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CORRELATION BETWEEN STRUCTURE AND TRANSPORT PROPERTIES OF POLYMERIC MEMBRANES FOR IMMUNOISOLATION

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Abstract

Laboratory-made asymmetric polyurethane membranes designed for immunoisolation were investigated. Two types of EK and ES membranes were prepared in different spinning conditions.

The membrane structure was characterised by the skin pore radius measurements using differential scanning calorimetry (DSC). Diffusive transport properties of membranes were determined by in vitro method for albumin and creatinine. The scanning electron microscopy (SEM) was applied to study the morphology of membranes.

It has been found that the DSC technique is a useful tool for the evaluation of pore radii in the skin layer for PU membranes. Calculated pore radii were in the range from 1.95 to 2.47 nm for the EK and ES types. A correlation between the skin pore radii and the transport properties was not found in this case of investigated membranes. However, the transport properties data can serve for the estimation of selectivity of membranes. Thus, the selectivity of membranes for solutes of various molecular size was estimated from the D_m/D_w ratio of diffusion coefficients for albumin and creatinine. The SEM micrographs reveal the finger-like internal structure of capillary membranes, as well as various skin thickness.

Keywords: differential scanning calorimetry, diffusive permeability, polyurethane membranes, scanning electron microscopy

Introduction

Polymeric semipermeable membranes are necessary for immunoisolation [1], where the transplanted tissues or cells are encapsulated in a membrane in order to protect it from immune rejection. The aim of the transplanted foreign cells or tissue is to replace a lost function in host tissues due to disease or degeneration. Cell therapy is a promising method for the treatment of a variety of diseases, including diabetes, liver dysfunction, haemophilia B, as well as disorders in the central nervous system (chronic pain syndrome) and neurodegenerative disorders such as Parkinson's and Alzheimer's diseases [1, 2].

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The selectively permeable membranes are formulated to allow small molecules such as nutrients to freely permeate into the encapsulated environment while hindering larger molecules and cells of the host immune system [1–3].

Recently, it has been proposed that new types of semipermeable biocompatible membranes based on PU polymers can be applied for the cell encapsulation [4–5]. Therefore, problems of characterization of membranes have to be solved from both the preparation and the application points of view.

In our earlier work [6] we applied the method based on differential scanning calorimetry recently proposed by Ishikiriyama *et al*. [7–9] to determine the pore size of capillary membranes.

This work is a continuation of our earlier research concerning characterization of the structure of polymeric membranes for immunoisolation. A correlation between the structure and transport properties of laboratory-made asymmetric polyurethane membranes was investigated.

Experimental

Materials

Aliphatic polyurethanes were synthesised by a two-step reaction, then the hollow fiber membranes were prepared by the phase inversion using the spinning method. The phase inversion process involves a ternary system comprised of a polymer, solvent and non-solvent. DMF and water were used as solvent and non-solvent, respectively.

Two types of polyurethane membranes were investigated: EK and ES types where the spinning solution and the spinning conditions were modified, respectively.

The characteristics of obtained membranes are given in Table 1.

Table 1 Characteristics of polyurethane membranes

Hollow fiber membrane	Wall thickness/μm	Inner diameter/μm
EK0	148	750
EK1	72	925
EK2	146	940
EK3	122	862
ES1	131	1032
ES2	168	662
ES3	229	953

Procedures

DSC measurements

The thermoanalytical measurements were carried out with a Perkin Elmer DSC 7 equipped with a cooling accessory CCA 7. The DSC 7 instrument was calibrated us-

ing the deionized water class RO (reverse osmosis) of conductivity 18.2 MΩ×cm, and pure indium metal as standards.

The hollow fibres were washed several times by isopropanol, then by deionized water class RO and maintained under reduced pressure during 2 h.

Then samples were securely wiped to remove the water from the capillary lumen, cut in pieces of about 4 mm and put into the DSC volatile sample pan.

The following cycle was proposed: sample was cooled from 30 to –50°C with a cooling rate of 50°C min^{-1}; maintained at –50°C for 10 min, heated from –50 to 10°C with a heating rate of 1°C min^{-1} and cooled from 10 to –50°C with a cooling rate of 3°C min^{-1}.

