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Surface modification of PE porous membranes based on the strong adhesion of polydopamine and covalent immobilization of heparin

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ABSTRACT

Based on the self-polymerization and strong adhesion characteristic of dopamine in wet conditions, the hydrophobic polyethylene (PE) porous membranes were surface-modified via simply immersing them into dopamine aqueous solution for 24 h. Subsequently, heparin was immobilized covalently onto the resultant membrane by the coupling between heparin and reactive polydopamine layer. Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy and X-ray photoelectron spectroscopy (XPS) were utilized to determine the chemical compositions of membrane surface, which confirmed the successful introduction of polydopamine and immobilization of heparin molecules. Scanning electronic microscopy (SEM) and atomic force microscopy (AFM) were employed to investigate the changes in surface morphologies after surface modification. The data of water contact angle measurements indicated that the hydrophilicity of PE membranes was remarkably improved after polydopamine coating and heparin immobilization. The results of *in vitro* hemocompatibility test proved that surface heparinization significantly suppressed the adhesion of platelet and enhanced the anticoagulation ability of PE membranes. This work offered a convenient approach to improve the permeability and biocompatibility of inert PE porous membranes for their biomedical and blood-contacting applications.

1. Introduction

Polyethylene (PE) is one of the commonest polymeric materials with nontoxicity, excellent mechanical strength, physical and chemical stability, high porosity and anti-degradation, as well as low cost. PE is widely used in biomedical fields such as blood taking bags, injection syringes, artificial organs and a variety of medical catheters. In recent years, PE porous membrane has been finding more and more applications in bio-separation, such as hemodialysis, hemopheresis and protein filtration. However, the blood compatibility of PE porous membrane as blood-contacting material is not satisfying due to its inert and hydrophobic surface. To improve the hydrophilicity and blood compatibility of PE porous membranes, surface modification often has to been performed before used in biomedical fields.

As is well-known, heparin, an efficient and confessed anticoagulant, is a kind of sulfated polysaccharide that contains sulfonic, sulfoamino and carboxyl groups. The heparin molecules could catalyze the combination of coagulation factor and anticoagulation factor, which plays a dominating role in the blood coagulation resistance properties [1,2]. Hence, surface heparinization is regarded as an effective way to improve the blood compatibility of hydrophobic polymeric membrane [3,4]. To protect the immobilized heparin from denaturation and keep the bioactivity, it is necessary to introduce a hydrophilic spacer between hydrophobic polymeric membrane and heparin in bioconjugation procedure [1,3]. The spacer can be generated by means of radiation grafting technique [5], plasma treatment [6], UV-induced graft [7], etc. yet these methods are somewhat complex with a bad influence on the bulk properties of membrane materials.

Recent bionics researches find that, L-3,4-dihydroxyphenylalanine (DOPA) and its catecholic derivatives, for instance, 3,4-dihydroxyphenethylamine (dopamine) is able to self-polymerize in aqueous solution and form strongly attachment to a wide range of substrates such as rocks, metals, polymers and wood. Based on the strong adhesion behavior of DOPA and dopamine, a new and facile approach for surface modification of solid materials is put forward [8–10]. Li et al. [11] demonstrated that dopamine could self-polymerize and adhere firmly onto the polysulfone (PS) membrane in solution under mild conditions. The as-prepared membranes were used for pervaporative desulfurization and exhibited satisfying separation performance. Recently, we successfully modified polyolefin porous membranes including PE, poly(vinylidene fluoride) (PVDF) and polytetrafluoroethylene (PTFE) via polydopamine coating method. It was found that the hydrophilicity, water perme-

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ability and anti-fouling ability of these membranes were improved significantly [12].

In our recent work, it was found that heparin could be covalently immobilized on the surface of PVDF porous membrane via polyDOPA surface modification technique mentioned above [13], but the detailed surface characteristics of the modified membrane was not reported yet. According to this modification method, the hydrophobic PE porous membranes were surface-modified by the self-polymerization and adhesion of dopamine in this work. Subsequently, heparin was covalently immobilized onto the surface of PE membrane via coupling with polydopamine active layer. The effects of polydopamine coating and heparin immobilization on PE membrane morphology, hydrophilicity, permeability and hemocompatibility were investigated in detail. It is expected that a convenient approach of surface hydrophilization and heparinization for PE porous membranes is established.

2. Experimental

2.1. Materials and reagents

PE porous membrane prepared by stretching method was used as hydrophobic membrane sample for surface modification in this work. The average pore size of PE membrane is 0.5 μm measured using a mercury porosimeter. 3,4-Dihydroxyphenethylamine (dopamine) was also purchased from Sigma–Aldrich and used as received. Tris (hydroxymethyl) aminomethane (Tris) and heparin sodium were obtained from Sinopharm Chemical Reagent Co., Ltd. The platelet-poor plasma (PPP) was supplied by the Blood Center of Zhejiang Province, China. All other chemicals were commercially analytical grade and used without further purification.

