Bull. Chem. Soc. Jpn., ***69***, 883—889 (1996)

Effects of the Molar Mass of a Solute on Permeability through Poly(vinyl alcohol) Gel Membranes

Masakatsu Yonese,* Masatoshi Kondo, Isamu Miyata, Sin-ichi Kugimiya, Shizuko Sato, and Masao Inukai

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467

(Received August 31, 1995)

The effects of the molar masses of solutes on permeability through poly(vinyl alcohol) PVA gel membranes were studied using polyethylene glycol having a wide range of molar masses and other solutes, such as electrolytes, glucose, and maltose. Furthermore, the effects of the network structure and fixed charges on the permeability were studied using opaque, transparent, and charged PVA gels. The permeability coefficients of solutes through PVA gel membranes (P) depended on the hydrodynamic radius of the solute (d_0) and the mesh sizes of the network (ξ). When interactions between the matrix and the solute were negligible, the normalized permeability coefficients (P/D_0) were found to be the scaling function of ξ/d_0.

Hydrogels have been widely applied to pharmaceutical fields, such as drug delivery systems and the matrices of immobilized enzymes.[1)] In these applications, the characteristics of gels, such as storage abilities and barrier effects, are used. Recently, they have attracted special interest as promising materials due to the development of basic studies concerning gels, such as phase transitions and mechanochemical reactions.[2—4)] Drug release from gel during deformation was reported to be controlled by a squeezing effect and a skin effect, i.e., the release is accelerated by the former effect, resulting from the efflux of water, and is suppressed by the latter effect, resulting from the formation of a dense surface layer.[5)] Even in release during deformation, the barrier effects of the network and the interaction between the gel matrix and solutes are basically important factors.[6)] The barrier effects depend on both the water content and the network structure.

In this report, the effects of the molar mass of a solute on permeability through a poly(vinyl alcohol) gel membrane were studied using polyethylene glycol having a wide range of molar masses, including other solutes. Furthermore, the effects of the network structure and fixed charges on the permeability of a solute were studied using opaque, transparent and charged PVA gels.

Poly(vinyl alcohol) (PVA) can be easily gelled from aqueous solutions by various crosslinking methods, i.e., freeze-thawing,[7)] freeze-drying, chemical crosslinking by using crosslinking agents,[8,9)] such as formaldehyde, and γ-ray irradiation.[10)] By repeating the freeze-thawing processes of PVA aqueous solutions, opaque PVA gels (PVA(FT)) are usually obtained, and transparent ones can be obtained by gelation prior to the phase separation.[11)] Although the network structure of the former gel is heterogeneous, due to the phase separation, that of the latter is homogeneous. In our laboratory, transparent and strong PVA gel membranes were found to be easily obtained without using any organic solvent by freeze-drying wet xerogel. The gels obtained by this method are denoted by PVA(FD).

PVA and borate anions form predominantly 1 : 2 type complexes and negative charged crosslinks are formed between PVA chains, although the resultant gels are very weak.[12,13)] By introducing borate crosslinks to neutral PVA gels prepared by the freeze-drying method, transparent PVA gels become negatively charged gels having sufficient strength for measuring the tensile stress and permeability.[14)] The thus-obtained dually crosslinked PVA gel is denoted by PVA(B) gel.

Experimental

Materials. PVA was of commercial origin (Katayama Chemical Industries Co., Ltd., degree of polymerization; 2000, tacticity; atactic) and was used after dialyzing. The degree of saponification and the amount of 1,2 glycol were determined to be 98.8% and 3.22 mol%. The weight-averaged molecular weight (M_w) was determined to be 1.07×10^5 g mol^{-1} by a light scattering method. Polyethylene glycol PEG was also of commercial origin (Katayama Chemical Industries Co., Ltd.). Their averaged molar masses were in the 200—50000 g mol^{-1} range. Bovine serum albumin BSA was obtained by removing fats from fraction V (Seikagaku Kogyo Co., Ltd.) using activated carbon according to Chen et al.[15)] Borax $Na_2B_4O_7\cdot10H_2O$ and other reagents were of special grades (Katayama Chemical Industries Co., Ltd.). Deionized and distilled water was used.

