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Tethering poly(ethylene glycol)s to improve the surface biocompatibility of poly(acrylonitrile-*co*-maleic acid) asymmetric membranes

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Abstract

To improve the surface biocompatibility, asymmetric membranes fabricated from poly(acrylonitrile-*co*-maleic acid)s (PANCMAs) synthesized by water-phase precipitation copolymerization were tethered (or immobilized) with poly(ethylene glycol)s (PEGs) by esterification reaction. Chemical changes on the membrane surface were characterized by Fourier transform infrared spectroscopy and elemental analysis to confirm the immobilization of PEG onto the PANCMA membranes. The hydrophilicity and blood compatibility of the PEG-tethered PANCMA membrane were investigated by water contact angle, water absorption, protein adsorption, plasma platelets adhesion and cell adhesion measurements, and the results were compared with the corresponding PANCMA membranes. It was found that, after the tethering of PEG, the hydrophilicity of the membrane can be improved significantly, and the protein adsorption, platelets adhesion and macrophage attachment on the membrane surface are obviously suppressed. Furthermore, not only the content of maleic acid in PANCMA, which influences the tethering density of PEG, but also the molecular weight of PEG has great effect on the surface modification of PANCMA membranes for biocompatibility.

Keywords: Polyacrylonitrile; Membrane; Surface modification; Biocompatibility; Platelets adhesion; Cell adhesion

1. Introduction

Polyacrylonitrile has been successfully applied as membrane materials in the fields of dialysis [1–3], ultrafiltration [4,5], enzyme-immobilization [6] and pervaporation [7]. It has also been reported as a membrane to support the attachment of hepatocytes in an artificial liver support system [8]. In addition, it has good membrane formation properties and acrylonitrile can be easily copolymerized with a variety of vinyl comonomers [9–15]. Copolymerization with hydrophilic monomer such as *N*-vinyl-2-pyrollidone has recently been described to improve the biocompatibility of polyacrylonitrile membrane [13,14], while that with other functional monomer can provide reactive groups for enzyme-immobilization [10] and/or further chemical reaction [15].

In our previous work, asymmetric hollow fiber membranes were fabricated from poly(acrylonitrile-*co*-maleic acid)s (PANCMAs) synthesized by water-phase precipitation copolymerization process, which provided plentiful functional groups for further modification [15]. Moreover, the content of reactive carboxyl groups could be controlled through adjusting the copolymerization condition. Most importantly, it was confirmed that the reactive carboxyl groups on membrane surface could be conveniently conversed into more active anhydride groups. These anhydride groups are able to undergo a ring-opening reaction easily with nucleophilic reagents containing hydroxyl or amine groups [16–18]. For examples, a series of novel glycopolymers with specific biological properties were obtained recently by the reaction of poly(styrene-*co*-maleic anhydride)s with amino sugars such as 1-amino-1-deoxy-β-D-galactose, 1-amino-1-deoxy-β-D-glucose and 1-amino-1-deoxy-β-D-lactose [16]. Poly(styrene-*co*-maleic anhydride)s were

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also reacted with poly(ethylene glycol) (PEG) to obtain amphiphilic graft copolymers with thermo-sensitive and/or pH-sensitive properties [17,18].

PEG is an uncharged polyether with the chemical formula, H–$(OCH_2CH_2)_n$–OH, which is the simplest structure of water-soluble polymers and is well known for its extraordinary ability to resist cell adhesion and protein adsorption because of its hydrophilicity, large exclusion volume, and unique coordination with surrounding water molecules in an aqueous medium. Especially, PEG has the unique properties of nontoxicity and nonimmuno-genecity which are very important for biomaterials. In recent years, the immobilization of PEG on material surface to improve the blood compatibility and to minimize cell adhesion is well-documented in Refs. [19–30].

Due to the relatively poor hydrophilicity and biocompatibility for the previously reported PANCMA membranes [15], their further applications in bioseparation and biomedical devices are limited. In this study, therefore, we investigate the capability of tethering (immobilizing) PEG to improve the surface biocompatibility of PANCMA membranes. For this aim, the hydrophilicity, protein adsorption, plasma platelets deposition and cell adhesion were mainly studied after the immobilization of PEG. The influences of the immobilization density and the molecular weight of PEG were also described.

2. Material and methods

2.1. Materials

All chemicals were analytical grade. Four PANCMAs, designated as PANCMA0, PANCMA3, PANCMA7 and PANCMA11 in the following text, were synthesized in our laboratory with a water-phase precipitation copolymerization process [15]. The number in the designation indicated that the mole fraction of maleic acid in the copolymer was 0, 3.69, 7.48 and 11.45 mol%, respectively. The molecular weights (M_v) of these copolymers are 25.6×10^4 g/mol for PANCMA0, 15.8×10^4 g/mol for PANCMA3, 15.1×10^4 g/mol for PANCMA7 and 14.5×10^4 g/mol for PANCMA11. Dimethyl sulfoxide (DMSO) was purified by vacuum distillation before used. Bovine serum albumin (BSA, purity > 98%) was purchased from Sino-American Biotechnology Co. and used as received. A 0.1 wt% BSA solution was prepared in a phosphate buffered saline (PBS) solution at pH 7.4. PEGs (Shanghai Chemical Reagent Co., China) with molecular weight ranged from 200 to 1000 g/mol were used as received. The nonsolvent selected for the coagulation bath for fabricating the asymmetric membrane was ultrafiltrated water, while deionized water was used for the filtration experiments.

