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THERMOANALYTICAL STUDIES OF POLYMERIC MEMBRANES FOR IMMUNOISOLATION

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Abstract

Preliminary studies concerning characterization of the structure of polymeric membranes for immunoisolation are reported. Laboratory-made cellulosic and polyurethane membranes for immunoisolation were investigated. Differential scanning calorimetry (DSC) was applied to determine the membrane structure, e.g. the pore diameter. The thermoanalytical measurements were carried out with a Perkin Elmer DSC 7 equipped with a CCA 7 cooling accessory. Diffusive transport across the hollow fiber membrane was evaluated *in vitro* by using albumin, creatinine and vitamin B_{12}. It was concluded that the DSC method is a useful tool for characterization of polymeric membranes for immunoisolation. Methodology, including experimental conditions, is proposed for capillary membranes.

Keywords: differential scanning calorimetry, immunoisolation, polymeric membranes

Introduction

The transplantation of cells as a method of treatment of patients with an organ deficiency has been extensively investigated for several years [1–6]. This method may be particularly successful in the treatment of diabetes by the implantation of pancreatic cells into diabetic patients. However, rejection by the immune system of the recipient comprises a major limitation to this method. To overcome this problem, it has been proposed that the implanted cells should be separated from the immunological system of the recipient by means of an artificial semipermeable membrane.

The biological efficiency of such a 'bioartificial pancreas' depends largely on the properties of the artificial membrane, which must be biocompatible and nondegradable in a biological environment. Moreover, such a membrane must allow the effective transport of nutrients and metabolites, while preventing the passage of antibodies and immune cells. A knowledge of the structure of the immunoisolating membrane is therefore crucial for its performance [7, 8].

In earlier work [9], we applied the method based on differential scanning calorimetry (DSC) recently proposed by Ishikiriyama *et al.* [10–12] to determine the pore diameter of a commercial cellulose capillary membrane.

In the present work, laboratory-made cellulosic and polyurethane membranes for immunoisolation were investigated by using DSC.

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Experimental

Materials

The following polymeric membranes were investigated: OC: cellulose acetate CA 398-10 (Eastman); PU-E2: polyurethane Elastollan 1164D (BASF); PU-E01: polyurethane Elastollan 1164D (BASF) modified by cellulose acetate CA 398-6 (Eastman).

The hollow fiber membranes were prepared by a phase inversion method in the Institute of Biocybernetics and Biomedical Engineering PAS.

Table 1 Characteristics of the hollow fiber membranes

Hollow fiber membrane	Outer diameter/μm	Wall thickness/μm
OC	924	45
PU-E2	850	75
PU-E01	650	100

Procedures

DSC measurements

The thermoanalytical measurements were carried out with a Perkin Elmer DSC 7 equipped with a CCA 7 cooling accessory.

The material (hollow fibres measuring about 10 cm) was washed several times with isopropanol, then with deionized water class RO and maintained under reduced pressure during 2 h.

The samples were thoroughly wiped to remove external water, cut into pieces measuring about 4 mm and placed into the DSC volatile sample pan.

Before measurements, the DSC 7 was calibrated. Deionized water class RO (of specific resistivity 18.2 MΩ cm) and indium were used as standards.

The following cycle was proposed: the sample was cooled from 20 to –40°C at a cooling rate of 100°C min^{-1}, heated from –40 to 20°C at a heating rate of 1°C min^{-1}, and cooled from 20 to –40°C at a cooling rate of 1°C min^{-1}.

Diffusive transport measurements

The diffusive permeability of membranes for small and large solutes was evaluated by using the method described by Granicka *et al.* [13].

In the tests, solutes involving molecules of different sizes were chosen i.e. albumin (M=69 000), vitamin B_{12} (M=1355) and creatinine (M=113).

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

The concentrations of albumin, creatinine and vitamin B_{12} were determined spectrophotometrically at 280, 235 and 361 nm, respectively, using a Shimadzu UV-160 spectrophotometer.

Scanning electron microscope (SEM) observations

Before observations, the membranes were immersed in liquid nitrogen.

The cross-sections of the membranes were observed by using a Jeol JSM-S1 (Japan) SEM.

Results and discussion

Figures 1 and 2 show the cross-sections of the OC and the PU-E2 hollow fibers, respectively, as observed by SEM. The cellulose membrane exhibits a very fine spongy structure, whereas the polyurethane membrane reveals a finger-like structure.

