Solute Diffusion in Poly(vinyl alcohol)/Poly(acrylic acid) Interpenetrating Networks

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ABSTRACT: Solute transport through interpenetrating polymeric networks of poly(vinyl alcohol) and poly(acrylic acid) at pH 3 or 6 was studied in order to investigate the influence of possible solute binding on the transport process through the networks. Diffusion of theophylline, vitamin B_{12}, and myoglobin was analyzed, and diffusion and partition coefficients were determined. Analysis using the free volume-based theory of Peppas and Reinhart indicated that solute binding occurred only in those hydrogels that were in the ionized state. ATR-FTIR spectroscopic studies were used to determine the level of binding in the case of myoglobin in contact with these IPN hydrogels.

Introduction

Hydrogels have become increasingly important for use in separation processes including microfiltration, ultrafiltration, gas permeation, pervaporation, dialysis, and reverse osmosis.[1] In the biomedical field, hydrogels are used in diagnostic, therapeutic, and implantable devices[2,3] (e.g., catheters, biosensors, artificial skin, controlled release drug delivery systems, and contact lenses). Hydrogels may contain functional groups that interact with the external environment (e.g., temperature, ionic strength, and pH of the swelling agent). Their response to environmental conditions may lead to increase or decrease of the mesh size of the hydrogel.[4−8] The hydrogel equilibrium swelling ratio is an important parameter because it describes the amount of water contained within the hydrogel at equilibrium; it is a function of the network structure, cross-linking ratio, hydrophilicity, and degree of ionization of the functional groups. In solute transport through hydrogels, size, shape, and solute ionization affect its diffusion through the network. If the gel and the solute are ionized, interactions may occur that may assist or hinder the diffusional process, depending on the charges on the membrane and solute.[9,10]

Solute transport through hydrogels has been extensively studied in recent years.[4−8] We have recently studied[10] the solute transport through ionic hydrogels as a function of mesh size and environmental conditions (i.e., pH and ionic strength) and determined that each factor plays a very important role in solute transport. We have also investigated the effect of pH on solute transport from ionized hydrogels[11] and have found that pH-dependent hydrogels could be prepared to exhibit constant solute transport; this behavior could be attributed to the effect of the pH on the relaxation, swelling, and release mechanism of the hydrogel. In solute transport through ionizable hydrogels, polymer/solute interactions are important in predicting the overall diffusion. Collins and Ramirez[12] studied these interactions and offered one of the earliest methods of quantitative analysis of such transport.

Previously, we studied such interactions using well-characterized interpenetrating networks of poly(vinyl alcohol) (PVA) and poly(acrylic acid) (PAA) by varying the content of PAA in the hydrogel membrane. We also compared the permeation of solutes through interpenetrating polymer networks (IPNs) at pH 3 (below the pK_a of PAA) and pH 6 (above the pK_a of PAA) and determined that permeation is a function of size exclusion parameters as well as polymer/solute interactions.

Size exclusion phenomena in hydrogels have been described by a wide range of free volume and other theories.[14−21] Prominent among them are the theories of Yasuda et al.[17] and Peppas and Reinhart[19] which are based upon the free volume theory for a three-component system and predict the dependence of the solute diffusion coefficient on solute size, mesh size, swelling, ratio, and other structural characteristics of the hydrogels. As none of these theories has addressed ionic interactions between solute and polymer, the purpose of this work was to reexamine these theories in view of new data on solute transport through such hydrogels. The polymers studied in this work were poly(vinyl alcohol) and poly(acrylic acid). Their structure, characteristics, and solute diffusion have been studied before.[20−23]

Experimental Section

Synthesis of Homopolymers. A 10 w/v % aqueous solution of PVA (Elvanol 85−82, E. I. du Pont de Nemours and Co., Wilmington, DE, degree of hydrolysis 99.6% with $\bar{M}_n$ = 48 237 and $\bar{M}_w$ = 103 699 according to Lark Enterprises, Webster, MA) was prepared by dissolving PVA in water at 90 °C for 6 h.

A 25% aqueous solution of glutaraldehyde was added to the PVA solution according to the desired cross-linking ratio. The cross-linking ratio, X, was defined as the ratio of moles of glutaraldehyde per mole of PVA repeating unit. In addition, a 10% H_2SO_4 solution (catalyst), a 50% methanol solution (quencher), and a 10% solution of acetic acid were added to the PVA solution at a 2:1:2:3 ratio. In a typical experiment for a cross-linking ratio of X = 0.01, 0.2 mL of sulfuric acid, 0.4 mL of methanol, 0.6 mL of acetic acid, and 0.4 mL of the glutaraldehyde solution were added to an aqueous solution containing 5 g of PVA and 50 mL of water. The solution was mixed very slowly and glutaraldehyde was added to initiate the cross-linking process. Hydrogel films were prepared by injecting the solution between two 75 × 50 × 1 mm microscope slides using a Pasteur pipet. The slides were separated by microscope slides to adjust the thickness. The solution was reacted in a 60 °C oven for 3 h and then cooled to room temperature. The ensuing membranes were placed in distilled water and washed for 5 days to remove un-cross-linked polymer chains and cross-linking agent.