2.2. Membrane fabrication

PANCMA powder was dried for at least 3 h at 50°C in vacuum oven, and then dissolved in DMSO at about 80°C for 24 h with vigorous stirring to form a homogeneous 4 wt% casting solution, which was allowed to stand overnight to remove air bubbles. After the air bubbles were removed, the casting solution was cast onto a clean glass plate using a casting knife with 100 μm gate opening. The nascent membrane was placed in the air (25 ± 1°C, 45–50% relative humidity) for 10 min, and then immersed in 22 ± 1°C ultrafiltrated water for 24 h. Finally, the membrane with a thickness of 32 ± 1.5 μm was preserved in 5 vol% formaldehyde solutions for further use.

2.3. Tethering poly(ethylene glycol) onto membrane

The PANCMA membrane was first washed with a water–ethanol–hexane sequence, and dried at room temperature. The dry PANCMA membrane was then refluxed in acetic anhydride for 1 h to ensure a high conversion of carboxyl to anhydride, and washed with acetone and completely dried [31]. Finally, this membrane was immersed in PEG with different molecular weight at 100°C under nitrogen atmosphere for about 16 h [29,30]. The resulted membrane was washed with large amount of deionized water to remove the unreacted PEG and dried completely at 40°C in vacuum oven. The grafting degree (DG) was calculated by the following equation:

$$\mathrm{DG}\ (\%) = \frac{w_g - w_0}{w_0} \times 100,$$

where w_0 and w_g are the weight of a membrane before and after tethering reaction, respectively. Moreover, the immobilization density of PEG was calculated from the value of $(w_g - w_0)$ and the molecular weight of the PEG used.

2.4. Fourier transform infrared spectroscopy

To investigate chemical changes between the original PANCMA and PEG-tethered membranes and confirm the immobilization of PEG on membrane surface, Fourier transform infrared spectroscopy (FT-IR, Vector 22) with an ATR unit (KRS-5 crystal, 45°) was used.

2.5. Elemental analysis

Elemental analysis was used to detect the difference of atomic composition between the original PANCMA and PEG-tethered membranes. The weight percentage of carbon, hydrogen and nitrogen of each sample was obtained from an elemental analyzer (EA1110, Carco Erba Co., Italy), and then that of oxygen was calculated from EA data.

2.6. Hydrophilicity measurements

The hydrophilicity of the membrane surface was characterized on the basis of water contact angle (CA) and water absorption measurements. Using a sessile drop method, water CA was measured at room temperature by a CA goniometer (KRÜSS DSA10-MK) equipped with video capture. A total of 10 μl of deionized water was dropped on a dry membrane with a micro-syringe in an atmosphere of saturated water vapor and then a CA was measured when the drop age was about 5 s. At least 10 CAs were averaged to get a reliable value. Water absorption was defined as $(w_2 - w_1)/w_1$, where w_1 and w_2 represent the weight of the dry membrane and the membrane soaked in water for 24 h at $22 \pm 0.5^{\circ}C$, respectively. The reported value was the average of at least three experiments and the standard deviation was within ca. $\pm 5\%$.

2.7. Filtration and protein adsorption

The protein adsorption on the membrane surface was studied by a dynamic filtration experiment, which was similar to that of Pieracci et al. [32]. Each membrane was first compacted for 30 min at 0.15 MPa. Then, the pressure was lowered to 0.10 MPa and the flux of deionized water (J_{w0}) was measured by weighing the permeate, till consecutive recorded values differed by less than 2% (J_0). Next, a 1 g/l BSA solution was added to the reservoir and the filtering experiment was performed at 0.10 MPa for 30 min, the permeate flux at the end of BSA solution filtration was denoted as J_p. After BSA solution filtration, the membrane was cleaned for 1 min, three times to remove weakly attached BSA, and then the deionized water flux (J_{w1}) was measured at 0.10 MPa. The membrane was filled with a 500 ppm NaOCl solution and filtered for 1 h at 0.10 MPa. Thereafter, the membrane was cleaned with deionized water, and the additional filtering of deionized water was performed for 20 min in order to completely remove the remaining NaOCl. The next measured deionized water flux was J_{w2}. The reported data were the mean value of triplicate samples for each membrane. The amount of adsorbed BSA that had not been removed by chemical cleaning was determined by measuring the weight of the membrane before and after the filtration experiment.

2.8. Adhesion of blood platelets

A sample of 20 ml of human fresh blood was taken by venipuncture of a sole healthy donor. The blood was mixed with trisodium citrate (1 part to 9 parts of blood) and centrifuged at 250*g* for 10 min to obtain platelet-rich plasma (PRP). The studied membrane was cut into $1 \times 1\,cm^2$ pieces and placed in a tissue culture plate. In all, 20 μl fresh PRP was dropped on the center of the sample and then incubated at 37°C for 30 min. The membrane was rinsed gently with a PBS solution, after which the adhered platelets were fixed with 2.5 wt% glutaraldehyde in PBS for 30 min. Finally, this sample was washed with PBS, and dehydrated with a series of ethanol/water mixtures of increasing ethanol concentration (30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% ethanol, 10 min in each mixture) [33,34]. The membrane surface was coated with gold and observed with scanning electron microscopy (SEM) at 500 or 1000 magnification.

