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The Biocompatibility Comparison of Modified Polysulfone by 2-Methoxyethylacrylate and the Sulfonated Hydroxypropyl Chitosan

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Abstract. In this paper, polysulfone materials were modified with 2-methoxyethylacrylate and the sulfonated hydroxypropyl chitosan in different graft method respectively. After being through chloromethylation and amination reaction of polysulfone, polysulfone-graft-poly (2-methoxyethylacrylate) (PSF-g-PMEA) was synthesized via Michael addition reaction, while the sulfonated hydroxypropyl chitosan (SHPCS) was grafted from polysulfone membrane material by Schiff-Base reaction. Scanning electron microscopy (SEM), water contact angles (WCA) measurement, protein adsorptions, hemolysis assay of the membranes were characterized and tested. The results showed that the water contact angle of modified polysulfone materials decreased to 60.5^{o}C and 31.8 ^{o}C, and the amount of protein adsorption declined at least 83.3%. Furthermore, the hemolysis ratios changed from 2.89% to 1.08%. All of results exhibited that modified polysulfone membrane materials have better biocompatibility than pure polysulfone materials and have potential application in biomedical materials.

1. Introduction

It is well known that biomaterials have played an enormous role in artificial organs, medical devices and especially hemodialysis membranes [1]. Cellulose and its ramifications are the first generation of polymers applied to dialyzers [2, 3]. However, physical structure performance of cellulose materials is a bit unsatisfactory so that its prospect is limited. A family of polymers such as polyurethane, polyethersulfone and polysulfone are the second generation of dialysis membranes, which have better structure performance of membrane and higher permeability than the first [4]. Nevertheless, the native polymers with adverse biocompatibility especially the blood compatibility can lead to coagulation and the formation of thrombus directly.

The objective of this paper is to obtain higher blood compatibility of polysulfone materials modified by using two kinds of hydrophilic materials in different methods. What's more, these modified materials are useful in the area of biomaterials.

2. Experimental

2.1. Synthesis of polysulfone-graft-poly (2-methoxyethylacrylate) (PSF-g-PMEA)
The fabrication process of PSF-g-PMEA includes three steps. Chloromethylation of PSf was performed to introduce the -CH_2Cl groups at first. The PSf-Cl membrane was subsequently incubated into ethylene diamine (EDA) at 25 ^oC for 20 min to obtain amino groups. Then the aminated polysufone membranes (PSf-NH_2), 2-methoxyethylacrylate and ethanol were added separately to a glass tube, followed by stiring at 25 ^oC for 20 h, the polysulfone-graft-poly (2-methoxyethylacrylate) (PSF-g-PMEA) membrane was fabricated eventually after being washed with ultrapure water and freeze-dried for12h.

2.2. Synthesis of polysulfone-graft- sulfonated hydroxypropyl chitosan (PSF-SHPCS)
Different from modification process mentioned above, the last step in the fabrication of polysulfone-graft- sulfonated hydroxypropyl chitosan is to make use of Michael addition reaction which is distinct. PSf-Cl membrane obtained by chloromethylation reaction was immersed into ethylene diamine (EDA) at 25 ^oC, the aminated polysufone membranes (PSf-NH_2) was prepared. Then the sulfonated hydroxypropyl chitosan was synthesized with chitosan via sulfonation reaction. Finally, the PSf-NH_2 membranes were added into a round bottom flask containing glutaraldehyde solution (1%, v/v) at 25 ^oC for 8 h under stirring slightly followed by adding a few drops of glacial acetic acid, the treated membranes were introduced into SHPCS aqueous solution at 25 ^oC for hours stirring slightly. After being washed with ultrapure water several times and freeze-dried for 12h, polysulfone-graft-sulfonated hydroxypropyl chitosan membrane (PSF-SHPCS) was prepared.

2.3. Surface characterization and biocompatibility assays
The native and modified membranes were characterized by scanning electron microscopy (SEM), water contact angle (WCA) measurement. Protein adsorption, platelet adhesion, and hemolysis assay were executed to evaluate the blood compatibility of membranes decorated by 2-methoxyethylacrylate and the sulfonated hydroxypropyl chitosan individually. It should be noted that these two types of modified membranes that we choose were both reacted for 20 hours so that the greatest grafted yield of modified membranes were attained respectively.

3. Results and discussions

3.1. Surface characterization
The SEM images of the surfaces and cross-sections of PSF, PSF-g-PMEA and PSF-SHPCS membranes are shown in Fig.1. It was observed that all the membranes showed no apparent distinction. The surface morphology images showed that the modified membranes were more coarse than the pristine membrane, which might be caused by the aggregation of the grafted modified materials ,and more points appeared on the PSF-SHPCS membrane than on the PSF-g-PMEA, which may be affected by the grafting yield of those two polymers .It is noticed that a unique asymmetric structure was observed in SEM images of cross-sections of all membranes, which indicated that special morphology of finger-like structure was not damaged during the procedure of modification.

