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Polysulfone hemodiafiltration membranes with enhanced anti-fouling and hemocompatibility modified by poly(vinyl pyrrolidone) *via in situ* cross-linked polymerization

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ABSTRACT

Poly(vinyl pyrrolidone) (PVP) and its copolymers have been widely employed for the modification of hemodiafiltration membranes due to their excellent hydrophilicity, antifouling and hemocompatibility. However, challenges still remain to simplify the modification procedure and to improve the utilization efficiency. In this paper, antifouling and hemocompatibility polysulfone (PSf) hemodiafiltration membranes were fabricated *via in situ* cross-linked polymerization of vinyl pyrrolidone (VP) and vinyltriethoxysilane (VTEOS) in PSf solutions and non-solvent induced phase separation (NIPS) technique. The prepared membranes were characterized by attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR), X-ray photoelectron spectroscopy (XPS) and scanning electron microscopy (SEM), which suggested that VP and VTEOS have been cross-linked copolymerized in PSf membranes. The modified PSf membranes with high polymer content showed improved hydrophilicity, ultrafiltration and protein antifouling ability. In addition, the modified PSf membranes showed lower protein adsorption, inhibited platelet adhesion and deformation, prolonged the activated partial thromboplastin time (APTT), prothrombin time (PT), and decreased the content of fibrinogen (FIB) transferring to fibrin, indicating enhanced hemocompatibility. In a word, the present work provides a simple and effective one-step modification method to construct PSf membranes with improved hydrophilicity, antifouling and hemocompatibility.

1. Introduction

In recent years, polysulfone (PSf) membrane has been widely applied in biotechnological applications, such as hemodiafiltration and protein separation, due to its excellent mechanical strength, chemical resistance, chemical and thermal durability [1–3]. However, the antifouling and hemocompatibility of the hydrophobic PSf membrane are not ideal [4–6]. Membrane fouling is often initiated by the accumulation/aggregation of suspended solids, colloidal particles and biomolecules on the surfaces and pores of the separation membranes, resulting in an increase in resistance to permeate flow [7,8]. In addition, the adsorption and deposition of proteins and platelets often cause thrombus formation and blood coagulation [9]. Therefore, it is necessary to improve the antifouling and hemocompatibility of PSf membrane applied in hemodiafiltration.

Hydrophilic modification is an effective and conventional method to enhance antifouling and hemocompatibility of the polymeric membranes. A water layer formed on the hydrophilic surface can inhibit the adsorption and adhesion of pollutants, proteins and platelets *via* repulsive hydration force, thus reducing fouling and improving hemocompatibility [10–13]. Extensive hydrophilic polymers and anticoagulants, such as poly(ethylene glycol) (PEG), poly(vinyl pyrrolidone) (PVP) and polyzwitterions, have been implemented to improve the fouling and hemocompatibility of the hydrophobic polymeric membrane [4,14–20]. PVP, a non-ionic water soluble polymer, has received much attention due to its good chemical stability, physiological inertness and biocompatibility [21,22]. It was initially used as a blood plasma substitute. Up to date, PVP has been employed as a hydrophilic agent to modify polymeric membranes.

Blending, surface coating and grafting methods have been reported to modify polymeric membranes [23–26]. Compared to other approaches, blending is an easier and more convenient method to improve the membrane surface and internal pore walls [27]. However, the elution of PVP from the blend membranes is almost unavoidable, leading to deterioration in long-term durability [28,29]. In order to avoid the elution of PVP, PVP-based amphiphilic copolymers, such as poly(styrene-acrylic acid-vinylpyrrolidone) (P(St-AA-VP)) [30], PVP-*b*-poly(methyl methacrylate)-*b*-PVP (PVP-*b*-PMMA-*b*-PVP) [22,31–34], PVP-*b*-poly(acrylate-*g*-poly(methyl methacrylate))-*b*-PVP (PVP-*b*-

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P(AE-*g*-PMMA)-*b*-PVP) [28], poly(styrene-acrylic acid)-*b*-PVP-*b*-poly(-styrene-acrylic acid) (P(St-AA)-*b*-PVP-*b*-P(St-AA)) [35], were synthesized and developed as the blend additives. In the amphiphilic copolymers, the hydrophilic PVP chains migrate to the membrane surface during the phase separation process to prevent the adsorption and adhesion of proteins and platelets, meanwhile, the hydrophobic chains mingle in the membrane bulk materials. As a result, the blend membranes with amphiphilic copolymers as additive exhibited enhanced antifouling and good hemocompatibility properties and long-term durability. However, the synthesis and purification of the amphiphilic copolymers often require multi-step procedures, increasing membrane fabrication costs and limiting their practical application. Therefore, it should be to simplify the modification procedure and to improve the utilization efficiency.

The *in situ* polymerization is an easy and effective method for the modification of polymeric membranes. Zhang et al. synthesized poly(polyethylene glycol monomethyl ether methyl methacrylate-methyl methacrylate) (P(PEGMA-MMA)) and poly(polyethylene glycol monomethyl ether methyl methacrylate-polytetrahydrofuran dimetha crylate ester) (P(PEGMA-PTMGDA)) in the poly(vinylidene fluoride) (PVDF) solutions *via* free radical polymerization to modify PVDF membranes with superior mechanical behaviors, enhanced antifouling properties, narrowly distributed pore size and molecular weight cut off [36,37]. However, the stability of the modified membranes might be insufficient, because crosslinking agent was not added in the polymerization. As a result, the *in situ* cross-linked polymerization was developed and has been used to modify polyethersulfone (PES) membranes [38–40]. Compared with the conventional blending, the *in situ* cross-linked polymerization approach improves the modification efficiency, avoids post-synthetic treatments and reduces the overall costs.

