Research article

polymers advanced technologies

Received: 25 December 2013, Accepted: 01 April 2014, Published online in Wiley Online Library: 29 May 2014

(wileyonlinelibrary.com) DOI: 10.1002/pat.3316

Insights into the surface property and blood compatibility of polyethersulfone/polyvinylpyrrolidone composite membranes: toward high-performance hemodialyzer

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Applications of blood purification membranes are fuelled by diverse clinical needs, such as hemodialysis, hemodiafiltration, hemofiltration, plasmapheresis, and plasma collection. For clinical usage, the adding of polyvinylpyrrolidone (PVP) is the general protocol for the design of antifouling and antithrombotic properties integrated artificial membranes. In the present work, to insight into the detailed surface properties and blood compatibilities of the PVP blended composite membranes, we synthesized a series of PVP polymers with different molecular weights using reversible addition fragmentation chain transfer polymerization and designed a series of polyethersulfone (PES)/PVP composite membranes by a physically blending method. The effects of PVP molecular weights and blending ratios on the surface properties and the blood compatibilities of the composite membranes were investigated in detail. The surface attenuated total reflection Fourier transform infrared spectra and scanning electron microscopy pictures indicated that the PVP was successfully immobilized into the membranes, and the composite membranes exhibited morphology transformation from finger-like structure to sponge-like structure, which indicated that the composite membrane had tunable porosity and permeability by adding PVP. The blood compatible tests revealed that the composite membranes showed increased hydrophilicity, decreased plasma protein adsorption, suppressed platelet adhesion, and prolonged blood clotting time compared with pristine PES membrane. These results indicated that the PES/PVP composite membranes exhibited enhanced antifouling and antithrombotic properties than the pristine PES membrane. Meanwhile, the results also suggested that the composite membranes with larger molecular weight PVP and higher blending ratios might show better blood compatibility. **Copyright © 2014 John Wiley & Sons, Ltd.**

Keywords: PES/PVP composite membranes; surface property; blood compatibility; hemodialyzer

INTRODUCTION

Recent advancements of modern medicine in blood purification membranes are fuelled by diverse clinical needs, such as the hemodialysis, hemodiafiltration, hemofiltration, plasmapheresis, and plasma collection.[1–3] The current clinical blood purification membranes are mostly fabricated by artificial polymeric materials, such as polysulfone and polyethersulfone (PES). However, these artificial polymers exhibited limited blood compatibility because of the hydrophobic surface and serious plasma protein adsorption.[4–7] Meanwhile, plasma protein adsorption may induce or accelerate the formation of thrombus, which can cause artery occlusion.[8] Therefore, the excellent hemocompatibility of artificial polymeric membranes has been considered as the key to approach the clinical hemodialyzer.[9]

Among the materials used in hemodialyzer fields, PES is one of the most important polymeric materials.[10–12] PES membranes show outstanding oxidative, thermal and hydrolytic stability, and good mechanical and film-forming properties. The membranes also showed high permeability for middle molecular hazardous proteins when used as hemodialysis membranes.[13–15] However, as a hydrophobic polymer, the blood compatibility of the PES membrane is not adequate, and injections of anticoagulants, such as heparin, are needed during hemodialysis.[16–19] In the past decades, with the aim of improved blood compatibility and reduced anticoagulant dosage, tremendous efforts had been taken to improve the hemocompatibility of PES membranes.[20–24] Many functional synthesized polymers and biopolymers have been introduced to modify the PES membranes, especially the polyvinylpyrrolidone (PVP). PVP, a kind of hydrophilic polymer without hydroxyl group and ionic group, is known to have good hydrophilicity, water solubility, nontoxicity, and biocompatibility[25,26] and has been applied in a wide variety of applications such as

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blood plasma substitute, biomaterials and coatings, medicine, cosmetics, and macromolecular additives.[27–30] In recent researches, PVP has been introduced onto the surface of PES polymeric membranes by various methods such as bulk blending,[8,19,31] surface plasma treatment,[32,33] surface grafting,[34] and surface coating.[35] Among the methods, blended composite membranes have always been recognized as the most industrially and clinically practicable method to improve surface property and reduce undesirable response between membrane materials and blood/tissues.[36,37] Moreover, as one of the good polymeric additives, PVP owns good miscibility with PES matrix.[38] Thus, the blending method will not change the mechanical property of the PES bulk matrix significantly because of the good miscibility between the mixed components.

In recent years, the physically blending of PVP with polymeric materials has been reported. Yoo *et al.*[39] investigated the effect of PVP molecular weight on the morphology of asymmetric polyimide membranes; and other researchers also studied the effect of PVP on the performances of filtration membranes.[40] However, the elution of PVP is unavoidable because of the good water solubility; and the molecular weights of PVP also have great effect on the surface properties and blood compatibilities of PES/PVP composite membranes. Till now, no sufficient studies have been reported on the measurement of the elution ratios of PVP quantificationally, and the surface property and blood compatibility of the PES/PVP composite membranes when different molecular weights PVP were blended.

In the present work, to insight into the detailed surface properties and blood compatibilities of the PVP blended composite membranes, a series of PVP polymers with different molecular weights were synthesized using reversible addition fragmentation chain transfer (RAFT) polymerization and used to prepare composite PES membranes by a physically blending method. The effects of PVP molecular weights and blending ratios on the surface properties of the composite membranes were characterized by scanning electron microscopy (SEM), attenuated total reflection Fourier transform infrared (ATR-FTIR), atomic force microscopy (AFM), and water contact angles. Meanwhile, the blood compatibilities of the composite membranes were systematically investigated by bovine serum albumin (BSA) protein adsorption, platelet adhesion, and activated partial thromboplastin time (APTT). The features of the PES/PVP composite membranes could be summarized as follows: (i) the membrane morphology and surface roughness were changed after blending PVP; (ii) the composite membranes exhibited better blood compatibility (suppressed platelet adhesion and prolonged blood coagulation time) compared with the pristine PES membrane; and (iii) the large molecular weight PVP can improve the blood compatibility more efficiently than that of low molecular weight PVP due to molecule elution.

