Analysis of solute diffusion in poly(vinyl alcohol) hydrogel membrane

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Received 1 April 1996; revised 17 September 1996; accepted 22 September 1996

Abstract

Measurements of diffusion and partitioning of solutes having molecular weights ranging 180–66 000 in PVA gel membranes with various crosslinking degree were carried out. With increasing solute size or decreasing number of average molecular weight between crosslinks of the membranes, both the solute permeability and partition coefficient decreased. In spite of similar solute sizes, the more hydrophilic solute ribonuclease showed higher permeability and partition coefficient than the less hydrophilic \textalpha-lactalbumin, probably due to interaction with the hydrophilic PVA. The solute diffusion through swollen gel membrane was analyzed by the equation based on free volume theory. In this analysis equation, the partition coefficient, which is defined as the ratio of solute concentration in gel membrane standardized by water volume in the membrane to that in bulk solution, was introduced as the probability of a diffusing species finding a mesh with a volume of at least the solute size. The efficiency of the proposed analysis equation was confirmed by the experimental results of the effects of solute size and water volume fraction in the membrane.

Keywords: Poly(vinyl alcohol); Hydrogels; Free volume theory; Partition coefficient; Lysozyme

1. Introduction

Hydrogel membranes in general have high hydrophilic nature, high biocompatibility and low fouling potential. These advantages have led to their use in laboratory, biological separations, and biomedical applications such as artificial skin and corneal prostheses. A well known example of commercial biological application is poly(vinyl alcohol) (PVA) gel membrane developed by Kuraray Ltd. for plasmapheresis. This membrane in hollow fiber form showed high hydraulic permeability and plasma flux [1].

In order to design the hydrogel membrane process efficiently, solute diffusion characteristics through water-swollen network must be clarified both experimentally and theoretically. From the experimental standpoint, such as effects of experimental conditions on solute permeability coefficients, many studies have been carried out [2–6].

Gel membranes are formed by polymeric networks with pores of molecular size, which is termed as macromolecular mesh [7]. Therefore, theories developed for microporous membranes, which are mainly characterized by the normalized size \( \lambda \) defined as the ratio of the solute diameter to the average pore diameter may not be appropriate for the analysis of gel membranes due to the uncertainty of \( \lambda \) in gel network...
Yasuda et al. developed theory for solute diffusion through hydrated polymer membrane based on the free volume theory [9–11]. They indicated that the experimental results of the dependencies of solute diffusion coefficient on the solute size and the degree of swelling were explained by the theory. Peppas and Reinhart presented a similar physical model for solute diffusion [8]. According to the theory, the normalized solute diffusion coefficient, that is the ratio of the solute diffusion coefficient in the swollen gel membrane, $D_{\text{gel}}$, to that in pure water, $D_{\text{water}}$, was expressed as follows.

$$
\frac{D_{\text{gel}}}{D_{\text{water}}} = B(v_d)\exp\left(-\frac{\pi r_s^2 l}{V_1(Q_m - 1)}\right)
$$

(1)

Where, $r_s$ is the Stokes hydrodynamic radius, $l$ is the characteristic length, $V_1$ is the average free volume of water, $Q_m$ is the volume degree of swelling of the network, and $H$ is the volume fraction of water in gel membrane. The term $B(v_d)$ denotes the probability of a diffusing species of volume $v_d$ finding a mesh formed by the crosslinked chains of the polymeric network, having a volume of at least $v_d$. By assuming that the normalized diffusion coefficient is linearly related to the mesh size, Peppas and Reinhart gave the expression for $B(v_d)$ and presented the following equation [8].

$$
\frac{D_{\text{gel}}}{D_{\text{water}}} = k_1 \frac{(M_c - M'_c)}{(M_n - M'_c)} \exp\left(-\frac{k_2 r_s^2}{Q_m - 1}\right)
$$

(2)

Here, $M_c$ is the average molecular weight between crosslinks, $M'_c$ is the threshold value of $M_c$, below which no diffusion of solute can occur, $M_n$ is the average molecular weight of the polymer before crosslinking. The constants $k_1$ and $k_2$ are structural parameters. They demonstrated that the previously published experimental data showed reasonable linear dependencies in the relations between $\log(D_{\text{gel}}/D_{\text{water}})$ and $r_s^2$, and between $\log(D_{\text{gel}}/D_{\text{water}})$ and $1/(Q_m - 1)$, as expected by Eq. (2). The validity of the free volume theory for diffusion through the gel membrane was also confirmed from the similar linear dependence of vitamin B$_{12}$ diffusion coefficient on $1/(Q_m - 1)$ [12].

