

Transport Properties of New Copolyether-Ester and Copolyether-Urethane Dialysis Membranes

INTRODUCTION

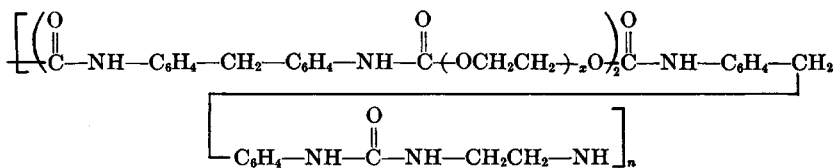
Polymeric materials suitable for hemodialysis membranes should be permeable, mechanically strong, and compatible with blood. Moreover, as the undesirable, toxic solutes in the blood are more clearly defined, more selective membranes are needed for improved dialysis treatment of uremic patients. One of the major toxic solutes to be passed by the membrane and eliminated from the blood is lipid-soluble urea, while lipid-insoluble glucose should be retained. Hydrophilic cellulosic membranes currently used for hemodialysis in general differentiate between solutes by molecular size. We are developing membrane materials in which selectivity also depends on solubility differences between solutes.

Our research program on the development of such membrane materials has included both the synthesis and study of the aqueous transport properties of several block copolymers. These copolymers consisted of hydrophilic segments, to impart the requisite water absorption and transport properties, and of hydrophobic or lipid-like segments, to impart solute selectivity and mechanical strength to the swollen films. Our preliminary results on the structure-transport relationships in a copolyether-ester system, consisting of hydrophobic poly(ethylene terephthalate) and hydrophilic polyoxyethylene glycol segments, have been described previously.¹ By varying the size of the ether segment, the transport properties of this copolymer can be examined as a function of the varying chemical and physical properties of the system, thereby indicating what factors favor high flow rates without loss of solute selectivity. To complete these early studies, we now report our results on the flow properties of another member of this copolyether-ester series, CPE 1000. Finally, we show how these initial findings have been used to develop a new copolyether-urethane material with improved transport properties.

EXPERIMENTAL

The copolyether-esters, prepared by transesterification of dimethyl terephthalate with polyoxyethylene glycol and ethylene glycol, have been described previously.¹ The material using the polyoxyethylene glycol, Union Carbide Corp. Carbowax 1000, is designated CPE 1000. Some data for the copolyether-ester CPE 1540, with the higher molecular weight polyoxyethylene glycol (Carbowax 1540), are included for comparison. In both materials, the molar ratio of ethylene glycol to polyoxyethylene glycol was 7/3. The weight per cent of polyether in CPE 1000 and CPE 1540 was 62.7% and 70.7%, respectively.

The copolyether-urethane was prepared in a two-step synthesis. First, the polyoxyethylene glycol (Carbowax 1540) was end-capped with methylene bis(4-phenylisocyanate) by heating both materials together in dimethyl sulfoxide (DMSO) for two hours at 90°C. Second, the resultant macrodiisocyanate was chain extended with ethylenediamine by the slow addition of the diamine in DMSO at 30–40°C. By pouring the resulting DMSO mixture into water, the copolyether-urethane was precipitated from solution and then isolated. A second precipitation was from dimethylformamide. When the starting isocyanate-to-glycol ratio was 2/1 or 3/2, the resultant copolymers produced useful water-swollen films. Only the more highly swollen 3/2 material (77.5% by weight polyether) designated CPU 1540-2-e was examined in this work:



CPU 1540-2-e
2439

The material based on a 5/4 ratio did not yield a useful polymer; a 2/1 polymer based on Carbowax 4000 produced water-swollen films that ruptured easily.

Results for mechanical property measurements for water-swollen samples of CPE 1000, CPE 1540, and CPU 1540-2-e are given in Table I. For comparison, data for cuprophane, the completely hydrophilic cellulose film currently used in the Kiel hemodialyzer, are also included in this table.