2.9. Macrophage adhesion

The murine macrophage suspension was prepared with the method reported previously [35]. The suspension was isolated from freshly killed mice using chloroform. The skin was sprayed with alcohol and the abdomen was opened. In all, 10 ml sample of Roswell Park Memorial Institute (RPMI) 1640 containing 10% fetal bovine serum (FBS), 100 g/ml penicillin and 100 μm/ml streptomycin was injected into the peritoneal cavity, and then the abdomen was gently massaged by fingers for 5 min. The peritoneum was carefully punctured, and then the washings were removed by a sterile pipet and placed in a sterile container to be centrifuged at 1000 rpm for 10 min to collect the macrophages. The macrophages obtained were grown in RPMI 1640 to obtain the macrophage suspension in which the cell concentration was 1×10^6 cells/ml.

The membrane ($10 \times 10\,mm^2$) was cleaned sequentially in an ultrasonic bath of ethanol solution for 10 min and rinsed in PBS. Then the sample was immersed in physiological saline (pH 7.4) to recondition for several hours. The cell suspension was inoculated on the surface of the membrane to assess the cell attachment. The incubation period was 48 h for the cell attachment test in a humidified atmosphere of 5% CO_2 in air at 37°C. Then the supernatant was removed, and the membrane was washed cautiously five times using PBS (pH 7.2), and the adherent cells were fixed by the addition of methanol for 5 min. The adherent cell density on the membrane was quantified on the basis of measurements obtained visually from at least five randomly selected fields ($0.24 \times 0.36\,mm^2$) using an Olympus TE300 phase contrast optical microscope. The mean values of triplicate samples for each membrane with the standard deviation were reported.

3. Results and discussion

3.1. Tethering PEG onto PANCMA membrane

FT-IR/ATR spectra of the studied membranes were measured to confirm the tethering of PEG on the

PANCMA membrane surface. Characteristic peaks of the PANCMA0 membrane can be observed at 2242 cm^{-1} (C≡N stretching vibration) and 1452 cm^{-1} (CH_2 scissoring vibration). The spectrum of PANCMA3 membrane shows an absorbance band at 1725 cm^{-1}, which is the characteristic peak for carboxyl group. Converting carboxyl into anhydride can be confirmed by the appearance of two absorbance bands at 1785 and 1825 cm^{-1}. Compared with the spectrum of PANCMA*n*, the characteristic bands of anhydride disappear in the spectrum of PANCMA3-g-PEG400, while the 1716 cm^{-1} for C=O stretching vibration of the ester group appears and the 1060 cm^{-1} band for C–O stretching vibration enhances.

The immobilization of PEG on PANCMA membrane was also demonstrated by elemental analysis summarized in Table 1, which reveals that the weight percentage of both oxygen and hydrogen has an obvious increase with PEG immobilization on the membrane. Furthermore, as can be seen from Fig. 1, with the increase of the content of maleic acid in PANCMA from 0 to 11.45 mol%, the DG and the immobilization density of PEG400 increase from 0 to 16.84 wt% and from 0 to 2.62×10^{-7} mol/cm^2. On the other hand, although the DG of PEG increases from 9.97 to 25.49 wt% for PANCMA3-g-PEG200 to PANCMA3-g-PEG1000 (Fig. 2), it was found on the basis of calculated immobilization density that, with the molecular weight of PEG increases from 200 to 1000 g/mol, the immobilization density of PEG on PANCMA membrane surface decreases from 1.49 to 0.76×10^{-6} mol/cm^2. It indicates that the tethering of PEG with high molecular weight is relatively difficult to take place.

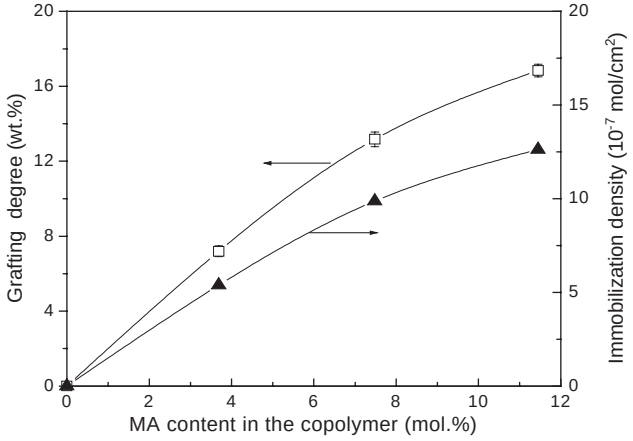

Fig. 1. Effects of maleic acid content in PANCMA membranes on the DG and immobilization density of PEG (PEG400).

