

The Transport Phenomena of Some Solutes through the Copolymer Membranes of 2-hydroxyethylmethacrylate (HEMA) with Selected Hydrophobic Monomers

Whan Gun Kim and Mu Shik Jhon†

Department of Chemistry, Korea Advanced Institute of Science and Technology, P.O. Box 150 Chongryangri, Seoul 131, Korea (Received November 15, 1984)

A series of copolymer membranes of 2-hydroxyethylmethacrylate (HEMA) with selected hydrophobic monomers were prepared without crosslinking agents. The equilibrium water content, the partition coefficient, and the permeability of the solutes such as urea, methylurea, 1,3-di-methylurea, and acetamide via these membranes were measured. The partition coefficient data show that as the hydrophobicity of solutes increased, the partition of solutes were dictated by hydrophobic interaction between solute and polymer matrix. Diffusion coefficients obtained in these experiments decrease as the water content of polymer membrane decreases. This decrease is blunt as the excess heat capacities, ϕC_p° (excess) in aqueous solution at infinite dilution of solute increases. To investigate the relationship between water content and diffusion coefficient, the results of the diffusion experiments were examined in light of a free-volume model of diffusive transport. The remarkable increase of urea mobility in the polymer network containing relatively larger bulk water can be considered as water structure breaking effect.

1. Introduction

Poly (hydroxyethylmethacrylate) (PHEMA), a synthetic hydrogel, was first synthesized by Wichterle and Lim in 1960¹. This polymer and many of its derivatives have been investigated extensively for possible biomedical applications². Especially, the study of transport phenomena in these hydrogel membranes³⁻⁷ has been accomplished to be used for hemodialysis membranes and controlled-release drug delivery system^{8,9}.

Two basic mechanisms have been considered in explaining solute transport through a polymer membrane; microporous type and partition type membrane. Chen¹¹ has described three different diffusion mechanisms from his water absorption studies. Previously, evidence is presented that the water in many hydrogel systems can exist in at least three different, structurally distinct forms^{12,13} and that the water structure perturbing capability of the polar organic solutes is a controlling factor in the permeation mechanism¹⁴.

Until now, although the study of crosslinker effect^{7,15} in HEMA system has been accomplished, the systematic transport study has not been done in the copolymer system between hydrophobic monomer and HEMA which are used for hard contact lens and drug delivery system etc. In this work, we investigate the transport phenomena of several copolymer hydrogel membranes to obtain the systematic informations about the role of water in transport mechanism and interaction between solute and polymer matrix.

Selected hydrophobic monomers are methylmethacrylate (MMA) methoxyethylmethacrylate (MEMA), and methoxyethoxyethylmethacrylate (MEEMA), and solutes are urea, methylurea, 1,3-dimethylurea and acetamide.

2. Experimental

Materials. HEMA and MEMA was obtained from Polysciences, Inc. They were purified by distilling under reduced pressure. MMA monomer obtained from Aldrich Co. was also distilled under reduced pressure. MEEMA monomer was purchased from Tokyo Kasei Co. It was purified by a procedure similar to that used for other monomers. All the solutes in this study were of reagent grade purity and used as received from E. Merck Co.

Polymer Preparation. Polymer formulations are listed in Table 1. Initiated monomer-solvent mixtures were poured between two shim separated glass plates and allowed to polymerize for 24 hours and then were put into oven at 60°C for 2 hours. The homogeneous gel formed were removed by soaking the glass plates in distilled water. All gels were equilibrated for at least 4 weeks in large volumes of frequently changed distilled water.

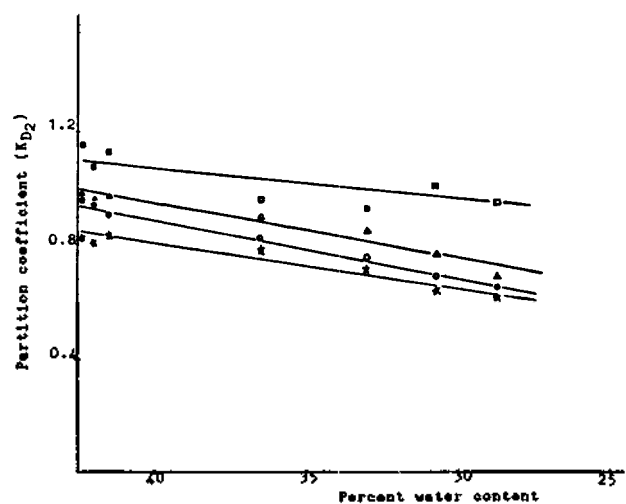
The detailed descriptions for the measurement of partition coefficient and permeability were reported in the previous paper⁷.