Reinhart and Peppas investigated the influence of crosslinking on diffusive properties [13]. They showed that the normalized diffusion coefficient depends on the value of $M_c$. However, it was concluded that the linear dependence of the diffusion coefficient on the mesh size, which is expressed by Eq. (2), was not correct. Thus, the appropriate expression for the probability $B(v_d)$ has not been presented.

In this work, the use of partition coefficient as the expression of $B(v_d)$ in the analysis equation for permeation rate based on the free volume theory has been proposed. PVA gel membranes with various mesh sizes were prepared by chemical crosslinking. The effects of solute size, solute hydrophobicity and water volume fraction, $H$, on the normalized diffusion coefficients were investigated and the efficiency of the proposed analysis equation was discussed.

2. Experimental

2.1. Polymer, crosslinking agent and solutes

Poly(vinyl alcohol) with weight average molecular weight of 50 000 (Aldrich) was obtained as a 99+% hydrolyzed powder. Glutaraldehyde (Aldrich, 50% aqueous solution) was used as a chemical crosslinking agent.

The solutes used were theophylline (Nacalai Tesque, Guaranteed Reagent), vitamin B$_{12}$ (Nacalai Tesque, Guaranteed Reagent), lysozyme from egg white (Seikagaku, 6X crystallized), ovalbumin (Sigma, Grade V, 98% purity), bovine serum albumin, BSA (Sigma, Fraction V powder, 98–99% purity), ribonuclease from bovine pancreas, RNase (Sigma, Type I, 85% purity) and $\alpha$-lactalbumin ($\alpha$LA) from bovine milk (Sigma, Type III, 85% purity). The molecular weights, Stokes radii, diffusion coefficients in water and total hydrophobicities of the solutes are listed in Table 1. The solute sizes increase in order of theophylline, vitamin B$_{12}$, lysozyme, ovalbumin and BSA. Although lysozyme, RNase and $\alpha$LA have similar solute sizes, hydrophilicities of the solutes decrease in order of RNase, lysozyme and $\alpha$LA. The solutes were dissolved in a phosphate buffered saline solution (0.0027 M KCl, 0.137 M NaCl, pH 7.4).
### Table 1
Properties of used solutes

<table>
<thead>
<tr>
<th>Solute</th>
<th>Molecular weight (g mol⁻¹)</th>
<th>( r_s ) (Å)</th>
<th>( D_{\text{water}} ) (cm² s⁻¹)</th>
<th>Total hydrophobicity ( \alpha )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theophylline</td>
<td>180</td>
<td>3.7 ( ^b )</td>
<td>( 6.54 \times 10^{-6} ) ( ^c )</td>
<td>-7.6</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>1355</td>
<td>8.4 ( ^b )</td>
<td>( 2.83 \times 10^{-6} ) ( ^c )</td>
<td></td>
</tr>
<tr>
<td>Lysozyme</td>
<td>14 600</td>
<td>14.6 ( ^d )</td>
<td>( 1.27 \times 10^{-6} ) ( ^c )</td>
<td>-7.6</td>
</tr>
<tr>
<td>Ovalbumin</td>
<td>45 000</td>
<td>17.6 ( ^f )</td>
<td>( 8.47 \times 10^{-7} ) ( ^e )</td>
<td></td>
</tr>
<tr>
<td>BSA</td>
<td>66 000</td>
<td>22.5 ( ^f )</td>
<td>( 6.98 \times 10^{-7} ) ( ^e )</td>
<td></td>
</tr>
<tr>
<td>Ribonuclease</td>
<td>13 700</td>
<td>14.6 ( ^d )</td>
<td>( 1.33 \times 10^{-6} ) ( ^c )</td>
<td>-8.7</td>
</tr>
<tr>
<td>( \alpha )-Lactalbumin</td>
<td>14 200</td>
<td>14.6 ( ^d )</td>
<td>( 1.21 \times 10^{-6} ) ( ^c )</td>
<td>-5.8</td>
</tr>
</tbody>
</table>

