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The Transport Phenomena of a Series of Amides through the Copolymer Hydrogel Membranes

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Hydrogel membranes were prepared by copolymerizing 2-hydroxyethyl methacrylate (HEMA) and N-vinyl-2-pyrrolidone (VP) in the presence of the solvent and the crosslinker tetraethyleneglycol dimethacrylate (TEGDMA). By changing the monomer composition and the crosslinker content, different membranes were synthesized. Using these membranes, relative permeabilities and distribution coefficients for amides including urea were measured. The water contents in membrane were also measured. On the basis of solute-membrane matrix interaction, the results were interpreted.

1. Introduction

Hydrogels are three dimensional networks of hydrophilic polymers, generally covalently or ionically crosslinked, which interact with aqueous solutions by swelling to be some equilibrium value. Because of high water contents, hydrogels are biocompatible, and used as materials of contact lenses, artificial kidney, and so forth.[1] Poly(HEMA) is the most widely used hydrogel and can be applied as a material for hemodialysis.[2] Uncrosslinked poly(VP) is extremely soluble in water and high concentrations of crosslinker (5-20%) are needed to produce a material with useful mechanical properties. Faster metabolic water transfer was obtained with diisocyanate crosslinker poly(VP) than the conventional cellulosic membranes.[3]

The transport phenomena through some poly(HEMA) membranes have been previously investigated.[4-6] Yasuda *et al.*[4,7] have analyzed the diffusion data, based on the free volume theory, for homogeneous hydrogel membranes.

With varying crosslinker concentration and water content, Wisniewski *et al.*[8] obtained diffusion data, which provided the additional information on the basic transport mechanisms for water in hydrogels and on the role of water in the transport of other solutes. Two basic mechanisms are the followings; 1) a microporous type membrane, which can act as a sieve with the solute molecules being transported through the minute pores of the membrane, and 2) a partition type, which further acts to slow the diffusion process due to the interaction between diffusing solute and membrane matrix or membrane water.

Lee *et al.*[9] investigated amide transport through poly(HEMA) membranes with varying crosslinker content. In the low crosslinker contents, the membrane behaves as pore type, and a linear relationship exists between molecular weight and relative permeability.

With increasing crosslinker content, the membrane behaves as partition type and the relationship is broken. In the partition membrane, urea has higher permeability, because urea with two amide groups has more hydrophilic interaction with the polymer matrix.

Transport of urea through hydrogel membranes was experimented in order to develop more efficient hemodialysis membranes.[2,3,10,11]

We investigated how crosslinker content and monomer composition affected the diffusion data, and compared with Lee *et al.*'s.

2. Theory

Relative Permeability. The equation used to obtain permeability U was derived elsewhere.[12]

$$\ln\left(\frac{2C_t}{C_0} - 1\right) = -U \cdot S \cdot \frac{2t}{V_1} \qquad (1)$$

where C_t, C_0, S and V_1 are the concentration at time, t, that at time 0, the surface area of membrane exposed to both solution, and the cell compartment volume, respectively.

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A plot of $\ln(\frac{2C_t}{Co}-1)$ versus time will yield a straight line with slope $=-\frac{2}{V_1}\cdot U\cdot S$. Substituting measured values of V_1 and S, one can obtain permeability U. Multiplying U by the thickness of membrane d gives relative permeability U_{re}.

Distribution Coefficient. The districution coefficient K_D is defined as the ratio of the concentration of a solute in the membrane phase to its concentration in the solution phase, the two phases being in equilibrium. The following equation was used.[13]

$$K_D = \frac{(C_s^o - C_s^s)\, V_s^o}{C_s^s \cdot V^m} \tag{2}$$

where C_s^o, C_s^s, V_s^o and V_m are the equilibrium concentration in the membrane phase, that of the surrounding solution, the volume of the surrounding solution and the volume of the swollen membrane, respectively.

Diffusivity. From the absolute reaction rate theory[14], the permeability U is given as

$$U = \frac{K_D \cdot D}{d} \tag{3}$$

By substituting the measured values of K_D, d, and U, one can obtain diffusivity D.

