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Solute diffusion in poly(vinyl alcohol)/poly(acrylic acid) composite membranes prepared by freezing/thawing techniques

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Composite membranes of poly(vinyl alcohol) and poly(acrylic acid) were prepared by freezing and thawing of aqueous solutions of the two components. The ensuing hydrogels and membranes exhibited crystallinity of up to 13.50% (on a swollen basis) due to crystallization of the poly(vinyl alcohol). The membranes prepared under these conditions exhibited size exclusion characteristics. Theophylline and FITC-dextran transport were investigated and the solute diffusion coefficients were correlated with the mesh size of the membranes. Copyright © 1997 Elsevier Science Ltd.

(Keywords: poly(vinyl alcohol); poly(acrylic acid); freezing/thawing)

INTRODUCTION

Poly(vinyl alcohol) (PVA) hydrogel membranes have been prepared and used over the past thirty years in a variety of chemical and biological separation applications[1–13]. Of particular importance have been recent efforts to produce PVA hydrogels of well characterized pore size and size distribution. For example, Paul and Ebra-Lima[1] and Ebra-Lima and Paul[2] studied their preparation and hydraulic permeability, whereas Katz and Wydeven[3,4], and Peppas[5] and Peppas and Merrill[6] investigated their preparation by irradiation methods and their reinforcement by heat treatment (annealing) techniques at moderate to high temperatures. Their hydraulic and solute permeability coefficients have been also investigated[7–13]. We have commented[13] on the relative importance of the water-filled pores vs the network structure of the membranes. PVA membranes have been used even for separation of gases[14]. Asymmetric PVA membranes have also been prepared and tested[15–18].

In recent years, there has been a renewed interest in biomedical applications of PVA especially through the use of preparation techniques that are based on benign manufacturing. Studies by Ikada and collaborators[19,20], our group[5,21] and others[22–25] have addressed methods of preparation preparing PVA membranes free of elutable impurities, such as emulsifiers, catalysts and unreacted crosslinking agents. In this sense, the use of crosslinking agent-free preparation methods has become very popular but also necessary[19–21]. The preferred preparation method for such medical or biological applications consists of a freezing–thawing process applied on pure aqueous solutions of PVA, or on solutions containing dimethyl sulfoxide (DMSO). In previous work[21,26], we summarized the historical development of these techniques.

In the freezing–thawing-based techniques[21], fine crystallites are formed due to the slow heat treatment. Their properties have been analysed to a great extent in recent monographs[27,28] and contributions[29–37]. In recent work[38], we analyzed the degree of crystallinity, mesh size and diffusive characteristics of PVA hydrogel membranes made by this technique.

As pure PVA hydrogels are insensitive to pH changes, several recent studies have been reported[39–59] where poly(acrylic acid) (PAA) has been mixed with PVA to produce pH-sensitive gels by the freezing–thawing process or other methods. Such studies have examined the methods of preparation and morphological changes of the ensuing materials[39–52], as well as diffusive properties and applications in the medical field[53–59]. Biomedical applications of such membranes or materials are particularly interesting because of the virtual lack of toxic additives or reactants during membrane preparation.

In the present work, we were particularly interested in the diffusive characteristics of PVA/PAA composite membranes, especially those produced by freezing/thawing techniques. Little is known about the mode of solute diffusion in such membranes. Reported applications include their use for pervaporation separation[54,55] or for protein transport in the presence of electrical fields[50,58]. Here, we analyse results of solute transport in PVA/PAA membranes using the free value theory in the spirit of our recent work on pure PVA membranes[38].

EXPERIMENTAL

Membrane preparation

PVA (Elvanol 9050, E.I. du Pont de Nemours and Co.,

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Wilmington, DE) with a degree of hydrolysis of 99.6%, $\bar{M}_n = 35\,420$, $\bar{M}_w = 79\,200$, and polydispersity index of 2.24, and PAA (Aldrich Chemical Company, Inc., USA), with $\bar{M}_w = 90\,000$ supplied in the form of a 25 wt% aqueous solution were used for membrane preparation.

Aqueous 15 wt% PVA solutions were prepared by dissolving preweighed quantities of dry PVA in deionized water and heating them at 90 ± 0.2°C for 6 h (see also Hickey and Peppas[38]). After cooling slowly to 25 ± 1°C, the PVA solution was mixed with the PAA solution by stirring at 25 ± 1°C for 8 h in order to achieve a homogeneous solution of the two polymers. Solutions with different PVA/PAA ratios were prepared by varying component composition, cast onto glass plates using a Gardner knife, and then placed at −20°C for 8 h. After the freezing process they were thawed to 25 ± 1°C and kept there for 5 h. This freezing and thawing cycle was repeated for an additional two to four times.