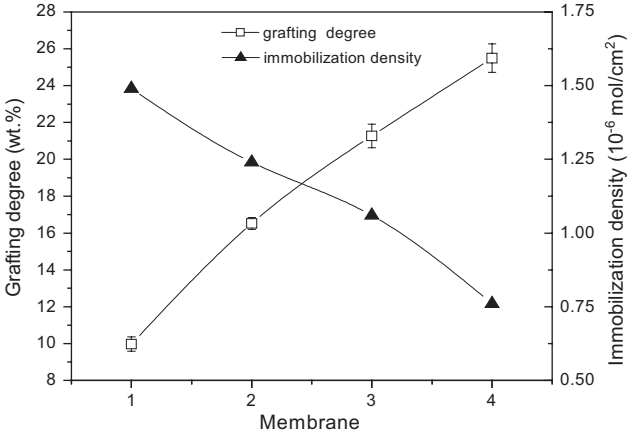

Fig. 2. Effects of the molecular weight of PEG on the DG and immobilization density of PEG: (1) PANCMA3-g-PEG200; (2) PANCMA3-g-PEG400; (3) PANCMA3-g-PEG600; (4) PANCMA3-g-PEG1000.

3.2. Hydrophilicity of the membranes

Water CA and water absorption measurements have been commonly used to characterize the relative hydrophilicity or hydrophobicity of the membrane surface. For membranes with comparable structures, relatively low CA value and high water absorption normally mean high hydrophilicity. It can be seen from Fig. 3(a) that the water absorption of the membrane rises with the increase of maleic acid content in PANCMA. The PEG400-tethered membrane showed almost two times of water absorption more than the corresponding PANCMA membrane. Results in Fig. 3(b) indicate that the PANCMA0 membrane has a maximum CA value (68.3°), and this value of all PEG400-tethered membranes and corresponding PANCMA membranes decreases with the content of maleic acid increasing from 0 to 11.45 mol%. Furthermore, the CA value of PEG400-tethered membranes is much lower than that of original PANCMA membranes. On the other hand, concerning the effect of PEG with different molecular weight, it was found that the PANCMA3-g-PEG400 membrane manifests the lowest CA value of 23.1° among all PEG-tethered membranes, which is a half of that for the original PANCMA3 membrane (48.2°). At the same time, the PANCMA3-g-PEG400 membrane also has the highest

Table 1
Elemental analysis data for the studied membranes

Sample	Nitrogen (wt%)	Carbon (wt%)	Hydrogen (wt%)	Oxygen (wt%)
PANCMA3	25.12	64.88	5.61	4.39
PANCMA7	22.83	63.32	5.41	8.44
PANCMA11	20.89	61.41	5.35	12.34
PANCMA3-g-PEG200	22.84	63.97	5.82	7.28
PANCMA3-g-PEG400	21.04	63.31	6.13	9.53
PANCMA3-g-PEG600	19.98	62.89	6.28	10.85
PANCMA3-g-PEG1000	18.79	62.47	6.44	12.29

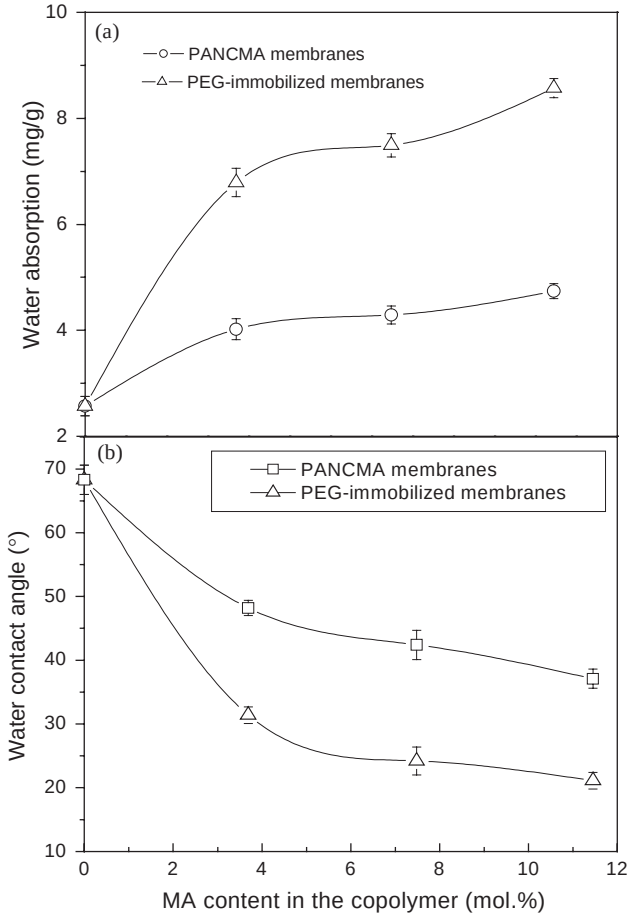

Fig. 3. Effects of maleic acid content in PANCMA on the water CA and water absorption of PANCMA and PEG-tethered (PEG400) membranes.

