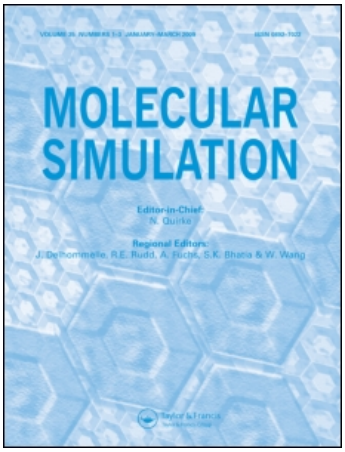

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Facilitated Transport of Lipophilic Toxins Through Polysulfone Membrane using Albumin as a Carrier

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Facilitated Transport of Lipophilic Toxins Through Polysulfone Membrane using Albumin as a Carrier

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The chloromethylated/aminated asymmetric polysulfone ultrafiltration membrane with finger pores was made by the phase inversion process. The albumin-fixed facilitated transport membrane was prepared by cross-linking bovine serum albumin (BSA) into the membrane with 1,1′-carbonyldiimidazole (CDI). It was used to remove a lipophilic toxin, bilirubin, from the simulation plasma. The experiment results showed that the transfer rate of bilirubin was obviously enhanced after fixing albumin into the high-flux asymmetric membrane. The clearance of bilirubin was 43.7%. In addition, the effect of membrane thickness on facilitated transport was discussed.

Keywords: Lipophilic toxins; Facilitated transport; Fixed-site; Albumin

INTRODUCTION

Blood detoxification is of therapeutic interest for various diseases caused by exogenous or endogenous intoxications (drug intoxications, renal and liver failure, metabolic disorders, and others) [1]. The removal of water-soluble substances is well established by dialysis procedure. However, an unsolved problem is the low dialyzability of lipophilic toxins. Such toxins have been shown to be responsible for the induction of hepatic encephalopathy in chronic liver diseases as well as of hepatic coma in acute hepatic failure. Because of their affinity to nondialyzable albumin, these toxins are not able to permeate into the dialysate solution [2]. Therefore, dialysis and ultrafiltration are not sufficient methods to remove the above-described toxins. Alternative methods using hemoperfusion over adsorbents are effective but are not specific enough, because they also remove essential substances like hormones which are linked to their own transport proteins.

Facilitated transport is a separation process by which an active chemical carrier will selectively bind with a permeate, transport it across a film and release the permeate at the other boundary [3]. It was first accomplished in liquid membranes, in which two aqueous phases were separated by an organic solvent containing carrier molecules. These membranes displayed a high selectivity due to a specific complexation (hydrogen bonding, electrostatic or hydrophobic interactions) of the solute by the selective carrier, but it suffered from several technological problems such as the low fluxes, the leaching of carriers and poor stability [4]. In an effort to overcome the problems of the liquid membranes, polymeric facilitated transport membranes have more recently been attracting attention on account of excellent stability as well as both high permeability and selectivity [5].

In the present study, the chloromethylated/aminated asymmetric polysulfone UF membrane with finger pores is made by the phase inversion process. Bovine serum albumin (BSA) molecules are immobilized as carriers of facilitated transport membrane, using 1,1′-carbonyldiimidazole (CDI) as a crosslinking reagent. The BSA-fixed membrane is used to remove the bilirubin from the simulation plasma, mixture solution of BSA and bilirubin. The experiment results show the transfer rate of lipophilic toxins is obviously enhanced after fixing albumin into the high-flux asymmetric membrane. The clearance of lipophilic toxins is 43.7%.

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THEORETICAL FOUNDATION

Based on the biochemical analysis, albumin molecules are able to exchange their ligands over short distance and, therefore, these ligands can cross the dense permselective skin of asymmetric membrane if acceptor albumin molecules are present inside the membrane. In this process, toxins are facilitated transport by albumin in the pores of support layer. The facilitated transport mechanism of the molecule in the asymmetric membrane will be reported later.

EXPERIMENTAL

Materials

Polysufone was a gift from Tianjin Institute of Textile Science and Technology (Tianjin, China). CDI was obtained from the Sigma Chemical Company (USA). BSA was purchased from Beijing Chemical Reagent Company (Beijing, China). Bilirubin was provided by Shanghai Weihui Chemical Factory (Shanghai, China). Acetone, hexamethylendiamine, dimethylacetamide, polyethylene glycol-1000 and metacetonic acid were obtained from Tianjin Chemical Reagent Company (Tianjin, China).

Membrane Preparation

Preparation of Chloromethylated Polysulfone Membrane

Chloromethylated polysulfone was prepared according to procedure described by Hao *et al.* using polysulfone [6].