Measurement of the Diffusion Coefficient of PEG. The diffusion coefficients of PEG in aqueous solutions were measured at 25 °C by dynamic light scattering (DLS 700Ar: Ootsuka Electronics Co., Ltd.). The correlation function of first order was analyzed by the cumulant method, and the z-averaged diffusion coefficient was obtained. From them, the hydrodynamic radii of PEG were obtained from Einstein–Stokes's equation by assuming a sphere.

Preparation of PVA Gel Membranes. PVA gel membranes were prepared by two methods, i.e., a freeze-drying method and a freeze-thawing method. Freeze-drying PVA gel membranes (PVA-(FD)) were prepared by following processes: (1) PVA aqueous solutions (4 w/v%, 15 cm^3) dissolved by heating at (most) 80 °C were poured into Petri dishes (diameter: 15 cm), and were dried for various numbers of days in a chamber (30 °C), as described in a previous paper, under the circumstance of a flow of dried air, which was passed through a column of dried silica gel.[16] (2) The dried samples were swollen for 24 h in saturated vapor pressure at 30—70 °C. (3) The swollen PVA samples were frozen at almost −50 °C for 5 h and dried in vacuo. Thus-obtained transparent xerogels were reswelled in water for 24 h before measuring the stress and permeability. Freeze-thawing PVA gel membranes (PVA-(FT)) were prepared by repeating 5 times the following processes: PVA aqueous solutions (10 w/v%, 8 cm^3) poured into the Petri dishes (diameter: 15 cm) were frozen at almost −40 °C in 10 h and thawed at 25 ° C for 14 h.

PVA gel membranes crosslinked by borate (PVA(B)) were prepared by immersing PVA(FD) gel membranes in a borax aqueous solution (0.03 $\mathrm{mol\,dm^{-3}}$, $\mathrm{pH} = 9.2$) for 24 h at 25 °C.

Measurement of the Density and Water Content of PVA Gel Membranes. The densities of PVA gels (ρ) were determined at 25 °C by a floating method, i.e., from the densities of mixed solvents comprising isooctane and carbon tetrachloride in which pieces of PVA gels were floated. The densities of the solvents were measured by a densitometer (Anton Paar DMA602). The water contents of PVA gels (W_{w}) were measured by the weight change after drying at 80 °C in vacuo for 24 h.

Measurement of Tensile Stress. A strip of PVA gel membrane (length, 4; width, 1; thickness, 0.1—0.25 cm) was fixed by clamps made of a plastic plate with a rough surface in order to prevent it from slipping off. The sample was suspended in water, and strains (γ) were imposed by using a manipulator. The tensile stress (σ) was measured using a strain gauge (Shinko Communication Industry Co., Ltd.) connected to a constant direct current source and a microvolt meter. The apparatuses were set up in an air-thermostatic bath (25 °C) in order to eliminate any temperature effect on the strain gauge, as shown in a previous paper.[17,18]

Measurements of the Membrane Permeability Coefficient. The membrane permeability coefficients were measured at 25 °C using the diffusion cell shown in Fig. 1. The membranes were fixed between compartment I (donor cell) and II (receptor cell), in which the volumes of a permeant solution and water were 50 cm^3, respectively. The surface areas of the membranes were 6.25 cm^2. From compartment II, sample solutions of V_{s} (1—3 cm^3) were withdrawn at arbitrary time intervals for determining the concentrations of the solutes and the same amounts of solvent were added at each sampling time.

The concentrations of the solutes were determined by three kinds of methods: The concentrations of chlorides were determined by the Mohr method; those of glucose, maltose and PEG were determined by a differential diffractometric method (RM102: Ootsuka Electronics Co., Ltd.); those of NaBA and BSA were determined by absorbance (284 and 280 nm respectively).

Determination of the Permeability Coefficient. When a solute has a low molar mass, such as KCl, NaBA, and glucose, the movement of water from compartment II to I due to a difference in the osmotic pressure can be negligible. Then, the total amount of solute permeating from compartment I to II until the ith sampling time (Q_i^{T}) is expressed by

$$Q_i^{\mathrm{T}} = C_i^{\mathrm{II}} V^{\mathrm{II}} + \left(\sum C_i^{\mathrm{II}}\right) V_{\mathrm{sam}}, \tag{1}$$

where C_i^{II} is the concentration of the solute in compartment II at the ith sampling, V^{II} is the volume of solution in compartment II and V_{sam} is the volume of the sampling solution.

