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Some Model Solute Affinity for a Tactic *p*-HEMA Membranes by K_D Measurement

Eun Hee Lee, Sang Il Jeon and Mu Shik Jhon†

Department of Chemistry, Korea Advanced Institute of Scienec and Technology, Seoul 131, Korea
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Two series of membranes have been prepared by postcrosslinking highly syndiotactic and isotactic poly (2-hydroxyethyl methacrylate), P(HEMA). The crosslinker used was hexamethylene diisocyante (HMDIC). The distribution coefficients (K_D,) of the model solutes such as urea (and thiourea), their derivatives, homologous alcohol series and amide sreies in water-swollen tactic P(HEMA) membranes at 25°C were mesaured. In addition, the concentration effects of acetamide and butyramide were also measured. On the basis of hydrophobic interation and the stsructural factors of tactic P(HEMA) membranes, the hydrophobic adsorption of the solutes in the polymer matrix were discussed. The results showed that the more hydrphobic the solute is, the higher the K_D, value is. And the polymer conformation also affects the distribution of solvents.

1. Introduction

Of particular interest in recent years have been those hydrogels[1,2] derived from polymers of methacrylic esters containing at least one hydroxyl group in the side chain. Since Wichterle and Lim[2] have emphasized crosslinked poly (2-hydroxyethyl methacrylare), p(HEMA) hydrogel as biomedically important material, ample studies about the hydrogzl have been accomplished.

The primary structure of homogeneous P(HEMA) hydrogel is covalently crosslinked three-dimensional network. In conjuntion with covalently bonded structure, P(HEMA) chains are held together by some noncovalent forces in a secondary structure giving hydrogel, which shows its characteristic swelling stability in water. It was reported that in aqueous solution gel-soute association by hydrogen bonding seems unlikely.[3] And the H-bonding interaction between model peptide group is small.[4] Hence the feasibility that these bonds contribute in a considerable way to the stabilization of secondary structure of P(HEMA) hydrogel is slight. Interactions between the hydrophobic portion of the polymer, the so-called hydrophobic bondings[5] are probably very important factor in holding P(HEMA) segments in an aqueous environment. The microsolvent addition experiments to the hydrogel seems to confirm this hypothesis.

In our experiments, we wish to report studies which support the hypothesis of hydrophobic interaction in the adsorption of water soluble solutes. We used ISO membranes and SYN membranes. Because isotactic P(HEMA) and syndiotactic P(HEMA) have different conformations, different results are expected.

The P(HEMA) membranes which have been studied previously[6,7] is relatively atactic in triad tacticity. Recently, Gregonis *et al.*[8] have mode highly syndiotactic and isotactic P(HEMA) by U. V. photolysis and coordination polymerization, repectively, and measured the equilibrium water swelling properties of these hydrogels. From these observation, they have proposed that the stereochemistry of the polymer chain is a factor in determining swelling behavior of the hydrophilic gel

In our experiments, we compared isotactic (ISO) membranes with syndiotactic (SYN) membranes to determine the effect of the addition of urea (and thiourea) and their dervitives, and water-solute organic solvents on the hydrated stereoregular P(HEMA) hydrogels, depending on the predominant hydrophobic interaction.

It is also determined the effect of concentration of acetamide and butyramide. To test the hydrophobic adsorption, we have therefore determined the distribution coeffIcients. From this, will be discussed that hydrophobic adsorption increases with more hydrophobic group. And it will be also discussed that conformional differences affects the distribution

coefficient.

2. Experimental Methods

Materials. Highly pure HEMA monomer of low diester content (<0.02%) purchased from Hydron Laboratories Inc. was used without further purification.Hexamethyene diisocyanate (HMDIC), used as a crosslinker, was purchased from Polyscince Inc. All solutes used in these experiments were of the purest grade available. And on further purifications were done in these cases.

Synthesis of P(HEMA). Linear P(HEMA) has been synthesized in highly syndoitactic and highly isotactic configurations.[8] Highly syndiotactic P(HEMA) was synthesized by radical polymerization at −50°C. The polymer was formed after 6 hrs. of U. V. (254 nm) photolysis of methanolic monomer solution, The initiator azobis (methyl isnbutyrate) was prepared by Motimer[9] previously.

Isotactic P(HEMA) was synthesized by anionic polymerization. To prepare highly isotactic P(HEMA), blocking group benzoxyethyl methacrylate (BEMA) was used. The anionic initiator for BEMA polymerization is *n*-butyllithium and copper iodide complex $Li^+(nBu)_2Cu^-$. Using this reagent, isotactic P(BEMA) was produced. The hydrolysis process[10] of isotactic P(BEMA) was somewhat different from Gregonis et al's.[8] The synthesized isotactic P(BEMA) was hydrolyed in the cosolvent of acetone, N,N-dimethylformamide (DMF), and methanol (volume ratio; 3:2:2) with aqueous potassium hydroxide for 30 min at 50°C. The reaction mixture was cooled to room temperxture and neutalized, and then the hydrolyzed product was precipitated in water. All the polymers obtained were redissolved and reprecipitated three times.

