Mass Transport Properties of Co(polyether)polyurethane Membranes II: Permeability and Sorption Characteristics

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Abstract □ A series of co(polyether)polyurethane polymers containing polyethylene glycol 600, 1000, or 1540 was synthesized, purified by reprecipitation, and cast into clear, tough, flexible membranes using the solution method. Hydration and membrane swelling increased with increasing polyethylene glycol molecular weight. Paroxypropione, 5-nitrosalicylic acid, sulfaguanidine, and phenylbutazone were used as penetrants at a 1 m*M* donor concentration. Transport rates through the 1540 and 1000 copolymer membranes were in decreasing order: paroxypropione > 5-nitrosalicylic acid > sulfaguanidine > phenylbutazone; however, through the 600 copolymer membrane the rates were paroxypropione ≫ 5-nitrosalicylic acid ~ sulfaguanidine. Phenylbutazone did not penetrate during the experiment. Good agreement was obtained between apparent diffusion coefficients calculated by both the time lag and nonsteady-state methods. Boundary layer effects were examined by variations in stirring speeds. Evidence that diffusion may occur primarily through the aqueous region of the hydrated membranes is presented.

Keyphrases □ Model membrane systems—polyurethane copolymers, permeability and sorption characteristics □ Copolymers, polyurethane—model membrane systems, permeability and sorption characteristics □ Permeability—polyurethane copolymers, model membrane systems, permeability and sorption characteristics

The systematic modification of a polymer structure to alter its diffusional characteristics is a promising approach for the development of new model membranes and drug delivery systems. It was suggested (1) that the hydrophilic–hydrophobic character of a membrane may be controlled by suitable structural modifications. Membranes, while combining the seemingly opposite properties of mechanical strength and the ability to swell in water, have been prepared by copolymerization of hydrophilic and hydrophobic reactants (2–4). The membranes formed from these copolymers allowed the transport of permeants at rates comparable to porous dialysis membranes, but with the apparent selectivity of partitioning-type membranes (5).

Therefore, a series of co(polyether)polyurethane polymers composed of hydrophilic polyethylene glycol 600, 1000, or 1540 blocks and hydrophobic urethan segments was synthesized and characterized as described previously (6). The purpose of this study was to determine the mechanism of diffusion for a group of ionizable permeants with a wide range of physical and chemical properties. Sorption of the permeants, paroxypropione, 5-nitrosalicylic acid, sulfaguanidine, and phenylbutazone, were examined. The system was also analyzed for boundary layer effects.

EXPERIMENTAL

Materials—Paroxypropione[1], 5-nitrosalicylic acid[1], sulfaguanidine[2], and phenylbutazone[2] were used as received.

Methods—Beer's law plots were prepared for each permeant at 27, 37, and 47° in 0.05 *M* phosphate buffer. A thermostated UV-cell holder was used to control sample temperatures during spectrophotometric[3] analysis.

Permeability of the polymer membranes was studied at 27, 37, and 47° using the described permeants at constant donor concentrations. A diffusion cell similar to one designed by Flynn and Smith (7) was used (6). The donor side was connected *via* tubing[4] from its sampling ports to a two-channel tubing pump[5] and an open donor solution reservoir. The receiving side of the diffusion cell was similarly connected to a UV micro flowcell[6] and the other channel of the tubing pump. The tubing on the receiving side, between the UV micro flowcell and tubing pump, was cut to facilitate filling the receiving side of the diffusion cell. Pieces of tubing[7] were used in the tubing pump drive, for connections to the sampling ports and UV micro flowcell, and to reconnect the break in the receiving side tubing after filling. Internal stirring speeds were controlled by using a synchronous motor[8] attached through an external gear system.

A diffusion experiment was begun by mounting a hydrated membrane between the halves of the diffusion cell. The assembled diffusion cell was placed into its cell holder which, in turn, was immersed in a specially constructed water bath maintained at the desired temperature ±0.3°. The receiving side of the diffusion cell, tubing, and UV micro flowcell were filled with preheated buffer by turning on the pump. In all cases, the buffer was 0.05 *M* phosphate at pH 7.5. The tubing was connected under the surface of the buffer to exclude air from the system.

The spectrophotometer, with the UV micro flowcell in place, was zeroed against the blank buffer in a 1-cm quartz cell. The connecting tubing on the donor side was then pumped full of preheated 0.001 *M* permeant in buffer from the 200-ml donor reservoir. To initiate diffusion across the membrane, preheated permeant solution was injected into the donor side chamber through a sampling port using a glass syringe. The donor side tubing from the donor reservoir, which had been left unattached so that solution could be injected, was secured to the sampling port, and the absorbance was recorded continuously *versus* time. Sink conditions were maintained in all cases. The two-channel tubing pump was set to deliver ~18 ml/min. The exact flow rate was determined prior to a diffusion experiment by measuring the amount of solution delivered in 3 min.