Distilled acrylic acid (AA, Aldrich Chemical Co., Milwaukee, WI) and water were combined in a 1:1 ratio. A quantity of

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Table 1. Solutes Used in the Diffusion Studies

solute	mol wt	pK_a	exp diff coeff (10^7 cm^2/s)	shape and dimens (Å)
theophylline	180	8.6		spherical
vitamin B_{12}	1355	neutral	37.9[26]	spheroid[27] 9.5 × 9.2 × 7.5
myoglobin	17200	7.0	12.8[26]	irregular[28] 12.5 × 17.5 × 22.5

0.5% ethylene glycol dimethacrylate (EGDMA, Aldrich) was added and the solution was thoroughly mixed. A quantity of 1% AIBN (Aldrich) was then added to initiate the reaction. Immediately, the solution was injected between two microscope slides as before and the reaction took place at 60 °C for 3 h. The films or membranes were placed in distilled water and washed for 5 days to remove unreacted monomer and cross-linking agent.

Synthesis of Interpenetrating Networks. Aqueous PVA and AA solutions were prepared separately. The two solutions were then mixed to obtain compositions with molar ratios of VA:AA of 60:40, 50:50, and 25:75. These solutions were cast between two microscope slides, cross-linked at 60 °C for 3 h, and washed for 5 days.

Equilibrium Swelling. The hydrogels were characterized by equilibrium swelling studies using techniques described in detail before.[13,23−25] To determine the equilibrium swelling ratio, a sample of each hydrogel (1 cm^2 square) was cut immediately after cross-linking. This sample was weighed in air and heptane (a nonsolvent). The sample was then placed in deionized water at 37 °C for 5 days to swell to equilibrium and weighed again in air and heptane. Finally, the sample was dried for 5 days at room temperature and weighed in air and heptane. Due to the ionization of PAA, buffer solutions of pH 3 and pH 6 were used in the equilibrium swelling studies for PAA and IPNs instead of water. The buffer solutions were prepared using 0.1 M dimethylglutaric acid (Sigma Chemical Co., St. Louis, MO). The pH was adjusted using 1.0 N NaOH. The equilibrium swelling ratio was determined in the same manner as PVA.

Diffusion Studies. Solute diffusion studies were performed at 37 ± 0.5 °C using a Valia-Chen diffusion cell (Crown Glass Co., Inc., Somerville, NJ). The apparatus consisted of two half-cells with a volume of 3 mL and a side opening with a diameter of 9 mm. A magnetic stir bar was placed in each half-cell for continued agitation. Between the two half-cells a pre-equilibrated membrane was securely placed and was protected from the atmosphere to prevent evaporation of the solvent from the membrane. Diffusion experiments were run at 37 °C as described before.[23,24] The solutes used in the diffusion studies varied in molecular weight, degree of ionization, and shape as shown in Table 1. Theophylline, vitamin B_{12}, and myoglobin were all purchased from Sigma Chemical Co., St. Louis, MO. For concentration detection purposes, theophylline and vitamin B_{12} had maximum wavelengths of 274 and 359 nm, respectively. The concentration used in the donor cell was 1 mg/mL for both solutes. Myoglobin had a maximum wavelength around 390 nm, and the concentration used was 10 mg/mL.

The solute partition coefficients were determined by equilibrating the membranes (approximately 1 cm^2) in water at 37 °C. They were then placed in 30 mL of solute of a known concentration. After 3 days, the absorbances of the solutions were measured. Solute concentrations were determined for each solution using a calibration curve. The solute concentrations of the membranes were calculated using a mass balance for the solute.

ATR-FTIR Spectroscopic Studies. Attentuated total reflectance-Fourier transform infrared (ATR-FTIR) spectroscopy was used to qualitatively investigate the interactions between the ionized membranes and ionized solutes. This technique was employed to determine if solute diffusion was hindered due to the interaction between the ionized solutes and ionized membrane. The interaction would be noted by the shifts in the functional groups (i.e., carbonyl groups) of the membrane. PVA, PAA, and IPN films were prepared by the same techniques as before on germanium crystals (Wilmad, Buena, NJ) using a spin-coating method. Reaction took place on these crystals and the ensuing films were transferred to an ATR-FTIR spectrophotometer (Model 800, Nicolet, Madison, WI). The relevant IR spectra were obtained in both the presence and absence of a dilute solution of the drugs or proteins tested.

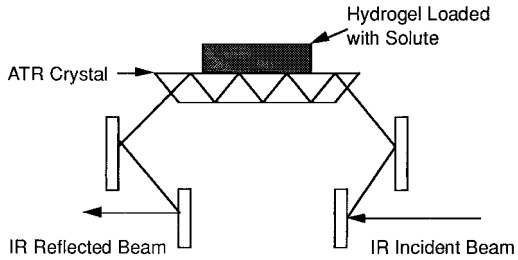

Figure 1. Setup of sample on the germanium crystal and infrared light path through ATR-FTIR.