TABLE 1: Composition of Polymerization Mixture for Membrane Preparation

Name	HEMA	MMA	MEMA	MEEMA	H ₂ O + EtOH (3:2)	Ethylene glycol	(NH ₄) ₂ S ₂ O ₈ (60%)	Na ₂ S ₂ O ₅ (12%)	unit: ml
A	10	.	.	.	4	6	1	1	
B	9	1	.	.	4	6	1	1	
C	8	2	.	.	4	6	1	1	
ME I	9	.	1	.	4	6	1	1	
ME III	7	.	3	.	4	6	1	1	
MEE I	9	.	.	1	4	6	1	1	
MEE III	7	.	.	3	4	6	1	1	

TABLE 2: Water Content of Polymer Membrane

Membrane	Water Content
A	41.6%
B	33.1%
C	27.8%
ME I	36.6%
ME III	30.8%
MEE I	42.0%
MEE III	42.4%

**Figure 1.** The partition coefficient of solute as a function of equilibrium water content of membranes at 25°C; (□) 1,3-dimethylurea; (Δ) methylurea; (○) urea; (*) acetamide.

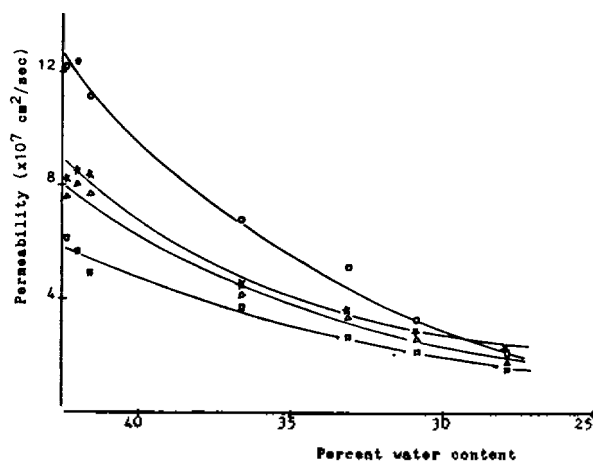
3. Results and Discussion

The percent water content of each polymer membrane is represented in Table 2. From Table 2, the decrease of percent water content can be found as the volume of hydrophobic monomer except MEEMA increases. It can be seen that MMA is most reactive but MEEMA doesn't show a great change according to monomer content increase, probably due to lower reactivity ratio. And also in case of MEEMA copolymer, it can be found that percent water content of polymer membrane increases compared with pure PHEMA, which can be due to more water content in pure MEEMA homopolymer.

To investigate gel-solute interactions, partition coefficients (K_{D_2}) were measured. The measured molar partition coefficients (K_{D_2}) of each solute are plotted against percent water content of polymer membranes in Figure 1. From these results, the following can be stated: With urea K_{D_2} is linearly correlated with the equilibrium water content of membranes at 25°C, but other solutes don't show these correlation. And it can be seen that the partition coefficient increase in proportion to the increase of the number of methyl group in solute for each polymer membrane.

Comparing urea with acetamide, the difference of affinity for these PHEMA-copolymer hydrogel membrane is smaller as water content of polymer membrane decreases.

This linear correlation of urea and acetamide indicates that the partition of these salts occur only into the water-containing regions, which are all interconnected. The appearance of devia-

**Figure 2.** The permeability of solute as a function of equilibrium water content of membranes at 25°C; (□) 1,3-dimethylurea; (Δ) methylurea; (○) urea; (*) acetamide.

tion from linear correlation in proportion to the increase of the number of methyl group in urea series shows the importance of gel-solute interaction, especially between the hydrophobic portion of the polymer^{16,17}. That is, it can be found that the so-called hydrophobic interaction^{18,19} is probably a very important factor in partition for polymer containing lower bulk water. In relatively higher bulk water region, it can be considered that the higher affinity of urea over acetamide is mainly governed by the electrostatic force because the difference of dipole moment of urea and acetamide seems to be somewhat large (4.56D for urea and 3.60D for acetamide) and also the decrease of this affinity difference in lower bulk water region is mainly done by the hydrophobic interaction.