However, when solutes are PEG of higher molar masses, the movement of water into compartment I can not be negligible. In this experiment, in order to eliminate any difference in the hydrodynamic pressure between both compartments, water was added just before each sampling time to compartment II so as to balance the heights of the surfaces of both solutions. Then, the total amount of permeating solute (Q_i^{T}) is expressed by the following equation instead of Eq. 1:

$$Q_i^{\mathrm{T}} = C_i^{\mathrm{II}} \left(V^{\mathrm{II}} + (1/2)\sum V_{i,\mathrm{ad}}\right) + \left(\sum C_i^{\mathrm{II}}\right) V_{\mathrm{sam}}, \tag{2}$$

where $V_{i,\mathrm{ad}}$ is the volume of added water into compartment II just before the ith sampling time to balance the heights of both solutions. The total volume of water transferred into compartment I (Q_v^{T}) is obtained approximately by the following equation:

$$Q_v^{\mathrm{T}} = (1/2)\sum V_{i,\mathrm{ad}}\,. \tag{3}$$

From the time courses of Q_i^{T} and Q_v^{T} in the steady states, the fluxes of the solute (J_{s}) and the volume fluxes of water (J_{v}) can be obtained.

According to irreversible thermodynamics,[19] the flux of the solute relative to that of water (J_{d} and J_{v}) are expressed by the following equations by approximating the difference of hydrodynamic pressure equal to 0:

$$J_{\mathrm{d}} = L_{\mathrm{D}}\Delta\pi, \tag{4}$$

$$J_{\mathrm{v}} = L_{\mathrm{PD}}\Delta\pi, \tag{5}$$

where $\Delta\pi$ is the difference in the osmotic pressure, and L_{D} and L_{PD} are phenomenological coefficients. The flux of the solute relative to the cell (J_{s}) is expressed by

$$J_{\mathrm{d}} + J_{\mathrm{v}} = (J_{\mathrm{s}}/C)(1 + CV_{\mathrm{s}}), \tag{6}$$

where C is the averaged concentration of the solute in the gel membrane and V_{s} is the partial molar volume of the solute. CV_{s}

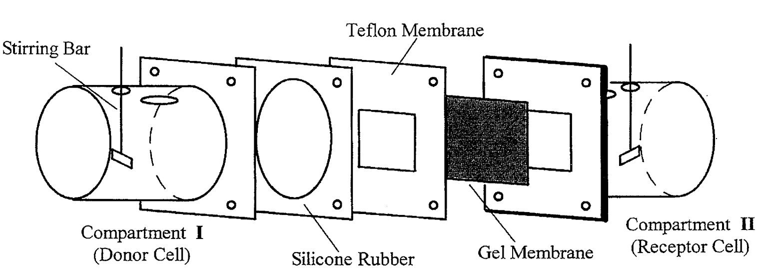

Fig. 1. Schematic diagram of diffusion cell.

is the volume fraction of the solute in the gel membrane, and is negligible in the case of dilute solutions. Then, J_s is expressed by

$$J_s = C(J_d + J_v). \qquad (7)$$

In the cases of dilute solutions, $\Delta\pi$ is obtained by van't Hoff's equation. Then, J_s and J_v are expressed by

$$J_s = -C(L_D + L_{PD})RT(C^{II} - C^{I}) \qquad (8)$$

and

$$J_v = -L_{PD}RT(C^{II} - C^{I}). \qquad (9)$$

In the cases of solutes of low molar mass, since J_v can be approximated to be 0, J_s is expressed by

$$J_s = -CL_DRT(C^{II} - C^{I}) \qquad (10)$$

$$= -P(C^{II} - C^{I})/L \qquad (11)$$

$$P = CL_DRTL, \qquad (12)$$

where P is the permeability coefficient and L is the thickness of the membrane.

In the cases of solutes of higher molar mass, since J_v can not be negligible, the value of P can be obtained from Eqs. 8 and 12 by using L_{PD} obtained from J_v.

Results and Discussion

Elastic Property of PVA(FD), PVA(FT), and PVA(B) Gel Membranes. PVA gel membranes prepared by the freeze-drying and freeze-thawing methods (PVA(FD) and PVA(FT)) were found to be quite different regarding their transparencies. PVA(FT) gel membranes were opaque but PVA(FD) gel membranes were transparent as well as PVA-(B). Although the network structures of PVA(FD) should be heterogeneous, those of PVA(FT) and PVA(B) should be homogeneous.