\( ^a \) [14]
\( ^b \) [15]
\( ^c \) Values at 298 K were estimated from the reported data at 310 K [15] by Stokes–Einstein equation.
\( ^d \) Estimated value from the sedimentation coefficient (1.9 \times 10^{-13} \text{ s}) [16]. The values for RNase and \( \alpha \)LA were assumed to be equal to that for lysozyme because they have similar sedimentation coefficients [16].
\( ^e \) Values at 298 K were estimated from the reported data at 310 K [16].
\( ^f \) [8]

2.2. Preparation of PVA gel membrane

The crosslinked polymeric networks of PVA were prepared by using a previously reported technique [13,17]. An aqueous 10 wt% PVA solution (10 ml) was mixed with a crosslinking solution (2.8 ml) for membrane casting. The crosslinking solution (7 ml) consisted of 3 ml 50 vol% methanol (quencher), 2 ml 10 vol% acetic acid (buffer), 1 ml glutaraldehyde (crosslinking agent) and 1 ml 10 vol% sulfuric acid (catalyst). The concentration of glutaraldehyde solution was varied from 2.5 to 10 vol% so that gel membranes could be prepared with initial crosslinking ratio, \( X \) from 0.005 to 0.020 moles of glutaraldehyde per mole of PVA repeating unit. The resultant mixture was then cast onto a glass plate of desired thickness (1000 µm) and placed in a drying oven at 37°C for 1 h crosslinking reaction time. The membrane obtained was swollen in water and stored for the partition and diffusion experiments.

2.3. Partitioning of solutes between gel membrane and bulk solution

To obtain partition coefficients of solutes between gel membrane and bulk solution, the gel membranes were soaked in solute buffer solution at 298 K for one day. The solute concentrations were 10 g dm⁻³ except for theophylline (5 g dm⁻³) and vitamin B₁₂ (5 g dm⁻³). The gel membranes taken out from the solute solutions were wiped carefully to remove the excess aqueous solution on the membranes, and were re-soaked in buffered saline solution (pH 7.4) at 298 K for one day. The concentrations of solutes released into the buffer solution were measured using a UV spectrophotometer (Hitachi, U-2000, wavelength: 271 nm for theophylline, 361 nm for vitamin B₁₂, 280 nm for lysozyme, ovalbumin, BSA, RNase and \( \alpha \)LA). Partition coefficient can be defined in two ways – one is the ratio of solute concentration in gel membrane standardized by the total membrane volume to that in bulk solution, and the other is the ratio of solute concentration in membrane standardized by water volume in the membrane to that in bulk solution. If we express the former as \( K \) and the latter as \( K' \), the two partition coefficients are related as follows where \( H \) is the water volume fraction.

\[
K = HK'
\]

(3)

2.4. Permeation experiments

Permeation experiments were carried out with PVA gel membranes having various crosslinking degrees using a diffusion cell. The diffusion cell consisted of two cylindrical half cells of volume 20 cm³ made of Pyrex glass. The gel membrane was sandwiched between two cells. The membrane area was 7.1 cm².
The solutions in the two cells were stirred by magnetic stirring bars at 250 rpm. The diffusion cell was placed in a water bath maintained at 298 K.

The feed solution was prepared by dissolving the solute in buffered saline solution (pH 7.4) described above. Solute concentration was 10 g dm\(^{-3}\) except for theophylline (5 g dm\(^{-3}\)) and vitamin B\(_{12}\) (5 g dm\(^{-3}\)). The receiving solution was the buffered saline solution. Samples of the receiving solution (1 cm\(^3\)) were taken at various intervals and solute concentrations were analyzed by spectrophotometer at the wave lengths described above. After taking out a sample of 1 cm\(^3\), 1 cm\(^3\) buffer solution was always added to the receiving solution. The change in concentration due to the addition of the buffer solution was taken into account in the calculation of the solute amounts transported.