The use of a donor solution reservoir ensured a constant donor solution concentration and thus eliminated the possibility that a significant portion of permeant would be sorbed by the membrane. Zentner *et al.* (8) discussed the treatment of diffusion data under these conditions.

Membranes were removed from the glass plates after hydration with buffer and were soaked for at least 20 min before use.

Permeability characteristics of the polymers were determined as a function of the drying time of the membranes, which were heated at 50° for up to 4 days. Normally, membranes were cast, dried at 50° overnight, and then stored in a desiccator at room temperature.

Permeability characteristics were also examined as a function of the length of time the membranes were stored in the desiccator after an initial drying time of 8–12 hr at 50°. Membranes cut from the same casting were stored for up to 10 days before hydrating and performing the diffusion experiments.

Distribution coefficients were determined in triplicate using a solution depletion method at 27, 37, and 47° for each permeant. The initial absorbate concentration was the same as the permeant donor solution

[1] Eastman Organic Chemicals, Rochester, NY 14650.
[2] Sigma Chemical Co., St. Louis, MO 63178.
[3] Model DB-G, Beckman Instruments, Fullerton, CA 92634.
[4] Teflon.
[5] Masterflex pump drive (5–100 rpm) with pump head No. 7016 and add-on pump head No. 7016, Cole-Parmer Instruments Co., Chicago, IL 60648.
[6] Model 8871, Beckman Instruments, Fullerton, CA 92634.
[7] Silastic, Tygon.
[8] Hurst Manufacturing Corp., Princeton, IN 47570.

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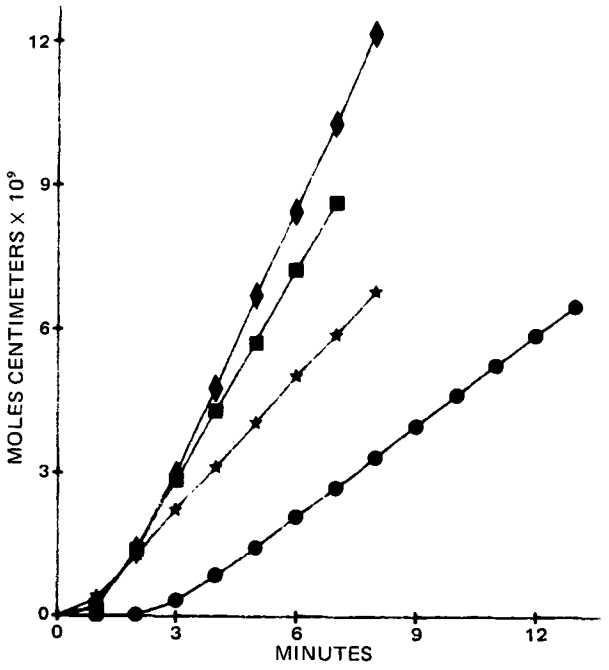

Figure 1—*Representative plot of diffusion through the 1540 copolymer membranes at 37° and 200 rpm for paroxypropione (◆), 5-nitrosalicylic acid (■), sulfaguanidine (★), and phenylbutazone (●) normalized for membrane thickness.*

concentration in the diffusion experiments. The time required to reach equilibrium for each polymer was estimated by preliminary absorption and diffusion experiments to be ~4 hr for the 1540 copolymer, 12 hr for the 1000 copolymer, and 24 hr for the 600 copolymer.

The permeant solution in each tube was assayed spectrophotometrically, and an experimental distribution coefficient was calculated by:

$$K = \frac{W_S/V_W}{C_S} \qquad \text{(Eq. 1)}$$

where K is the distribution coefficient, W_S is the equilibrium weight of permeant sorbed calculated from the concentration of the solution before and after sorption, V_W is the membrane wet volume, and C_S is the absorbate concentration in micrograms per milliliter remaining in solution after absorption completion.

To use this method, it was necessary to obtain a value for V_W. After absorption was complete, the membranes were removed from the solutions and dried overnight between two sheets of filter paper at 50°. Each membrane was then weighed to obtain the membrane dry weight, which was converted to wet volume, V_w, by:

$$V_w = \frac{V_R W_D}{\rho_D} \qquad \text{(Eq. 2)}$$

where W_D is the dry weight of the membrane, ρ_D is the dry density, and V_R is the ratio of the wet membrane volume to the dry membrane volume. The ρ_D and V_R values were averages calculated from the wet and dry dimensions of three sample membranes of each type of polymer as described earlier (6).