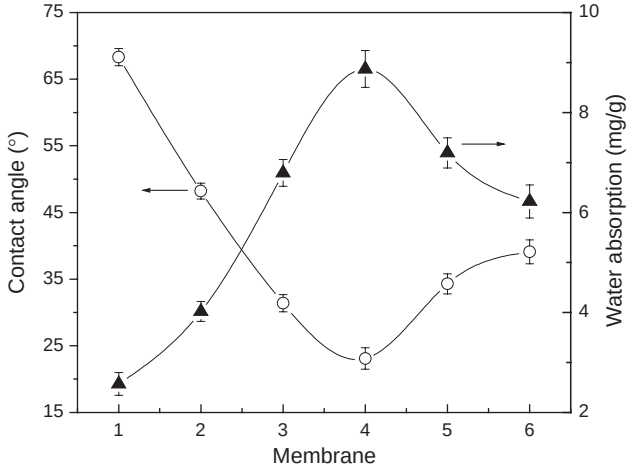

Fig. 4. Effects of the molecular weight of PEG on the water CA and water absorption of PEG-tethered membranes: (1) PANCMA0; (2) PANCMA3; (3) PANCMA3-g-PEG200; (4) PANCMA3-g-PEG400; (5) PANCMA3-g-PEG600; (6) PANCMA3-g-PEG1000.

Table 2
Filtration performances of the PANCMA and PANCMA-g-PEG membranes[a]

Membrane	J_{w0} (l/m^2 h)	J_p (l/m^2 h)[b]
PANCMA0	158.5±6.5	17.5±1.5
PANCMA3	323.4±16.8	120.2±5.6
PANCMA3-g-PEG200	372.6±22.3	197.6±5.7
PANCMA3-g-PEG400	499.9±21.8	312.8±18.3
PANCMA3-g-PEG600	450.6±13.5	253.2±12.7
PANCMA3-g-PEG1000	311.9±15.6	150.6±6.0
PANCMA7	378.5±15.1	190.9±13.4
PANCMA7-g-PEG400	574.3±17.2	393.8±7.9
PANCMA11	436.8±21.8	250.6±10.0
PANCMA11-g-PEG400	506.3±15.2	375.3±15.0

[a] The filtration test was conducted at a constant transmembrane pressure of 0.1 MPa and a system temperature of 22±0.5°C.
[b] The amount of adsorbed BSA on the membrane after chemical cleaning.

water absorption in comparison with other PEG-immobilized membranes (Fig. 4). The effects of the maleic acid content and the molecular weight of PEG on the hydrophilicity of PEG-tethered membranes can be ascribed to the DG and the calculated immobilization density shown in Figs. 1 and 2, respectively. With the content of maleic acid increasing, the DG and the calculated immobilization density of PEG400-tethered membrane increase simultaneously; therefore, the hydrophilicity of PEG400-tethered membrane is improved in step. When keeping the maleic acid content in PANCMA as 3.69 mol%, as mentioned above in Fig. 2, although PANCMA3-g-PEG200 membrane has the highest immobilization density, the short PEG chain with less hydrophilic –CH_2–CH_2–O– segment brings about relatively low hydrophilicity on the membrane surface than that of PANCMA3-g-PEG400 membrane. On the other hand, PEG600 and PEG1000 are more difficult to be tethered on the membrane surface; therefore, the hydrophilicity of the corresponding membranes also decreases. To obtain an optimal hydrophilicity, a moderate molecular weight of PEG should be suitable because of the balance between immobilization density and hydrophilic chain segments.

3.3. Filtration properties and bovine serum albumin adsorption

Table 2 shows the results of water and BSA solution filtration to investigate whether the PEG immobilization affects the filtration performance of the membranes or not, because the pore shape and size may be changed during the modification process. It was found that with the increase of maleic acid content, the flux of water and BSA solution increase for both PANCMA and PEG-tethered membranes. And with the exception of

PANCMA3-g-PEG1000 membrane, all membranes immobilized with PEG have higher flux values than the corresponding PANCMA membranes. These results indicate that surface modification by PEG immobilization can improve the filtration performance of the membrane due to the enhancement of hydrophilicity.

Figs. 5 and 6 show the results of BSA adsorption on the studied membranes. It was found that with the content of maleic acid increasing, the BSA adsorption on the PANCMA and PEG400-tethered membranes reduces and the PEG400-tethered membrane has a lower value than the original PANCMA membrane (Fig. 5).

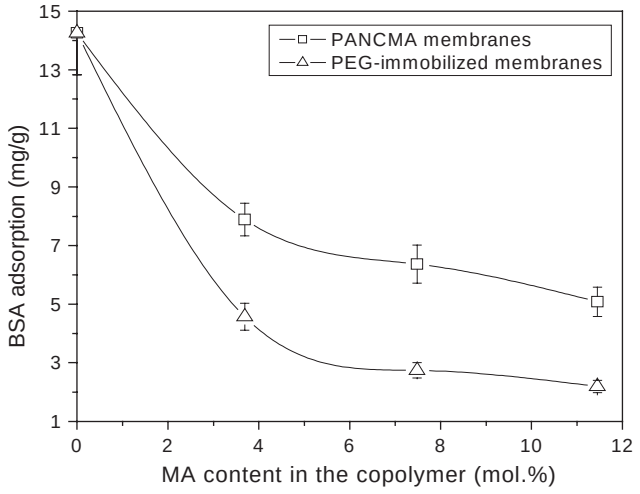

Fig. 5. Relationship between BSA adsorption and maleic acid content in PANCMA for both PANCMA membranes and PEG-tethered (PEG400) membranes.