Polymer solutions were prepared using chloromethylated polysulfone as the base polymer, dimethylacetamide as solvent, polyethylene glycol-1000 as additive and metacetonic acid aqueous solution (10 vol%) as a non-solvent. To synthesize flat membranes, polymer solutions films were cast on a glass plate with a finely polished glass rod. The temperature of glass plate was kept at 70°C. The cast solution was exposed to an atmosphere for 15–60 s, and then immersed in a non-solvent bath where the polymer precipitation occurs and the membrane is formed. Then the membrane was washed with deionized water for 24 h.

Preparation of Aminated Polysulfone Membrane

One chloromethylated polysulfone membrane disk (47 mm diameter) was shaken for 5 h at 313 K in 10 ml of 0.2 M hexamethylendiamine solution. After amination, the membrane was washed five times with deionized water at room temperature.

The SEM micrographs given in Fig. 1 shows the surface and cross section of aminated polysulfone membrane. As clearly seen here, the membrane indicates an asymmetric and open pore structure, which may lead to high internal surface area with low diffusive resistance.

Preparation of BSA-fixed Membrane

One aminated polysulfone membrane disk was shaken for 1 h at room temperature in a solution of 100 mg CDI per 10 ml acetone. They were then rinsed with acetone three times in 30 min and dried. The CDI-activated membrane was stored in a dry atmosphere until further use to avoid hydrolysis of the imidazole groups.

One CDI-activated membrane disk was given in 10 ml of 1% BSA in 0.1 M bicarbonate buffer pH 8.4 and shaken overnight at room temperature. Afterwards the membrane was washed with 0.5 M NaCl and water extensively.

The final membrane thickness was measured by a micrometer (least count 12 μm). The amount of BSA bound was determined by the variation of the absorbance of the BSA solution at 280 nm before and after cross-linking.

Transport Experiments

The experimental apparatus was shown in Fig. 2.

The BSA-fixed membrane was put on the joint mouth of diffusion cell, with the permselective layer

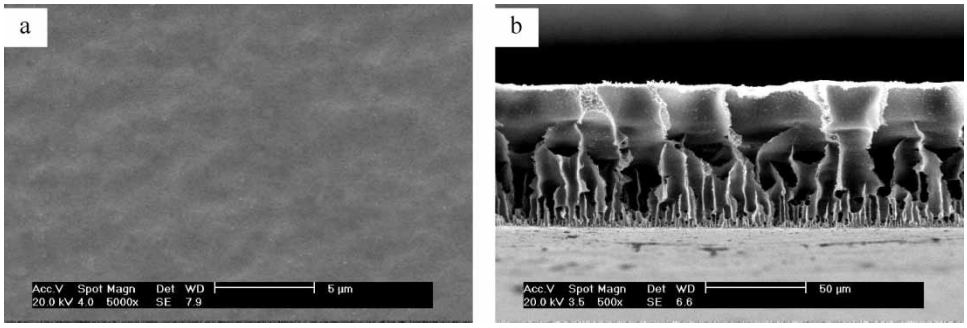

FIGURE 1 SEM of aminated polysulfone asymmetric membranes. (a) Surface; (b) cross section.

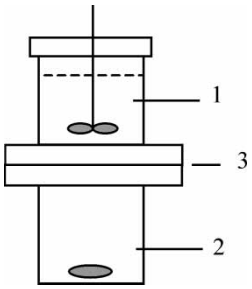

FIGURE 2 Schematic diagram of diffusion experiment. (1) BSA solution; (2) mixture solution of bilirubin and albumin; (3) facilitated transport membrane.

towards the bottom, and the thicker microporous support layer towards the top. The bottom cell contained the mixture solution of bilirubin and albumin, the other was filled with albumin solution. Thus the bilirubin molecules were facilitated transport by the albumin molecules in the membrane under the driving force of concentration gradient. At a given time interval, the solution concentration of the upper cell was determined spectrophotometrically by measuring the absorption at 460 nm.

RESULTS AND DISCUSSION

Effect of Glass Plate Temperature on Membrane Structure

The biological carrier cannot be immobilized perfectly into the pores of thicker microporous layer of traditional asymmetric membranes due to the thin dense skin still exiting at the bottom of microporous support layer. We increased the temperature of the glass plate to eliminate the thin dense skin at the bottom of microporous layer according to the network of polymer and micelle aggregate of polymer being sensitive to temperature [7]. The SEM of aminated polysulfone membranes is shown in Fig. 3 where the backs of membranes are observed. When the temperature of glass plate was kept at 70°C pores at the bottom were exposed so that the flux was large and carriers could be fixed in the pore easily. The pores at the bottom were closed when the glass plate was kept at room temperature.