Results and Discussion

Hydrogel Characterization. PVA was chemically cross-linked at 60 °C for 3 h. Swelling studies in distilled water and pH 3 and pH 6 buffer solutions were performed to characterize the membranes at 37 °C. The technique used and analysis of the results have been reported before by Peppas and Barr-Howell.[29] Table 2 summarizes the nominal cross-linking ratio and the polymer volume fractions of the relaxed and swollen states of the gel samples at pH 3 and pH 6. The polymer volume fraction in the equilibrium swollen polymer decreased as the PAA content increased, indicating significant swelling of the more hydrophilic compound.

The equilibrium polymer volume fraction, $v_{2,3}$, and the associated equilibrium volume swelling ratio, Q, of the hydrogel can be affected by the ionic strength, temperature, and pH of the swelling agent. In our studies, the ionic strength and temperature were kept constant at 0.2 N and 37 °C, respectively. The pH of the swelling agent was 6.7 for the PVA homopolymer due to its neutral nature. At pH 3, the PAA membranes were not ionized (pK_a = 4.7) while at pH 6 they were in the ionized form.

Table 2 also lists the equilibrium swelling ratios for PAA and PVA/PAA IPN membranes swollen in pH 3 and 6 buffer solutions. The results indicate that swelling increased as the pH increased. They also indicate that as the percentage of PAA increased in these membranes, the equilibrium swelling ratio increased. Due to the ionic nature of PAA, the IPNs and PAA membranes swelled much more than that PVA, which was neutral. Previously,[4,5] we studied the effects of pH on the swelling ratio and observed the same behavior as above.

Analysis of Cross-Linked Structure. The molecular weight between cross-links, $\bar{M}_c$, was calculated from the swelling data using eq 1 as discussed by Peppas and Merrill.[30]

$$\frac{1}{\bar{M}_c} = \frac{2}{\bar{M}_n} - \frac{\frac{\bar{v}}{\bar{V}_1}[\ln(1 - v_{2,s}) + v_{2,s} + \chi v_{2,s}^2]}{v_{2,r}\left[\left(\frac{v_{2,s}}{v_{2,r}}\right)^{1/3} - \frac{1}{2}\left(\frac{v_{2,s}}{v_{2,r}}\right)\right]} \quad (1)$$

Here, $\bar{M}_n$ is the number-average molecular weight of the polymer before cross-linking (=48 237), $\bar{v}$ is the specific volume of PVA (0.788 cm^3/g), $\bar{V}_1$ is the molar volume of

Table 2. Cross-Linking Ratio and Polymer Volume Fractions of PVA and PAA Homopolymer Hydrogels and PVA/PAA IPN Hydrogels in pH 3 and 6 Buffers at 37 °C

membrane code	PAA content (%)	solvent pH	nominal cross-linking ratio X ($\times 10^3$)	polym vol frac, $v_{2,r}$	polym vol frac, $v_{2,s}$	equil swelling ratio Q
PVA200	0	6.7	10.0	0.1094	0.1053	9.52
PP18	40	3	6.7	0.2575	0.0361	17.73
PP19	40	6	6.7	0.2655	0.0110	39.48
PP22	75	3	3.9	0.3937	0.0350	28.57
PP23	75	6	3.9	0.4025	0.0158	63.49
PAA001	100	3	1.8	0.5919	0.0085	36.21
PAA002	100	6	1.8	0.6105	0.0085	118.0

Table 3. Cross-Linking Densities and mesh Sizes Of the Homopolymers and PVA/PAA IPNs

PAA content (%)	swelling pH	nominal cross-linking ratio X ($\times 10^3$)	mol wt between cross-links, $\bar{M}_c$	mesh size (Å)	cross-linking density $\rho_x \times 10^4$ (mol/cm^3)
0	6	1.0	2500	98	4.16
40	3	6.7	29380	319	2.88
40	6	6.7	29380	420	2.88
75	3	3.9	31700	341	2.87
75	6	3.9	31700	502	2.87
100	3	1.8	35000	398	2.36
100	6	1.8	35000	589	2.36

water (18.1 cm^3/mol), $v_{2,r}$ is the polymer volume fraction in the gel in the relaxed state, $v_{2,s}$ is the polymer volume fraction in the gel in the swollen state, and χ is the interaction parameter[30] of PVA−water (=0.494).

For PAA-based gels, a modified swelling equation developed by Brannon-Peppas and Peppas[31] to account for the ionic nature in the homopolymers and IPNs was used. For PAA analysis, $\bar{M}_n$ was 75 000 as discussed before,[31] the specific volume of PAA was 0.951 cm^3/g, the Flory interaction parameter was approximately 0.5, and the dissociation constant was pK_a = 4.7.