Diffusive transport measurements

The diffusive permeability of membranes for small and large solutes was evaluated using the method described by Granicka *et al*. [12].

Solutes of different size molecules, i.e. albumin (M=69000), and creatinine (M=113), have been chosen for the test.

Single hollow fibers were stored for 30 min in 70% ethanol and 30 min in sterile distilled water, filled with the test solute solution in saline, sealed on both ends, and immersed in the beaker with the continuously mixed saline. The samples were collected from the beaker at appropriate time intervals to measure solute concentrations.

Concentrations of albumin and creatinine were determined spectrophotometrically at 280 and 235 nm respectively using a Shimadzu UV-160 spectrophotometer.

SEM observation

The structures of membranes were observed by using scanning electron microscopy (SEM) (Jeol JSM-S1). The membranes were immersed in liquid nitrogen before observation.

Results and discussion

The capillary membrane structure, i.e. the capillary cross-section and the cross-section sector is shown in Figs 1 and 2, respectively. The capillary membranes are asymmetric with a thin skin layer (Fig. 1). The finger-like structure and various skin thickness was observed for all polyurethane membranes.

The skin pore radii for the polyurethane membranes having asymmetric structure with a thin skin layer were determined from the DSC cooling curve [6]. The method is based on calorimetric analysis of a liquid–solid transition (e.g. of pure water) in a liquid-filled porous materials, originally developed by Ishikiriyama *et al.* [7–9]. They proposed a new method for determining the pore size distribution in porous materials from the freezing or melting curves of freezable pore water by using DSC technique.

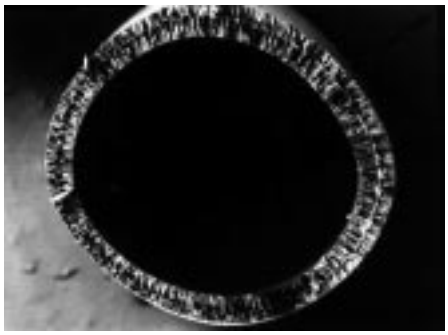

Fig. 1 Scanning electron micrograph of EK1 membrane (cross-section); magnification: 70×

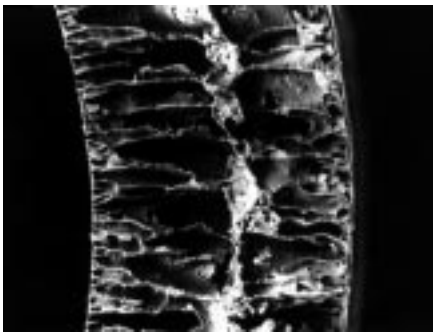

Fig. 2 Scanning electron micrograph of EK1 membrane (cross-section sector); magnification: 600×

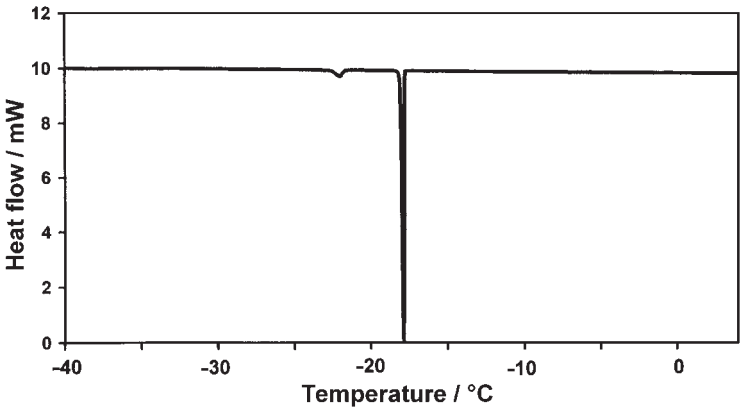

Fig. 3 DSC cooling curve for EK2 polyurethane membrane. Cooling rate: 3°C min^{-1}

Assuming (1) a cylindrical pore model and (2) that the layer thickness of non-freezable pore water is 1.0 nm, the pore radius R can be expressed in the case of freezing by the following equation:

$$R = \frac{56.36}{\Delta T} + 0.1\,(\mathrm{nm}) \tag{1}$$

where $\Delta T(=T-T_0)$ is the depression of freezing temperature of the freezable pore water, T_0 is the triple point of the bulk water, and T is the freezing temperature.