Table 1. The compositions of the PES/PVP flat-sheet composite membranes

Membrane no.	The molecular weight of PVP	PES (wt%)	PVP (wt%)
FSM-0	—	20	—
FSM-1	N1	20	5
FSM-2	N2	20	5
FSM-3	N3	20	5
FSM-4	N4	20	5
FSM-5	N5	20	5
FSM-5-2	N5	20	2
FSM-5-4	N5	20	4
FSM-5-7	N5	20	7

MATERIALS AND METHODS

Materials

Carboxyl-terminated trithiocarbonate (CTA) was synthesized according to the procedure of an earlier literature.[41] PES (PES, Ultrason E6020P) was purchased from BASF, Germany. *N*-vinylpyrrolidone (VP; 99%) was purchased from Alfa Aesar. *N*, *N*-dimethylacetamide (DMAc; AR, 99.0%) was purchased from Chengdu Kelong Inc. (Chengdu, China) and used as the solvent. 4,4′-Azobis(4-cyanovaleric acid) (ACVA) was purchased from Aladdin Chemical Reagent Co. and used as the initiator. BSA (fraction V) was obtained from Sigma Chemical Co. All the other

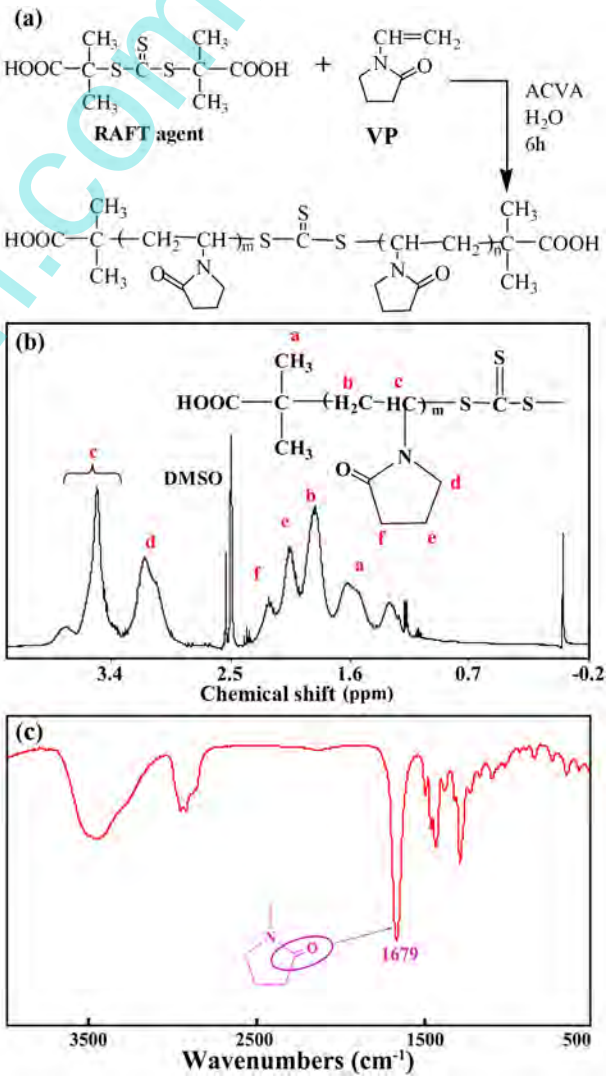

Figure 1. (a) The chemical structure of carboxyl-terminated PVP synthesized by RAFT polymerization, N1, with the lowest molecule weight; (b) ^{1}H NMR spectrum of carboxyl-terminated PVP; and (c) FTIR spectrum of carboxyl-terminated PVP. This figure is available in colour online at wileyonlinelibrary.com/journal/pat

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Table 2. Composition and molecular weight data of the synthesized PVP[a]

No.	N5	N4	N3	N2	N1[d]
[CTA] (mmol/l)	0.06	0.12	0.36	0.90	1.80
$M_\eta \times 10{,}000$[b]	12.1	7.3	3.5	1.2	0.8
Conversion %[c]	100	100	100	96.9	87.4

[a]Synthesis condition: VP, 7.21 g; ACVA, 0.07 g; T_p, 80°C; t_p, 5 hr; and H_2O was used as solvent.
[b]Viscosity-average molecular weight.
[c]Conversions were determined gravimetrically.
[d]GPC result: Mn = 8580; Mw/Mn = 2.2.

chemicals (analytical grade) were obtained from Aladdin Chemical Reagent Co., China, and used without further purification.

Synthesis and characterization of polyvinylpyrrolidone

Polymerization of *N*-VP was carried out in a sealed tube. The general procedure was as follows: VP, CTA, ACVA, and H_2O were added into the tube. After bubbling for 30 min with nitrogen, the reaction mixture was heated to 80°C under a nitrogen atmosphere, and the polymerization was carried out for 5 hr. After precipitating in ethyl ether, the product of PVP was dried under vacuum at 50°C overnight. In this study, PVP with different designed molecular weights were synthesized and termed N1, N2, N3, N4, and N5.

To prepare FTIR samples, the as-prepared PVP was dissolved in DMAc and cast on a potassium bromide disk with the thickness of about 0.8 mm. The FTIR spectra were measured with FTIR Nicolet560 (Nicol American). The ^{1}HNMR spectra were recorded in DMSO-*d* with a Varian Unity Plus 300/54 NMR spectrometer. Viscosity-average molecular weights were measured by viscosimeter using H_2O as solvent at 25°C. The molecular weight of N1 was also measured by using gel permeation chromatography (GPC) measurement using a polystyrene calibration, which was based on the liquid chromatography analysis using an aqueous gel permeation column and performed by using a PL220 GPC analyzer (Britain), and H_2O was chosen as the eluent.

Preparation and characterization of polyvinylpyrrolidone blended polyethersulfone membranes

The PES/PVP membranes were prepared by a phase inversion technique. PES and the synthesized PVP were dissolved in the solvent DMAc by vigorous stirring until clear homogeneous solution was obtained. The concentration of PES was 20% (wt%), and the compositions of the PES/PVP flat-sheet composite membranes are shown in Table 1.