RESULTS AND DISCUSSION

Fabrication of the polymers into membranes results in the exposure of a large surface area of polymer to the potentially deleterious effects of light and moisture. No changes were observed in the diffusional characteristics of the membranes with increases in either drying or storage time.

Figure 1 is a representative plot showing the diffusion of all four permeants at 37° through the 1540 copolymer membrane. This plot was normalized for thickness of the membrane by multiplying the moles of permeant diffused by the thickness of the membrane. The rank order of transport was paroxypropione > 5-nitrosalicylic acid > sulfaguanidine > phenylbutazone in both the 1540 and 1000 copolymer membranes. The rank order of transport was paroxypropione ≫ sulfaguanidine ≥ 5-nitrosalicylic acid in the 600 copolymer. Phenylbutazone did not penetrate during the experiment.

Figure 2 is a composite plot representing the permeability of paroxypropione through the three different membranes at 37°. The rank order of permeability was 1540 copolymer > 1000 copolymer ≫ 600 copolymer.

The apparent permeability coefficient, P', for each permeant was calculated from steady state using:

$$P' = \frac{(dm/dt)(h_m)}{(A)(C_d)} \qquad \text{(Eq. 3)}$$

where dm/dt is the steady-state slope (mass per second), h_m is the membrane thickness (centimeters), A is the diffusional area of the membrane (square centimeters), and C_d is the donor solution concentration (moles).

The apparent diffusion coefficient, D', was calculated for each permeant in each polymer, except 5-nitrosalicylic acid and sulfaguanidine in the 600 copolymer, by:

$$D' = \frac{h_m^2}{(6)(t_L - t_c)} \qquad \text{(Eq. 4)}$$

where t_L is the apparent lag time intercept and t_c is the time required for the receiving side chamber contents to reach the UV micro flowcell. The term t_c is given by:

$$t_c = \frac{3.7 \text{ ml}}{\text{pumping rate (ml/sec)}} \qquad \text{(Eq. 5)}$$

where 3.7 ml is the volume of the section of tubing leading from the diffusion cell to the UV micro flowcell. The results of the permeability experiments are shown in Table I for the 1540 copolymer.

Under certain circumstances, it may not be feasible to continue a diffusion experiment until steady-state diffusion is reached (9). An equation was derived to evaluate the diffusional parameters during the nonsteady-state period (10, 11):

$$\log \frac{M}{t^{1.5}} = \log \frac{8C_d K}{\sqrt{\pi h_m^2}} + \frac{3}{2}\log D' - \frac{h_m^2}{9.2D'}\frac{1}{t} \qquad \text{(Eq. 6)}$$

where M is the amount permeated at t, the corrected time $(t - t_c)$ in seconds; C_d is the concentration of the donor solution (M); K is the distribution coefficient; and h_m is the thickness of the membrane. Use of the equation is restricted to early nonsteady-state diffusion across a single barrier. From the slope of a plot of $\log M/t^{1.5}$ *versus* $1/t$, the apparent diffusion coefficient of the permeant in the membrane can be calculated.

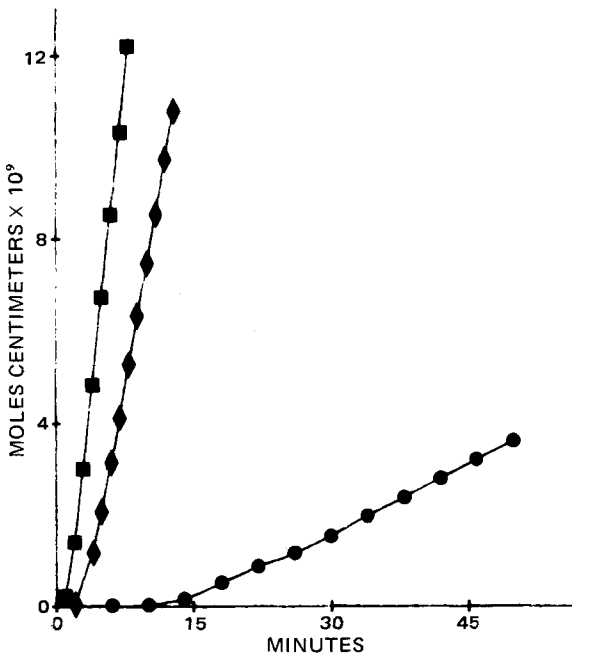

Figure 2—*Representative plot of diffusion of paroxypropione at 37° through 600 copolymer (●), 1000 copolymer (◆), and 1540 copolymer (■) membranes at 30, 200, and 200 rpm, respectively, normalized for membrane thickness.*