The experimental values of $\bar{M}_c$ are listed in Table 3. In general, the presence of PAA led to a more open network structure with higher $\bar{M}_c$ values. The hydrogel mesh size, ξ, was calculated using eq 2.

$$\xi = v_{2,s}^{-1/3}\left[C_n\left(\frac{2\bar{M}_c}{\bar{M}_r}\right)\right]^{1/2} \qquad (2)$$

Here, C_n is the Flory characteristic ratio (=8.3) for PVA[23] and 6.7 for PAA,[23] and l is the carbon−carbon bond length (=1.54 Å).

The cross-linking density of the membranes was calculated using eq 3.

$$\rho_x = \frac{1}{vM_c} \qquad (3)$$

Table 3 lists the calculated values of the mesh size and the cross-linking density for each hydrogel as a function of cross-linking ratio and pH. The data indicate that as the cross-linking ratio decreased, the mesh size increased. Thus, as the amount of cross-linking agent decreased, the space between the cross-links became larger. It was also noted that the mesh size was dependent on the pH of the swelling solution for ionic membranes.

Diffusion Analysis. The solute diffusion coefficients through these hydrogels were determined through diffusion studies. The solutes used varied in molecular weight and degree of ionization and included theophylline (MW = 180, pK_a = 8.6), vitamin B_{12} (MW = 1355, neutral solute), and myoglobin (MW = 17 200, pK_a = 7.0). Figure 2 presents typical data of the theophylline permeated through PVA/PAA IPN membranes as a function of normalized time. In all experiments, the time was normalized by dividing by the square of the

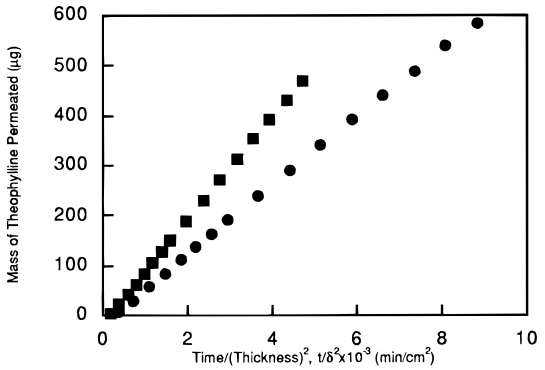

Figure 2. Diffusion of theophylline through PVA/PAA IPN membranes containing 40% PAA and with a mesh size, ξ, of 319 Å at pH 3 (●) and 420 Å at pH 6 (■).

equilibrium membrane thickness. The solute size, membrane mesh size, pH, and degree of ionization of the membrane and solute were determined to investigate their effects on solute diffusion. Permeation of theophylline through the membranes at both pH 3 and pH 6 was linear, and the amount permeated at pH 6 was greater than the amount permeated at pH 3. As the size of theophylline was much smaller than the mesh size of the IPN at both pH 3 and pH 6, these data cannot be explained in terms of solute size exclusion only. At pH 6, both theophylline and the membrane were ionized. Due to their opposite charges, ionic interaction and binding could be occurring, thus hindering the permeation of theophylline in the membrane at pH 6. At pH 3, theophylline was not ionized and binding did not occur. However, due to the increased mesh size of the membranes at pH 6 and the small solute size compared to the membrane mesh size, solute binding did not dominate the permeation of theophylline.

Permeation of vitamin B_{12} showed a short lag period at the beginning of each permeation study which was attributed to low vitamin B_{12} permeation due to size exclusion phenomena. This was indicated in the figures by the curvature of the line at the beginning of each study. Afterward, permeation proceeded linearly. The equivalent molecular diameter of vitamin B_{12} (d = 16.6 Å) is smaller than the mesh sizes of these membranes. At pH 6, solute permeation was greater because of the more space available for diffusion. As vitamin B_{12} was

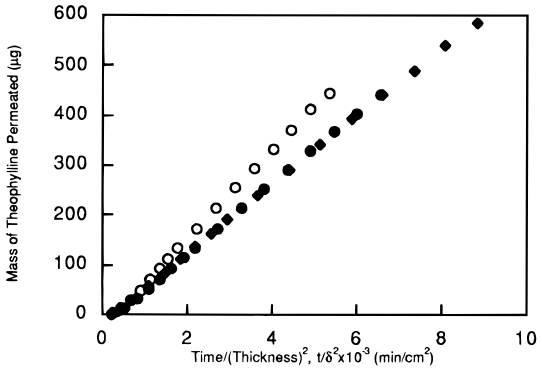

Figure 3. Diffusion of theophylline through PAA homopolymer and PVA/PAA membranes at pH 3: 40% PAA, mesh size, ξ, of 319 Å (◆), 75% PAA, mesh size, ξ, of 341 Å (●), and 100% PAA, mesh size, ξ, of 398 Å (○).

a neutral solute, there were no polymer/solute interactions.