2.2. Suface modification of PE porous membranes

Dopamine was dissolved in a mixed solvent of Tris–HCl buffer solution (10 mM, PH 8.5) and ethanol (V_{tris}:$V_{ethanol}$ = 9:1) to obtain dopamine solution (2.0 g/L). The clean and hydrophobic PE membranes were immersed in above-mentioned solution and shaken at 20 °C for 24 h. Then the membranes were taken out and followed by an entire washing with ethanol and deionized water alternately. The resultant membranes were used for characterization and further surface modification.

The above dopamine-coated PE membranes were immersed into heparin solution (PBS buffer solution as solvent, pH 7.4) at 4 °C for a predesigned time (T). The heparin concentration (C) in solution ranged from 0.25 to 2.0 g/L. Then the membranes were taken out and rinsed with deionized water and ethanol entirely in order to remove physically adsorbed heparin. After dried to constant weight in vacuum oven at 40 °C, the resultant modified membranes were used for characterization.

The immobilized amount (IA) of heparin onto the dopamine-coated membranes was determined by measuring the changes in membrane weight after surface modification process. It was calculated by the following equation:

$$IA = \frac{W_h - W_d}{A}$$

where IA represents immobilization amount (μg/cm^2), W_d and W_h (μg) are the weight of the membranes after dopamine coating and heparin immobilizing respectively, A (cm^2) is the surface area of the membrane.

2.3. Characterization of the membrane surface

The chemical compositions in the near surface of PE porous membranes were analyzed by X-ray photoelectron spectroscopy (XPS, PHI 5000C ESCA System) with Mg Kα excitation radiation ($h\nu$ = 1253.6 eV). The whole and narrow scan spectra of all the elements with high resolution were both recorded by RBD 147 interface (RBD Enterprises, USA) through the software. Binding energies were calibrated by using the containment carbon (C_{1s} = 284.7 eV). Attenuated total reflectance Fourier transform infrared spectra (ATR-FTIR, Nicolet NEXUS 670) were used to measure the changes in various functional groups on PE membrane surface before and after modification. The spectra were measured in a wave number range of 4000–600 cm^{-1}.

The surface morphology of membrane was observed by field emitting scanning electronic microscopy (FESEM, SIRION-100, FEI Co., Ltd.). The surfaces of PE porous membrane samples were coated with gold prior to examination. An atomic force microscopy (AFM, SPI3800N, Seiko instrumental) was also employed to analyze the surface topography. The AFM images were acquired in the tapping mode with silicone tip cantilevers. The root mean square (RMS) was used to evaluate the surface roughness of the unmodified and modified PE porous membranes based on 5.0 μm × 5.0 μm scan area. The average of three measurements was reported.

The surface hydrophilicity of membrane was characterized by water contact angle measurement (CA, OCA20, Dataphysics). The water droplet (volume = 1.0 μL) permeation process was recorded by speed optimum video measuring technology. The measurement were performed at 20 °C and 70% relative humidity.

2.4. The permeation experiments

The pure water flux of PE membrane was measured by a home-made filtration apparatus, with a tested membrane area of 4.9 cm^2. Each membrane sample was soaked in 50% ethanol solution for at least 1 h and pre-compacted with deionized water for 10 min at 0.15 MPa before measurement. Then, the pressure was lowered to 0.1 MPa, and the deionized water flux was obtained by measuring the volume of permeate liquid. The J was defined as follows:

$$J = \frac{V}{ST}$$

where J is the deionized water flux (L/m^2 h), V is the volume of the permeated water (L), S and T are the effective filtration area (S = 4.9 cm^2) and tested time (h). Each reported J value was mean of three measurements.

2.5. Platelet adhesion

5 mL anticoagulant human fresh blood was added into centrifuge tube and subsequently centrifuged at l000 rpm for 7–8 min to obtain the top layer of PRP. At room temperature (25 °C), membrane samples (1.0 cm × 1.0 cm) were placed on a piece of clean filter paper. 40 μL PRP was dropped on each sample, maintaining contact for 30 min. Then the samples were carefully rinsed in PBS (PH 7.2) to remove non-firmly adsorbed platelet. After fixed with 1 wt.% glutaraldehyde solution for 30 min, the samples were washed with triple-distilled water several times. The platelet adsorbed on the surface was dehydrated with 30, 40, 50, 60, 70, 80, 90, 100% (v/v) ethanol/water solution for 10–20 min of each in sequence. After natural drying in the air, the resultant samples were stored in dryer and observed with field emitting scanning electronic microscopy (FESEM, SIRION-100, FEI Co., Ltd.).

2.6. Plasma recalcification time (PRT)

The human fresh platelet-poor plasma (PPP, no Ca^{2+}) and 0.025 M $CaCl_2$ aqueous solution were placed in water bath at 37 °C for 30 min. 0.1 mL preheated PPP was droped on each sample in a 24-well cell culture plate and incubated statically at 37 °C for 1 min.