The time courses of the stress of PVA gel membranes were measured by imposing strains by steps. The stresses of PVA-(FD) and (FT) gel membranes under each strain showed short relaxation, and attained equilibrium states after about 1—2 min. However, the stresses of the PVA(B) gel membrane showed a rather long relaxation, and took almost 20—30 min to attain the equilibrium states. Figure 2 shows the equilibrium tensile stresses of these PVA gel membranes (σ) as a function of the strain (γ). From these linear relations, the elastic moduli (G) were obtained; the results are given in Table 1 together with other results, such as the water contents (W_w) and densities (ρ). The results of G for PVA-(FD) gels increased along with decreasing W_w. The number of the last part in the notation i.e., 74 in PVA(FD)-74, means water content (%). The values of G of PVA(FD)-74 were smaller than that of PVA(B)-74. The borate crosslinks are considered to result in greater values of G and ρ. It should be noted that PVA(B)-74 was prepared by immersing PVA-(FD)-62 in a borax solution. The increase in W_w from 0.62 to 0.74 resulted from the predominant effect of electrostatic repulsion of negative-charged borate crosslinks.[20)]

Table 1. Characteristic Values of PVA Gel Membranes

Membrane	W_w	l/mm	$G/10^3$ Pa	ρ/gcm^{-3}
PVA(FD)-62	0.617	0.181	1750	1.12
PVA(FD)-74	0.737	0.125	616	1.06
PVA(FD)-82	0.819	—	220	1.01
PVA(B)-74	0.737	0.137	1170	1.12
PVA(FT)-84	0.842	0.225	336	1.04

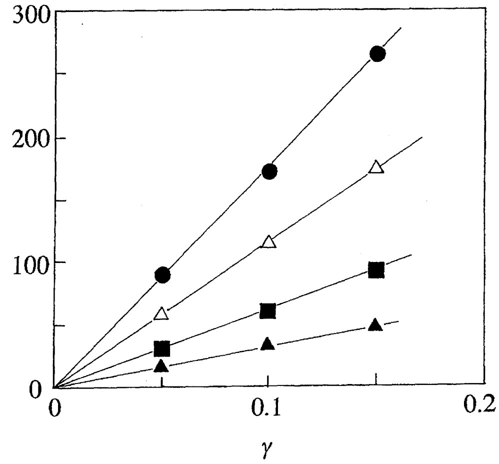

Fig. 2. Equilibrium tensile stress σ of PVA gels as a function of γ. PVA(FD)-62: ●, PVA(FD)-74: △, PVA(B)-74: ■, PVA(FT)-84: ▲.

Permeability Coefficients of Solutes through PVA Gel Membranes. The permeability coefficients (P) of electrolytes through PVA(FD)-62 and -82 gel membranes were measured, and their ratios to diffusion coefficients extrapolated to zero concentration (C=0) D_0; the normalized permeability coeficients (P/D_0), are shown in Fig. 3 as a function of their molar masses (M). Although the results of P were on the order of KCl>NaCl>LiCl, contrary to their molar masses, because of their hydration, the value of P/D_0 of each membrane was almost constant and their averaged values were 0.129 and 0.244 for PVA(FD)-62 and -82 gel membranes, respectively. As increasing with the water contents, the values of P/D_0 were found to increase as well as the results of gelatin membranes.[6)]

The permeability coefficients (P) of PVA gel membranes were measured using solutes of higher molar masses (M),

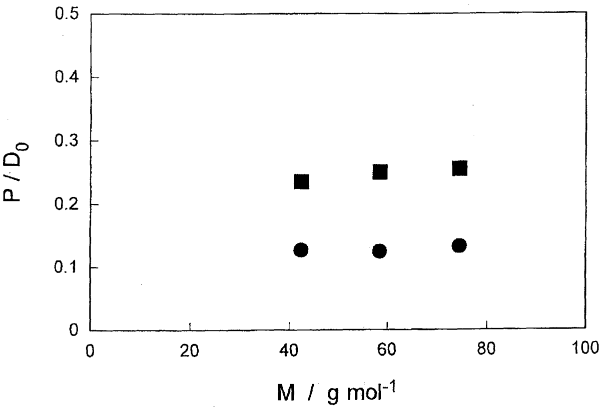

Fig. 3. Normalized permeability coefficient P/D_0 of electrolytes as a function of molar mass M of solute. PVA(FD)-62: ●, PVA(FD)-82: ■.

such as sodium benzoic acid NaBA, glucose, maltose, and polyethylene glycols PEG of various molar masses, which were in the range of 200—50000 g mol^{-1}. Figure 4 shows the results of P of the PVA-62 membrane, including the results of LiCl, NaCl, and KCl. As increasing with M, the values of P decreased, except for electrolytes of small molar mass.

