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Zwitterionic glycosyl modified polyethersulfone membranes with enhanced anti-fouling property and blood compatibility

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ABSTRACT

In this study, novel zwitterionic glycosyl modified polyethersulfone (PES) ultrafiltration membranes were prepared via *in-situ* cross-linking polymerization coupled with phase inversion technique, and the following reactions. The membranes were characterized by Fourier transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA), scanning electron microscopy (SEM), ^{1}HNMR spectrum, and static water contact angles (WCAs) measurements. The modified membranes showed excellent anti-fouling property, and the flux recovery ratio could reach almost 100%. Meanwhile, the blood compatibility of the membranes was measured by protein adsorption, platelet adhesion, activated partial thromboplastin time (APTT), and thrombin time (TT). The results implied that the zwitterionic glycosyl modified PES membranes had good anti-fouling property and blood compatibility.

1. Introduction

Polyethersulfone (PES) membrane has already been used in hemodialysis, water purification and also in gas separation for its famous chemical resistance, stability at high temperature, mechanical and film-forming properties [1–4]. However, when blood contacts with the membrane, protein adsorption usually happens on the surface at first and further platelet adhesion and aggregation, leading to subsequent biological responses such as thrombus formation and immune-responses. Therefore it is necessary to modify PES membrane to improve its antifouling property and blood compatibility.

In recent years, many attempts have been carried out to modify PES membrane [5,6], including bulk modification, blending method, coating method, surface-initiated ATRP, and so on. Blending method is the simplest and effective approach to modify the membrane surface and membrane pore surface [7,8]. However, many hydrophilic compounds will be eluted out when they migrate to the membrane surface [9,10]. The recently developed *in-situ* cross-linking polymerization is a novel and facile method to prepare ultrafiltration membrane to aim at effectively reducing the elution [11,12].

Membrane fouling is a process where solutes or particles deposit on membrane surfaces or into membrane pores, which would result in a decrease in the membrane performance. There were many factors which affected the interaction between membrane surface and proteins, such as membrane surface charged character, surface free energy and topological structure, solution environment (e.g. pH, salt concentration, ionic strength, temperature), and protein characters [13,14]. However, there was no direct evidence to explain the correlations between the membrane hydrophilicity, the membrane surface charge density and the fouling, many attempts have been done to modify membranes with enhanced anti-fouling property [15–17]. The hydrophilicity of a polymeric material is usually considered as the key point to decrease fouling and the hydrophilic surfaces tend to create a "hydration shell" when solutions contact with the membrane surfaces [15,16]. In recent years, many investigations [15,18,19] illustrated that zwitterionic polymers have excellent non-fouling ability. It is also generally accepted that the repulsive forces working between the charged surfaces and the co-ions in the feed solution prevented the solute deposition on the membrane surfaces, thus reducing the fouling. In addition, the fouling could be reduced by incorporating ionizable functional groups [15,20,21].

In the present study, we hope to prepare a new kind of membrane which has excellent anti-fouling property and good blood compatibility. Firstly, epoxy group decorated PES membrane was prepared via cross-linked free radical polymerization coupled with liquid–liquid phase separation technique. Owing to the

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environmental friendly nature and multi-hydroxyl structure, carbohydrate-containing compound N-methyl-D-glucamine (NMG) was anchored onto the membrane surface and membrane pore surface by an opening ring reaction. Then 1, 3-propanesultone was used as quaternization agent to convert the NMG into polyzwitterions. BSA solution was used to investigate the membrane anti-fouling property. While, the blood compatibility was investigated by protein adsorption, activated partial thromboplastin time (APTT), thrombin time (TT), and platelet adhesion.

2. Materials and experiment

2.1. Materials

Polyethersulfone (PES, Ultrason E6020P) was obtained from BASF, Germany. Glycidyl methacrylate (GMA, 97%, Aladdin), 1, 3-propanesultone (99%, Aladdin), azoisobutyronitrile (AIBN, 99%, Aladdin), N-methyl-D-glucamine (NMG, 99%, Aladdin), N, N′-methylenebisacrylamide (MBA, 97%, Aladdin), dimethylacetamide (DMAC, 99%, kelong), and dimethyl sulfoxide (DMSO, 99.8%, Aladdin) were used as received. Bovine serum albumin (BSA, fraction V) and bovine serum fibrinogen (FBG) were obtained from Sigma Chemical Co. Micro BCA™ protein assay reagent kits were purchased from PIERCE. APTT and TT reagent kits were obtained from SIEMENS. Deionized water was used throughout the study.

