(3):221-227
4. DiRamio JA,et al., Biotechnol. Progr. 2008;21(4):1281 - 1288.
5. Nho YC, Kwon OH. Radiat. Phys. Chem. 2003;66(4):299-307
6. Tsai W.B. et al., J. Biomed. Mater. Res. Part A, 2003; 67: 1255-1268