Menbrane Preparation. After dissolving the vacuum dried tactic P(HEMA) in dry N,N-dimethylacetamide thoroughly, desired amount of crosslinking agent, HMDIC (2.5 mole %), and the catalyst (dibutyltin dilaurate: 6.6×10^{-5} mol/*l*) were mixed well with it. The mixture was poured on a polypropylene mold. Crosslinking was carried out in a closed oven under dry nitrogen atmosphere for 24 hrs. And then, the solvent was slowly evaporated in a stream of clean air for 24 hrs. The polypropylene sheet to which the dried membrane stuck was placed under vacuum for 10 hrs. and dipped into distilled water for 12 hrs. This was partially dehydrated under vacuum for 5 hrs., and then, membrane was slowly drawn apart from polypropylene sheet. All the membranes were equilibrated in distilled water for at least one month during which the water was freqently replaced,

Distribution Coefficient. The distribution coefficient is defined is the ratio of the concentration of a solute in the membrane phase to its concenrtation in the solution phase, the two phases being in equilibrium. In our method, the distribution coefficient is determined by using the two-step sorption and desorption technique[12] because of good reproducibility. Here, the distribution coefficient, K_{D_2} is defined as

$$K_{D_2}=\frac{G_S^0}{G_m}\left(\frac{C_{S2}^S}{C_{S1}^S-C_{S2}^S}\right) \tag{1}$$

where G_S^0, G_m, C_{S1}^S, and C_{S2}^S are the weight of the surrounding solution, the weight of the swollen membrane, the concentration of the solute in the surrounding solution after sorption, and that after desorption, respectively.

This use of K_{D_2} differs slighly from the conventional one since the concentration in the membrane is molality whereas that in surrounding medium is molarity.[13]

Presoaked membranes at 25°C were surface dried between damp filter paper and placed in the stoppered bottle containing known weight of solution (5 m*l* = 4.95−4.89g according to the model). The stoppered bottle was lefted in a constant temperature (25°C) bath for two days. After reaching an equilibrium then removed, surface dried and placed in a bottle containing triply distilled water for two days at 25°C. Form first equilibrium ,we obtained C_{S1}^S and from second equilibrium C_{S2}^S was obtained. The sample was analyzed with a differential refractometer.

The relationship between the actual concentration of the solution and the refractive index of the solution relative to pure water determined by the differential refractometer shows $\Delta d=K\Delta C$. Therefore, the relative refractive index was substituted for the actual concentrations in equation (1) to obtain equation (2).

$$K_{D_2}=\frac{G_S^0}{G_m}\left(\frac{C_{S2}^S}{C_{S1}-C_{S2}^S}\right)=\frac{G_S^0}{G_m}\left(\frac{\Delta d_2}{\Delta d_1-\Delta d_2}\right) \tag{2}$$

where Δd_1, Δd_2 are the reading of differential refracto meter for C_{S1}^S and C_{S2}^S.

3. Results and Discussion

The distrbution coefficient (K_{D_2}) of homologous alcohol series, amide series, and ureas (and thioureas) and their derivatives are plotted againt the number of carbon atoms (n) as shown in Figure 1 to 3. All of them show that there is an affinity for less polar aliphatic solutes which suggests that this effect depends on the number of C atoms.

Figure 1 shows that there is an affinity order for homologous alcohol series. The order of the solutes in K_{D_2} magnitude is as follows:

1-Pentanol > 1-Butxnol > 1-Propanol > 1-Ethanol

the more hydrophobic group the solute has, the higher the interaction is. With regard to homologous aliphatic series, a regular pattern is apparent (Traube's rule).[14]

In the amide series, the same pattern is obtained (see Figure 2).