The flux \(N\) is given by

\[ N = \frac{V}{A}\frac{dC_{b1}}{dt} = K_0(C_{b2} - C_{b1}) \]  

(4)

where \(V\) is the receiving solution volume, \(A\) is the membrane area, \(K_0\) is the overall mass transfer coefficient and \(C_{b2}\) and \(C_{b1}\) are the bulk concentrations in feed and receiving solutions, respectively. The overall mass transfer coefficient is expressed as the sum of the individual resistances.

\[ \frac{1}{K_0} = \frac{L}{P} + \frac{1}{K_f} + \frac{1}{K_r} \]  

(5)

Here, \(P\) is the membrane permeability, \(L\) is the membrane thickness, and \(K_f\) and \(K_r\) are the mass transfer coefficients in feed and receiving solutions. To consider the contribution of \(K_f\) and \(K_r\) to \(K_0\), we prepared PVA/chondroitin sulfate blend membrane (blend weight ratio - PVA : chondroitin sulfate=10 : 3), which showed more than two times higher permeability than that of PVA membrane with the largest mesh size. In the case of laying two blend membranes, it was found that the value of \(K_0\) decreased to just the half of that of the single membrane. This means that the contribution of \(K_f\) and \(K_r\) is negligibly small and the resistance of the membrane phase is predominant. Therefore, also in the case of PVA membranes with lower permeability, the liquid-phase mass transfer resistance can be neglected. When the membrane resistance is predominant, Eq. (4) is rewritten as

\[ N = \frac{P}{L}(C_{b2} - C_{b1}) \]  

(6)

As the solute is transported into the receiving phase, the solute concentration in the receiving phase increases and the driving-force for the solute transport changes. From the initial slope of the relation between the amounts transported and time, the flux was obtained. The membrane permeability \(P\) was calculated from Eq. (6) by using zero value as \(C_{b1}\). The membrane thickness \(L\) was measured by a micrometer (Japan Micrometer, DMII).

The solute diffusivity in the gel membrane \(D_{gel}\) was evaluated using the following equation where \(K\) is the measured partition coefficient.

\[ D_{gel} = \frac{P}{K} \]  

(7)

3. Analysis of solute diffusion in gel membrane

Based on the free volume consideration, the normalized diffusion coefficient in gel membrane is expressed as Eq. (1). In order to make this theory more quantitative, the term \(B(v_d)\) must be determined. The term \(B(v_d)\) is a proportionality factor dependent upon the size and shape of the mesh formed by the crosslinked chains [8]. The characteristics of \(B(v_d)\) are as follows. For chains far apart from each other so that there are no entanglements, the solute diffusion is not obstructed by the chains. In such a case, \(B(v_d)\) must be unity unless there is no interaction between polymer chain and solute. On the other hand, when the polymer chains are well crosslinked and no solute diffusion occurs, \(B(v_d)\) must be zero.

Based on these characteristics of \(B(v_d)\), we propose the use of partition coefficient \(K'\) as \(B(v_d)\). As described above, the partition coefficient \(K'\) is defined as the ratio of solute concentration in gel membrane standardized by the water volume in the membrane to that in bulk solution. It should be noted that \(K'\) is different from \(K\) based on the solute concentration in gel membrane standardized by the total membrane volume.

The partition coefficient is driven by interactions between the solute and the polymer chains, while diffusion is driven by the mobility of the chains in glassy and rubbery polymers. Here, the tendency of the magnitude of the partition coefficient may be sometimes contrary to that of the diffusivity, that is, the polymer in which solute has higher partition coefficient may sometimes show lower diffusivity.
Table 2
Characteristics of PVA gel membranes