Table I—Results of Diffusion Experiments [a] with the 1540 Copolymer

Permeant	Temperature	Apparent Permeability Coefficient × 10^6, cm^2/sec		Apparent Diffusion Coefficient × 10^8, cm^2/sec	
		30 rpm	200 rpm	30 rpm	200 rpm
Paroxypropione	27°	1.2	2.2	2.3	5.1
	37°	1.8	3.0	3.6	7.5
	47°	2.1	3.3	4.7	8.7
5-Nitrosalicylic acid	27°	1.3	1.8	3.4	6.3
	37°	1.6	2.4	4.4	9.7
	47°	1.8	2.9	5.6	13.0
Sulfaguanidine	27°	1.0	1.4	5.9	12.0
	37°	1.1	1.5	8.2	16.0
	47°	1.2	1.8	8.2	22.0
Phenylbutazone	27°	0.60	0.8	1.4	2.4
	37°	0.73	1.1	1.9	3.2
	47°	1.0	1.4	2.5	4.2

[a] Each value is the mean of three experiments.

This approach was used for the calculation of D' for the diffusion of 5-nitrosalicylic acid and sulfaguanidine across the 600 copolymer since penetration was relatively slow. Boundary layer effects were negligible in this membrane. Permeability data are given in Table II.

Since paroxypropione penetrates the 600 copolymer rapidly enough to use the lag time steady-state method to calculate D', the applicability of Eq. 6 was tested by calculating D' utilizing both methods. The resulting apparent diffusion coefficient from the lag time was 1.5×10^{-9} cm^2/sec, while the diffusion coefficient calculated using the nonsteady-state method was 1.2×10^{-9} cm^2/sec.

Boundary layer effects can be seen in Table I. The apparent permeability coefficient for the permeants in the 1540 copolymer increased with an increasing stirring rate. In Fig. 3, the apparent permeability coefficients from a series of diffusion experiments for 5-nitrosalicylic acid through the 1540 copolymer at 37° are plotted *versus* stirring rates of 10–200 rpm. The apparent permeability coefficient increased with increasing stirring rate due to a reduction in thickness of the boundary layers on either side of the membrane. The boundary layer contribution was observed because of the relatively high diffusion coefficients of 5-nitrosalicylic acid in the 1540 copolymer.

This change is predicted for a series barrier where the boundary layers contribute a significant amount of resistance to the overall barrier resistance (8, 12–14). If diffusional processes are assumed to offer the most resistance to the overall permeation process, then under steady-state diffusion conditions and boundary layers of equal thickness:

$$F = \frac{C_d}{\frac{2h_l}{D_{aq}} + \frac{h_m}{KD}} \qquad \text{(Eq. 7)}$$

where F is the flux, C_d is the penetrant concentration in the bulk donor solution, h_l is the boundary layer thickness, h_m is the membrane thickness, D_{aq} is the diffusion coefficient for the permeant in the aqueous phase, D is the diffusion coefficient for the permeant in the membrane, and K is the distribution coefficient. The terms in the denominator are defined as the aqueous boundary layer resistance and the membrane resistance to diffusion, respectively (15).

Table II—Results of Diffusion Experiments with the 600 Copolymer at 30 rpm

Permeant	Temperature	Apparent[a] Permeability Coefficient × 10^8, cm^2/sec	Apparent Diffusion Coefficient × 10^9, cm^2/sec
Paroxypropione	27°	11.0	1.6
	37°	17.0	2.6
	47°	27.0	4.8
5-Nitrosalicylic acid	27°	—	—
	37°	1.3	0.6
	47°	2.6	1.4
Sulfaguanidine	27°	0.5	0.5
	37°	0.5	0.8
	47°	0.9	1.9

[a] Apparent P is the product of D and the distribution coefficient.

Boundary layer effects were not significant in the 600 copolymer since an increase in P' for paroxypropione in the 600 copolymer at 37° was not seen with increased stirring rates. Thus, P' was calculated as 1.7×10^{-7} cm^2/sec at both 30 and 200 rpm.

The apparent diffusion coefficient, D', was also affected by changes in boundary layer contributions (Table I). This effect on D' is due to the use of t_L, which is sensitive to the effects of the boundary layers.