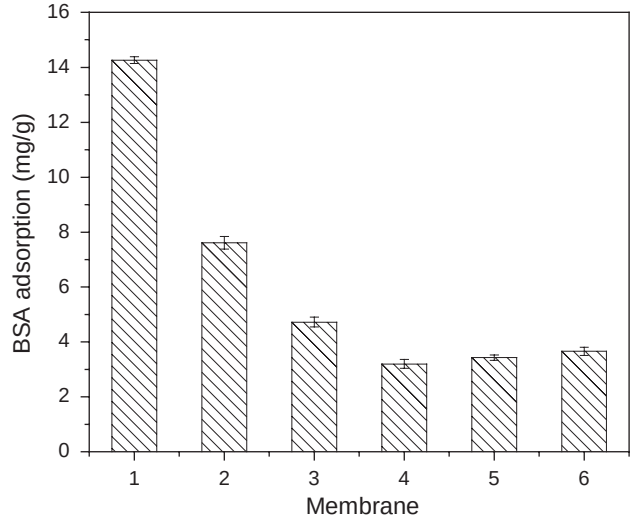

Fig. 6. Relationship between the molecular weight of PEG and the BSA adsorption on PEG-tethered membranes: (1) PANCMA0; (2) PANCMA3; (3) PANCMA3-g-PEG200; (4) PANCMA3-g-PEG400; (5) PANCMA3-g-PEG600; (6) PANCMA3-g-PEG1000.

From Fig. 6, in all membranes immobilized with different molecular weight of PEG, PANCMA3-g-PEG400 membrane has a lowest BSA adsorption value and it reduces about 77.56% and 57.9% compared with PANCMA0 and PANCMA3 membranes, respectively. It has been well known that the hydrophobic interaction between the material surfaces and proteins plays a very important role in the nonselective adsorption of protein. Materials possessing hydrophilic surface normally show relatively low nonselective adsorption for proteins or cells. Moreover, for PEG modified materials, the prevention of protein adsorption is also due to the steric repulsion by the surface-tethered PEG chains and has relation to the grafting density [19,23].

3.4. Platelet and macrophage adhesion

To our knowledge, when a material contacts with blood, proteins will be first adsorbed instantaneously on the surfaces and deformed, then platelets will be adsorbed, activated and aggregated, so platelets play a major role in the thrombus formation. Therefore, a study on platelets adhesion to evaluate the blood compatibility of separation membrane is important. Figs. 7 and 8 show the situation of platelets adhered on the surface of PANCMA and PEG-tethered membranes from platelets-rich plasma (PRP). It can be seen from Fig. 7(a)–(c) that many platelets adhere on PANCMA membrane surface, while all PEG-tethered membranes show a sharp suppress on platelets adhesion. Moreover, with the increase of the content of maleic acid, platelets adhered on both PANCMA and PEG-tethered membranes decrease obviously. Results in Fig. 8 indicate that, compared with PANCMA0 and PANCMA3 membranes, platelets adhered on the membranes immobilized with different molecular weight of PEG decrease, and PANCMA3-g-PEG400 membrane is the best one to suppress platelets adhesion. As mentioned above, PANCMA3-g-PEG400 has low protein adsorption and the protein adsorption is the first step for platelets adhesion. It has been well accepted that PEG has a unique nonadhesive property to proteins, blood components and cell. The specific character of PEG has been explained by the excluded volume effect and the dynamic motion of fully hydrated flexible chains [21]. Our work proves that the blood compatibility of the PANCMA membrane can be highly improved by tethering PEG chains on the membrane surface. This result is in full agreement with those of Refs. [19,20].

Macrophage is a kind of immune cell and performs various functions such as migration, phagocytosis, secretion, antigen presentation and survival through precisely modulated adhesion, in living bodies. However, the molecular mechanism in macrophage adhesion is complex, dynamic and not yet fully understood.