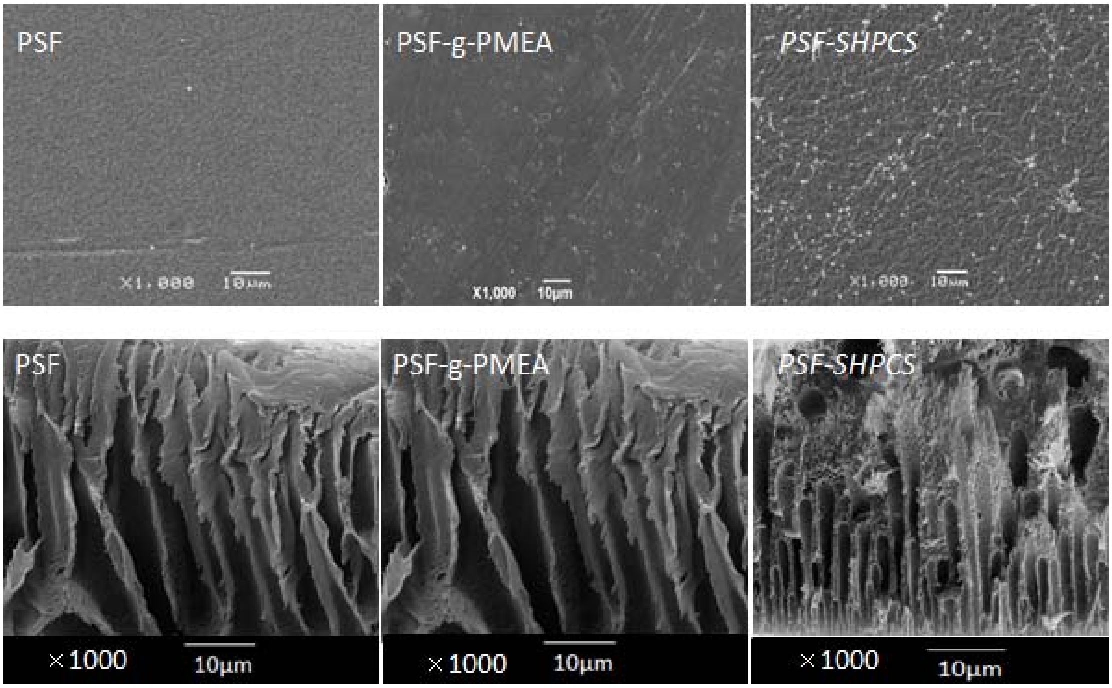

Figure 1. The SEM images of surface and across-section views for the membranes.

Static contact angle is a measurement to characterize hydrophilicity, which is also a simple method to evaluate the wettability .The contact angles of the native membrane and modified ones with equal grafting yield are shown in Table 1. The contact angles decreased obviously when the2-methoxyethylacrylate and the sulfonated hydroxypropyl chitosan were introduced into the copolymer separately. It worth noting that the contact angle of PSF-SHPCS membrane was decreased sharply to 31.8°when heparin like SHPCS were grafted. Meanwhile, the contact angle of PSF-g-PMEA modified membrane was higher than PSF-SHPCS .This might be resulted from the better hydrophilicity of SHPCS than PMEA .It could be inferred that the hydrophilicity of polysulfone membrane modified by SHPCS was significantly improved compared to membrane modified by PMEA.

Table 1. The static contact angles for the membranes.

Samples	Water contact angle(°)
PSF	79.8°±0.3
PSF-g-PMEA	60.5°±0.5
PSF-SHPCS	31.8°±0.3

3.2. Biocompatibility of the modified membrane

The amount of protein adsorbed on the membrane is regarded as a vital parameters to evaluate the blood compatibility of materials .The results of protein adsorption are shown in Fig.2. The protein adsorption amounts of PSF was 21 μg/cm^2, but the protein adsorption amounts of PSF-g-PMEA and PSF-SHPCS membranes were 3.5 μg/cm^2 and 3.0 μg/cm^2 ($P < 0.05$). It can be found that the amount of protein adsorption apparently decreased after 2-methoxyethylacrylate and the sulfonated hydroxypropyl chitosan grafted onto membrane, even though the protein adsorption amounts between PSF-g-PMEA and PSF-SHPCS showed no distinct difference. These results demonstrated that the resistance of protein adsorption of the modified membranes had improved to great extent, which are consistent with analysis mentioned above.

