Surface modification of titanium substrate by a novel copolymer containing sulfobetain and phosphonic acid functionalities: synthesis, characterization and platelet compatibility evaluation

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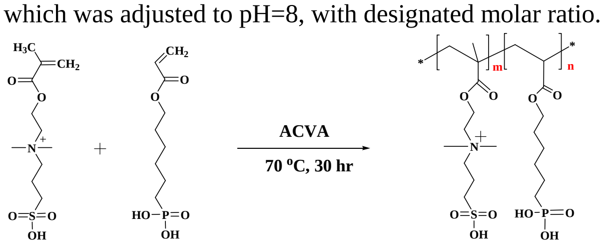
Statement of Purpose: Despite of the widely usage in clinical applications, the titanium-based material still face various challenges, such as hemocompatibility and anti-biofouling characteristics. The objective of this investigation was to develop a novel surface modification strategy for titanium-based material to improve platelet-contacting characteristics that is important in rigorous blood-contacting cardiovascular applications. In this work, a novel multi-functional copolymer, which composed of 6-acryloyloxy hexyl phosphonic acid (AcrHPA) and sulfobetaine methacrylate (SBMA) units will be synthesized by free radical copolymerization. The phosphonic acid groups within this novel copolymer can impart covalent binding to the titanium substrate while the zwitterionic sulfobetaine functionalities are believed to reduce the platelet adhesion and activation on this copolymer modified titanium surface. To impart a better hemocompatibility, various ratios of zwitterionic SBMA were mixed with AcrHPA for copolymerization. The chemical characteristics of these copolymers as well as the surface properties of the Ti substrate modified by these copolymers will be analyzed. In addition, the hemocompatibility of these copolymer-modified Ti substrates will be assayed by the in vitro platelet adhesion testing.

Methods:

Synthesis of poly(AcrHPA-SBMA) copolymer: The synthesis scheme for copolymers was shown in Scheme 1. AcrHPA and SBMA (sulfobetaine methacrylate) monomers were dissolved in 0.2 M phosphate buffer, which was adjusted to pH=8, with designated molar ratio.



Scheme 1. Synthesis procedure for of poly(AcrHPA-SBMA) AnSm copolymers

Preparation of polymer layer on Ti substrate: An aqueous polymeric solution (10mg/mL^{-1}) was spun-coated onto the titanium disk at a speed of 1000 rpm or 2000rpm for 30 s. The disks were then heated in an oven at 140˚C for 24 h.

Surface characterization and platelet adhesion studies: The polymer layer was characterized by sessile drop, SEM, AFM and ESCA. The *in vitro* platelet adhesion experiment was performed as similar to that was performed earlier in our group [1].

Results: By plotting copolymer compositions against monomer feed composition, the copolymerization is almost ideal statistical, since the data points are lying close to the diagonal line. Determination of copolymerization parameters according to the method of Kelen and Tüdös results in r_1=0.726 for AcrHPA and r_2=0.826 for SBMA, indicating that the copolymers show a slight tendency to add the monomers not perfectly statistical but in a random order.

The TGA results indicated that the thermal-cracking temperature of both homopolymers and all of copolymers are above 200°C, much higher than the temperature utilized in heat treatment after the spin coating process.

The static water contact angle values of specimens mention above are shown in Fig. 1. It was noted that an increase in SBMA content has resulted in a decrease in contact angle values.

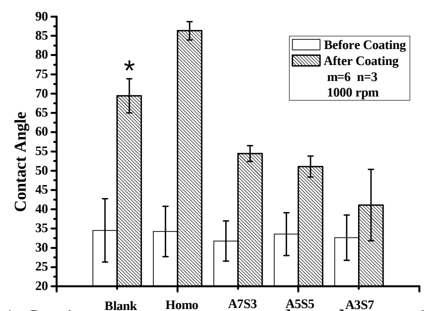


Fig.1 Static water contact angle values; * Bare titanium was dried in vacuum (140°C, 24 hr)

Platelets adhesion and activation can be utilized to assess the hemocompatibility of the blood-contacting materials. There were lots of platelets adhered on the nontreated Ti substrate and most polymer overcoats except A3S7 (Fig. 2). Nevertheless, most adherent platelets remained spherical and separated without pseudopodium.

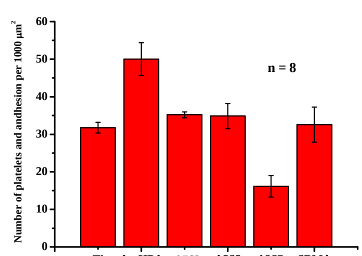


Fig. 2 The platelets adhesion density on various surfaces

Conclusions: These results revealed that surface modification with the copolymer containing both zwitterionic and phosphonic acid functionality is an effective method to improve hemocompatibility for the Ti substrate.

Reference:

1. Shen CH, Lin JC. Langmuir 2011;27:7091-8