Water Content. Water content is defined as follows;

$$\%\ \text{water content} = \frac{\text{wet membrane weight} - \text{dry membrane weight}}{\text{wet membrane weight}} \times 100.$$

3. Experiment

Membrane Preparation. HEMA, VP, and TEGDMA are purchased from Poly Sciences Inc. HEMA and VP were distilled in vacuum before polymerization to remove inhibitor. The redox initiators used are sodium metabisulfite and ammonium persulfate. The solvents are mixtures of water and ethylene glycol. In order to synthesize transparent hydrogels, solvent compositions were controlled. The formulation of the monomer mixture is listed in Table 1. The mixture was transferred between two glass plates with a spacer and polymerized at 37 °C for one day. After polymerization, the membranes were allowed to equilibrate in the distilled water for three weeks so that initiators and unreacted monomers might be removed from the polymer matrix.

Relative Permeability. The Leonard-Bluemle (L-B) cell being used in this study has been used in other experiments.[9,12] The characteristics of our L-B cell are; $S = 12.57\,cm^2$, $V_1 = V_2 = 250\,cm^3$. The membrane was fixed between the two compartments of the L-B cell. One compartment was charged with the distilled water and the other with the solution whose concentration was about 10 g/*l*. The solutes used are various amides including urea and are listed in Table 2. Each compartment was stirred at a constant rate (about 130 RPM) in order to eliminate the boundary layer effect. The changes of concentration in the solution compartment were checked by means of the differential refractometer (Brice-Phoenix differential refractometer, the Virtis Company). After dissembling the L-B cell, the thickness of the membrane was measured with the micrometer (Model 549, Testing Machines Inc.). All experiments were done at 25 °C.

TABLE 1: Recipe of the Monomer Solutions for the Membrane Preparation

	A	B	C	D	E	F	G	E	H
HEMA	10.0	9.0	8.0	7.0	6.0	6.0	6.0	6.0	6.0
VP	0	1.0	2.0	3.0	4.0	4.0	4.0	4.0	4.0
TEGDMA	1.4	1.4	1.4	1.4	1.4	0.3	0.8	1.4	2.0
H_2O	4.0	4.0	4.0	5.0	5.0	7.0	6.0	5.0	5.0
Ethylene Glycol	6.0	6.0	6.0	5.0	5.0	3.0	4.0	5.0	5.0
$(NH_4)_2S_2O_8$ (6 % solution)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
$Na_2S_2O_5$ (12% solution)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0

TABLE 2: Solutes

Solutes	Structural formula	Molecular weight	Cylindrical diameter(A)[15]
Urea	NH_2-C(=O)-NH_2	60.06	4.82
Acetamide	CH_3-C(=O)-HN_2	59.07	5.05
Propionamide	CH_3CH_2-C(=O)-NH_2	73.10	5.35
n-Butyramide	$CH_3CH_2CH_2$-C(=O)-NH_2	87.12	6.32
Malonamide	NH_2-C(=O)-CH_2-C(=O)-NH_2	102.09	5.56

Distribution Coefficient. A known volume of solution ($V_s^o = 10\,ml$, $C_s^o \approx 10\,g/l$) was delivered into the bottle. After removing the surface water on a swollen membrane we put the membrane into the bottle. The stoppered bottle was lefted in the constant temperature bath (25 °C) for one day. Then equilibrium concentration of the surrounding solution (C_s^s) was measured with the differential refractometer. The thickness of the membrane was measured with the micrometer and the area with the calipers. Multipling the thickness by the area gives the volume of the solution-swollen membrane (V^m).

Water Content. After weighing the wet membrane, the membrane samples were dried in a vacuum oven at 60 °C for a day. Then the weight of the dried membrane was measured.

4. Results and Discussion

Assuming that HEMA, VP, and TEGDMA were com-

pletely polymerized, the contents of the elements in the polymer matrix were calculated from the recipe in Table 1. The elemental analysis of the dried membrane was done at Korea Research Institute of Chemical Technology. The calculated value and the experimental value from elemental analysis are listed in Table 3. The experimental carbon contents of the polymer matrix are always smaller than the calculated ones owing to other impurities. The experimental hydrogen contents are larger than the calculated, since water is absorbed to the dried membrane during the elemental analysis. The experimental nitrogen contents are always smaller than the calculated. The reason is given below. The reactivity ratio of the monomers is given as HEMA:Styrene = 0.65:0.57, and Styrene:VP = 15.70:0.045.[16] Without considering the interaction between the monomers, we can estimate that HEMA is about 400 times as reactive as VP. Because the reactivity of VP is very low compared to HEMA and poly(VP) is soluble in water, we can consider that the VP content of the synthesized membrane is smaller than the used one. Only the VP contains nitrogen, so the practical nitrogen content is smaller than the calculated. With the assumption that HEMA and TEGDMA were completely polymerized, the practical formulations of the membrane were calculated from the data of the elemental analysis. The practical formulations of the membrane are listed in Table 4. A considerable fraction of the VP monomer didn't be polymerized into the network and did only the role of the solvent.