2.2. Preparation of PGMA modified membranes

Polyglycidyl methacrylate (PGMA) was firstly synthesized via *in-situ* cross-linking polymerization of GMA in PES solution. PES (16 wt.%) was dissolved in the DMAC by vigorous stirring until clear homogeneous solution was obtained. After that a mixture of GMA, AIBN and MBA (both the AIBN and MBA amounts were 1 mol.% with respect to the GMA) was added into the solution, the reaction was conducted at 75 °C for 24 h under nitrogen atmosphere. After the reaction, the solution was cooled to room temperature and vacuum degassed, and then was directly prepared into membranes by casting and liquid–liquid phase separation technique, with the membrane thickness of 55 ± 5 μm. The resultant membranes were naturally peeled off the glass plate surfaces and subsequently washed with water at least 12 h to remove the residual solvent, and were stored in water prior to utilization. In this study, three kinds of PGMA modified membranes were prepared with the weight percentages of the PGMA in the casting solutions as 2%, 4%, and 6%, and the membranes were termed as M-G-2, M-G-4 and M-G-6, respectively.

2.3. Chemical modification of the PES/PGMA membranes

Chemical modification of the M-G membranes consisted of two steps, namely the ring-opening reaction with NMG and the quaternization reaction with 1, 3-propanesultone as shown in Scheme 1.

The M-G membranes were firstly dehydrated with increasing alcohol (25%, 50%, 70%, 90% and 100%) successively. Then the membranes were immersed in NMG alcohol solution (the mole ratio of the NMG to the GMA was controlled at 1.1:1) at 30 °C for 24 h, and then washed with adequate water and alcohol to remove the residual NMG. After grafting the NMG, the PGMA changed into PGN, and the membranes were termed as M-N-2, M-N-4 and M-N-6, respectively. To prepare zwitterionic glycosyl modified membranes, the M-N membranes were dehydrated with increasing alcohol (25%, 50%, 70%, 90% and 100%) successively. Then the membranes were placed in 1, 3-propanesultone alcohol solution (the mole ratio of the 1, 3-propanesultone to the PGN was controlled at 1.1: 1) at 30 °C for 48 h. After the reaction was completed, the PGN changed into PGNS and the membranes were washed with adequate water and alcohol to remove the residual 1, 3-propanesultone. The modified membranes were termed as M-S-2, M-S-4, and M-S-6, respectively. In addition, pure PES (16 wt.%) membrane was also prepared as control, and termed as M-0.

2.4. Characterization of the membranes

The chemical compositions of the modified PES membranes were firstly characterized using FTIR spectrophotometer (Nicolet 560, Nicolet Co., American). The samples were prepared by dissolving the membranes in DMSO and casting on potassium bromide (KBr) disks, and then dried by an infrared light. To prepare ^{1}HNMR samples, the M-0, M-G, M-N and M-S membranes were dissolved in deuterated dimethyl sulfoxide (DMSO-D_6), and a Varian UNITY INOVA-400 was used to get the NMR spectra. The cross-linking network was observed in Fig. S1 (see Supporting Information, S1).

The thermal stability of the membranes was investigated from 30 °C to 800 °C at a heating rate of 5 °C/min under a dry nitrogen atmosphere by using thermogravimetric analysis (TGA, TG209F1, Netzsch, Germany) instrument.

To observe the surface and cross-section morphologies, the membranes were frozen in liquid nitrogen, broken and sputtered with gold layers, and the scanning electron microscopy (SEM) pictures were observed using a JSM-7500F (JEOL, Japan) with the voltage of 5 kV. The PGMA dissolved in DMSO to form the microgel particles and these would be observed in Fig. S2 (see Supporting Information, S2).

2.5. Water contact angle

The hydrophilicity of the membranes was characterized by water contact angle measurement using a contact angle goniometer (OCA20, Dataphysics, Germany) equipped with video capture. A piece of 1 × 1 cm^2 membrane was attached on a glass slide and mounted on the goniometer. At least eight measurements were averaged to get a reliable value, and the measurement error was ±3°.

2.6. Permeation properties

Water flux was measured at room temperature by using the apparatus as described in a previous study [22]. A dead-end ultrafiltration (UF) cell with an effective membrane area of 3.9 cm^2 was used. In order to get steady filtration, the test membranes were pre-compacted each time at the pressure of 0.14 MPa by the feed solutions for 20 min. After that, the fluxes were tested at 0.07 MPa. An air compressor supplied the pressure. The water flux was calculated using Eq. (1).

$$\text{Flux}\ (\text{mL/m}^2\ \text{h mmHg}) = \text{V/S} \cdot \text{T} \cdot \text{P} \quad (1)$$

where V (mL) is the volume of the permeated solution; S (m^2) is the effective membrane area; t (h) is the time of the solution collecting; and P (mmHg) is the pressure applied to the membrane.

To investigate the anti-fouling property of the M-0, M-N, M-S membranes, bovine serum albumin (BSA) solution was used, for which BSA was dissolved in isotonic phosphate-buffered saline solution (PBS, pH 7.4) with a concentration of 1.0 mg/mL. The permeation experiments were carried out as follows:

(1) the test membrane was pre-compacted at 0.14 MPa about 20 min by deionized water; (2) the water flux was measured at 0.07 MPa; (3) the membrane was pre-compacted at 0.14 MPa about 20 min by the BSA solution flow; (4) the flux of the BSA solution was measured at 0.07 MPa; and (5) the used membrane