The membrane surfaces were investigated by ATR-FTIR and AFM. The hydrophilicity of the membrane surface was characterized on the basis of contact angle measurement using a contact

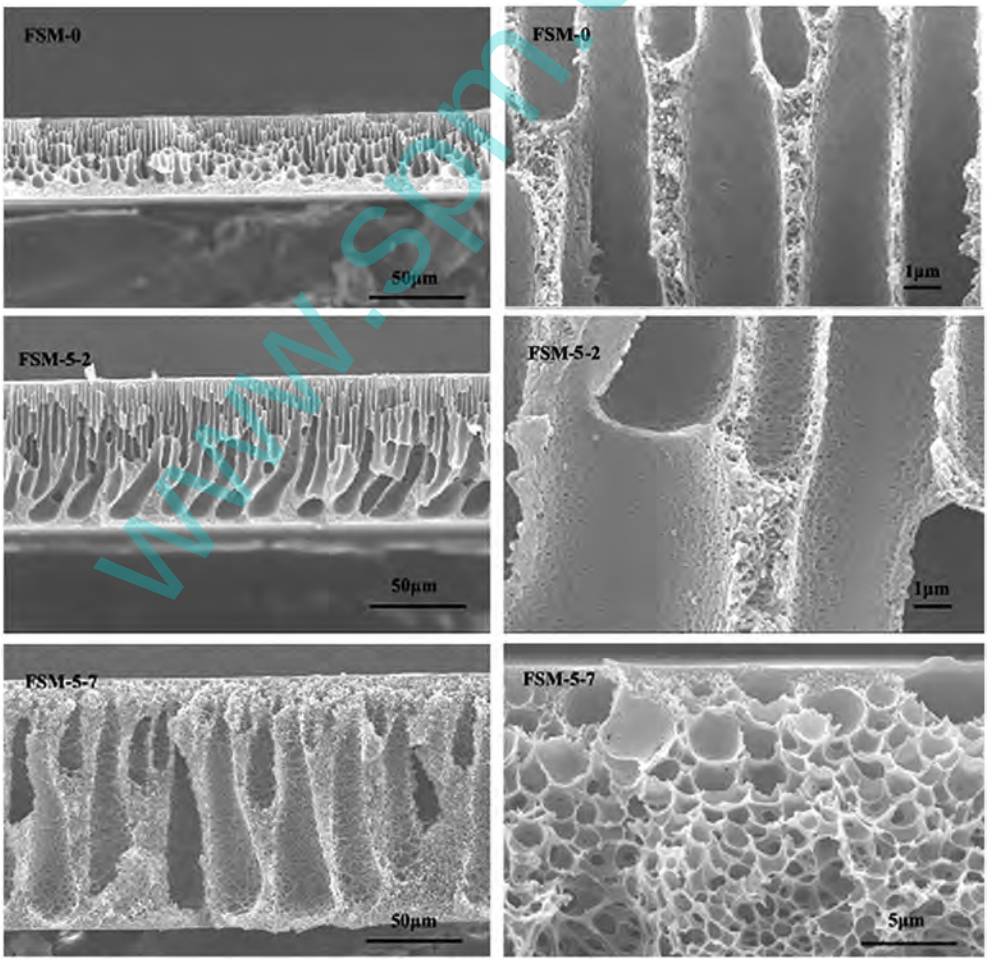

Figure 2. Scanning electron microscopy cross-sectional views of the PES (FSM-0) and PES/PVP composite membranes (FSM-5-2 and FSM-5-7).

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angle goniometer (OCA20, Dataphysics, Germany) equipped with video capture. A piece of 2 cm× 2 cm membrane was attached on a glass slide and mounted on the goniometer. For the static contact angle measurements, a total of 3 μl double distilled water was dropped on the airside surface of the membrane at room temperature, and the contact angle was measured after 5 and 30 sec. At least eight measurements were averaged to obtain a reliable value. The measurement error was ±3°.

Elution of polyvinylpyrrolidone from the membranes

In order to quantificationally determine the elution amounts of the PVP from the composite membranes, a series of PES/PVP solutions were prepared, with the concentrations of 20 and 5 wt% for PES and different PVP, respectively. Then, determined amounts of the solutions were prepared into flat-sheet membranes using phase inversion technique, and then the membranes were washed with double distilled water for 1 week at room temperature, and the extracted water was changed every 6 hr. Finally, the membranes were freeze-dried. The eluted PVP was expressed by the elution ratio using the following equation.

$$\text{Elution ratio}\ (\%) = 100 \times (M_a - M_b)/M_a (1)$$

where M_a presents the mass of PVP and PES in the casting solution; M_b presents the obtained mass of the composite membrane after completely washing.

Blood compatibility

Protein adsorption

The protein adsorption experiments were carried out with BSA solution (1 mg/ml, PBS solution, pH 7.4). The membrane with an area of $1\times 1\ cm^2$ was incubated in PBS solution for 24 hr and then immersed in the protein solution for 2 hr at 37°C. After the protein adsorption, the membrane was gently rinsed with PBS solution and then immersed in glass tubes containing 2% (wt%) SDS aqueous solutions for 1 hr at 37°C to remove the proteins adsorbed on the membranes. The amount of the protein eluted in the SDS solution was quantified by Micro BCA™ protein assay reagent kit. More than 95% of the adsorbed protein could be eluted into the SDS solution. And then the adsorbed BSA amount was calculated.