The change of the water content in the hydrogel membranes is plotted in Figure 1 as a function of monomer composition. As the volume % of VP in the monomer increases, the water content of the hydrogel increases. The reason is that VP is more hydrophilic than HEMA, and as the content of VP increases, the practical quantity of the solvent used increases as illustrated in Table 4. In Figure 2, one can see that as the crosslinker content increases, the water content of the hydrogel decreases. As the crosslinker content increases, the hydrogel becomes more compact and the vacant volume between the polymer matrix decreases. Hence, the water content of the hydrogel naturally decreases.

In our works, first, the permeation data of the hydrogels with different monomer composition are investigated. And second, the permeation data of the hydrogels with different crosslinker content are dealed with. The relative permeabilities of the solutes through the hydrogel membranes, whose

TABLE 3: Content of Each Element in the Dried Membrane

	C		D		E		G	
Membrane	Calc.	Exp.	Calc.	Exp.	Calc.	Exp.	Calc.	Exp.
Carbon	57.3	55.61	58.1	55.58	59.0	55.69	59.1	55.18
Hydrogen	7.9	8.18	8.0	8.12	7.9	8.09	7.9	8.07
Nitrogen	2.2	1.15	3.2	1.96	4.31	2.24	4.6	1.85

Unit (%)

TABLE 4: Copolymer Formulations Estimated from Elemental Analysis

	C	D	E	G
HEMA	8.0	7.0	6.0	6.0
VP	1.4(2.0)	1.8(3.0)	2.1(4.0)	1.6(4.0)
TEGDMA	1.4	1.4	1.4	0.8
Solvent	10.6(10.0)	11.2(10.0)	11.9(10.0)	12.4(10.0)

( ): Used volume, from Table 2. Unit(ml)

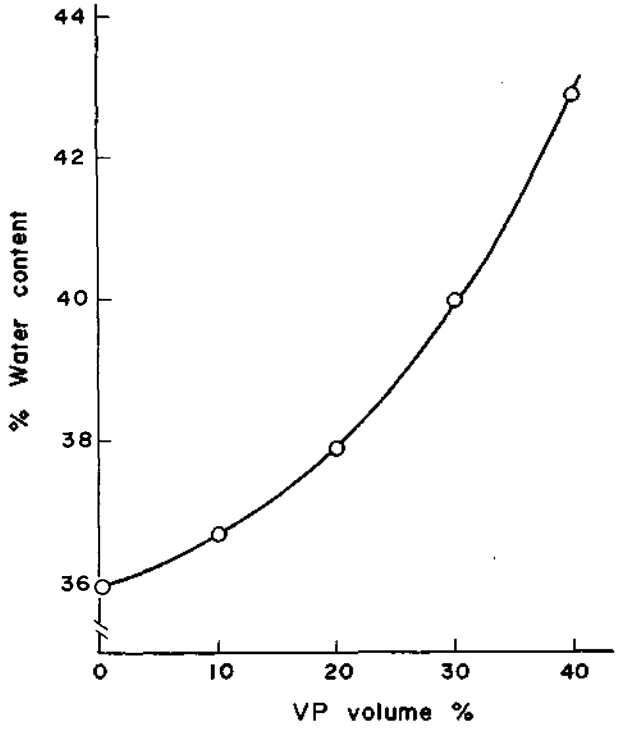

Figure 1. Dependence of % water content on volume % of VP in the comonomer.