Comparison of Clearance between BSA-fixed Membrane and Blank Membrane

Comparison of clearance between blank membrane (no BSA-fixed membrane) and BSA-fixed membrane is shown in Fig. 4. The clearance is defined as

$$\mathrm{CL} = (1 - \frac{C_A}{C_{A0}}) \times 100\%$$

where C_{A0} and C_A are the initial concentration of bilirubin and bilirubin concentration in the mixture solution of BSA and bilirubin, respectively.

It can be seen that the clearance of bilirubin is enhanced greatly after BSA is fixed into the pores of membranes. The clearance of bilirubin is 43.7% by BSA facilitated transport membrane, and yet 3.34% by blank membrane. It proves that bilirubin molecules in the BSA solution are facilitated transport over the dense skin of the membrane by the BSA molecules in the pores of support layer.

Effect of Membrane Thickness on Facilitated Transport

Figure 5 shows the effect of membrane thickness. The clearance of bilirubin of 120 μm thickness membrane is the highest, next is of 137 μm thickness, and the last is of 84 μm thickness. We offer two reasons for the results. On the one hand, the flux decreases with increasing membrane thickness because the diffusion rate in the membrane is inversely proportional to the membrane thickness. On the other hand, the amount of carriers increases with the membrane thickness due to membrane structures almost regardless of the thickness, and the facilitation factor increases with increasing amount of carriers.

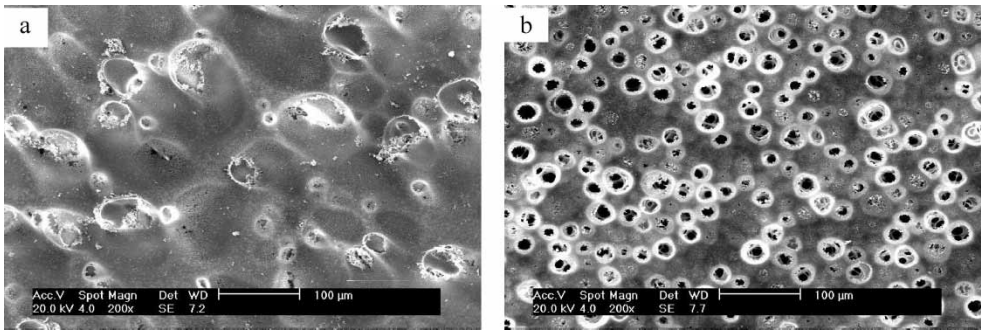

FIGURE 3 SEM of back of aminated polysulfone asymmetric membranes. (a) When the glass plate was kept at room temperature; (b) when the glass plate was kept at 70°C.

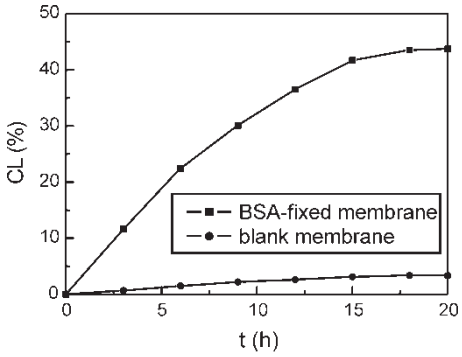

FIGURE 4 Comparison of CL between blank membrane and facilitated transport membrane (membrane thickness: 120 μm; $C_{A0} = 20$ μmol/l).

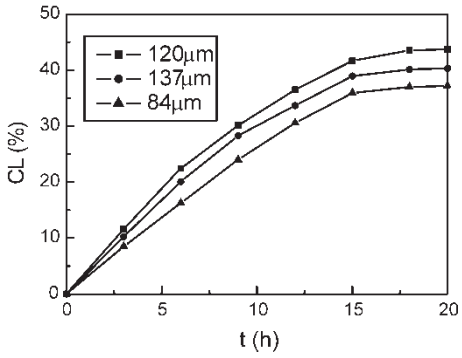

FIGURE 5 The effect of membrane thickness on facilitated transport ($C_{A0} = 20$ μmol/l).

CONCLUSIONS

From the scanning electron micrographs of the aminated membranes, finger pores in the support layer were observed. The surface was very fine and close, and at the bottom pores were exposed. These membrane can be used to fix the carrier molecules.

BSA-fixed membrane can well remove the lipophilic toxin, bilirubin, from the albumin solution. The clearance of bilirubin was 43.7%.

Acknowledgements

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