The quantity of solute permeated was plotted versus normalized time to determine the effects of mesh size on permeation of solutes. Figure 3 shows typical data of the permeation of theophylline through each membrane at pH 3. It can be seen that the extent of permeation of theophylline through membranes containing 40% and 75% PAA (mesh size, $\xi = 319$ and 341 Å, respectively) was the same. For the PAA homopolymer (mesh size, $\xi = 398$ Å) permeation was greater. However, at pH 6, the permeation of theophylline was essentially the same for all of the membranes. At pH 6, polymer/solute interactions existed, but because the size of theophylline was very small compared the mesh sizes of the membranes, these interactions did not dominate the diffusion of theophylline.

Polymer/solute interactions do not occur in the permeation of vitamin B_{12} at pH 3 and pH 6. Therefore, size exclusion phenomena dominate the diffusion process. At pH 3, vitamin B_{12} was shown to have permeated more slowly through PVA/PAA membrane containing 40% PAA (mesh size, $\xi = 319$ Å). As the mesh size increased, the permeation of vitamin B_{12} increased.

Permeability coefficients, P, were calculated from the data obtained in the permeation experiments using the following equation:

$$-\ln\left(1 - \frac{2c_t}{c_0}\right) = \frac{2A}{V}Pt \tag{4}$$

Here, c_t is the solute concentration in the receptor cell at time t, c_0 is the initial solute concentration of the donor cell, V is the volume of each half-cell, A is the effective area of permeation, and P is the membrane permeability coefficient.

The diffusion coefficient was calculated from the permeability coefficient, P, and the partition coefficient, K_d, as shown in the following equation:

$$D_m = \frac{Pl}{K_d} \tag{5}$$

Here, l is the membrane thickness in the swollen state at constant pH, and K_d is the ratio of the solute concentration in the membrane, c_m, to the solute concentration in the solution at equilibrium, c_s. Equation 6 was used to calculate the partition coefficient.

$$K_d = \frac{c_m}{c_s} = \frac{V_s(c_0 - c_e)}{V_m c_0} \tag{6}$$

Here, V_s and V_m are the volume of the solute in solution and the membrane, respectively, c_0 is the initial concentration of the solute in solution, and c_e is the solute concentration in the solution at equilibrium. Table 4 lists the partition coefficients for each membrane and solute. At pH 6, the partition coefficients were found to be higher for all solutes, indicating a higher affinity for the membranes than at pH 3. In the case of theophylline and myoglobin, this was due to the binding of the solute to the membranes. This would be correct, as at pH 6 there is complete ionization of the membrane. However, the values of K_d for myoglobin are extremely high, indicating significant binding in the membrane.

Vitamin B_{12} was found to have the smallest partition coefficients, which may be attributed to its nonionization. At pH 6, the partition coefficients of theophylline and vitamin B_{12} in membranes that contained 75% and 100% PVA were similar.

Although theophylline was a smaller molecule than vitamin B_{12}, the partition coefficients for theophylline were higher. In this case, polymer/solute interactions occurred, allowing binding to take place between the membrane and theophylline. The partition coefficients were higher at pH 6 due to the binding of theophylline to the membranes.

The highest partition coefficients were observed for myoglobin at pH 6 due to the size and shape of myoglobin as well as the permanent binding between myoglobin and the membranes.

These partition coefficients and data from the permeability studies were used to determine the diffusion coefficients of each solute through the membranes which are listed in Table 5. Comparisons are made to the diffusion coefficients of the solutes through water. The table shows that the diffusion coefficients were higher at pH 6 for theophylline. Although binding occurred between the membranes and theophylline, it did not dominate the diffusional process due to the size of theophylline ($d = 9.4$ Å) relative to the mesh sizes of the membranes which are listed in Table 5. The diffusion coefficients for vitamin B_{12} were also higher at pH 6 and were comparable to those of vitamin B_{12} in

Table 4. Solute Partition Coefficients in PAA Homopolymer and PVA/PAA Membranes Swollen at pH 3 and 6 at 37 °C

swelling pH	PAA compn of IPN (%)	solute	partition coeff, K_d
3	40	theophylline	25.1
		vitamin B_{12}	17.7
		myoglobin	
6	40	theophylline	32.6
		vitamin B_{12}	19.1
		myoglobin	11300
3	75	theophylline	27.7
		vitamin B_{12}	15.6
		myoglobin	
6	75	theophylline	31.4
		vitamin B_{12}	16.2
		myoglobin	12300
3	100	theophylline	36.5
		vitamin B_{12}	9.2
		myoglobin	
6	100	theophylline	31.9
		vitamin B_{12}	17.0
		myoglobin	4650

Table 5. Solute Diffusion Coefficients through IPN Hydrogel Membranes at 37 °C

solute	PAA compn of IPN (%)	swelling pH	mesh size (Å)	diff coeff $D_m \times 10^7$ (cm²/s)	diff coeff in water $D_{water} \times 10^7$ (cm²/s)
theophylline	40	3	319	49.6	
		6	420	60.2	
	75	3	341	47.8	
		6	502	58.4	87.4 (37 °C)
	100	3	398	45.3	
		6	589	59.8	
vitamin B_{12}	40	3	319	28.7	
		6	420	31.8	
	75	3	341	27.6	
		6	502	34.3	37.9 (37 °C)
	100	3	398	31.9	
		6	589	35.7	
myoglobin	40	3	319		
		6	420	0.17	
	75	3	341		
		6	502	0.16	12.8 (25 °C)
	100	3	398		
		6	589	0.16	

water at 37 °C. This indicated that vitamin B_{12} freely diffuses through the membrane. Myoglobin diffusion coefficients were not calculated at pH 3 as there was no discernible diffusion. At pH 6, the diffusion coefficients were smaller than through water at 25 °C, which was attributed to permanent binding of myoglobin in the membrane.