The contribution of boundary layer resistance to the overall resistance of the barrier can be evaluated by plotting $1/P'$ *versus* $1/h_m$, as suggested by Hwang *et al.* (14), using

$$1/P' = \frac{1}{P} + \frac{2h_l}{D_{aq}}\frac{1}{h_m} \qquad \text{(Eq. 8)}$$

where P is the permeability coefficient adjusted for the boundary layer contribution. The slope of such a plot is the resistance due to the boundary layer, R_{2h_l}, and the reciprocal of the intercept is P. Figure 4 shows such a plot for the diffusion of 5-nitrosalicylic acid at 37° through the 1540 copolymer at four stirring speeds. Table III contains the values of P and D for the four stirring speeds. These P and D values are essentially constant when compared to Fig. 3, which suggests that the boundary layer contribution was largely eliminated.

Figure 5 shows that the relative contribution of the membrane resistance to the overall barrier resistance increases with increasing stirring rate. The resistance of the membrane, R_m, is given by:

$$R_m = \frac{h_m}{P} \qquad \text{(Eq. 9)}$$

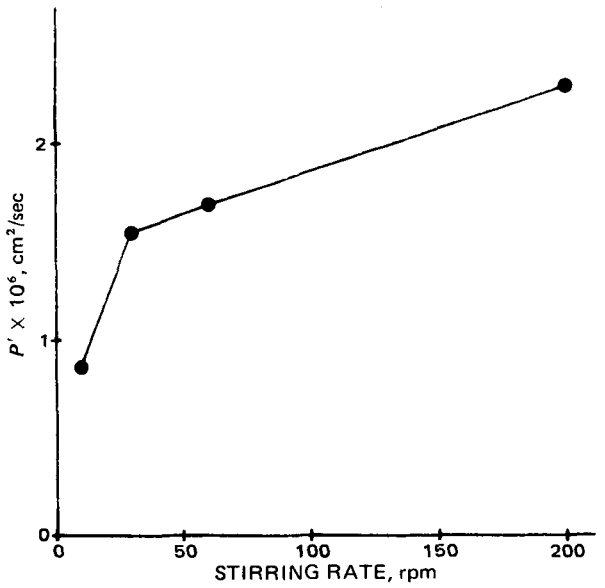

Figure 3—*Effect of stirring rate on the apparent permeability coefficient of 5-nitrosalicylic acid in the 1540 copolymer at 37°.*

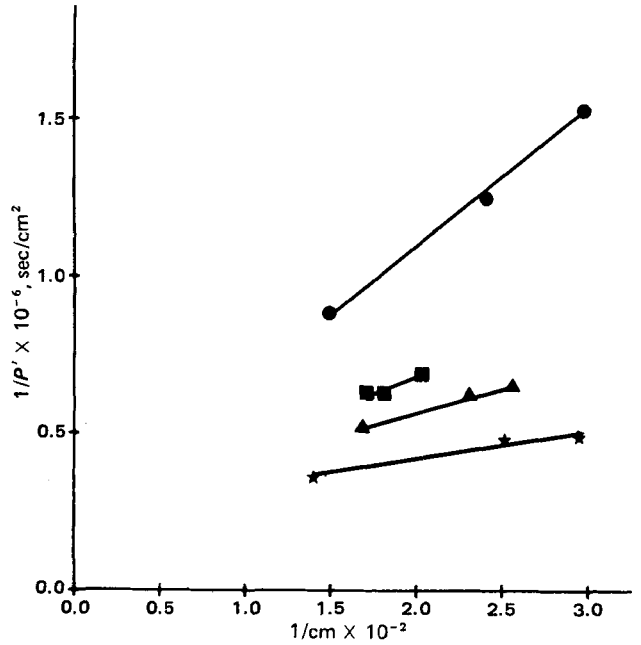

Figure 4—*Analysis of boundary layer effects of the diffusion of 5-nitrosalicylic acid in the 1540 copolymer at 37° and stirring speeds of 10 (●), 30 (■), 60 (▲), and 200 (★) rpm.*

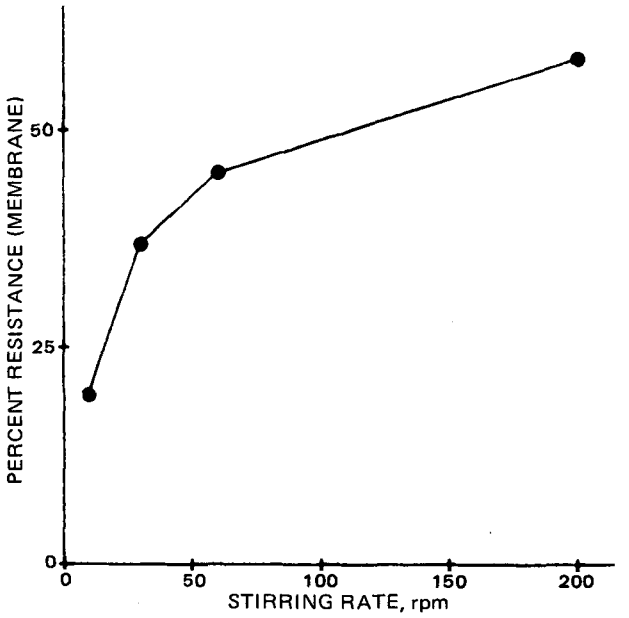

Figure 5—*Effect of stirring rate on the contribution of membrane resistance to the overall resistance of the barrier at 37° for 5-nitrosalicylic acid in the 1540 copolymer.*