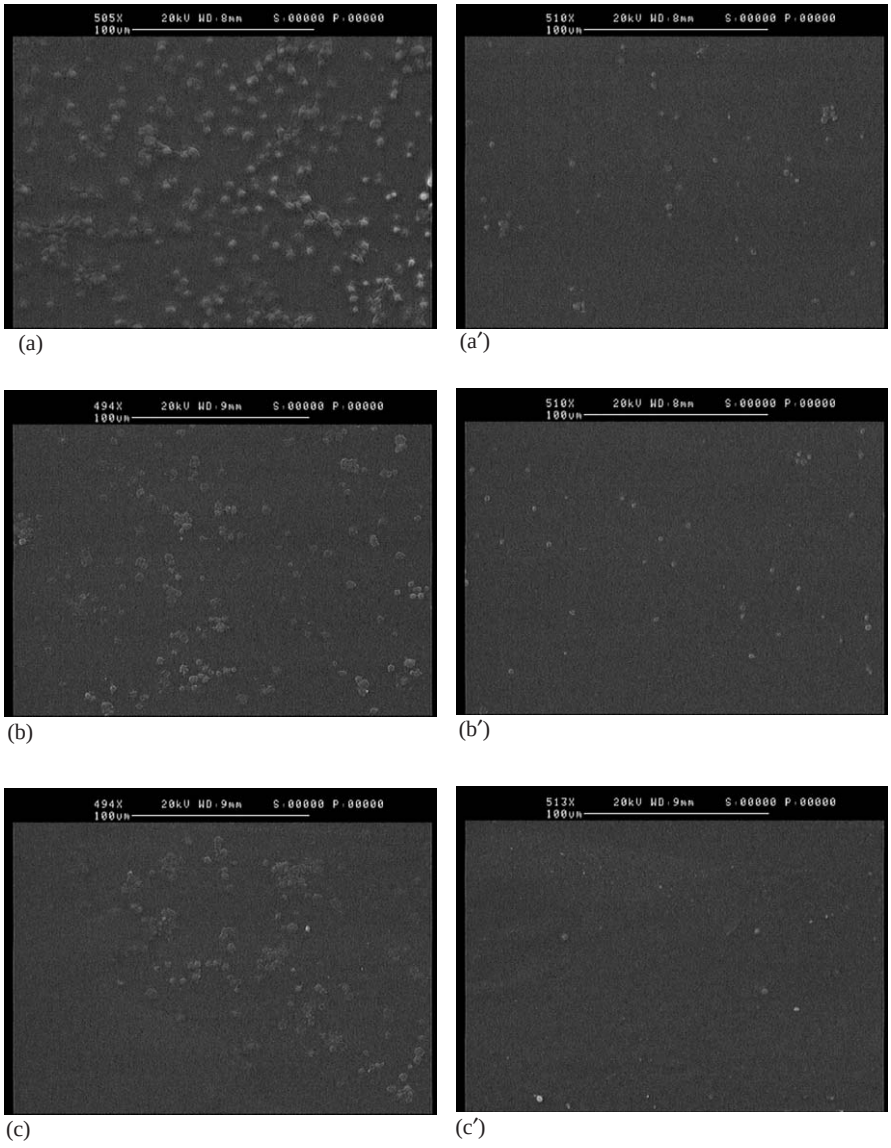

Fig. 7. Adhesion of blood platelets on the surface of PANCMA and corresponding PEG-tethered membranes: (a) PANCMA3; (a′) PANCMA3-g-PEG400; (b) PANCMA7; (b′) PANCMA7-g-PEG400; (c) PANCMA11; (c′) PANCMA11-g-PEG400.

Generally speaking, the fewer amount of macrophage adhered onto the material surface, the better the blood compatibility of the material is, which is to say that the immunological reaction or immunological rejection will decrease after the material has been planted into the living body. The results of macrophages adhesion on the PANCMA0, PANCMA3 and PEG-tethered membrane surface are shown in Figs. 9 and 10, respectively. It demonstrates clearly that, with the increase of the content of maleic acid, the number of macrophages adhered on all PANCMA and PEG-tethered membranes decreases significantly, which indicates that the increase of maleic acid content and PEG immobilization density on the membrane surface induces the reduction of macrophage adhesion. Moreover, in all membranes immobilized with different molecular weight of PEG, the PANCMA3-g-PEG400 has the lowest adhered cell number due to the best hydrophilicity and the lowest protein adsorption among the studied membranes. These results again show that the biocompatibility of the membrane can be highly improved by tethering PEG chains on the membrane surface.

4. Conclusions

Asymmetric membranes fabricated from poly(acrylonitrile-*co*-maleic acid)s (PANCMAs) were immobilized with PEG by esterification reaction. Both water contact angle and water absorption measurements demonstrate