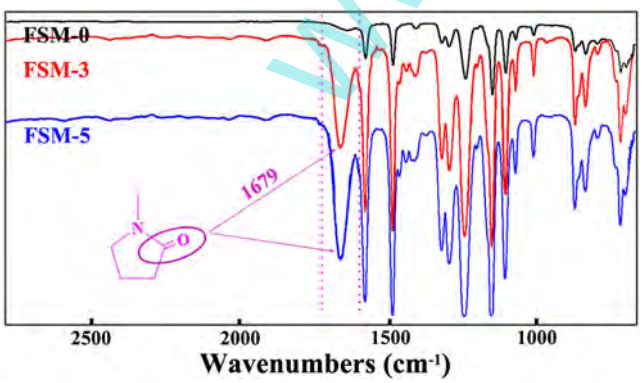

Figure 3. Attenuated total reflection Fourier transform infrared spectra for the membrane surfaces of PES and the PES/PVP composite membranes with different PVP molecular weights. This figure is available in colour online at wileyonlinelibrary.com/journal/pat

Platelet adhesion

Healthy human fresh blood (male, 30 years old) was collected using vacuum tubes, containing sodium citrate as an anticoagulant (anticoagulant to blood ratio, 1: 9 *v/v*). The blood was centrifuged at 1000 rpm for 15 min to obtain platelet-rich plasma (PRP) or at 4000 rpm for 15 min to obtain platelet-poor plasma.[21,42]

The PES and modified PES membranes were immersed in PBS solution and equilibrated at 37°C for 1 hr. The PBS solution was removed, and then 1 ml of fresh PRP was introduced. The membranes were incubated with PRP at 37°C for 2 hr. Then, the PRP was decanted off, and the membranes were rinsed three times with PBS solution. Finally, the membranes were treated with 2.5% (wt%) glutaraldehyde in PBS at 4°C for 1 day. The samples were washed with PBS solution, subjected to a drying process by passing them through a series of graded alcohol-PBS solutions (25%, 50%, 75%, and 100%) and isoamyl acetate–alcohol solutions (25%, 50%, 75%, and 100%).[43] The platelet adhesion was observed using an S-2500C microscope (Hitachi, Japan).

Clotting time

To evaluate the antithrombogenicity of the membrane, APTT was measured by an automated blood coagulation analyzer CA-50 (Sysmex Corporation, Kobe, Japan). The APTT was measured as follows: the samples ($0.5\times 0.5\ cm^2$, three pieces)

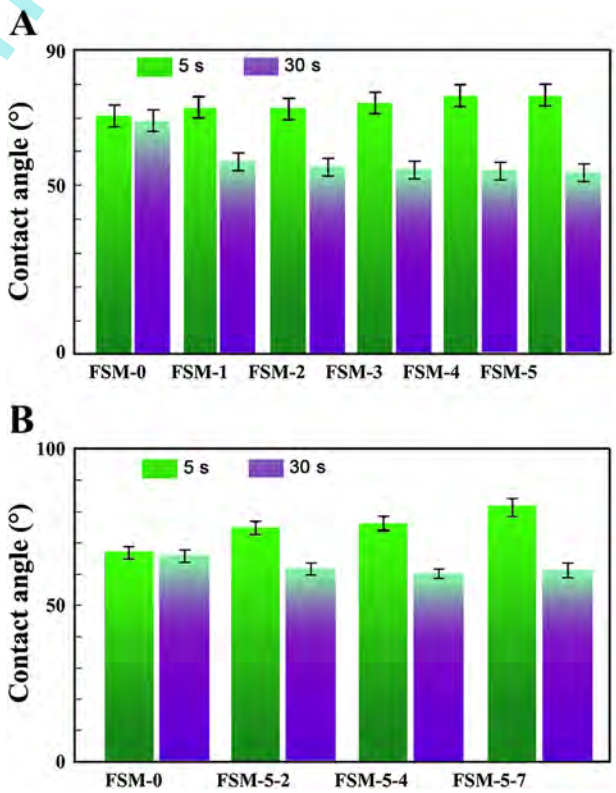

Figure 4. The contact angles of PES and PES/PVP composite membranes ($n = 3$). (A) Membranes blended by different molecular weights of PVP; (B) membranes blended by different amounts of N5. The measurements are carried out both at 5 and 30 sec contacting time. This figure is available in colour online at wileyonlinelibrary.com/journal/pat

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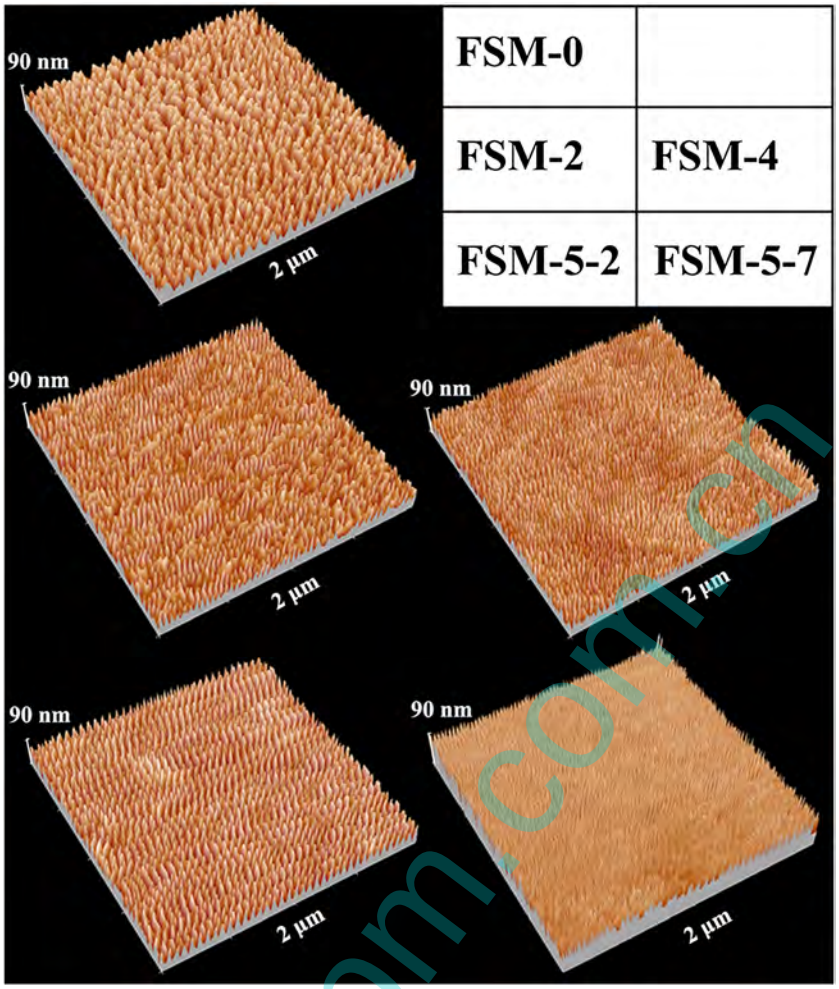