Analysis of Diffusion Studies. The theory proposed by Peppas and Reinhart[19] can be used to describe solute permeation through highly swollen, nonporous hydrogels. As mentioned before, this theory predicts that the solute diffusion coefficient is related to the solute size, equilibrium degree of swelling, and other structural parameters of the membranes according to eq 7.

$$\frac{D_{SM}}{D_{SW}} = k_1\left(\frac{\bar{M}_c - \bar{M}_c^*}{\bar{M}_n - \bar{M}_c}\right)\exp\left(-\frac{k_2 r_s^2}{Q-1}\right) \qquad (7)$$

Here, D_{SM} and D_{SW} are the solute diffusion coefficients in the hydrogel and water, respectively, $\bar{M}_c$ is the molecular weight between cross-links, k_1 and k_2 are structural parameters of the polymer/water system, $\bar{M}_c^*$ is the critical molecular weight between cross-links below which diffusion could not occur, $\bar{M}_n$ is the molecular weight of the polymer before cross-linking, r_s is the Stokes hydrodynamic radius of the solute, and Q is the equilibrium volume swelling ratio of the hydrogel. The theory suggests that a plot of $\ln(D_{SM}/D_{SW})$ versus $r^2/(Q-1)$ would yield a straight line. The experimental results were plotted for PVA/PAA membranes containing 40%, 75%, and 100% PAA using both methods, as shown in Figure 4. A straight line was obtained for each hydrogel composition studied. However, according to the theory,[19] all data should collapse into one line. This was a clear indication that although the membranes are highly swollen, ionic interactions between the solute and the membrane lead to derivations from the theory. As the amount of PAA increased in the membrane, the polymer/solute interactions increased. Although the mesh size increased, the permeation of ionic solutes decreased evidently due to an increase of polymer/solute interactions, which were not considered in the development of the previous theory.[19]

Study of Interactions between PAA Hydrogel and Myoglobin. ATR-FTIR spectroscopy was used to study the polymer/solute interactions in ionic systems by measuring vibrational and rotational transitions of

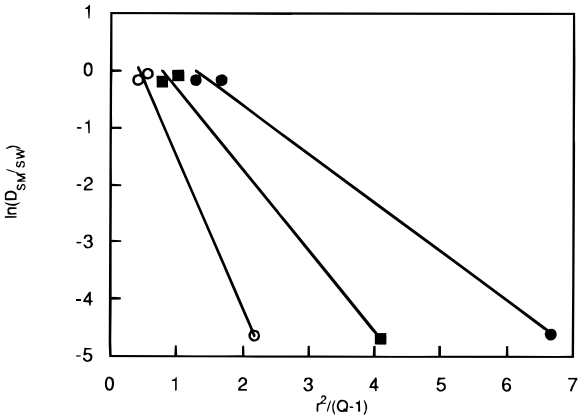

Figure 4. Diffusion data for PVA/PAA membranes containing 40% PAA (●), 75% PAA (■), and 100% PAA (○) fitted to the Peppas−Reinhart model.

functional groups. To analyze these interactions, a sample was centrally placed on a germanium crystal. The hydrogel sample was placed in a concentrated drug solution for 2 days in order to load the drug into the hydrogel. The sample was then placed on the crystal and spectra were taken to determine any interactions between the drug and polymer. Since the beam penetrates a small distance into the sample, care was taken to place the sample in intimate contact with the surface of the crystal. For comparison, the spectra of swollen hydrogel without the drug and the drug itself were analyzed.

ATR-FTIR spectroscopy was used to study the interactions between PAA hydrogel and myoglobin. A spectrum of the clean germanium crystal was used as the background. The spectrum of the hydrogel swollen at pH 6 in the absence of solute was compared with the spectra of myoglobin and a swollen hydrogel loaded with myoglobin. The background was subtracted from each spectrum to eliminate noise.