Formamide < Acetamide < Propionamide < Butyramide

Above results are also consistent with alcohol series. From our results, it is reasonable that alkyl groups enhance the affinity. The affinity of the tactic P(HEMA) hydrogel for homologous alcnhol solutes and amide solutes, which is due to the CH_2 groups, strongly suggest a hydrophobic interaction. Sloutes which decrease the solvent power of water will induce the creation of additional bonding between hydrophobic residues in the polymer network. Hyrophobicity is a controlling on the preferential sorption of alcohol (and amide) solutes in the tactic P(HEMA) hydrogel in the water-containing system: the magnitude of this effect increases with decreasing polarity of the compound sorbed as seen in

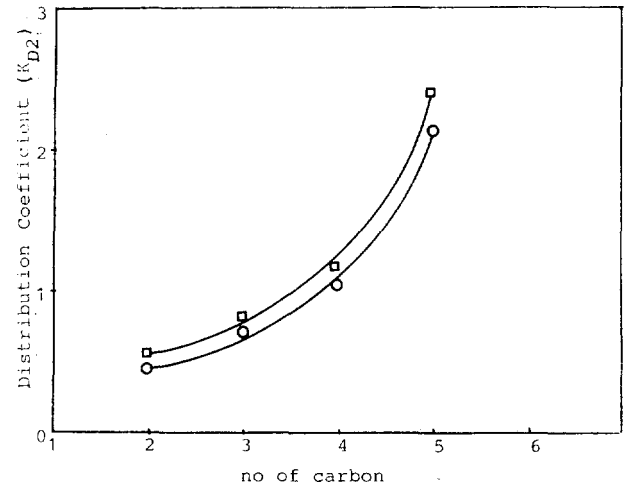

Figure 1. The distribution coefficient of alcohol solutes in HEMA membranes as a function of carbon unmber at 25°C; (□), for the isotactic precursor; (○), for the syndiotactic precursor.

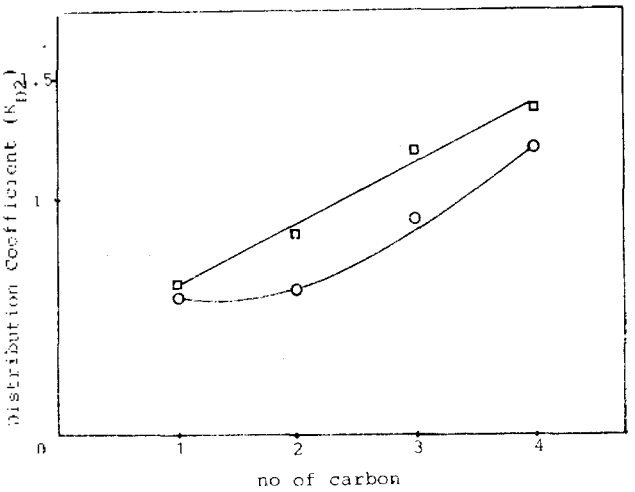

Figure 2. The distribution coefficient of amide solutes in HEMA membranes as a function of carbon unmber at 25°C; (□), for the isotactic precursor; (○), for the syndiotactic precursor.

Figure 1 and Figure 2.

For all solutes, ISO membranes have higher distribution coefficient values than SYN membranes. This difference can explained in terms of Russell *et al.*, s[15] CPK^R space-filling molecular models. The conformational difference between isotactic P(HEMA) and syndiotactic P(HEMA) is that the hydrophilic polar groups for isotactic P(HEMA) are all displaced outward from the helical backbone, giving a helix conformation which has a hydrophobic inner surface and hydrophilic outer surface. This is not the case for syndiotactic P(HEMA), where polar and apolar groups are inters persed along the helix .This may be partly account for the differences observed in the swlling behavior of isotactic and syndiotactic P (HEMA).[8] The membranes of isotactic precursor are more hydrated compared to the ones of its syndiotactic counterpart. From adove report, it is apparent that SYN membrane is more hydrophobic than ISO. And then it is expected that in the same solute, SYN membrane would

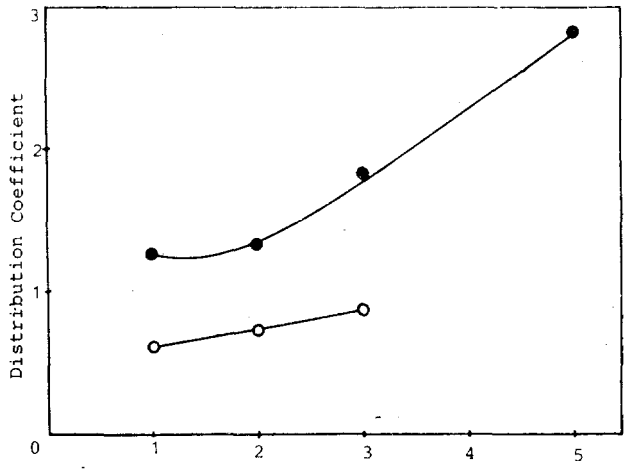

Figure 3. The distribution cofficient of urea thiorea sulutes in SYN membranes as a function of carbon unmber at 25°C; (●), thiourea and its derivatives; (o), urea and its derivatives.