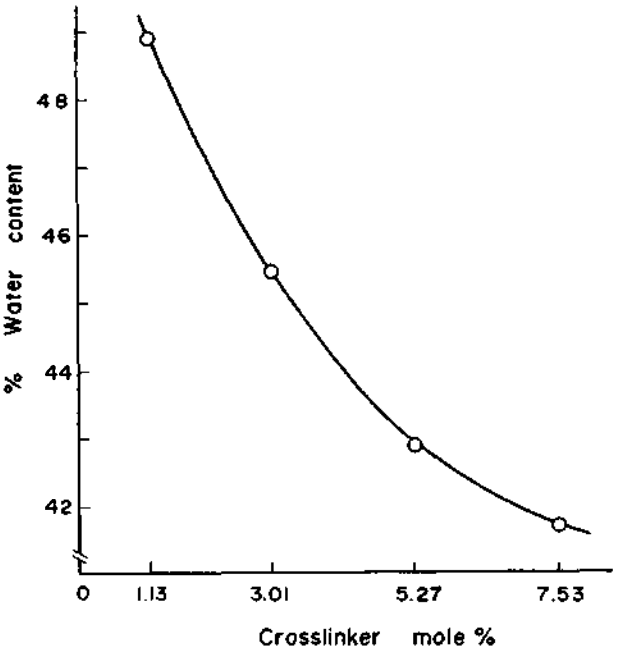

Figure 2. Dependence of % water content of HEMA-VP gels on crosslinker mole %.

monomer compositions were varied, were illustrated in Figure 3. It can be seen that as the VP volume % in the comonomer increases, the relative permeability of each solute increases. As the VP content increases, the water content of the membrane and the free volume through which the solutes move increase. Then, the relative permeabilities increase.

The K_D data as a function of monomer composition are listed in Table 5. As VP contents increase, the K_D values increase. The order of the solutes in K_D magnitudes is as follow; *n*-butyramide > propionamide > acetamide, urea > malonamide. The more hydrophobic is the solute, the higher is the K_D value.

TABLE 5: Distribution Coefficient (K_D)

VP volume %	0	10	20	30	40
Urea	0.548	0.578	0.631	0.709	0.762
Acetamide	0.558	0.581	0.647	0.697	0.710
Propionamide	0.691	0.721	0.754	0.763	0.780
n-Butyramide	0.912	0.925	0.935	0.939	0.953
Malonamide	0.410	0.412	0.453	0.492	0.531

Figure 4 indicates that as VP contents increase, the diffusivities increase, and the smaller is the cylindrical radius of the solute, the more diffusive is the solute.

Next, the dependence of the permeation data on the crosslinker contents are analyzed. The relative permeabilities as a function of the crosslinker content are shown in Figure 5. In the low crosslinker content (less than 2.0 mole%), the order of the U_{re} is completely reverse to the order of the molecular weight of the solute. With increasing the crosslinker contents, the polymer matrix becomes more compact, the free volume decreases, and the U_{re} of urea decreases more slowly than that of acetamide, and in the range of higher crosslinker content beyond 2.0 mole%, the U_{re} of urea is larger than that of acetamide. This fact indicates that in the range of high

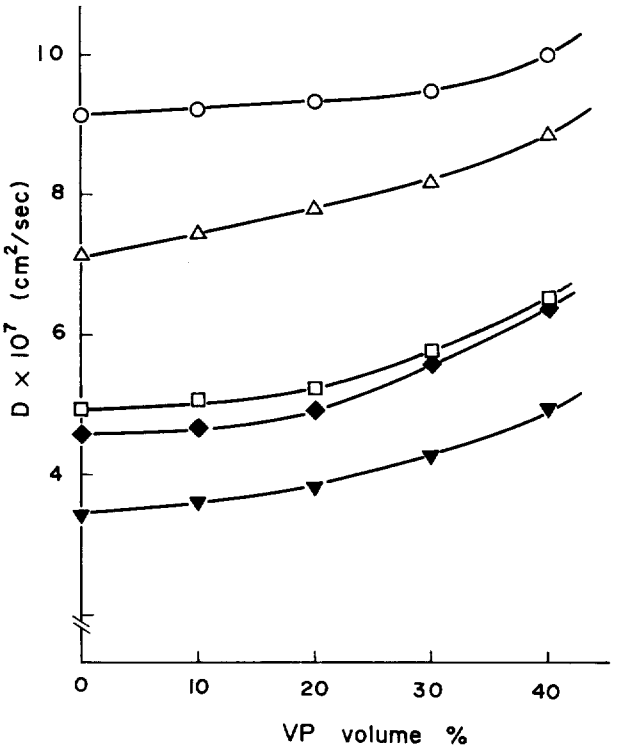

Figure 4. Dependence of diffusivity on VP volume %. Same representation as Figure 3.