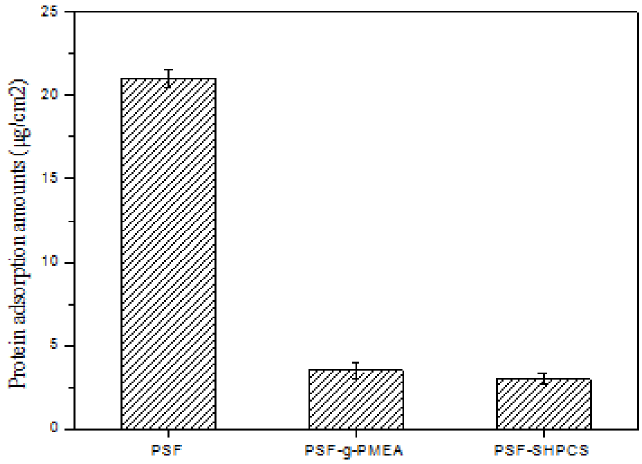

Figure 2. BSA adsorption on the surfaces of neat and modified membrane with different copolymers. Data are expressed as the mean ± SD of three independent measurements.

The shapes and number of the adhered platelet observed by scanning electron microscopy are recognized as important factors to assess the blood compatibility [5]. As it shows in Fig.3, the adhering platelets were assembled on the neat membrane. It was found that the amounts of adhered platelet on the pristine PSF were higher than that on PSF-g-PMEA and PSF-SHPCS membranes. Besides, the "pseudopods" were not observed on modified membranes which means the shape of adhered platelet are not changing a lot. It can be inferred that the blood compatibility of both modified membranes were improved.

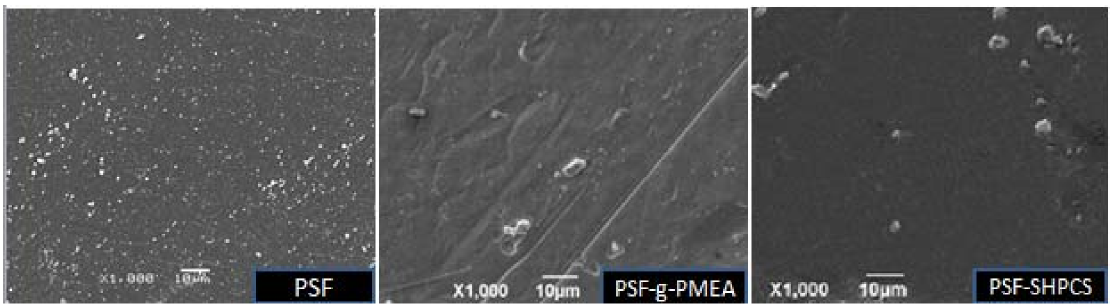

Figure 3. The SEM images of platelets adsorbing onto PSF, PSF-g-PMEA, PSF-SHPCS membranes. Magnification: 1000 ×

Fig.4. showed the hemolysis ratios of membranes. The hemolytic rate of PSF-g-PMEA decreased 68.85% compared with the PES membrane. While the hemolysis ratios of PSF-SHPCS declined 62.63%. So it suggested that blood compatibility of membrane materials grafted with 2-methoxyethylacrylate and the sulfonated hydroxypropyl chitosan could effectively enhanced.

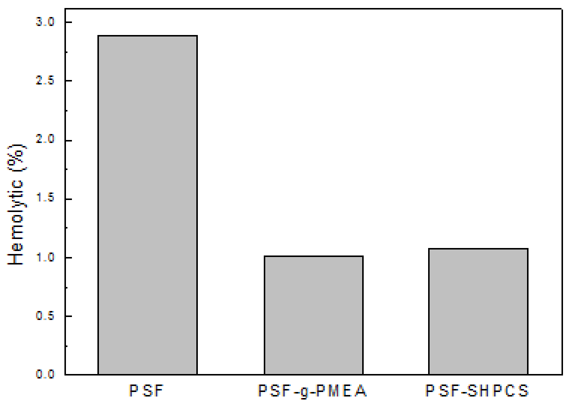

Figure 4. The hemolysis ratios of the membranes grafted with different polymers respectively.

4. Conclusion

The modified membrane material PSF-g-PMEA was synthesized by Michael addition reaction. The sulfonated hydroxypropyl chitosan was grafted onto membrane via Schiff-Base reaction. In spite of distinct reaction, both kinds of modified membrane materials showed lower contact angle, fewer amount of adsorbed protein and adhered platelet and lower hemolysis rate compared with pristine polysulfone materials. Specifically, the contact angle decreased at least 19.3 ^{o}C, the hemolysis ratio dropped 62.63%, which demonstrated the biocompatibility of modified membrane were greatly improved. It worth noting that the biocompatibility of modified material (PSF-SHPCS) seemed better than the other one according to test data. Hence, these modified materials have potential to be used in the field of biomaterials.

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