<table>
<thead>
<tr>
<th>$X$ (mol/mol)</th>
<th>$M_t$ (g mol$^{-1}$)</th>
<th>$M_c^{*}$ (g mol$^{-1}$)</th>
<th>$\rho$ (mol cm$^{-1}$)</th>
<th>$\xi$ (Å)</th>
<th>$H$ (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.005</td>
<td>11700</td>
<td>8800</td>
<td>1.08×10$^{-2}$</td>
<td>297</td>
<td>0.957</td>
</tr>
<tr>
<td>0.015</td>
<td>6800</td>
<td>2900</td>
<td>1.87×10$^{-2}$</td>
<td>165</td>
<td>0.883</td>
</tr>
<tr>
<td>0.018</td>
<td>5400</td>
<td>2400</td>
<td>2.35×10$^{-4}$</td>
<td>139</td>
<td>0.862</td>
</tr>
<tr>
<td>0.020</td>
<td>2900</td>
<td>2200</td>
<td>4.38×10$^{-4}$</td>
<td>92</td>
<td>0.811</td>
</tr>
</tbody>
</table>

However, we treated the diffusion in gel membranes. The gel membranes usually have high water content, that is, a large pore portion in the total volume. In such gel membranes, the partition coefficient occasionally may be determined simply by the space volume (mesh size), by the exclusion effect rather than the interaction between the solute and polymer chain. Further, it is well known that the network of the gel fluctuates in time and space. However, the cooperative diffusion coefficient of the gel is much smaller than that of the small solute [18] and therefore, the polymer network of the gel behaves as fixed obstacle for the diffusion of small molecules in the gel [19]. Here, we can treat the gel membrane as the rigid porous material. When the interaction between the solute and the polymer is negligible and the water content in the gel membrane is high, the diffusion coefficient of the solute are determined only by the mesh size of the polymer network and size of the solute [19]. In this case, the probability of a diffusing species of volume $V_d$ finding a mesh formed by the crosslinked chains of the polymeric network, $B(V_d)$, is influenced by the magnitude of the free space divided by the polymer chain rather than by the mobility of the polymer chain. Therefore, both the partition coefficient and $B(V_d)$ are dependent on the mesh size.

The partition coefficient $K'$ satisfies the conditions which $B(V_d)$ shows. $K'$ is unity similar to $B(V_d)$ when the polymer chains are far apart from each other, while $K'$ and $B(V_d)$ become zero when the polymer chains are well crosslinked and the mesh size is smaller than the solute size. Because $B(V_d)$ is the probability of the solute finding the position for diffusion in the mesh structure, it takes some value $\phi$, which is smaller than unity due to the exclusion effect when the mesh size is comparable to the solute size. The partition coefficient $K'$ also takes the same value of $\phi$ due to the same exclusion effect.

Because the PVA gel membrane had a high water volume fraction as shown in Table 2, the interaction between the solute and PVA may not be so significant. Therefore, an attempt was made to use the partition coefficient as $B(V_d)$ to analyze the diffusion through the PVA gel membrane even though it is a rough approximation.

Using $K'$ as $B(V_d)$, Eq. (1) is rewritten as

$$\frac{D_{gel}}{D_{water}} = K' \exp \left( -\frac{\pi \rho^2}{V_1} \right)$$

The efficiency of Eq. (8) was examined comparing with experimental results in the following section.

4. Results and discussion

4.1. Characteristics of gel membranes

The water volume fraction $H$ for each membrane prepared with various initial crosslinking ratios $X$ are listed in Table 2. The value of $H$ was calculated from the water weight fraction $W$, obtained by the swelling experiment at 298 K using specific volume of water (1.003 cm$^3$ g$^{-1}$) and PVA (0.788 cm$^3$ g$^{-1}$ [13]), as $W \times 1.003 / [W \times 1.003 + (1 - W) \times 0.788]$. The average molecular weight between crosslinks $M_c$ was calculated using the following Flory-Rehner expression [20,21] and are listed in Table 2.

$$\frac{1}{M_c} = \frac{2 \nu / \hat{V}_1 [ln(1 - v_2) + v_2 + \chi v_2^2]}{(v_2^{1/3} - v_2/2)}$$