Figure 5. Atomic force microscopy morphologies for PES and the PES/PVP composite membranes, with a scanning area of 2 μm× 2 μm. (The Z range scales are all 90 nm). This figure is available in colour online at wileyonlinelibrary.com/journal/pat

were incubated with 0.1 ml healthy human blood plasma at 37° C for 30 min, and then the APTT was measured.[44]

RESULTS AND DISCUSSIONS

Synthesis and characterization of polyvinylpyrrolidone

Carboxyl-terminated PVP was prepared via successive RAFT polymerization using S, S′-bis (α, α′-dimethyl-α-acetic acid)-trithiocarbonate as the RAFT agent, which had extremely high chain transfer efficiency and controlled radical polymerization, because the carbon attached to the labile sulfur atom is tertiary and bears a radical-stabilizing carboxyl group. In addition, the applied RAFT agent owns exceptional water solubility because of the carboxyl group and thus more suitable for the aqueous polymerization of PVP comparing with using the other RAFT agent. The molecular formula of the synthesized PVP is shown in Fig. 1a.

The VP polymerizations in the presence of S, S′-bis (α, α′-dimethyl-α-acetic acid)-trithiocarbonate were carried out at 80° C, using ACVA as the initiator, where the initial CTA concentrations were 0.06, 0.12, 0.36, 0.9, and 1.8 mmol/l. The monomer conversions were determined gravimetrically, and the viscosity-average molecular weights (M_η) were also measured. The Mn of N1 was also measured by using GPC method, which was similar with M_η. The molecular weights (M_η) of the synthesized PVP are shown in Table 2. As shown in the table, the molecular weight decreased obviously when the CTA concentrations changed from 0.06 to 1.8 mmol/l.

Figure 1b shows the ^{1}H-NMR spectrum of the obtained PVP. PVP was verified by the signals at *d* 3.90–3.35 ppm (s, H, –CH–N), *d* 3.25–2.91 ppm (s, 2H, –CH_2–N), *d* 2.30–1.39 ppm (s, 2H, –CH_2–C=O, –CH_2–C–), and *d* 1.59 ppm (s, 3H, –CH_3). PVP was also

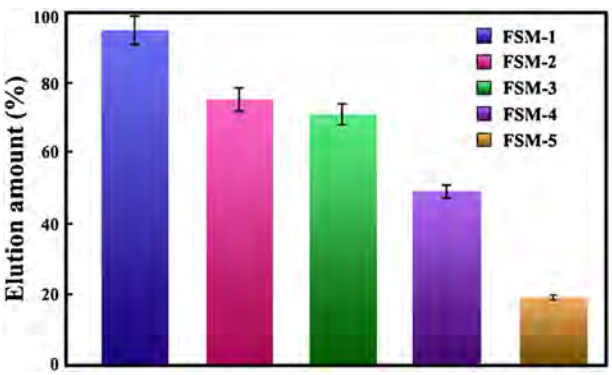

Figure 6. Elution ratios of PVP with different molecular weight in modified PES membranes. This figure is available in colour online at wileyonlinelibrary.com/journal/pat

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characterized by FTIR, as shown in Fig. 1c. The characteristic peak of the bond of PVP at 1679 cm^{-1}(>C=O stretching) was observed.

Membrane preparation and characterization

The PES/PVP composite membranes were prepared by a liquid–liquid phase inversion technique, and the physical blending weight ratios of PES to PVP were shown in Table 1. In order to evaluate the effects of the PVP components on the structures of the composite membranes, the SEM, ATR-FTIR, water contact angle, AFM, and PVP elution ratio for the composite membranes were investigated in detail.

Scanning electron microscopy micrographs of the membranes

Figure 2 shows the cross sections of the PES and PES/PVP composite membranes (blend with N5) at the same spin-coating condition. A characteristic morphology of asymmetric membrane consisting of a dense top layer and porous sublayer with a finger-like structure was observed for all the membranes.[45,46] For the PVP blended composite membranes (FSM-5-2 and FSM-5-7), the top skin layer and the finger-like structure were observed with a little change, porous sublayer was formed, and larger quantities of micropores in the finger-like structure were observed when PVP was added into PES matrix, especially the FSM-5-7. This should be attributed to the hydrophilic structure of PVP and the affinity between the PES chains and PVP; the PVP polymer would assembly with PES chains during the aqueous phase separation of the membrane fabrication. Then, when PVP weight ratio increased, the porous structure views became to transform from finger-like structure to sponge-like structure gradually. For FSM-5-7, both the skin layer and sublayer showed sponge-like structure with many connected porous structures and microspores. It is believed that the main factors for the formation of this structure is that the PVP chains may increase the viscosity of the casting solution then decrease the driving force and the relative diffusion rate of the solvent and nonsolvent during phase separation. The decreased diffusion rate then lead the cast solution to take a longer time to complete the process of membrane formation and then formed a sponge-like structure[47]; meanwhile, the sponge-like structure may result in firmly twisted PES/PVP chains in the membranes, which could greatly reduce the elution of hydrophilic PVP chains during preparation and then enhance the stability. And the increased viscosity of casting solution also increases the thickness of the prepared membrane. The SEM pictures suggested that the inner structures of the composite membrane had been altered after blending the PVP, which indicated that the composite membrane own increased porosity and permeability, and the membrane cross-section morphologies could be adjusted by changing the amounts of PVP.