Table III—Dependence of Apparent Permeability Coefficient on Stirring Rate and Adjustment for Boundary Layer Effect of Diffusion of 5-Nitrosalicylic Acid in 1540 Copolymer Membrane at 37°

Revolutions per Minute	Membrane Thickness × 10^3, cm	Apparent Permeability Coefficient × 10^6, cm^2/sec	Permeability Coefficient × 10^6, cm^2/sec	Diffusion[a] Coefficient × 10^8, cm^2/sec
10	3.4	0.66	4.7	2.3
	4.2	0.80		
	6.7	1.14		
30	5.5	1.60	4.0	1.9
	4.9	1.45		
	5.8	1.61		
60	5.9	1.9	3.9	1.9
	4.3	1.6		
	3.9	1.5		
200	3.4	2.0	4.1	2.0
	4.0	2.1		
	7.1	2.8		

[a] Calculated from P/K where $K = 20.8$.

where h_m is the membrane thickness (taken as 5.08×10^{-3} cm) and P is the reciprocal of the intercept of Eq. 8.

The diffusion data adjusted for boundary layer effects for the 1540 copolymer and the 1000 copolymer are given in Tables IV and V. The diffusion data for the 600 copolymer were not adjusted for boundary layer effects since no significant effects were observed. The adjusted P and D values are in the same rank order as the apparent permeability and apparent diffusion coefficients but are preferred since they represent the diffusional properties of the membrane alone and not the contribution of the boundary layers.

For each permeant, as the percent polyethylene glycol (or the percent water absorbed) increased, an increase in the magnitude of the diffusion coefficient was observed (Fig. 6). These results suggest that the extent of hydration of the membrane greatly influenced the diffusivity of a permeant in these membranes.

This dependence of D on the hydration state of the membrane may be explained by the free volume theory (16, 17), which is given by:

$$\ln D = \ln D_{aq}\phi q_2 - V^*/V_{f,1}\left(\frac{1}{H} - 1\right) \qquad \text{(Eq. 10)}$$

where D is the diffusion coefficient for the permeant in the swollen membrane, D_{aq} is the aqueous diffusion coefficient for the permeant, ϕq_2 is the probability of finding a hole unobstructed by polymer large enough for the molecule to diffuse through, V^* is a characteristic volume pa-

Table IV—Results of Diffusion Experiments for the 1540 Copolymer at 200 rpm Adjusted for Boundary Layer Effects

Permeant	Temperature	Slope[a] × 10^2, sec/cm	Intercept × 10^5, sec/cm^2	r^2	Permeability Coefficient × 10^6, cm^2/sec	Diffusion[b] Coefficient × 10^7, cm^2/sec	Percent[c] Resistance due to Membrane
Paroxypropione	27°	5.4	3.4	0.961	2.9	0.7	77
	37°	9.7	1.6	0.937	6.4	1.7	45
	47°	7.4	1.3	0.954	7.9	2.5	46
5-Nitrosalicylic acid	27°	9.7	3.2	0.996	3.2	1.2	62
	37°	12.0	1.9	[d]	5.2	2.5	45
	47°	9.0	1.7	0.98	5.8	3.2	49
Sulfaguanidine	27°	11.0	5.2	0.998	1.9	1.7	71
	37°	12.0	3.9	0.963	2.5	2.6	62
	47°	9.1	3.8	0.922	2.6	3.5	68
Phenylbutazone	27°	20.0	9.2	0.998	1.1	0.4	70
	37°	17.0	6.3	0.988	1.6	0.5	66
	47°	11.0	5.0	0.944	2.0	0.7	69

[a] Slope of line constructed from the results of three diffusion experiments. [b] Calculated from P/K. [c] Percent of total barrier resistance provided by the membranes based on a membrane thickness of 0.00508 cm. [d] Estimated from only two data points.