Here, $\nu$ is the specific volume of PVA, $\hat{V}_1$ is the molar volume of water (18 cm$^3$ mol$^{-1}$), $\chi$ is the Flory PVA–water thermodynamic interaction parameter (0.494 [22]) and $v_2$ is the polymer volume fraction at swelling, which is equal to $(1 - H)$. Because the value of $M_n$ for PVA used in this work was not reported, it was estimated as half the average molecular weight of
50000 [23]. The theoretical $\bar{M}_c$ value, $\bar{M}_c^{id}$, in the case where all crosslinking agents react with polymer can be obtained by Eq. (10) using the crosslinking ratio $X$ and the molecular weight of PVA repeating unit $M_r$ (44).

$$\bar{M}_c^{id} = \frac{M_r}{X}$$

(10)

These values are also listed in Table 2. The values of $\bar{M}_c$ obtained experimentally were more or less smaller than those of $\bar{M}_c^{id}$.

The crosslinking density $\rho$ and the mesh size $\xi$ were determined from $\bar{M}_c$ by Eq. (11) [13] and Eq. (12) [24], respectively.

$$\rho = \frac{1}{(\nu\bar{M}_c)}$$

(11)

$$\xi = l_c(2\bar{M}_c/M_r)^{1/2}C_n^{1/2}v_2^{-1/3}$$

(12)

Here, $l_c$ is the C–C bond length ($1.54 \text{ Å}$), $C_n$ is the characteristic ratio which was reported to be 8.9 for PVA [24]. The results of these calculations are shown in Table 2.

With the increase in the crosslinking ratio $X$, the degree of crosslinking increases, which leads to higher crosslinking density and lower $\bar{M}_c$, as shown in Table 2. Therefore, the increase in $X$ brings about decrease in both mesh size and water volume fraction $H$. The mesh size of the membrane prepared with $X=0.020$ was about two times the Stokes diameter of BSA listed in Table 1.

4.2. Partition properties

The relation between the partition coefficient $K'$ and the Stokes radius of solute is shown in Fig. 1. With increasing Stokes radius, $K'$ decreased. The values of $K'$ for lysozyme, RNase and $\alpha$LA were certainly different although they have similar Stokes radius. As described above, the hydrophilicities of the solutes increase in order of $\alpha$LA, lysozyme and RNase. Because PVA is highly hydrophilic, it is expected that a more hydrophilic solute is more likely to be distributed in the PVA gel membrane due to the interaction with PVA. The $K'$ values obtained increased in the order of $\alpha$LA, lysozyme and RNase, which is in agreement with the order of hydrophilicity. However, further investigation is necessary to clarify whether such interaction between PVA and solute influences the partition coefficient.
Fig. 4. Effect of Stokes radius on permeability $P$ and $D_{gel}$. • theophylline, ◇ vitamin $B_{12}$, △ RNase, ■ lysozyme, □ αLA, ○ ovalbumin. ◆ BSA: crosslinking ratio $X=0.005$ ($M_c=11700$).

4.3. Permeation properties

The effect of Stokes radius on the membrane permeability $P$ and solute diffusion coefficient in swollen gel membrane, $D_{gel}$ are shown in Fig. 4. The permeability and $D_{gel}$ decrease abruptly with the Stokes radius. For example, the permeability for theophylline was more than $10^3$ times that for BSA although the Stokes radius of BSA is only 6 times higher than that of theophylline. Lysozyme, RNase and αLA, which have similar Stokes radii, showed different permeability probably due to the difference in hydrophilicity. The more hydrophilic RNase showed about ten times higher permeability than the more hydrophobic αLA. This may mean that the separation based on not only the solute size but also the degree of hydrophilicity is possible for the gel membrane.

The effect of the crosslinked structure of PVA networks on solute diffusion can be observed by plotting the permeability as a function of $M_c$. The results are shown in Fig. 5. As $M_c$ decreases, that is, as the network becomes more crosslinked, the permeabilities and $D_{gel}$ for vitamin $B_{12}$ and lysozyme decrease significantly. The relation between the normalized diffusion coefficient $D_{gel}/D_{water}$ and $M_c$ is also shown in Fig. 5. The threshold of $M_c$ for lysozyme permeation was approximately estimated at $M_c^*=2800$ by extrapolating the data. The threshold for BSA permeation through the PVA gel membrane was reported as $M_c^*=3500$ [13]. By taking into account the smaller size of lysozyme, the obtained threshold $M_c^*$ for lysozyme is reasonable, compared with that for BSA. With respect to the transport of the smaller vitamin $B_{12}$, $M_c^*$ is considered to be fairly small and the exact value of $M_c^*$ could not be determined in this work.