The ensuing membranes were allowed to dry completely at 25 ± 1°C. All films were annealed at 60°C for 24 h in a thermostated oven. The annealed films were immersed in a phosphate buffer with pH = 7 at 25 ± 1°C and kept there until further use.

Membrane characterization

Samples of the previously prepared PVA/PAA membranes (1 × 1 cm^2) were swollen in a buffer solution at pH = 7. Some loss of weight was observed at the beginning of the swelling studies, but after approximately 50 h the membranes achieved constant weight, which did not change for 25 days.

The volumes of the hydrogel sample before equilibrium swelling in a buffer solution, $V_{d,g}$, and after equilibrium swelling, $V_{g,s}$, were determined according to Peppas and Barr-Howell[60], using equations (1) and (2)

$$V_{g,d} = \frac{W_{a,d} - W_{n,d}}{\rho_n} \tag{1}$$

$$V_{g,s} = \frac{W_{a,s} - W_{n,s}}{\rho_n} \tag{2}$$

where $W_{a,d}$ and $W_{a,s}$ are the sample weights in air before and after swelling, respectively, and $W_{n,d}$ and $W_{n,s}$ are the sample weights in a nonsolvent (heptane with $\rho_n = 0.684\,g\,cm^{-1}$ at 25 ± 1°C) before and after equilibrium swelling, respectively.

The equilibrium volume swelling ratio, Q, was determined as the ratio of the two volumes.

$$Q = \frac{V_{g,s}}{V_{g,d}} \tag{3}$$

and the polymer volume fraction, $v_{2,s}$, was calculated as

$$v_{2,s} = \frac{1}{Q} \tag{4}$$

The number average molecular weight between crosslinks, $\bar{M}_c$, was calculated using equation:

$$\frac{1}{\bar{M}_c} = \frac{2}{\bar{M}_n} - \frac{\frac{\bar{v}}{V_1}\left[\ln(1 - v_{2,s}) + v_{2,s} + \chi v_{2,s}^2\right]}{\left(v_{2,s}^{1/3} - \frac{1}{2} \cdot v_{2,s}\right)} \tag{5}$$

where $\bar{M}_n$ was calculated as the arithmetic average of the individual $\bar{M}_n$ values, according to the PVA and PAA contents in the membrane. The parameter χ was determined by Peppas and Merrill[6] for PVA and varied between 0.494 and 0.512. Similarly, the value for PAA was 0.51. Thus, a value of $\chi = 0.51$ was used here. Similarly, $\bar{v}$ was approximated as 0.788 cm^3 g^{-1}, since the membranes were predominantly PVA. Finally, $V_1 = 18.1\,cm^3\,mol^{-1}$ for water. The mesh size was calculated using equation (6).

$$\xi = v_{2,s}^{-1/3} \cdot \sqrt{C_n}\sqrt{2\bar{M}_c/M_r} \cdot l \tag{6}$$

where $C_n = 8.3$ (for membranes containing predominantly PVA), M_r is the average of the molecular weights on the repeating units of PVA (= 44) and PAA (= 72), and $l = 1.54$ Å.

Mechanical studies

The mechanical stability of the PVA/PVA membranes prepared was tested using tensile experiments. Typically, equilibrium swollen membranes were cut with a dumbbell-shaped die of length 3.8 cm, end with 0.6 cm and neck width 0.2 cm. Small deformation, constant-rate-of-extension experiments were performed in a tensile tester (model 4301, Instron, Canton, MA) under an extension rate of 2 mm min^{-1}. The stress vs strain behaviour was recorded and the intial modulus, E_0, was calculated. The degree of crystallinity was measured by differential scanning calorimetry (d.s.c.) as discussed before[38].

Permeation studies

Solute permeation experiments were performed as before[38] using a side-by-side diffusion apparatus (Crown Glass Co. Inc., Somerville, NJ, USA), consisting of two cylindrical glass-stirred diffusion cells, surrounded by water jackets. A membrane was placed between the two cells and its ends were covered with Parafilm^R to prevent membrane drying. Each half-cell had a volume of 3 ml. The open area between the half-cells was 0.64 cm^2.

Theophylline (Sigma Chemical Company, St Louis, Missouri, USA) with a molecular weight of 180.2 and a hydrodynamic radius[61] of 3.7 Å and fluorescein isothiocyanate (FITC)-dextran (Sigma Chemical Co., St Louis, USA) with a molecular weight of 4400 and a hydrodynamic radius[62] of 16.5 Å were used for these studies.