Table V—Results of Diffusion Experiments for the 1000 Copolymer at 200 rpm Adjusted for Boundary Layer Effects

Permeant	Temperature	Apparent Permeability Coefficient $\times 10^6$, cm²/sec	Permeability Coefficient $\times 10^6$, cm²/sec	Apparent Diffusion Coefficient $\times 10^8$, cm²/sec	Diffusion Coefficient $\times 10^7$, cm²/sec	Percent[a] Resistance due to Membrane
Paroxypropione	27°	1.3	1.5	2.3	0.25	90
	37°	1.7	2.6	3.1	0.49	69
	47°	2.2	5.1	4.6	1.10	47
5-Nitrosalicylic acid	27°	0.8	1.3	2.7	0.45	68
	37°	1.0	1.3	4.1	0.58	76
	47°	1.0	1.3	5.3	0.72	79
Sulfaguanidine	27°	0.5	0.6	4.1	0.50	86
	37°	0.6	0.9	6.0	0.86	76
	47°	0.6	0.9	6.7	1.00	76
Phenylbutazone	27°	0.2	0.2	0.7	0.07	—
	37°	0.3	0.4	0.9	0.11	90
	47°	0.5	0.7	1.2	0.19	68

[a] Percent of total barrier resistance provided by the membrane based on a membrane thickness of 0.00508 cm.

rameter for the permeant, $V_{f,1}$ is the free volume of water, and H is the hydration of the membrane expressed as (wet volume − dry volume)/wet volume.

The hydration of the membrane calculated as a weight fraction was used here as an approximation for H as discussed earlier (16). For a more rigorous treatment, the volume fraction may be used to calculate H.

Plots of the diffusion coefficient *versus* $(1/H - 1)$ for each permeant (except phenylbutazone) at 37° were made according to Eq. 10 and are shown in Fig. 7. The hydration of each polymer, H, was determined at room temperature and was used in all plots. While the water content of hydrogels are not necessarily temperature independent (18, 19), Refojo and Yasuda (20) showed changes in water content of only 3–4% for some hydrogels over 10–90°. Thus, changes in membrane hydration with temperature would be expected to be quite small and result in only slight differences in slope between the free volume plots at various temperatures.

Methods to correct the data for temperature-induced changes in swelling (hydration) were developed (18); but due to insufficient data, no correction for this effect was made here. The linearity of the free volume plots implies that the transport of the solutes through these membranes occurs primarily in water-filled pores or channels within the membranes.

The free volume theory of diffusion is most often applied to noninteractive systems in which the distribution coefficients range from 0 to 1. Therefore, further study may be required to confirm the applicability of the free volume theory of diffusion in these more interactive polymer–permeant systems.

Other evidence for the existence of small pores is given by the magnitude of the activation energy of diffusion for the permeants in the membrane (7–20 kcal/mole) compared to the activation energy of diffusion for a permeant in water (~4 kcal/mole) (9). This increase implies that the polymer chains form small pores that can impede the transport of the permeant through the aqueous regions in the membrane; thus, more energy is required for diffusion. It was suggested (17) that the hydrated polymer chains are relatively mobile, so that the size and shape of the water-filled pores or channels changes continuously.

The ability of the polymers to absorb the permeants was studied using a solution depletion method at three temperatures. The results are given in Table VI. The magnitude of the distribution coefficients indicates that a significant amount of permeant was sorbed. The rank order of the distribution coefficients was paroxypropione > phenylbutazone > 5-nitrosalicylic acid > sulfaguanidine. The distribution coefficients are not simply the result of permeant dissolved in water present inside the swollen membrane since, if this were the case, the K values would range between zero and 1. Since the sorption experiments were done in buffer at pH 7.5, 5-nitrosalicylic acid (pKa 2.3) and phenylbutazone (pKa 4.4) were almost completely ionized and paroxypropione (pKa 7.8) was ~50% ionized. At pH 7.5, sulfaguanidine (pKa 2.8) was essentially unionized.

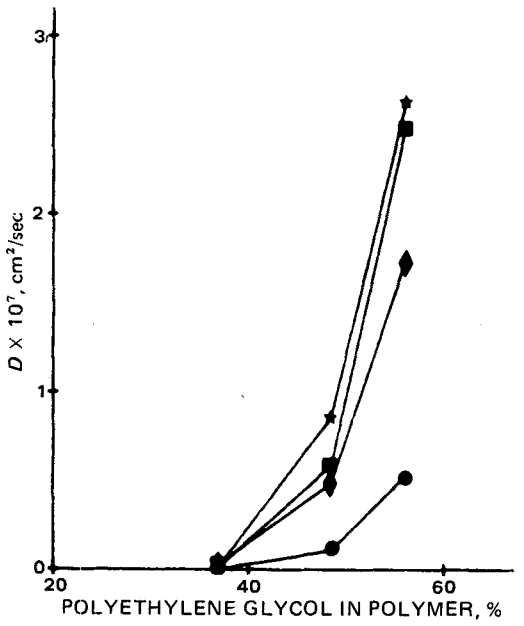

Figure 6—*Effect of polyethylene glycol content on the diffusion coefficients for paroxypropione (◆), 5-nitrosalicylic acid (■), sulfaguanidine (★), and phenylbutazone (●) at 37°.*