The normalized permeability coefficients (P/D_0) of PVA-(FD)-62 gel membrane are shown in Fig. 5 as a function of the molar mass of solutes (M) in log–log form together with the results of PVA(FT)-84 and PVA(B)-74. The diffusion coefficients of PEG were measured (as mentioned later) by using dynamic light scattering, except for PEG of low molar masses; those of other solutes were obtained from references. In the region of low molar masses, such as LiCl, NaCl, and KCl, the values of P/D_0 of PVA(FD)-62 were constant (as mentioned before). However, as increasing with M slightly more, such as NaBA (M=144), D-glucose (M=180), maltose (M=360), PEG200 and PEG500, the values of P/D_0 were found not to be constant, and to decrease. As increasing with M of PEG, furthermore, they abruptly decreased. The result of NaBA through PVA(B)-74 (indicated by ■) was found to be smaller than the curve of other neutral solutes. This deviation results from the electrostatic effects between NaBA and the negative charges of the borate crosslinks.[14] From the results of PVA(FD)-62, PVA(FT)-84, and PVA(B)-74, the decreasing curves of P/D_0 were found to depend not only on W_w, but also on other properties of gel membranes, such as their fixed charges and network structures. It should be noted that the value of P is proportional to the diffusion coefficient (D), as shown in Fig. 3, only when the mesh sizes of the gel membranes are much larger than the size of the solute and the interaction between the matrix and the solute is negligible.

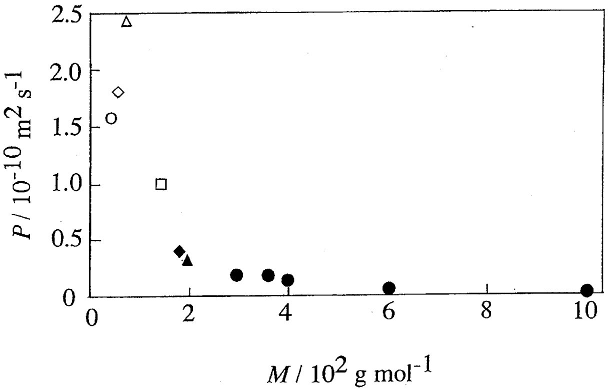

Fig. 4. Permeability coefficient P of various solutes through PVA(FD)-62 gel membrane as a function of molar mass M. ○: LiCl, ◇: NaCl, △: KCl, □: NaBA, ◆: glucose, ▲: maltose, Marks ● show the results of PEG (M= 20—1000 g mol^{-1}).

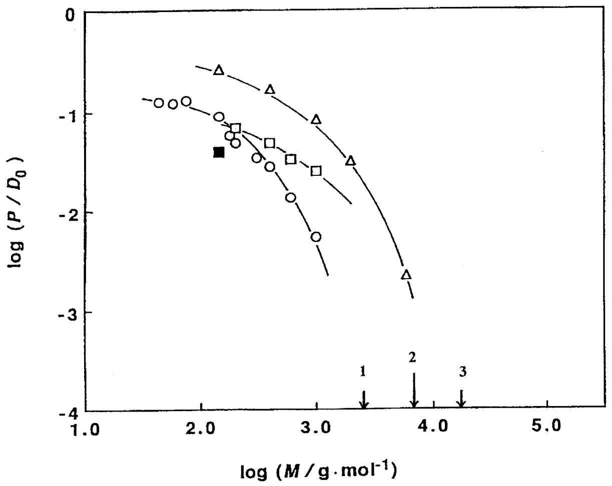

Fig. 5. Normalized permeability coefficient P/D_0 as a function of molar mass M of solute. PVA(FD)-62: ○, PVA(FT)-84: △, PVA(B)-74: □. The mark ■ shows the result of NaBA through PVA(B)-74 membrane. Arrows show the values of M_{cutoff} of PVA membranes obtained from Fig. 8. Numbers: 1; PVA(FD)-62, 2; PVA(B)-74, 3; PVA(FT)-84.