The donor cell was filled with a 0.1 g l^{-1} aqueous solution of the solute, while the receptor cell was filled with deionized water. The whole system was agitated with magnetic stirrers and the contents of the receptor cell were replaced with fresh deionized water every 15 min for theophylline and every 60 min for FITC-dextran diffusion studies. The sample's absorbance was determined immediately upon removal from the receptor cell with an ultraviolet–visible (u.v.–vis) spectrophotometer (model 559, Perkin Elmer, Norwalk, CT). Theophylline and FITC-dextran concentrations were calibrated at the absorbance peaks of 271 nm and 237 nm. respectively. All diffusion experiments were performed at 25 ± 1°C over an average run time of 8 h.

The solute partition coefficient was measured by equilibrating thin sections of the membranes in a concentrated solution for 7 days and calculating the ratio of the soluble concentration in the membrane (by difference) to that in the solution.

RESULTS AND DISCUSSION

PVA/PAA composite membranes were produced by

Table 1 Preparation conditions and swelling behaviour of PVA/PAA composite membranes

PVA/PAA membrane composition (PVA/PAA ratio)	Number of freezing/thawing cycles	Time of freezing (h)	Equilibrium swelling ratio, Q
90/10	1	8	8.61
85/15	1	8	11.06
80/20	1	8	14.44
75/25	1	8	17.51
90/10	3	8	7.60
85/15	3	8	9.30
80/20	3	8	11.90
75/25	3	8	14.30
90/10	5	8	7.18
85/15	5	8	8.33
80/20	5	8	10.43
75/25	5	8	10.88

Table 2 Characterization of PVA/PAA composite membrane swollen at 25°C

Membrane composition	Swollen membrane thickness, δ (cm)	Equilibrium swelling ratio, Q	Polymer volume fraction, $v_{2,s}$	Polymer–water interaction parameter, χ
I				
PVA[a]	0.029	4.40	0.227	0.495
PVA/PAA[a] (90/10)	0.028	7.60	0.132	0.502
PVA/PAA[a] (85/15)	0.025	9.30	0.107	0.496
PVA/PAA[a] (80/20)	0.028	11.90	0.084	0.489
PVA/PAA[a] (75/25)	0.028	14.30	0.069	0.487
II				
PVA[b]	0.029	4.00	0.250	0.495
PVA/PAA[b] (90/10)	0.031	7.18	0.139	0.505
PVA/PAA[b] (85/15)	0.040	8.33	0.120	0.499
PVA/PAA[b] (80/20)	0.038	10.43	0.096	0.493
PVA/PAA[b] (75/25)	0.043	10.88	0.092	0.492

[a] Crystalline PVA in membrane is 12.86%
[b] Crystalline PVA in membrane is 13.92%

freezing and thawing of aqueous solutions of the two polymers. They were strong, thin films and swelled to equilibrium in a few hours at 25°C. *Table 1* summarizes the membrane compositions, duration of freezing and number of freezing/thawing cycles used. The values of the equilibrium swelling ratio were determined at 25°C and varied between 7.18 and 17.51. Clearly, as the PAA content increased the membrane swelling ratio increased significantly due to the ionization of the carboxylic groups of PAA. Some of the most swollen composite membranes contained 25% PAA and swelled to equilibrium values of $Q = 17.51$, corresponding to $v_2 = 0.057$. Previous freezing/thawing studies have indicated[45,52,53] that the main reason for the solidification observed during this process is the crystallization of PVA. The ionic component PAA is typically entangled between the semicrystalline PVA chains but may also interact by forming hydrogen bonds[39,46] through the carboxyl functional groups. In our studies, hydrogel membranes prepared after one cycle were highly swollen (see *Table 1*) and extremely difficult to handle. It was noted that as the number of cycles increased, the swelling ratio decreased significantly. For example, for PVA/PAA membranes containing 20% PAA, the swelling ratio was 14.44 (corresponding to 6.9% polymer in the swollen gel) after one cycle, but decreased to 10.43 (corresponding to 9.6% polymer in the gel) after five cycles. These results were compared to Q values of membranes prepared under the same conditions but containing only PVA[38], where the swelling ratio was 4.45. Clearly, the presence of ionizable PAA led to a significant increase in the swelling. This has also been noted in some very recent studies by Lee *et al.*[63] that were published during the proofreading stage of this paper.

Table 2 summarizes the equilibrium polymer volume fraction and other characteristics of PVA/PAA membranes. D.s.c. studies revealed that the first set of membranes (Set I) indicated by the symbol (a) had an average crystalline PVA content at equilibrium of 12.86%, whereas the second set of membranes (Set II) indicated by the symbol (b) was slightly more crystalline at 13.92% crystalline PVA.