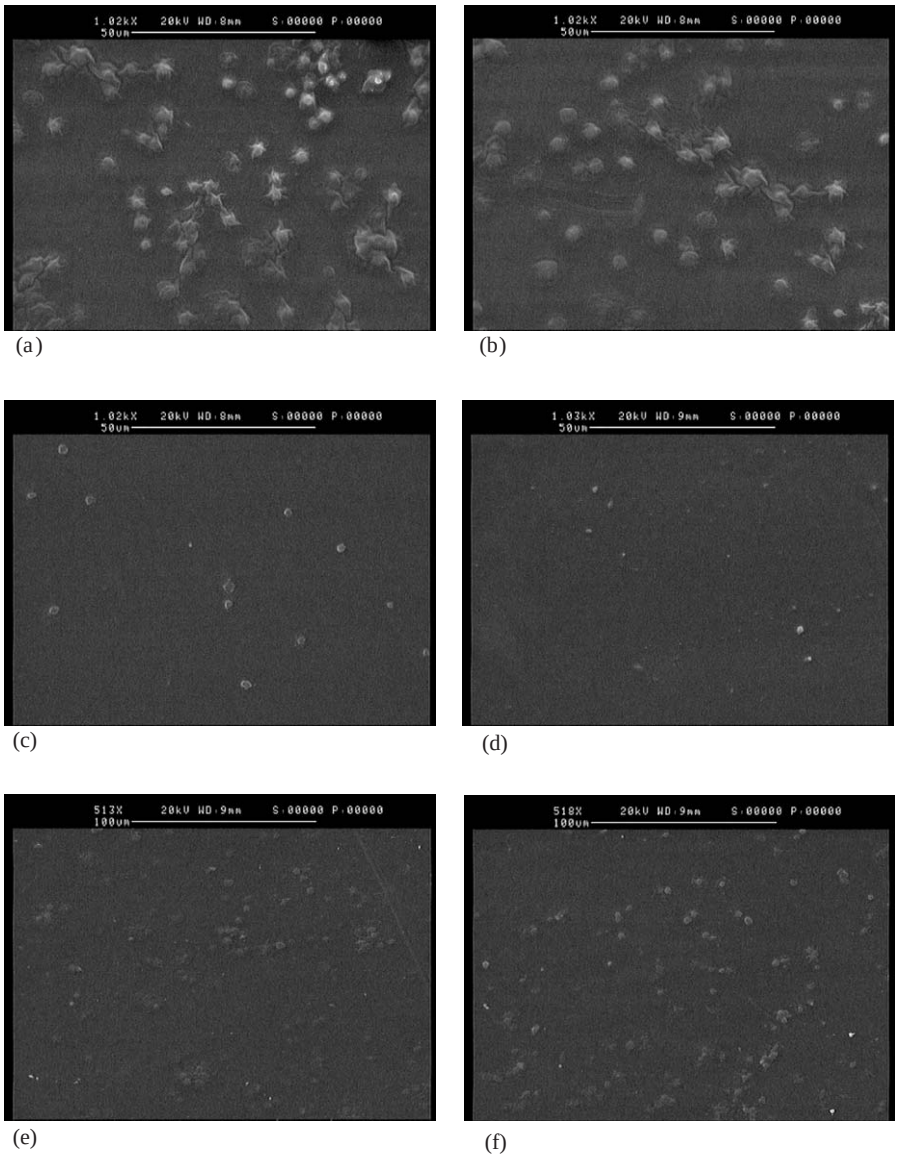

Fig. 8. Adhesion of blood platelets on PANCMA and different PEG-tethered membrane surfaces: (a) PANCMA0; (b) PANCMA3; (c) PANCMA3-g-PEG200; (d) PANCMA3-g-PEG400; (e) PANCMA3-g-PEG600; (f) PANCMA3-g-PEG.1000.

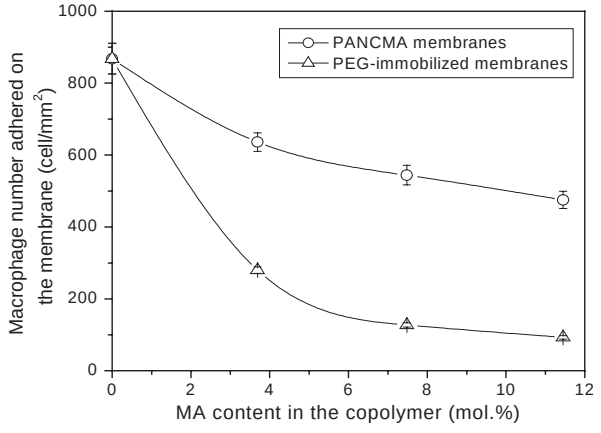

Fig. 9. Effects of maleic acid content in PANCMA on macrophage adhesion for both original PANCMA membranes and PEG-tethered (PEG400) membranes.

that the hydrophilicity of the membranes can be improved by increasing the content of maleic acid and the PEG immobilization density. The amount of BSA absorption, plasma platelets adhesion and macrophages adhesion on the PEG-tethered membranes decrease in comparison with those of the original PANCMA membranes. In all PEG-tethered membranes, it was found that PANCMA3-g-PEG400 has the best hydrophilicity, lowest protein adsorption and best blood compatibility due to the balance between PEG immobilization density and hydrophilic chain segments. These preliminary results prove that the hydrophilicity and blood compatibility of PANCMA membranes can be effectively improved by adjusting the content of maleic acid in the copolymer and the molecular weight of PEG immobilized on the membrane surface.

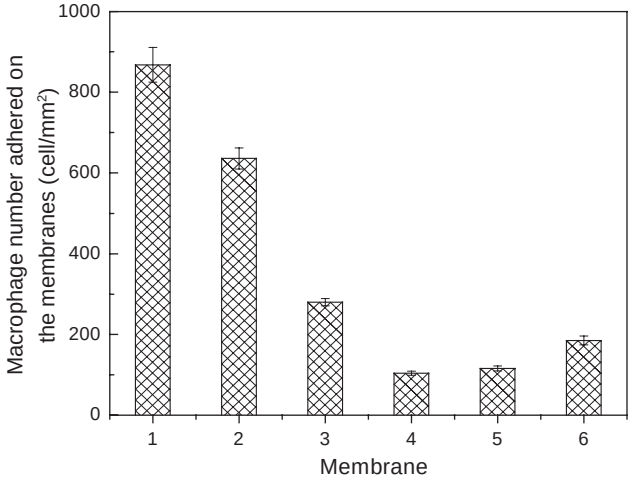

Fig. 10. Number of macrophage adhered on the PANCMA0, PANCMA3 and different PEG-tethered membrane surfaces: (1) PANCMA0; (2) PANCMA3; (3) PANCMA3-g-PEG200; (4) PANCMA3-g-PEG400; (5) PANCMA3-g-PEG600; (6) PANCMA3-g-PEG1000.

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