Figure 2. shows that the calculated permeability coefficients (P) are plotted against percent water content of polymer membranes. The permeability data show that in urea series, the smaller the molecular weight of solute, the faster the permeation rate. And in the light of similar molecular weight (about 60) of two salt solutes (urea and acetamide), it can be seen that urea showing higher affinity is found the faster permeation rate in relatively higher bulkwater content region. But as the quantity of bulk water content fall off, their difference decreases remarkably, and it is even represented that two curves intersect each other in the lowest water content region. It can be suggested that the hydrophobic interaction between the hydrophobic methyl group of acetamide and polymer matrix contributes to permeation in lower water content region as it has been seen that the difference of affinity between urea and acetamide is smaller according to water content decrease.

The apparent diffusion coefficient D_{AM} of a permeant which is a criterion for its mobility within membrane phases, is obtained from

$$P = K_D D_{AM} \quad (1)$$

where P and K_D have been previously defined. The calculated diffusion coefficients are plotted against percent water content of polymer membranes in Figure 3. From diffusion data, it can be seen that in urea series, the larger the molecular weight of solute, the diffusion coefficients of solute show a good linear dependence on the percent water content. That is, as the

molecular weight increases the change of diffusivity is lax. And in lower bulk water content region it is also represented that two curves of urea and acetamide intersect each other as permeability data shows.

In view of pore-partition transport mechanism, it can be found that this system have the pore and the larger the molecular weight, its mechanism approaches toward partition mechanism. To investigate the relation between diffusion coefficient and water content, we use theoretical prediction based on the free-

volume concept of diffusive transport in hydrated homogeneous membranes²⁰, and that the relation is given as follows:

$$\ln(D/D_0) = -\beta x(1-\alpha)/(1+x\alpha) \quad (2)$$

were $x = (1-H)$, $\alpha = V_p/V_w$, $\beta = V^*/V_w$, D = experimental diffusion coefficient (D_{AM}), D_0 = diffusion coefficient of water in pure water, V_w = free volume in unit volume of pure water, V_p = free volume in unit volume of polymer phase, V^* = a characteristic volume parameter describing the diffusion of a permeant molecule in the medium, and H = water content.

It is possible to rearrange eq. (2) in order to obtain a linear plot. That is,

$$(\ln D/D_0)^{-1} = -\frac{1}{\beta(1-\alpha)}x^{-1} - \frac{\alpha}{\beta(1-\alpha)} \quad (3)$$

The D_0 values for each solute are represented in Table 3, Figure 4 is a plot $(\ln D/D_0)^{-1}$ vs. x^{-1} for all solutes. This figure shows that although these hydrogels have ingredient which is different from each other, the linearity of the plot is represented without great deviation. It can be suggested that the structural factors for these water-swollen hydrogels are similar and that the permeation of solutes occurs predominately through the porous regions of the network. However, in the homogeneous membrane model used in this interpretation, the water-filled space through which transport of permeants can occur would be conceived as fluctuating pores or channels of the polymer matrix which are not fixed either in size or in location.

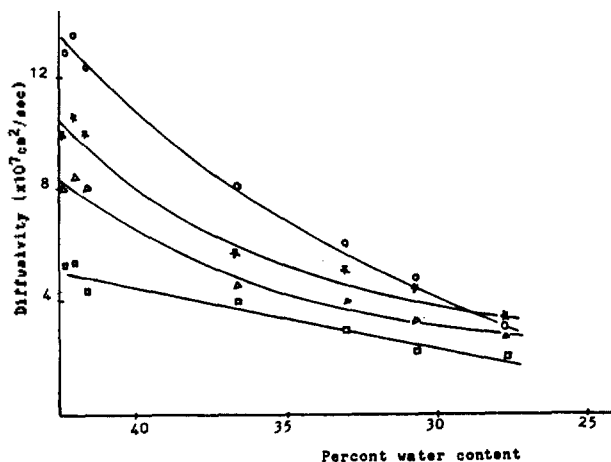


Figure 3. The diffusivity of solute as a function of equilibrium water content of membranes at 25 °C; (□) 1,3-dimethylurea; (Δ) methylurea; (○) urea; (*) acetamide.

TABLE 3: The Molecular Parameter for the Solutes

Solutes	Abbreviation	Molecular weight	$\phi C_p(\text{excess})^{22}$ in Aqueous Solution (cal deg ⁻¹ mol ⁻¹)	Diffusion Coefficient ^a in Aqueous Solution at 25°C ($\times 10^5$ cm ² /sec)
Urea	u	60.06	-5.8	1.382
Methylurea	mu	74.08	10.7	1.168
1,3-dimethylurea	dmu	88.11	25.6	0.998
Acetamide	a	59.07	9.2	1.252

^aLongworth, *J. Phy. Chem.*, **67**, 689 (1963).