Figures 5−7 show the ATR-FTIR spectra of the hydrogel, myoglobin, and the combined system and identify the bands at which stretching and vibration may be occurring. Table 6 indicates the relevant peaks in the hydrogel, myoglobin, and membrane loaded with myoglobin. Peaks between 1000 and 2000 cm^{-1} which were observed in myoglobin and in the loaded hydrogel, but in the hydrogel without myoglobin. However, peaks observed in the loaded myglobin hydrogel spectrum were also observed in the pure myoglobin spectrum

Table 6. Analysis of FTIR Spectra of PAA Hydrogel, Myoglobin, and PAA Hydrogel Loaded with Myoglobin at pH 6

		wavenumbers (cm^{-1})		
peak	functional vibration	PAA hydrogel	myoglobin	hydrogel loaded with myoglobin
A	OH^-	3370	3370	3370
B	OH^- stretching, hydrogen bonding		2964	2964
C	OH^- (associated carboxylic acid vibration)	2363	2363	2363
D	OH^- (associated carboxylic acid vibration)	2336	2338	2338
E	C═O stretching	1734	1734	1728
F	C═O stretching, intramolecular hydrogen bonding	1635	1635	1635
G	$(C{=}O)^-$	1558	1558	1550
H	$C(=O)-O^-$ symmetric stretch		1400	1393
I	C−O stretching (dimer)		1262	1262
J	C−O stretching (monomer)		1069	1083

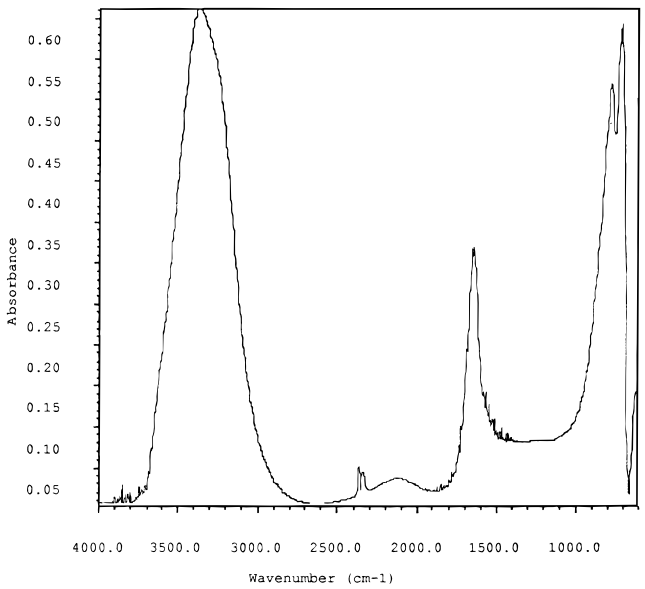

Figure 5. ATR-FTIR spectrum of a swollen PAA hydrogel at pH 6.

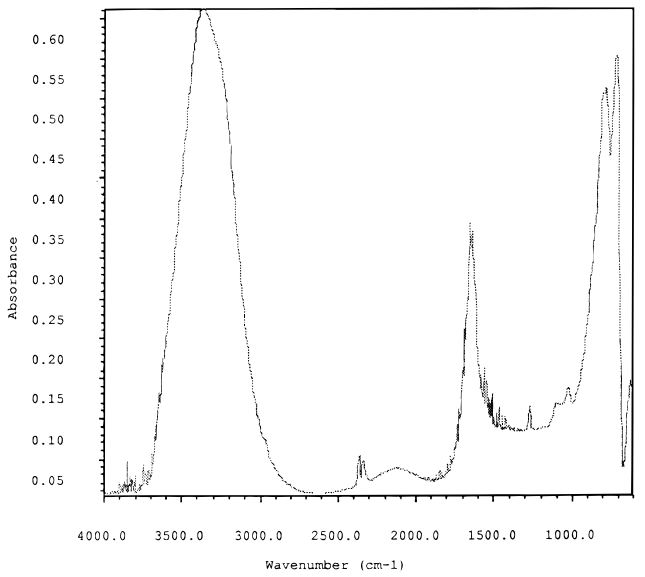

Figure 6. ATR-FTIR spectrum of myoglobin solution.

albeit shifted. Each sample exhibited OH^- stretching due to hydrogen bonding and carboxylic vibrations and CO^- due to intramolecular bonding in the same regions. Peak E represents C═O stretching at 1734 cm^{-1} but is seen at 1728 cm^{-1} in the loaded hydrogel. Peak G represents the ionized carbonyl group at 1558 cm^{-1} but is seen at 1550 cm^{-1} in the loaded hydrogel. Peaks H and J, which represent $C(=O)-O^-$ symmetric stretching

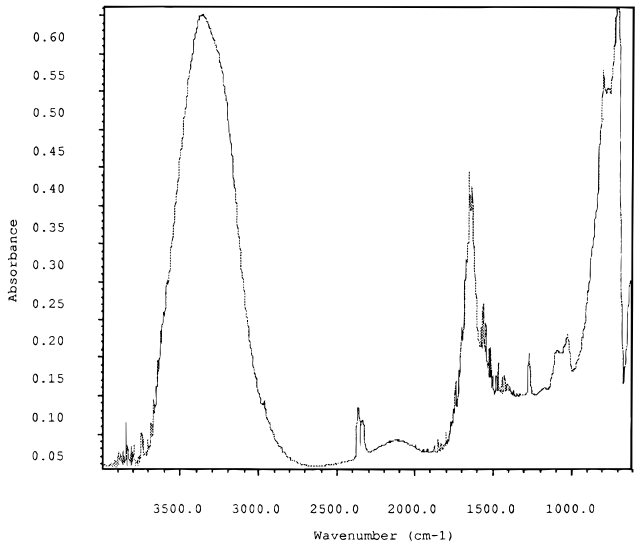

Figure 7. ATR-FTIR spectrum of a swollen PAA hydrogel loaded with myoglobin at pH 6.