Attenuated total reflection Fourier transform infrared spectra for the membrane surfaces

The ATR-FTIR spectra for the membrane surfaces of pure PES (FSM-0) and PES/PVP composite membranes are shown in Fig. 3. It could be seen that the most significant changes between PES and the PES/PVP composite membranes were the appearance of the peak at 1679 cm^{-1}, which was the characteristic peak of the PVP as mentioned earlier. And compared with FSM-3, the intensity of the characteristic peak of PVP in FSM-5 was stronger because of the larger molecular weight of N5, which thus may lead to higher remained amount and hard to be eluted.

Contact angle

Contact angle is a convenient way to assess the hydrophilic/hydrophobic of the membrane surface.[48] Figure 4 shows the static water contact angles of the prepared PES and PES/PVP composite membranes. From Fig. 4A, it could be found that the initial contact angles (5 sec) of the composite membranes increased after blending PVP, compared with that of PES membrane; and the same phenomenon was observed for the composite membranes with different blending amounts of N5, as shown in Fig. 4B. However, as we have known, PVP is a good hydrophilic material, and the presence of PVP in the membrane should enhance the hydrophilicity of the matrix; nevertheless, the initial water contact angles reflected opposite results in this study. To further study the hydrophilic/hydrophobic property of the membrane matrix, the water contact angles for 30 sec were also recorded as shown in blue column of Fig. 4. The results of all PES/PVP composite membranes exhibited decreased water contact angles than pristine PES membranes. Meanwhile, to further confirm the hydrophilicity of PES/PVP composite membranes, we have prepared the evaporation membrane using solvent vaporizing method, the blend ratios of PES/N5 were 20/0, 20/2, 20/4, and 20/7, respectively, the same as those by phase inversion method. The average static water contact angles of the evaporation membranes were 80.1°, 71.7°, 67.5°, and 55.4°, respectively. It could be found that the water contact angles decreased with the increase of N5 blending amounts.

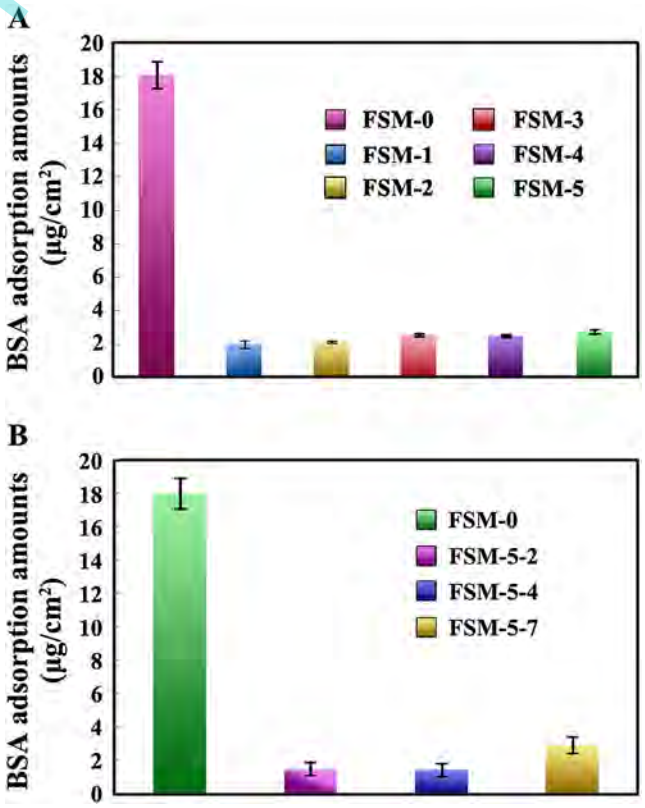

Figure 7. Protein adsorption amounts onto PES and the PES/PVP composite membranes. This figure is available in colour online at wileyonlinelibrary.com/journal/pat

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These results indicated that the hydrophilicity of the PVP blended membrane increased compared with that of pristine PES. Furthermore, the increased initial water contact angles, shown in Fig. 4, could be attributed to the surface morphology changes of the composite membranes during the aqueous phase inversion processing, and it could be detected by AFM micrographs and will be discussed in next section.

Atomic force microscopy

Figure 5 demonstrates the three-dimensional AFM images for the modified PES membrane surfaces at a scan size of 2 μm× 2 μm. It was observed that the morphologies of the surfaces were changed after blending PVP. Compared with that of the pristine PES membrane, it was observed that the size of surface tiny grooves and fine holes decreased with the increase of the PVP molecular weights for the FSM-2 and FSM-4, and the same phenomenon was found for the increased blending ratios of FSM-5-2 and FSM-5-7.

Although, it was observed that the size of surface tiny grooves and fine holes decreased, the surface roughness still remains unknown. For quantitative analysis, the roughness of the membrane surface was obtained from the AFM images using CSPM software (version 4.60) (Angstrom Advances. Inc, USA). The surface roughness parameters (nm) of the membranes were expressed in terms of the mean roughness (Sa), the root mean square of the Z data (Sq) and the ten-point height (Sz). For FSM-0, FSM-2, FSM-4, FSM-5-2, and FSM-5-7 membranes, the surface roughness parameters (nm) were FSM-0 (Sa:14, Sq:16, Sz:66.1), FSM-2 (Sa:15.4, Sq:17.5, Sz:76.8), FSM-4 (Sa:21.1, Sq:24, Sz:70.9), FSM-5-2 (Sa:16.7, Sq:19, Sz:90), and FSM-5-7 (Sa:51.3, Sq:60.1, Sz:323), respectively. These results suggested that the roughness for the composite membranes increased with the increase of the PVP molecular weights (FSM-2 and FSM-4) and the blended N5 amounts (FSM-5-1 and FSM-5-5) in the membranes. These data indicate that the increased initial water contact angles may have directly connected with the increased surface roughness.

Recently, many researches reported that the hydrophilicity/hydrophobicity of the material surface had a great connection with the surface morphology.[49–51] A hydrophilic surface could be transformed into a super-hydrophobic one via changing the surface morphology.[52] A hydrophobic surface could be obtained from the increase of the surface roughness,[52,53] and the water contact angle increased when the material surface switched to a relative rough one, although the material matrix was hydrophilic. In this study, the increase of the initial water contact angles for the PES/PVP membranes could be attributed to the surface roughness increment.