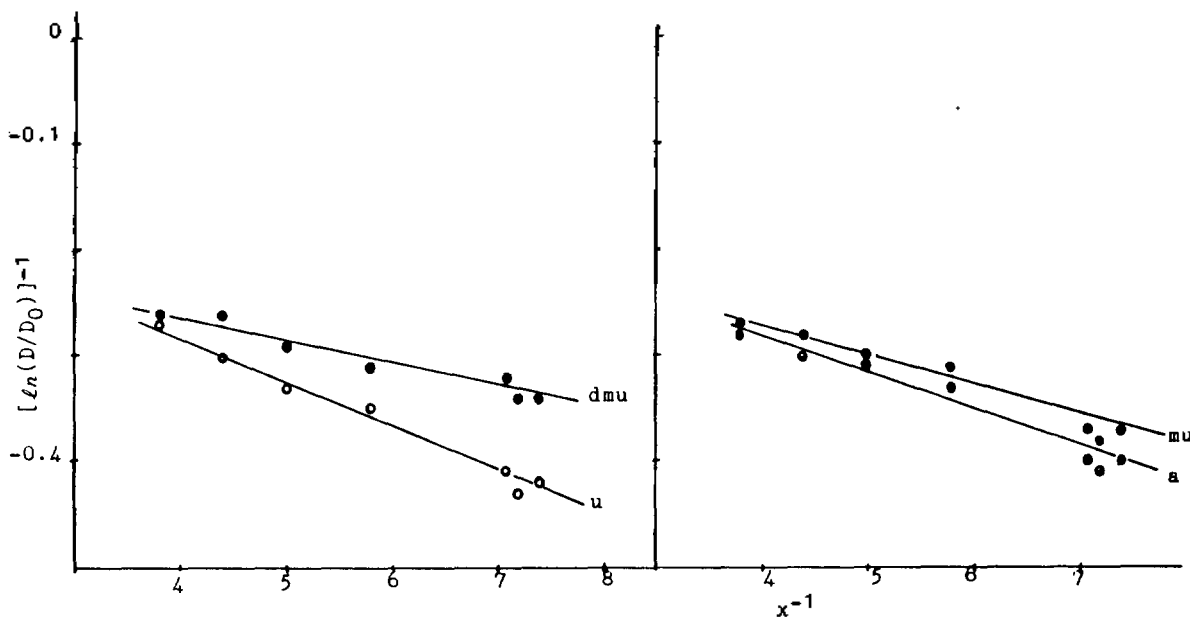


Figure 4. Relation between diffusion coefficient and water content.

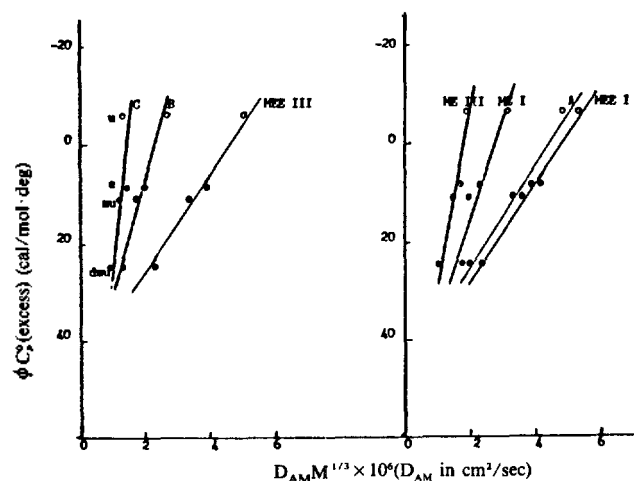


Figure 5. The correlation between the excess molal heat capacity, ϕC_p^e ; and the diffusivity parameter $D_{AM} M^{1/3}$ at 25°C within each polymer membrane.

In relatively higher bulk water region, Figure 3 shows that urea has faster mobility than other solutes, especially than acetamide having similar molecular weight. To explain this phenomena, the concept of water structure-breaking and-making effect of solutes can be used. This concept which has been used as a powerful indirect tool for interpreting solute-water interactions in aqueous solution^{21,22} has been applied to the diffusion¹⁴.