TABLE I
Water Absorption Data, Flow Parameters,^a and Mechanical Properties^b

	CPE 1000	CPE 1540	CPU 1540-2-e	Cuprophane
ϕ_w , cc water/cc wet membrane	0.524	0.664	0.805	0.676
Polymer, g/cc wet membrane	0.638	0.464	0.391	0.664
L_p , cm ³ /dyne-sec glucose	— ^c	4.4×10^{-14}	7.7×10^{-14}	9.1×10^{-14}
ω , moles/dyne-sec ethyl carbamate	10.1×10^{-17}	15.3×10^{-17}	22.7×10^{-17}	5.8×10^{-17}
glucose	1.9×10^{-17}	4.2×10^{-17}	6.2×10^{-17}	2.4×10^{-17}
ethyl carbamate/ glucose	5.3	3.6	3.6	2.4
Tensile strength, ^b psi	726	256	321	3630
Elongation, ^b %	268	107	826	17

^a The average solute concentration is 0.05 *M*; L_p and ω are normalized to 1 cm thickness and unit membrane area, 1 cm².

^b Determined for water-swollen membranes.

^c Wet membrane deformed under pressure.

All CPE films were prepared by solution casting from methylene chloride.¹ Those of CPU 1540-2-e were cast from DMF solution (10% by weight) and dried at 70°C. All water-swollen films were generally 1 to 3 mils thick. The procedures for determining the water absorption properties and flow parameters of films have been described previously.^{1,2} The filtration coefficient L_p is defined as the volume flow (cc/sec per unit membrane area) per unit pressure difference (dynes/cm²) across the membrane at zero osmotic pressure difference:

$$L_p = (J_v/\Delta P)_{\Delta\pi=0}.$$

The solute permeability coefficient ω is the solute flow (moles of solute passing through unit membrane area per unit time) per unit osmotic pressure difference (dynes/cm²) at zero volume flow:

$$\omega = (J_s/\Delta\pi)_{J_v=0}.$$

RESULTS AND DISCUSSION

To increase aqueous transport of both solvent and solute across a swollen polymeric membrane, it is generally necessary to increase the water content ϕ_w , or overall hydrophilic character of the membrane material. However, this also results in loss of solute selectivity or differentiation which depends on the type and amount of polymer present in the water-swollen membrane. From our previous results on water absorption properties and solute solubilities within the copolyether-ester system,¹ the more hydrophilic CPE 1540 would be expected to be generally more permeable but less selective to solute type than the CPE 1000. Our current study of flow parameters using two very different types of solutes, lipid-insoluble glucose and lipid-soluble ethyl carbamate, con-

firms this prediction (Table 1). Within the CPE polymer system, the relative magnitudes of the solute permeability coefficients ω for each solute are still determined primarily by the total hydrophilic character of the swollen polymer, whereas the selectivity, or ratio of ω values for each polymeric material, reflects more the hydrophobic, or lipid-like, properties of the polymer.

To achieve high flow rates and yet retain solute selectivity, our results indicate that it is advantageous to increase both the hydrophilic and the hydrophobic properties of the copolymer. Although these desired properties result from opposed structural trends, selective transport could be optimized in such block copolymers by using different and more effective hydrophobic blocks. Since the hydrophobic portion could then be reduced without losing solute selectivity, a more hydrophilic material could result.

We have now demonstrated this approach with the related copolyether-urethane system, CPU 1540-2-e. The urethane system was of interest because it offered better hydrolytic stability and more promising blood compatibility³ than the ester system. In comparison, the water content φ_w is higher and the polymer content lower for the swollen CPU material (Table I). Accordingly, the magnitude of the flow parameters ω and L_p has increased, yet the solute selectivity has remained fairly high. Thus, new polymers with improved aqueous transport properties and solute selectivity can be produced by increasing the lipophilic nature of the material while also keeping the water content necessarily high.

References

1. S. K. Brauman and B. K. Fritzinger, *J. Biomed. Mater. Res. Symposium*, **1**, 31 (1971).
2. B. K. Fritzinger, S. K. Brauman, and D. J. Lyman, *J. Biomed. Mater. Res.*, **5**, 3 (1971).
3. J. L. Brash, B. K. Fritzinger, and B. H. Loo, Stanford Research Institute, Project No. PYU-5091, Annual Report No. 4, under Contract No. PH 43-64-84, National Heart Lung Institute, October 1970; J. W. Boretos, D. E. Detmer, and J. H. Donachy, *J. Biomed. Mater. Res.*, **5**, 373 (1971).

SHARON K. BRAUMAN
BRUCE K. FRITZINGER

Polymer Chemistry Program
Stanford Research Institute
Menlo Park, California 94025

Received October 22, 1971

Revised April 19, 1972