The mechanical stability of the membranes was characterized by determining their initial moduli which varied from 0.42 to 0.96 MPa.

The number average molecular weight, $\bar{M}_c$, and the equilibrium mesh size, ξ, were determined and calculated as indicated above. The values determined are summarized in *Table 3*. In general, the equilibrium mesh size was larger than that of PVA membranes prepared by the

Table 3 Network characterization and solute diffusion coefficients through equilibrium swollen PVA/PAA composite membranes at 25°C

Membrane composition	Equilibrium swelling ratio, Q	Number-average molecular weight between crosslinks, $\bar{M}_c$	Mesh size, ξ (Å)	Solute diffusion coefficient $D_c \times 10^8$ (cm^2 s^{-1})	
				Theophylline ($r_s = 3.7$ Å)	Dextran ($r_s = 16.5$ Å)
I					
PVA[a]	4.40	1750	71.7	5.9 ± 0.09	2.81 ± 0.05
PVA/PAA (90/10)	7.60	7900	129.7	6.86 ± 0.45	3.05 ± 0.10
PVA/PAA (85/15)	9.30	11 550	167.0	6.35 ± 0.15	2.82 ± 0.25
PVA/PAA (80/20)	11.90	13 550	197.1	6.92 ± 0.08	3.42 ± 0.36
PVA/PAA (75/25)	14.30	16 200	228.0	9.24 ± 0.38	3.69 ± 0.27
II					
PVA[b]	4.00	1575	59.3	5.67 ± 0.12	2.23 ± 0.05
PVA/PAA (90/10)	7.18	6850	121.3	7.69 ± 0.44	2.51 ± 0.17
PVA/PAA (85/15)	8.33	9175	141.6	11.16 ± 0.33	3.40 ± 0.07
PVA/PAA (80/20)	10.43	13 500	179.3	9.92 ± 0.26	3.69 ± 0.20
PVA/PAA (75/25)	10.88	13 750	182.8	12.64 ± 0.21	4.39 ± 0.13

[a] Crystalline PVA in membrane is 12.86%
[b] Crystalline PVA in membrane is 13.92%

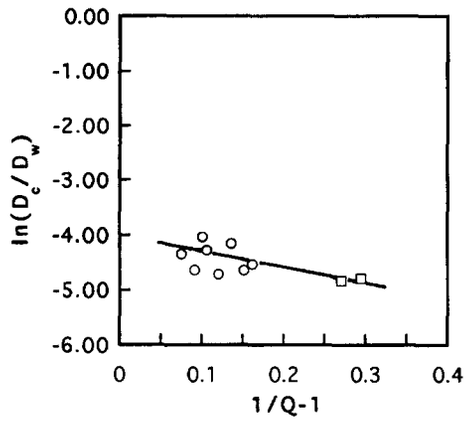

Figure 1 Normalized theophylline diffusion coefficients through semicrystalline, freezing/thawing processed PVA/PAA membranes as a function of the hydration factor $(Q-1)^{-1}$, of the membranes at 25°C

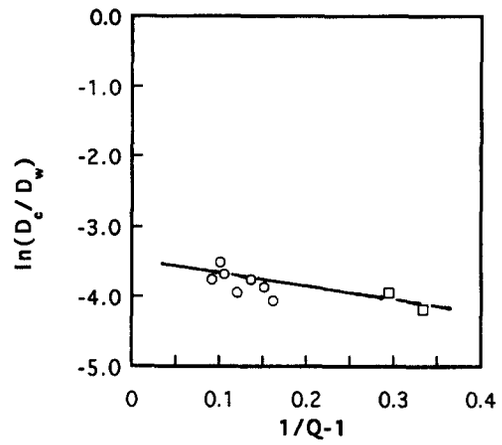

Figure 2 Normalized FITC-dextran diffusion coefficients through semicrystalline, freezing/thawing processed PVA/PAA membranes as a function of the hydration factor, $(Q-1)^{-1}$, of the membranes at 25°C

same techniques, as previously reported by us[38]. This was due to the ionic nature of PAA. Indeed, a pure PVA membrane prepared under the same conditions exhibited a mesh size of 71.7 Å. It was also noted that a small increase of the degree of crystallinity (Set II vs Set I) led to a significant degree of the mesh size. Previously, Rhim *et al.*[54] discussed the preparation of composite PVA/PAA membranes with the same compositional characteristics but heat treated at high temperatures instead of the freeze/thawing processing. They found that such membranes could be used for pervaporation separation, a conclusion that can be explained by the mesh sizes reported here.