4.4. Efficiency of proposed model

Eq. (8), proposed in this work, is changed to the following equation.
The equation is:

\[
\frac{D_{gel}}{D_{water}}/K' = \exp\left(-\frac{\pi r_0^2 (1/H - 1)}{V_1}\right)
\]

(13)

From this equation, a linear relationship is expected in the plot of \(\log\left(\frac{D_{gel}}{D_{water}}/K'\right)\) vs. \(r_0^2\). This plot is shown in Fig. 6. A linear relationship was obtained. Although lysozyme, RNase and \(\alpha\)LA have fairly different permeabilities as shown in Fig. 4, the values of \(\frac{D_{gel}}{D_{water}}/K'\) for these solutes become almost the same. Although a more hydrophilic solute shows higher \(D_{gel}\), the term \(\frac{D_{gel}}{D_{water}}/K'\) is not influenced by solute hydrophilicity because the interaction between solute and membrane is included in the coefficient \(K'\) and such an interaction is compensated in \(\frac{D_{gel}}{D_{water}}/K'\). The intercept at \(r_0^2 = 0\) was about unity, which is in agreement with the expectation from the tendency that as the solute size decreases, the diffusion through the gel membrane approaches to that in water.

Fig. 7 shows the plot of \(\log\left(\frac{D_{gel}}{D_{water}}/K'\right)\) vs. \((1/H-1)\). For lysozyme, a linear relation was observed. This is in agreement with the expectation from Eq. (8). Because vitamin B₁₂ is a small solute, the effect of \((1/H-1)\) was not clear in this experimental region. As the value of \((1/H-1)\) approaches zero, that is, \(H\) approaches unity, the value of \(\frac{D_{gel}}{D_{water}}/K'\) is expected to approach unity. As shown in Fig. 7, this tendency was confirmed experimentally.

The results of Figs. 6 and 7 confirmed the efficiency of the analysis equation proposed in this work, from the effects of both the solute size and water volume fraction.

Although our analysis method was useful for the PVA gel membrane, it is not general and has limited application. For the gel membrane with much lower water volume fraction, where the interaction between the solute and polymer influences the partition coefficient significantly, and the mobility of the polymer chain influences \(B(v_0)\), our analysis method may not be useful.

5. Conclusions

(1) PVA gel membranes with various crosslinking degrees were prepared by chemical crosslinking of dilute aqueous polymer solutions. Their molecular characteristics were analyzed by equilibrium swelling experiments. The average molecular weight between crosslinks \(M_c\) was found to be of the range 2900–11700, which corresponded to mesh sizes from 92 to 297 Å.

(2) Partition coefficients between the gel membrane and bulk water, and the membrane permeabilities were obtained. The partition coefficients and permeabilities decreased with increase in the solute size. In spite of similar solute size, the more hydrophilic solute ribonuclease showed higher partition coefficient and higher permeability than \(\alpha\)-lactalbumin, probably due to the interaction with the hydrophilic PVA. It was found that partition coefficients and permeabilities decreased monotonously with increasing crosslinking degree.

(3) The new analysis equation based on the free volume theory was presented by modifying the previous equation, and the solute diffusion through swollen PVA gel membrane was analyzed using the
equation. In the proposed equation, the partition coefficient was introduced as the probability of a diffusing species finding a mesh with a volume of at least the solute size. The efficiency of the proposed analysis equation was confirmed experimentally from the dependency on the solute size and water volume fraction in the membrane.