As a measure of the water structure-perturbing capability of solutes²³, the excess apparent molal heat capacities ϕC_p^e (excess) has been used. Table 3 gives the molecular parameter for the solutes used in this experiments. Figure 5 is a plots of ϕC_p^e (excess) vs. $D_{AM} M^{1/3}$ for each polymer membranes. This figure shows a good linear correlation and that as the content of bulk water decrease, this effect diminish. It can be found that in polymer membrane containing relatively larger bulk water, the greater the structure breaking effect, the permeation is promoted and in the polymer membrane containing relatively smaller bulk water, this effect does not play a important role in permeation but rather hydrophobic interaction does.

4. Conclusion

The following conclusions can be drawn about the systems studies.

As the hydrophobicity of solute increased, the solutes were not partitioned only into the water-containing regions but the partition of solutes were dictated by hydrophobic interaction between solute and polymer matrix.

Structural factor for these water-swollen methacrylate copolymer hydrogels are similar and the permeation of solutes

occurs through "fluctuating pores".

Water structure breaker increases the permeability but the decrease of water content in polymer membrane bring the opposite effect.

References

- (1) O. Wichterle and D. Lim, *Nature*, **185**, 117 (1960).
- (2) B.D. Ratner and A.S. Hoffman, "Hydrogel for Medical and Related Applications," J.D. Andrade, Ed., pl, *Amer. Chem. Soc. Syn. Ser.*, **31**, 1976.
- (3) H. Yasuda, L.D. Ikenberry, and C.E. Lamaze, *Die Makro. Chemie*, **125**, 108 (1969).
- (4) M.F. Refojo, *J. Appl. Poly. Sci.*, **9**, 3417 (1965).
- (5) S. Wisniewski and S.W. Kim, *J. Mem. Sci.*, **6**, 299 (1980).
- (6) K.H. Lee, J.G. Jee, M.S. Jhon, and T. Ree, *J. Bioeng.*, **2**, 269 (1978).
- (7) S.C. Yoon and M.S. Jhon, *J. Appl. Poly. Sci.*, **27**, 3133 (1982).
- (8) G.M. Zentner, J.R. Cardinal, and S.W. Kim, *J. Pharm. Sci.*, **67**, No. 10, 1352 (1978).
- (9) L. Olanoff, T. Koinis and J.M. Anderson, *ibid.*, **68**, No. 9, (1979).
- (10) S.J. Wisniewski, D.E. Gregonis, S.W. Kim, and J.D. Andrade "Hydrogel for Medical and Related Applications," J.D. Andrade, Ed., p. 80, *Amer. Chem. Soc. Sym. Ser.*, **31**, 1976.
- (11) R.Y.S., Chen, *Polymer Preprints*, **15**, 387 (1974).
- (12) M.S. Jhon and J.D. Andrade, *J. Biomed. Mater. Res.*, **7**, 509 (1973).
- (13) H.B. Lee, M.S. Jhon, and J.D. Andrade, *J. Colloid and Interface Sci.*, **51**, 225 (1974).
- (14) S.C. Yoon and M.S. Jhon., *J. Appl. Poly. Sci.*, **27**, 4661 (1982).
- (15) T.A. Jadwin, A.S. Hoffman, and W.R. Vieth, *J. Appl. Poly. Sci.*, **14**, 1339 (1970).
- (16) M.F. Refojo, *J. Poly. Sci., Part A-1*, **5**, 3103 (1967).
- (17) Asa C. Haglund and N.V.B. Marsden, *J. Poly. Sci. Poly. Lett. Ed.*, **18**, 271 (1980).
- (18) C. Tanford, "The Hydrophobic Effect—Formation of Micelles and Biological Membranes," Wiley-Interscience, New York, 1973.
- (19) F. Franks, in "Water a Comprehensive Treatise," Plenum Press, Vol. 4, Chapter 1, New York, 1975.
- (20) H. Yasuda, C.E. Lamaze and A. Peterlin, *J. Poly. Sci., Part A-2*, **9**, 1117 (1971).
- (21) H.S. Frank and F. Franks, *J. Chem. Phys.*, **48**, 4746 (1968).
- (22) E.G. Finer, F. Franks, and M.J. Tait, *J. Amer. Chem. Soc.*, **94**, 4424 (1972).
- (23) O.D. Borner, J.M. Bednarek, and R.K. Arisman, *J. Amer. Chem. Soc.*, **99**, 2898 (1977).