Fig. 1 Scanning electron micrograph of hollow fiber OC membrane (cross-section). Magnification ×1000

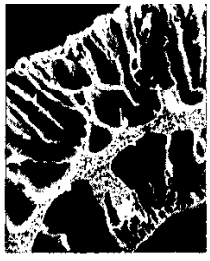

Fig. 2 Scanning electron micrograph of hollow fiber PU-E2 membrane (cross-section). Magnification ×3000

The DSC heating curve for the OC membrane is shown in Fig. 3. Two endothermic peaks were observed. The first peak, on the low-temperature side, is assigned to the melting of ice inside the pores of the membrane, and the second, dual peak, on this high-temperature side, is due to the melting of ice adhering to the membrane wall and/or in the fiber lumen. From the DSC curve, the pore radii are calculated according to the method developed by Ishikiriyama *et al.* [10–12]. They proposed a

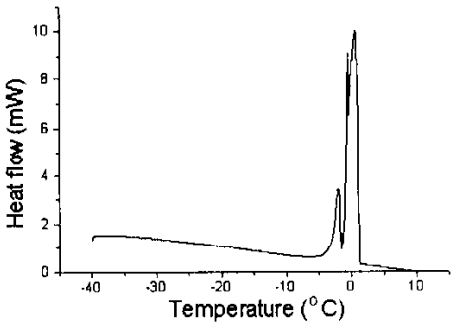

Fig. 3 DSC heating curve of OC membrane

new method for determining the pore size distribution in porous materials from the freezing or melting curves of freezable pore water by using a DSC technique.

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 by the following equations:

$$R = \frac{33.3}{\Delta T} + 0.68 \qquad \text{(in the case of melting)} \tag{1}$$

$$R = \frac{56.36}{\Delta T} + 0.1 \qquad \text{(in the case of freezing)} \tag{2}$$

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

The pore radii of the OC membrane calculated from Eq. (1) range from 7.6 to 21.5 nm (Table 2).

Table 2 Calculated pore radii of membranes

Membrane	Pore radii range/nm
OC	7.6–21.5
PU-E2	2.5–3.2
PU-E01	4.8–6.2

For the polyurethane membranes, having an asymmetric structure with a thin skin layer, the pore radii were calculated from the cooling curve (cf. Eq. (2). An example of the DSC cooling curve for the PU-E01 membrane is shown in Fig. 4. For better peak separation, we applied a low cooling rate, i.e. 0.5°C min^{-1}. The results of the calculations are given in Table 2.

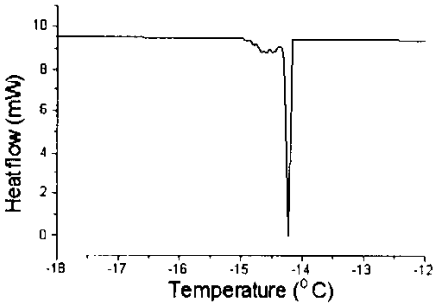

Fig. 4 DSC cooling curve of PU-E01 membrane

The DSC results obtained were compared with the permeability characteristics of the investigated membranes for immunoisolation.

Table 3 lists the diffusive permeability results for small and large solutes.

Table 3 Diffusive permeability of membranes for small and large solutes

Membrane	Diffusive permeability, P/ml min^{-1} m^{-2}		
	Albumin	Vitamin B_{12}	Creatinine
OC	0.31	23.7	5.6
PU-E01	3.2	5.6	4.3
PU E2	0.059	0.73	7.5

The OC membrane has good selectivity. Its permeability for low solutes such as vitamin B_{12} is higher than for those for large solutes e.g. albumin.

The permeability of the PU-E01 membrane for large and small solutes is comparable. This may be explained by the presence of defects in the skin layer of the membrane [14].

In the case of the PU-E2 membrane, the permeability of albumin is lower than that for the OC membrane, proving that the former has smaller pores than those of the latter. Moreover, the PU-E2 membrane has a better permeability for low molecules, e.g. vitamin B_{12} and creatinine, than for a large molecule such as albumin. This proves the good selective property of this membrane.

These results seem to prove that a correlation exists between the membrane structure determined by the DSC method and its permeability characteristics. However, the evaluation of such a correlation, especially for asymmetric membranes, necessitates further investigation.

Conclusions

The method proposed by Ishikiriyama *et al.* was applied to determine the structure of hollow fiber polymeric membranes for immunoisolation.

The DSC results obtained roughly correlate with the diffusive permeability data.

It was concluded that the DSC method is a useful tool for the characterization of polymeric membranes for immunoisolation.

Further studies are planned as concerns an asymmetric polyurethane membrane for immunoisolation.

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