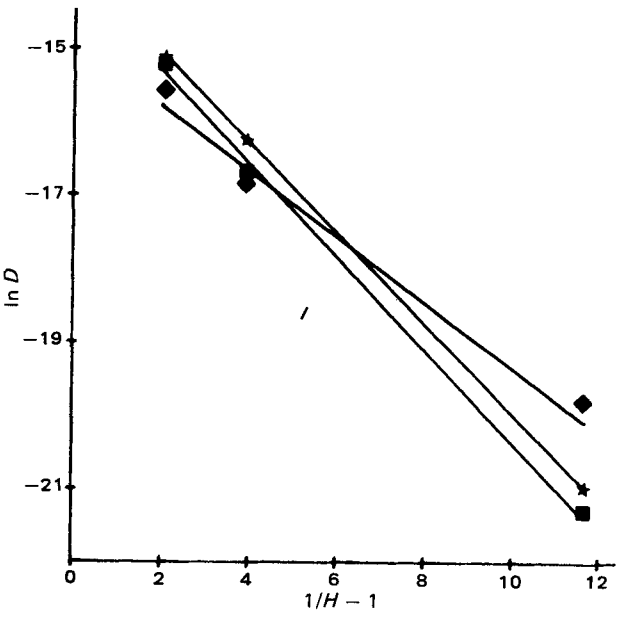

Figure 7—*Free volume plot for co(polyether)polyurethane membranes at 37° for paroxypropione (◆), 5-nitrosalicylic acid (■), sulfaguanidine (★), and phenylbutazone (●).*

Table VI—Distribution Coefficients for Permeant–Polymer Systems

Permeant	Temperature	Distribution Coefficient[a] 600 Copolymer	1000 Copolymer	1540 Copolymer
Paroxypropione	27°	74.8	58.6	40.2
	37°	63.3	53.2	37.0
	47°	51.3	46.5	31.9
5-Nitrosalicylic acid	27°	26.7	28.3	25.4
	37°	17.7	22.3	20.8
	47°	13.2	18.5	17.7
Sulfaguanidine	27°	9.8	12.7	11.5
	37°	7.2	10.2	9.7
	47°	4.7	8.2	7.6
Phenylbutazone	27°	36.3	35.4	31.3
	37°	33.3	34.3	30.0
	47°	30.1	36.2	29.1

[a] Mean of three determinations.

This finding suggests that these polymers are capable of sorbing both the unionized and ionized forms of the molecules.

It can also be seen that, except for paroxypropione, the distribution coefficients are rather insensitive to polymer composition and the resulting hydration state of the membrane. For penetrants insensitive to polymer composition, it is difficult to deduce whether the hydrophilic or the hydrophobic portion is primarily responsible for sorption. In the case of paroxypropione, the increase in the distribution coefficient with decreasing polyethylene glycol content of the polymer suggests an affinity for a more hydrophobic environment. This finding lends support to other suggestions (3, 21) that the hydrophobic urethan block may provide a site for permeant interaction with these types of polymers.

It appears that the permeant loading of the membranes may be affected by the distribution coefficient of the drug, but the lack of correlation between the distribution coefficient and permeability indicates a lack of support for diffusion through the membrane material itself. Perhaps in polyethylene glycol copolymer membranes prepared with polyethylene glycols with molecular weights of <600, the distribution coefficient would be a better predictor of membrane permeability.

Highly ionic species are readily transported, and the apparent consistency of the data with the free volume theory for diffusion is consistent with the transport of some permeants through aqueous channels. That sorption of the various permeants by these membranes was demonstrated need not eliminate the aqueous channel mechanism of diffusion in favor of a partitioning mechanism. The sorption of permeants by the membrane may be, for example, a reversible binding of the permeant to the polymer chains. This would increase the membrane concentration of permeant but not necessarily require that the permeant dissolve in the polymer and diffuse through the polymer phase of the membrane. The permeant might alternatively desorb back into and subsequently diffuse through the aqueous phase. The path taken by the permeant through the swollen membrane depends on the relative permeability of the permeant in the aqueous and polymer phases (9). The ability of the polymer to absorb the penetrant had no predictive relationship with diffusion through the membranes.

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