Blood compatibility on poly (acrylic acid- sulfobetaine methacrylate) polyelectrolyte multilayers modified surface

Wei-Hsuan Kuo[a], Meng-Jiy Wang[a], Wei-Bor Tsai[b], and Chiapyng Lee[a].
[a] Department of Chemical Engineering, National Taiwan University of Science and Technology, Taipei 106, Taiwan, R.O.C
[b] Department of Chemical Engineering, National Taiwan University, Taipei 106, Taiwan, R.O.C

Statement of Purpose:

Non-fouling surface has been widely used as blood-compatible materials for antithrombogenic implants. Various surface modification methods such as self-assembled monolayers (SAMs), graft polymerization, surface grafting, and layer-by-layer polyelectrolyte multilayers (PEM) were employed to create nonfouling surfaces. Layer-by-layer PEM method shows particular advantages of facile preparation and excellent nonfouling effect. Phosphobetaine, sulfobetaine, and carboxybetaine were zwitterionic molecules reported recently to present resistance to protein and cell adsorptions [1,2]. In this study, layer-by-layer PEM decorated substrates with a top layer of poly(acrylic acid- sulfobetaine methacrylate) (poly(AA-SBMA)) were prepared to investigate the inhibition of platelet adhesion and the effect of surface on the activation of platelet .

Methods:

Poly(AA-SBMA) copolymer firstly was synthesized by free radical polymerization, and purified by dialysis and freeze-drying. The layer-by-layer PEM modified surfaces were prepared by adding polyelectrolyte solutions (120 μL/well for 20 min) into tissue culture polystyrene (TCPS) 96-well plate via electrostatic interaction and rinsing with DI H_2O for each layer. In this study, the poly(AA-SBMA) PEM modified surface is composed of 4 layers TCPS substrate / poly(ethylene-imine) (PEI)/ poly(acrylic acid- azidoaniline) (PAA-Az) / PEI / poly(AA-SBMA)).

The platelets adhesion analyses were based on the literature [3]. The platelet suspension was adjusted to 5×10^7 platelets/mL with platelet suspension buffer (PSB), and platelet suspension (100 μL/well) were added to the wells to adhere for 1 hr at 37°C. The number of adhered platelets was determined by a lactate dehydrogenase (LDH) activity method.

Results and Discussion:

Figure 1 shows platelets adhesion on PEM modified surface prepared on different substrates (TCPS, polydimethylsiloxane (PDMS), and polyurethane (PU)). Poly(AA-SBMA) modified surfaces on all substrates demonstrated excellent resistance to platelet adhesion compared with on TCPS and on PEM modified surfaces with a top layer of PEI. The morphology of the activation of adhered platelets on TCPS substrate, PEI, PAA, poly (AA-SBMA) modified surfaces were examined by SEM photographs (Figure 2). On the TCPS and PEM modified surfaces with a top layer of PEI, it showed that numerous platelets were adhered with spread morphology. On the PEM modified surface with a top layer of PAA, the number of adhered platelets decreases significantly and the platelets showed less activated than on the TCPS substrates. It is noted that, on the PEM modified surfaces with a top layer of poly(AA-SBMA), not only the number of platelet is limited but also the platelet showed completely non-activated morphology. The results indicated that the poly(AA-SBMA) on PEM surfaces inhibits the platelet activation and adhesion effectively. The high resistance of platelet activation on poly(AA-SBMA) modified surface is closely related to the physical-chemical properties such as the functionalities and protein adhesion of the modified surfaces and were investigated by different analytical methods including electron spectroscopy chemical analysis (ESCA) and Quartz Chrystal microbalance (QCM) which will be reported in the conference.

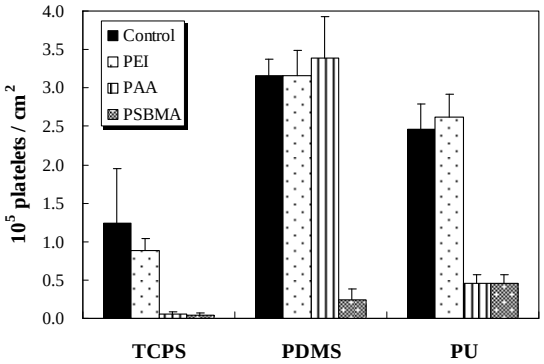
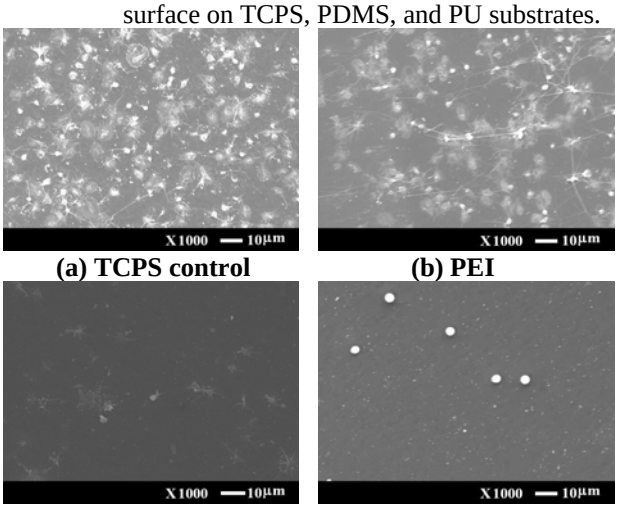


Figure 1 Platelets adhesion of different PEM modified surface on TCPS, PDMS, and PU substrates.



(a) TCPS control **(b) PEI**

(c) PAA **(d) poly (AA-SBMA)**

Figure 2 SEM photographs of platelets adhered onto (a) TCPS substrate (control), (b) PEI, (c) PAA, and (d) PSBMA PEM modified surface.

Conclusions:

Poly(AA-SBMA) copolymer PEM modified surfaces resist platelet adhesion and activation effectively on various substrate materials. The further investigations of the SBMA/AA monomer ratio, experimental parameters such as effects of pH and salt concentrations would assist to develop a material with "platelet adhesion-free" surfaces with excellent blood compatibility.

References:

[1] S. Chen et al., J Am Chem Soc, 2005; 127:14473-14478.
[2] Z. Zhang et al., Langmuir, 2006; 22: 10072-10077.
[3] W.B. Tsai et al., J. Biomed. Mater. Res. Part A, 2003; 67: 1255-1268.