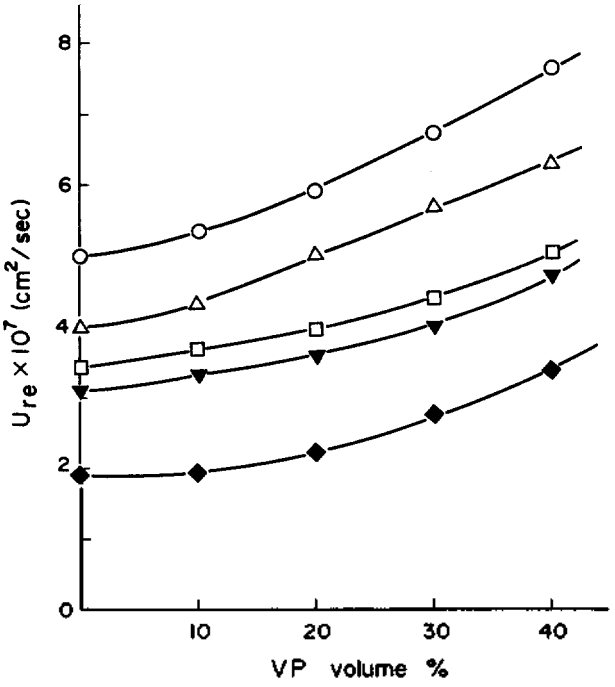

Figure 3. Dependence of relative permeability on VP volume%. ○: Urea, △: acetamide, □: prioionacide, ▼: *n*-butyramide, ◆: Malonamide.

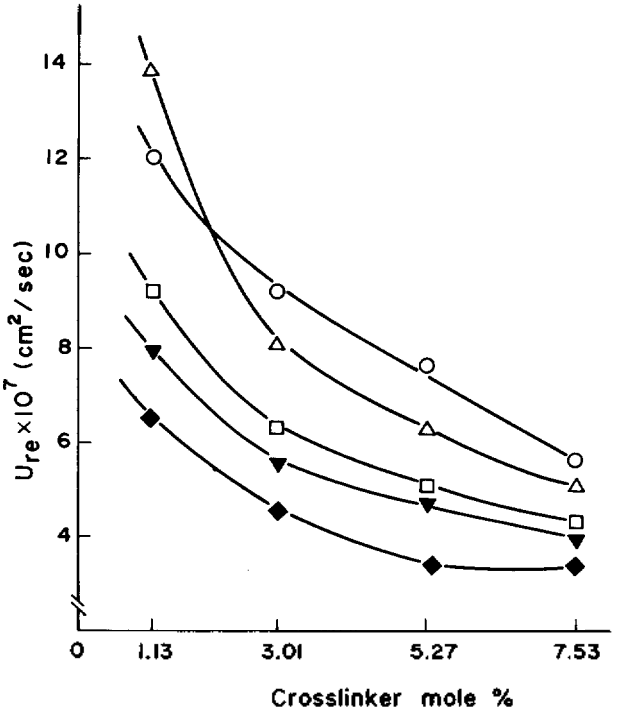

Figure 5. Dependence of relative permeability on crosslinker mole %. Same representation as Figure 3.

crosslinker content there are certain interactions between the solutes and polymer matrix. This interaction is the hydrogen bonding between the amides and the polymer matrix as shown in Figure 6. The carbonyl group of HEMA is not hydrogen-bonded, because it is near the polymer backbone.[17] Because urea has two amide groups, urea is more hydrogen-bonded with the polymer matrix than other solutes and the U_{re} of urea is larger than that of acetamide in the range of high crosslinker content.

In Table 6, one can see that with increasing the crosslinker contents, the K_D values decrease.

The diffusivities are plotted in Figure 7. As the crosslinker contents increase, the diffusivities decrease. The diffusivities of urea and malonamide with two amide groups decrease more slowly than those of other solutes, since they are more hydrogen-bonded with the polymer matrix.