Elution of polyvinylpyrrolidone from the modified polyethersulfone membranes

In order to determine the elution amount of PVP with different molecular weights from the composite membranes quantificationally,

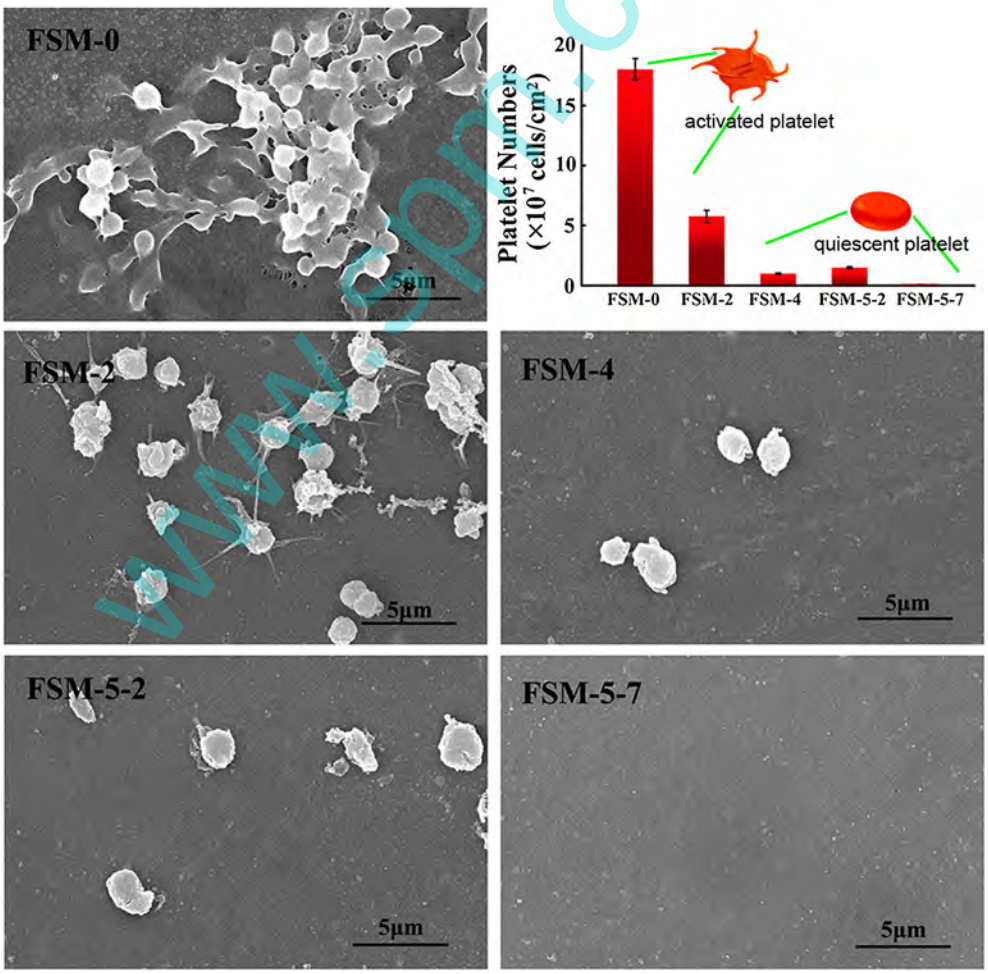

Figure 8. Scanning electron microscopy pictures for platelet adhesion on the membranes (×3000). The inserted table indicates the average number of the adhering platelets onto the membranes from platelet-rich plasma estimated by six scanning electron microscopy images.

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the elution ratios were calculated by eqn (1), and the data are shown in Fig. 6. It could be found that with the increase of the PVP molecular weights, the elution ratio decreased. The elution ratio nearly reached 100% when N1 was blended; however, only less than 20% of N5 was eluted from the membrane. When the chain length was short as for N1, it was easy to be eluted from the PES matrix because of the good water solubility. The results suggested that large molecular weight of PVP, as an additive material, could avoid the elution of PVP from the bulk membrane.

Blood compatibility

Protein adsorption

It is well known that the hydrophobic interaction between a material surface and protein plays a very important role in the nonselective adsorption of protein. Materials that possessed hydrophilic surface tend to exhibit relatively low nonselective adsorption for protein or cells.[54] The vitro protein adsorption experiment is a critical index for the evaluation of membrane clinical dialysis performance. Protein adsorption on membrane surfaces is a common phenomenon and is always considered as the first step of many undesired blood responses, such as the coagulation and thrombus. Protein adsorption is affected by numerous factors including protein size, charge, hydrophilicity/hydrophobicity, pH, surface charge, surface topology, intermolecular forces between the adsorbed molecules, the strength of functional groups, the composition of the protein solution, and the chemistry of the surface.[55] It is reported that a membrane that was modified by hydrophilic polymer could reduce protein adsorption and improve its blood compatibility.[56,57]

In the present work, the surfaces of the membranes were studied in relation to the adsorption of BSA *in vitro*, as shown in Fig. 7. It was found that all the PES/PVP composite membranes showed significant lower BSA adsorption than the pristine PES membranes. From FSM-1 to FSM-5, the protein adsorption amounts increased slightly with the increase of the molecular weight of PVP, and the protein adsorption amounts increased with the increase of the amounts of N5 as well. The increase of protein adsorption amounts could be attributed to the altered interface property induced by the PVP blending, which may increase the porosity of membrane and thus increase the protein adsorption. In general, the BSA adsorption data indicate that the PES/PVP composite membranes own superior antifouling properties. The improved antiprotein adsorption property might assist to improve the antiplatelet adhesion properties of the PES/PVP composite membrane, which will be discussed in the following sections.