Theophylline and FITC-dextran permeation studies were used to determine the size exclusion characteristics of these samples. The receptor solute concentration was determined as a function of time and the solute permeability coefficient, P, was calculated using equation (7).

$$\ln\left(1-\frac{2c_t}{c_0}\right) = -\frac{2A}{V}Pt \tag{7}$$

Here, c_0 was the initial solute concentration in the donor cell, c_t was the solute concentration in the receptor cell at time t, A was the area of the cell opening (effective area for permeation), and V was the cell volume.

The calculated values of the permeability coefficients, P, were used to calculate the solute diffusion coefficient, D_c, using equation (8)

$$D_c = \frac{P\delta}{K} \tag{8}$$

Here, K was the partition coefficient and δ the (equilibrium) thickness of each membrane. The partition coefficient was determined experimentally as $K = 0.36 \pm 0.04$ for theophylline, and as approximately equal to 1 for FITC-dextran.

Based on these studies, *Table 3* summarizes the values of the solute diffusion coefficient, D_c, for theophylline and FITC-dextran in selected PVA/PAA membranes studied.

As discussed by Reinhart and Peppas[12], a correlation between the normalized solute diffusion coefficient, D_c/D_w, and the term $(Q-1)^{-1}$ should provide a straight

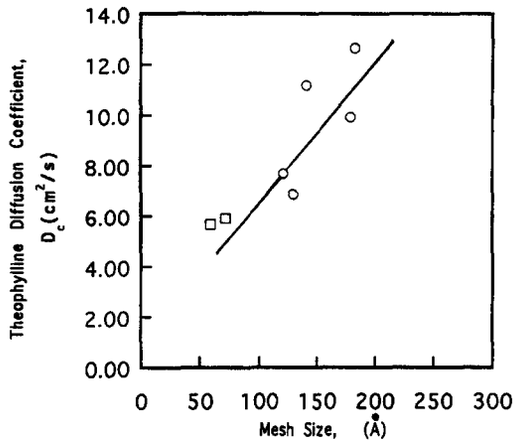

Figure 3 Theophylline diffusion coefficient as a function of the mesh size of PVA/PAA membranes at 25°C

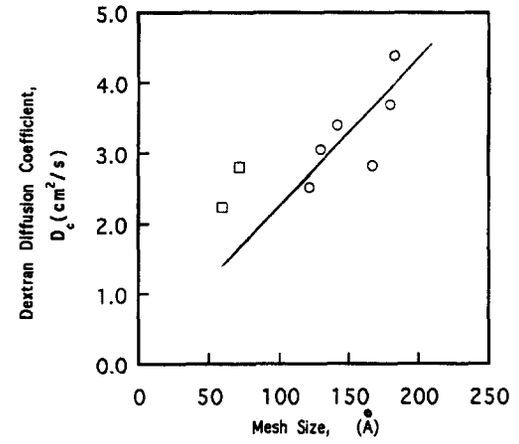

Figure 4 FITC-dextran diffusion coefficient as a function of the mesh size of PVA/PAA membranes at 25°C

line. These data are presented in *Figures 1* and *2* for theophylline and FITC-dextran (linear regression correlation coefficients of $r^2 = 0.965$ and 0.971 respectively). Here, D_w is the theophylline diffusion coefficient in pure water which was calculated as $7.16 \times 10^{-6}\,cm^2\,s^{-1}$ from data of Harland and Peppas[61] at 37°C, corrected for temperature and water viscosity to 25°C, and as $1.46 \pm 10^{-6}\,cm^2\,s^{-1}$ for FITC-dextran[61] of molecular weight 4400. Thus, these results clearly indicate that the Reinhart–Peppas analysis[12] can be used to analyse the observed size exclusion during solute diffusion. Beyond this, as the latter analysis is applied to amorphous networks, the remarkably good agreement of the data with this same theory indicates that the PVA crystallites responsible for the three-dimensional network structure are probably of small size, as indicated also by Cha *et al.*[37].

Figures 3 and *4* show the dependence of the solute diffusion coefficients, D_c, on the mesh size between physical crosslinks. It is evident that a size exclusion effect was observed which was prominent at the lower mesh sizes. These results indicate that solute transport through freezing/thawing processed PVA/PAA membranes is significantly slower than through chemically crosslinked membranes[64].

Clearly, such membranes can be used for separations as they are expected to provide reasonable barriers for solute transport.

CONCLUSIONS

We have shown that strong PVA/PAA membranes can be prepared by freezing/thawing of aqueous PVA and PAA solutions. Diffusion studies with theophylline and FITC-dextran showed a size exclusion phenomenon that was attributed to the physical network created by the crystallites of the system.

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