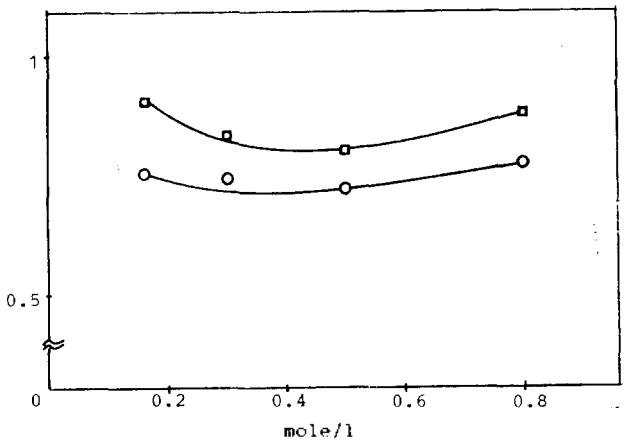

Figure 4. The distribution coefficient of caetamide solutes in HEMA membranes as a function of concentration at 25°C; (□), for the isotactic precursor; (○), for the syndiotactic precursor.

have higher distribution coefficient than membrane. But in our previous reports the distribution coefficient is linearly dependent to the equilibrium water content in membranes at 25°C.[10,16] The linear correlation indicates that the partition of the solutes also occurs into the water-containing region which is all interconnected. As ISO membranes are more hydrated than SYN membranes, it is suggested that the hydrogen bonding effect is significant between solutes and polymer matrix. In our experiments, SYN membranes, hydrophobic mature never overcomes ISO membranes' water content effect.

In Figure 3, in ureas (and thioureas) one can see that an affinity is increased as follows:

Urea < N-Methylurea < N-Ethylurea

Thiourea<N-Methylthiourea<N,N'-Dimethylthiourea< N,'N-Diethylthiourea

Here the affinity is increased by N-methylation. A higher K_{D_2} value is found for the N-ethyl dervative in comparison with the N-methyl derivative, And N,N'-methylation has mroe hydrphobic nature than N-ethylation. It is apparent that, within the concentration ragne studied, substitiuton

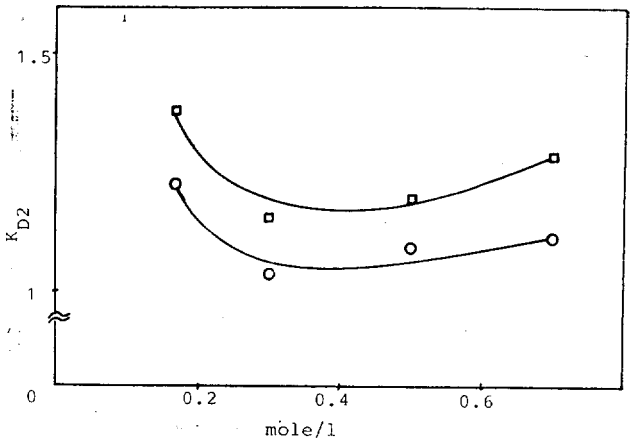

Figure 5. The distribution coefficient of butyramide solutes in HEMA membranes as a function of concentration at 25°C; (□), for the isotactic precursor; (○), for the syndiotictic precursor.

of methyl groups for hydrogen atoms on urea and thiourea fits reaonably well in terms of a hydrophobic mechanism. From Figure 3. one can see that thiourea has higher K_{D_2} value than urea. This is due to the higher affinity to the membrane for thiourea than urea.

In Figure 4 and 5, one can see that the K_{D_2} values show a minimum as concentration increases. From our previous report;[17] it is suggested that water content is varied with concentration. In these cases hydrogen-bonding between solutes and tactic P(HEMA) hydrogel must be an important effect. In the same membrane, butyramide has higher K_{D_2} value than acetamide over a concentration range of 0.176–0.8*M*. Solutes' hyorophobic nature is a major effect in partitioning polymer matrix. In the same solute, ISO membranes have higher K_{D_2} value than SYN membranes. In this case, gel–solute association by the hydrogen bonding is a major effect.

4. Conclusion

The distribution coefficients for the two series of tactic P(HEMA) membranes with the crossliker, HMDIC, are obtained.

Distribution coefficients were measured for urea (and thiourea) and its derivatives and homologous alcohol series, as well as amide series with the water-swollen tactic P-(HEMA) membranes. Distribution coefficient data of tactic P(HEMA) membranes increase with the increase in hydrophobic groups.

From this, it is assumed that the more hydrophobic the solute is, the higher the polymer-solute affinty is. ISO membranes show the higher K_{D_2} values than SYN membranes for all solutes concentration ranges, This trend is consistent with the water contents of water-swollen tactic P(HEMA) membranes.

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