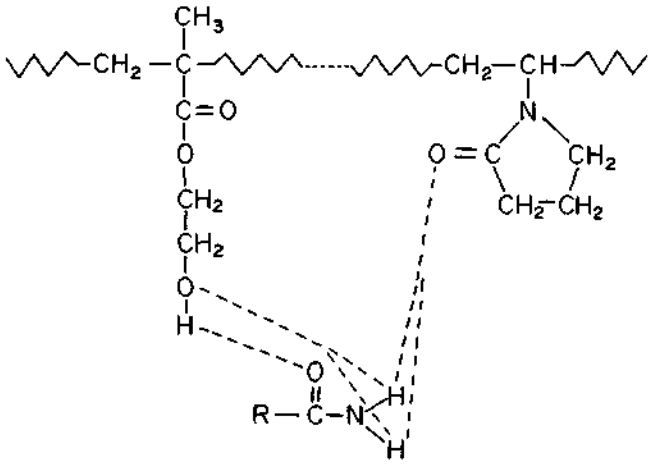

Figure 6. Hydrogen-bonding between amides and polymer matrix.

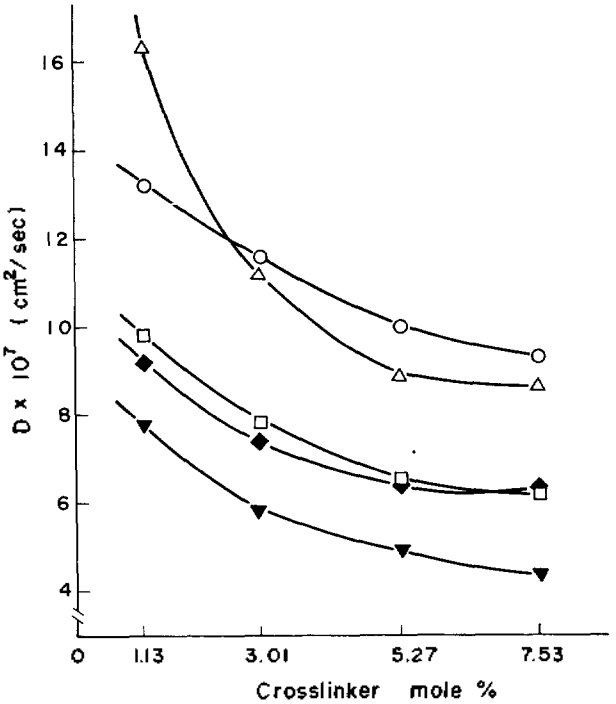

Figure 7. Dependence of diffusivity on crosslinker mole %. Same representation as Figure 3.

TABLE 6: Distribution Coefficient

Crosslinker mole%	1.13	3.01	5.27	7.53
Urea	0.912	0.792	0.762	0.608
Acetamide	0.852	0.719	0.710	0.593
Propionamide	0.939	0.812	0.780	0.695
n-Butyramide	1.02	0.965	0.953	0.918
Malonamide	0.710	0.613	0.531	0.526

5. Conclusions

The transport phenomena of a series of amides through the copolymer (HEMA-VP) hydrogel membranes were studied. With varying monomer composition and crosslinker content, we measured water contents, relative permeabilities, and distribution coefficients.

As the volume fraction of VP in the comonomer increases, the water content of the hydrogel increases, since VP is more hydrophilic than HEMA and VP which didn't be polymerized into the network did the role of the solvent. Also, the relative permeabilities, the distribution coefficients and the diffusivities increase monotonously with increasing the volume fraction of VP in the comonomer.

As the crosslinker content increases, the hydrogel becomes more compact and the water content decreases. Also, the relative permeabilities, the distribution coefficients and the diffusivities decrease. Because in the range of the high crosslinker content, the amides are hydrogen-bonded with the polymer matrix, urea with two amide groups and small molecular weight, has the highest U_{re} value among the amides. If this hydrogel membrane is applied to the artificial kidney, the one with high crosslinker content may be efficient in removing urea from the blood.

Lee *et al.*[9] have studied the transport phenomena of a series of amides through the poly(HEMA) membranes. With varying the crosslinker contents, they measured the transport parameters. Comparing with their works, the volume of the solvent which we put into the monomer mixture was twice, but other conditions were similar. Because our HEMA membranes were less compact, the U_{re} was larger and the selectivity of urea on U_{re} was a little lower in our experiment than in theirs. If we use half the volume of the solvent, our selectivity on U_{re} may increase significantly.

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