and C−O stretching, respectively, were also shifted in the loaded hydrogel. Each of these shifts can be attributed to the binding of myoglobin to the membrane. Therefore, these ATR-FTIR studies indicate a significant binding of myoglobin on PAA hydrogels at the pH values relevant to the diffusion experiments. This binding would explain the significant reduction of myoglobin transport in these gels.

Implications of Binding on Solute Transport Theory. The previous conclusions can be used in a quantitative way to identify the shift in diffusional binding. For example, recently am Ende and Peppas[22,33] proposed a modification of the Peppas−Reinhart theory (eq 7) which takes into consideration the binding (and the associated shifts of the IR spectra) as shown in eq 8.

$$\frac{D_{SM}}{D_{SW}} = k_1\left(\frac{\bar{M}_c - \bar{M}_c^*}{\bar{M}_n - \bar{M}_c}\right)\exp\left(-\frac{k_2 r_s^{\,2}}{Q-1}\right) - k_3\exp\left(\frac{\Delta H^{ab}}{kT}\right) \tag{8}$$

Here, k_3 is a constant dependent on solute and polymer system and ΔH^{ab} is a term proportional to the shift in spectral frequency. Examination of the data of Figure 4 indicates that the solute diffusion coefficient decreased significantly (in some cases by 2−3 orders of magnitude) as the PAA content of the PVA/PAA content increased from 40% to 100%. Thus, if we consider the data of Figure 4 represented by the symbol (●) as the ones observed under the lowest binding, the additional reduction of the diffusion coefficient may be attributed

Table 7. Solute Transport Analysis Using the Modified Binding Equation[23,33]

PVA/PAA compn (PAA content %)	intercept of logarithmic form of eq 8 ln k_1'	preexponential term k_1'	diffusional constant λ_1
40	1.07	2.90	0.85
75	1.12	3.06	1.42
100	1.15	3.16	2.64

to binding and can be calculated from the last term on the right-hand side of eq 8.

For example, the diffusion data for the solutes studied here through the IPN membranes containing 40% PAA can be expressed as

$$\frac{D_{SM}}{D_{SW}} = k_1' \exp\left(-\frac{\lambda_1 r_s^2}{Q-1}\right) \tag{9}$$

Analysis of the data of Figure 4 with this equation leads to calculation of the values presented in Table 7. Clearly, these results indicate a significant solute binding in the more ionic hydrogels. A significant binding between solute and polymer is seen as an increase of the diffusional term, λ_1, from 0.85 in the 40% PAA hydrogel to 2.64 in the pure PAA hydrogel. This significant binding can be related to the spectral shifting term ΔH^{ab}, which increases as binding increases. If all other parameters are equal, solute binding in gels increasing from 40% to 100% PAA leads to a threefold increase in energetic shifting. The associated change in the pre-exponential term, k_1', cannot indicate a significant change of the mesh size, to which this term is related, as shown by eqs 8 and 9.

Conclusions

PVA, PAA, and IPN hydrogels were prepared to study the effect of ionization on solute diffusion at pH 3 and pH 6 (above and below the pK_a of PAA). Each membrane was well characterized through swelling studies, and the molecular weight between cross-links, the mesh size, and the cross-linking density were calculated. Solute diffusion was studied as a function of pH, mesh size, and PAA content. The results indicated that for vitamin B_{12} permeation was greater at pH 6 at which the hydrogel was expanded and the mesh size was greater. The permeation of theophylline was greater at pH 6, although the membrane and theophylline were ionized.

Polymer/solute binding may have occurred but because the mesh size of the membrane was significantly larger than the solute size, the interactions did not dominate diffusion. Myoglobin did not permeate through the membranes at pH 3 within 18 h due to the immediate binding of myoglobin as it was placed in contact with the membrane. At pH 6, permeation of myoglobin did occur. Myoglobin permeated through the membranes that contained higher amounts of PAA (75% and 100%) at a linear rate, but the rate changed after 2.5 h due the polymer/solute interactions occurring between the membranes and myoglobin.

The data did not fit the theoretical predictions of our equations[19] due to the polymer/solute interactions that occurred between the membrane and the solutes. To further support the polymer/solute interactions, ATR-FTIR quantitatively confirmed the polymer/solute interactions by showing a shift in the carbonyl region of the spectra. These data could be explained by a modification of the previous theory[23] by including a binding term for reduction of the solute diffusion.

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