In this study, we aim to enhance the anti-fouling and hemocompatibility properties of PSf membranes through *in situ* cross-linked polymerization. Generally, VP and vinyltriethoxysilane (VTEOS) were polymerized and cross-linked in PSf solutions. After being vacuum degassed, the obtained solution was directly used to fabricate membranes *via* non-solvent induced phase separation (NIPS) technique. The morphology, surface chemistry and hydrophilicity of the prepared membranes were investigated in detail. The ultrafiltration experiments for pure water and bovine serum albumin (BSA) solution were applied to characterize the fouling resistance property. In addition, BSA adsorption, platelet adhesion and morphology, activated partial thromboplastin time (APTT), prothrombin time (PT) and the content of fibrinogen (FIB) transferring to fibrin were measured to detect the hemocompatibility of the obtained membranes.

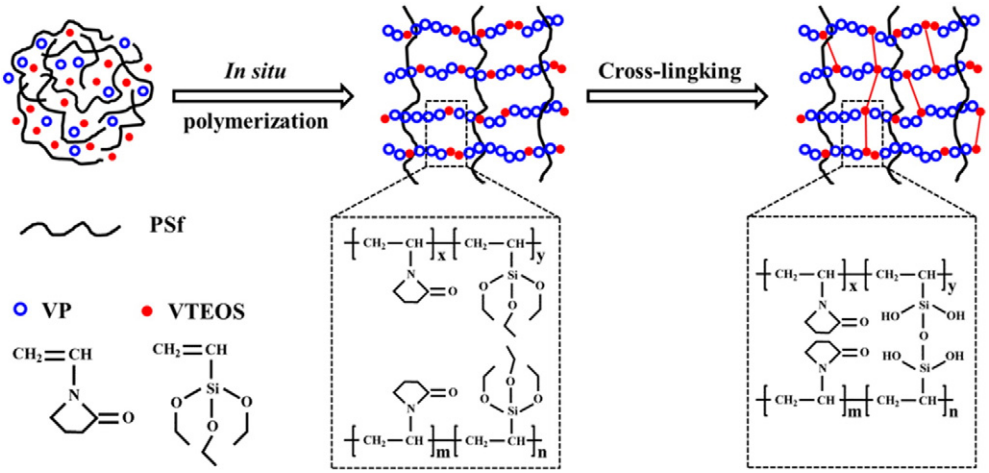
2. Experimental

2.1. Materials and reagents

Polysulfone (PSf, S6010) was bought from BASF SE. Vinyltriethoxysilane (VTEOS), *N*-vinyl pyrrolidone (VP), azobisisobutyronitrile (AIBN), bovine serum albumin (BSA) and lysozyme (Lyz) were purchased from Aladdin, China. VTEOS and VP were purified with basic alumina and activated carbon before use, respectively. AIBN was recrystallized from ethanol. Platelet-rich plasma (PRP) and platelet-poor plasma (PPP) were supplied by the Blood Center of Ningbo, China. Activated partial thromboplastin time (APTT), Prothrombin time (PT) and The content of fibrinogen (FIB) transferring to fibrin reagent kits were purchased from Shanghai Sun Biotech Co., Ltd., China. All other regents, such as *N*,*N*′-dimethylacetamide (DMAc) and ethanol, were brought from Sinopharm Chemical Reagent Co., Ltd., China.

2.2. Membrane preparation

The PSf membranes were prepared *via* the *in situ* cross-linked polymerization and the classical non-solvent induced phase separation (NIPS) technique. In a typical procedure, PSf (16 g), VP, VTEOS and AIBN (2 mol% with respect to VP and VTEOS) were dissolved in DMAc under mechanical stirring and N_2 protection to get a transparent reaction solution. The total weigh of the reaction solution was 99 g, and the malar ration of VP to VTEOS was locked at 2.5. Then the polymerization was carried out at 80 °C for 12 h with stirring and N_2 atmosphere, and stopped by quenching in ice water. Subsequently, acetic acid solution (1 mL) was added into the obtained solution under stirring for 2 h to improve the hydrolysis of the ethoxysilyl groups (Si—O—C_2H_5) and subsequent condensation of the silanol groups (Si—OH). After being vacuum degassed, the casting solution was spread onto a glass plate and immersed into a water bath at 30 °C for liquid-liquid phase separation. Then the solid membrane was immersed in distilled water at 80 °C for 24 h to thoroughly remove unreacted monomers and solvent, and further improve the cross-linking polymerization. The fabricated PSf microporous membranes with a thickness of 68 ± 5 μm were dried *via* freeze drying and designated as M0, M1.5, M3, M4.5, M6 and M7, respectively. The numbers denoted the corresponding weight percentages of monomers of VP and VTEOS in the casting solution. The *in situ* cross-linked polymerization of VP and VTEOS in PSf solution was presented in Scheme 1.



Scheme 1. *In situ* cross-linked polymerization of VP and VTEOS in PSf solution.