The DSC cooling curve for the EK3 membrane is shown in Fig. 3, as an example. Two exothermic peaks can be distinguished: the first peak at lower temperatures is attributed to the freezing of water confined in membrane pores; the second peak, at higher temperatures, is assigned to the freezing of bulk water [6–9]. Thus, the first peak corresponds to the pore size distribution, and the pore radii are calculated from Eq. (1).

The results i.e. the range of pore radii in the skin layer and the peak pore radius $r_{p\,DSC}$ are given in Table 2.

Table 2 Skin pore radii of membranes based on DSC curves

Membrane	Pore radii/nm (range)	$r_{p\,DSC}$/nm
EK0	2.31–2.47	2.39
EK1	2.36–2.47	2.31
EK2	1.99–2.15	2.08
EK3	1.95–2.08	2.04
ES1	2.37–2.48	2.39
ES2	2.24–2.34	2.33
ES3	2.26–2.32	2.30

The calculated skin pore radii of polyurethane membranes ranged from 1.95 to 2.48 nm. Thus, it has been found that all membranes are similar, if the skin pore radii is concerned. It is known that the permeation of the low and large solutes through the membrane is controlled by the skin layer.

Table 3 Transport properties of membranes for large and small solutes

Membrane	Albumin		Creatinine	
	Diffusive permeability P/ml min^{-1} m^{-2}	Diffusion coefficient ratio D_m/D_w	Diffusive permeability P/ml min^{-1} m^{-2}	Diffusion coefficient ratio D_m/D_w
EK0	1.25±0.32	0.051±0.013	35.94±10.65	0.106±0.031
EK1	2.75±0.01	0.054±0.001	41.21±4.57	0.059±0.007
EK2	0.36±0.11	0.014±0.004	8.74±0.19	0.026±0.001
EK3	0.44±0.01	0.015±0.002	40.29±2.09	0.098±0.005
ES1	3.42±0.36	0.123±0.130	45.37±5.69	0.120±0.015
ES2	0.95±0.17	0.025±0.008	30.17±3.57	0.102±0.012
ES3	2.45±1.39	0.153±0.087	30.28±12.41	0.122±0.028

The transport properties of polyurethane membranes were characterized in vitro by using albumin and creatinine. The results of diffusive permeability for large and small solutes are given in Table 3.

With regard to transport properties it is required to form of a highly selective membrane – i.e. a membrane with high diffusive selective permeability in the low molecular mass nutrient range and low diffusive permeability in the high molecular mass immunoglobulin range.

The permeability of membranes having different wall thickness has been compared using the diffusion coefficient ratio D_m/D_w (Table 3). It is defined as the ratio of diffusion coefficients of a solute in membrane and in water.

It has been observed that various transport properties are not correlated with the skin pore radii which are rather uniform for all membranes. However, information on the selectivity of membranes can be obtained from the transport properties. Thus, the best selectivity is observed for the EK3 membrane amongst EK types and the ES2 amongst ES types. The respective D_m/D_w are 0.015 for albumin and 0.098 for creatinine in the case of EK3, and 0.025 for albumin and 0.102 for creatinine in the case of ES2.

Conclusions

SEM micrograph reveal the finger-like internal structure of capillary membranes, as well as various skin thickness.

The DSC technique seems to be useful tool for the evaluation of pore radii in the skin layer for PU membranes. Calculated pore radii were in the range from 1.95 to 2.47 nm for EK and ES types investigated.

The selectivity of membranes for solutes of various molecular size can be estimated from the D_m/D_w ratio of diffusion coefficients.

More detailed and complementary investigation is still needed.

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