6. List of symbols

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>membrane area (cm²)</td>
</tr>
<tr>
<td>B</td>
<td>probability of diffusing species of volume v_d finding a mesh having a volume of at least v_d</td>
</tr>
<tr>
<td>C_b1</td>
<td>bulk solute concentration in receiving solution (mol cm⁻³)</td>
</tr>
<tr>
<td>C_b2</td>
<td>bulk solute concentration in feed solution (mol cm⁻³)</td>
</tr>
<tr>
<td>C_p</td>
<td>characteristic ratio for PVA</td>
</tr>
<tr>
<td>D_p</td>
<td>solute diffusion coefficient in gel membrane (cm² s⁻¹)</td>
</tr>
<tr>
<td>D_water</td>
<td>solute diffusion coefficient in water (cm² s⁻¹)</td>
</tr>
<tr>
<td>H</td>
<td>volume fraction of water in gel membrane</td>
</tr>
<tr>
<td>K</td>
<td>partition coefficient: ratio of solute concentration in gel membrane standardized by total membrane volume to that in bulk solution</td>
</tr>
<tr>
<td>K'</td>
<td>partition coefficient: ratio of solute concentration in gel membrane standardized by water volume in membrane to that in bulk solution</td>
</tr>
<tr>
<td>K_i</td>
<td>overall mass transfer coefficient (cm s⁻¹)</td>
</tr>
<tr>
<td>k_i</td>
<td>mass transfer coefficient in feed solution (cm s⁻¹)</td>
</tr>
<tr>
<td>k_r</td>
<td>mass transfer coefficient in receiving solution (cm s⁻¹)</td>
</tr>
<tr>
<td>k_2</td>
<td>structural parameter of Eq. (2)</td>
</tr>
<tr>
<td>L</td>
<td>membrane thickness (cm)</td>
</tr>
<tr>
<td>l_c</td>
<td>C-C bond length (Å)</td>
</tr>
<tr>
<td>M_c</td>
<td>average molecular weight between crosslinks (g mol⁻¹)</td>
</tr>
<tr>
<td>M'_c</td>
<td>threshold value of M_c (g mol⁻¹)</td>
</tr>
<tr>
<td>M_c ₜₜ</td>
<td>theoretical M_c value (g mol⁻¹)</td>
</tr>
<tr>
<td>M_n</td>
<td>average molecular weight before crosslinking (g mol⁻¹)</td>
</tr>
<tr>
<td>M_r</td>
<td>molecular weight of repeating unit of polymer (g mol⁻¹)</td>
</tr>
<tr>
<td>N</td>
<td>solute flux (mol/(cm² s))</td>
</tr>
<tr>
<td>P</td>
<td>membrane permeability (cm² s⁻¹)</td>
</tr>
<tr>
<td>Q_sn</td>
<td>equilibrium degree of swelling</td>
</tr>
<tr>
<td>r_s</td>
<td>Stokes radius of solute (cm)</td>
</tr>
<tr>
<td>V</td>
<td>receiving solution volume (cm³)</td>
</tr>
<tr>
<td>V_1</td>
<td>average free volume of water (cm³)</td>
</tr>
<tr>
<td>V_2</td>
<td>molar volume of water (cm³ mol⁻¹)</td>
</tr>
<tr>
<td>v_d</td>
<td>volume of diffusing species (cm³)</td>
</tr>
<tr>
<td>v_p</td>
<td>polymer volume fraction at swelling</td>
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<tr>
<td>W</td>
<td>weight fraction of water in gel membrane</td>
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<tr>
<td>X</td>
<td>initial crosslinking ratio</td>
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6.1. Greek letters

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
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</thead>
<tbody>
<tr>
<td>χ</td>
<td>polymer-solvent Flory interaction parameter</td>
</tr>
<tr>
<td>φ</td>
<td>probability of solute finding position for diffuse in the mesh structure when the mesh size is comparable to solute size</td>
</tr>
<tr>
<td>λ</td>
<td>normalized size: ratio of solute radius to characteristic half dimension of pore</td>
</tr>
<tr>
<td>ν</td>
<td>specific volume of PVA (cm³ g⁻¹)</td>
</tr>
<tr>
<td>ρ</td>
<td>crosslinking density (mol cm⁻³)</td>
</tr>
<tr>
<td>ξ</td>
<td>average mesh size (Å)</td>
</tr>
</tbody>
</table>

References