Platelet adhesion

For blood-contacting clinical dialyzer, the adhesion of platelets to the hydrophobic surfaces is a key event in thrombus formation. When material surface contacts with blood, the initial blood response is the adsorption of plasma proteins followed with platelet adhesion and activation of the coagulation pathways, leading to thrombus formation. Platelet can be activated by the adsorbed proteins; the activated platelets then accelerate thrombosis and led to further coagulations. Thus, in this study, the morphologies of the adherent platelets and the adhered platelet number were investigated to evaluate the blood compatibility of the composite membranes.

Figure 8 shows a typical scanning electron micrograph of the platelets adhering to the membranes. Both the outspread and pseudopodium deformation of the platelet were obviously suppressed, which indicated low platelet activation and improved blood compatibility for the PES/PVP composite membranes. By comparing the figures with the same amplification multiple, it was observed that numerous platelets were aggregated and cumulated on the PES membrane surface. The platelets spread flattened and irregular shapes, and a lot of pseudopodium was observed; which indicated that thrombus formation might occur at the surface of the PES membrane, and this was a life-threatening phenomenon for patients. But for the blended membranes (FSM-4, FSM-5, FSM-5-2, and FSM-5-7), the amount of adhered platelets were greatly suppressed; and the platelets expressed rounded morphology with nearly no pseudopodium and deformation, and most platelets retained their discoid shape on the PES/PVP composite membranes. However, some aggregated and activated platelets were also observed on the surface of FSM-1 membrane, and this might be resulted from the elution of the low molecular weight PVP from the PES matrix. Furthermore, it was found that the amounts of adhered platelet decreased with the increase of the N5 amounts, and nearly no adhered platelet was observed on FSM-5-7. The superior antiplatelet adhesion ability of FSM-5-7 should be attributed to the decreased PVP elution ratio of N5 and increased blended amounts than the other composite membranes.

Clotting time (activated partial thromboplastin time)

To further study the blood compatibility of the composite membranes, the APTT was measured, as shown in Fig. 9. The APTT test

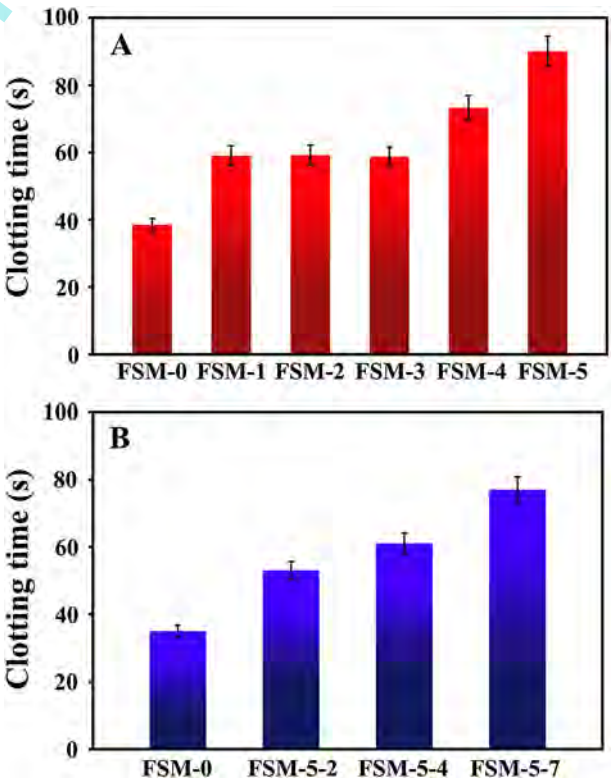

Figure 9. Activated partial thromboplastin times (APTTs) for the PES and modified PES membranes ($n = 3$). (A) Composite membranes with different PVP molecular weights and (B) composite membranes with different blending amounts of N5.

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exhibits the bioactivity of intrinsic blood coagulation factors. Compared with the pristine PES membrane, the APTTs for all the composite membranes increased significantly. As shown in Fig. 9A, it was found that the APTTs for the composite membranes increased with the increase of the molecular weight of PVP, which were coincident with the elution ratios of the PVP amount from composite membranes (Fig. 9A). And this indicated that the elution of the PVP from the composite membranes could be avoidable by the blending high molecular weight PVP, and thus the higher blood anticoagulant ability could be achieved. It was also found that with the increased amounts of N5 in the composite membranes, the APTT increased to nearly twice than the pristine PES membranes when the amount of N5 was 7 wt%. The enhancement in anticoagulant activity after blending PVP might be attributed to the surface-immigrated PVP brush and also the depressed platelet adhesion and activation.

CONCLUSION

In this study, highly blood compatible PES/PVP composite membranes with antifouling and antithrombotic properties were prepared via a physical blending method. To explore the effects of the surface properties and blood compatibilities by the blending of PVP in detail, different molecular weights of PVP were synthesized via RAFT polymerization and then blended with PES to achieve the PES/PVP composite membranes. The surface ATR-FTIR spectra and SEM pictures indicated that the PVP was successfully immobilized into the membranes, and the composite membranes exhibited morphology transformation from finger-like structure to sponge-like structure, which indicated that the composite membrane had tunable porosity and permeability by adding PVP. The results of the blood compatible tests revealed that the composite membranes showed increased hydrophilicity, decreased plasma protein adsorption, suppressed platelet adhesion, and prolonged blood clotting time compared with pristine PES membrane. Meanwhile, the results also suggested that the composite membranes with larger molecular weight PVP and higher blending ratios might show better blood compatibility because the high elution ratio of low molecular weight PVP. These results indicated that the PES/PVP composite membranes exhibited enhanced antifouling and antithrombotic properties than the pristine PES membrane and might have a promising future and favorable long-term utilization in clinical hemodialyzer and other advanced separation.

Acknowledgements

This work was financially sponsored by the National Natural Science Foundation of China (No. 51073105, 51173119, and 51225303). We would also thank our laboratory members for their generous help and gratefully acknowledge the help of Ms. H. Wang of the Analytical and Testing Center at Sichuan University, for SEM observation, and Ms. Liang of the Department of Nephrology at West China Hospital, for the human fresh blood collection.

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