Estimation of Mesh Size of Network. The average size of the network in a gel should control the diffusion of a solute. When the size of the network is larger than that of the solute, the solute can diffuse. The average size of the swollen network, i.e., the mesh size (ξ), can be obtained by the following equation:[21,22]

$$\xi = \alpha_s n^{1/2} b, \tag{13}$$

where n is the number of repeating units between adjacent crosslinks, b is the bond length, and α_s is the swelling ratio. When the molar mass between the adjacent crosslink is M_c and that of repeating unit is M_r, n is obtained by the following equation;

$$n = 2M_c/M_r. \tag{14}$$

When the volume fraction of a polymer in an isotropic swollen gel is v_p in an equilibrium state, α_s can be obtained by

$$\alpha_s = v_p^{-1/3}. \tag{15}$$

The values of M_c of PVA gel membranes were estimated from their tensile stress (σ) by using Flory's theory for swollen gels, which was derived by assuming an ideal rubber and a constant volume,[21]

$$\sigma = RTv_p^{-2/3} w_p (v_g M_c)^{-1} (1 - 2M_c/M_n)(\alpha - \alpha^{-2}), \tag{16}$$

where M_n is the number-averaged molar mass of PVA, α is the deformation of the network structure by an elongation ($\alpha = l/l_0 = 1+\gamma$), v_p, and w_p are the volume fraction and the weight fraction of PVA in the swollen gel, and v_g is the specific volume of the gel. By assuming that PVA gels are ideal rubbers, the values of M_c were estimated; the results are given in Table 2. The values of v_p were obtained by using a specific volume of dried PVA (ρ_{PVA}=1.27 g cm^{-3}),[22]

$$v_p = \rho/\rho_{\text{PVA}}. \tag{17}$$

From the results of M_c and v_p, the mesh sizes (ξ) of PVA gel membranes were estimated using b=0.154 nm as the C–C bond length of PVA; they are given in Table 2.

Table 2. Molar Mass between Closslinks (M_c) and Mesh Size (ξ) of PVA Gel Membranes

Membrane	M_c/kgmol^{-1}	ν_p	α_S	Q	$\langle R_0^2\rangle^{1/2}$/nm	ξ/nm
PVA(FD)-62	3.05	0.335	1.44	2.99	1.86	2.67
PVA(FD)-74	6.21	0.217	1.66	4.61	2.59	4.31
PVA(FD)-82	11.94	0.143	1.91	6.99	3.59	6.68
PVA(B)-74	3.89	0.229	1.57	4.37	2.21	3.47
PVA(FT)-84	8.67	0.131	2.05	7.63	3.11	6.38

Figure 6 shows ξ as a function of the water content (W_w). The values of ξ increased along with increasing W_w, and those of PVA(FT)-84 and PVA(B)-74 gel membranes were found to deviate slightly from the curve of PVA(FD). Peppas et al. reported that ξ of PVA gels crosslinked by glutaraldehyde were in the 6—13 nm range.[22] Then, the PVA gels used in this experiment were found to possess a relatively small network structure.

The values of ξ of the gels were reported to be scaled by the following equation,[24,25]

$$\xi \propto Q^{3/4}, \tag{18}$$

where Q is the equilibrium swelling ratio. Q is obtained from ν_p,

$$Q = 1/\nu_p. \tag{19}$$

As shown in Fig. 7, the values of ξ for PVA(FD) gel membranes showed a good linear relation as a function of $Q^{3/4}$. The result of PVA(B)-74 was on the line of PVA(FD), but the result of PVA(FT)-84 deviated from it. PVA(FD) and PVA(B)-74 gel membranes were transparent, i.e., the network structure should be homogeneous. On the other hand, PVA(FT)-84 was opaque (as mentioned before), i.e., the network structures should be heterogeneous. Therefore, the deviation of the latter gel from a line is considered to result from the heterogeneous network structure.

Effects of the Size of a Solute and the Mesh Size on Permeability. Diffusion coefficients (D) of PEG were measured by dynamic light scattering; the results were found to be linear functions of the concentrations in the region of low concentrations. The extrapolated values to infinite dilution (D_0) were obtained over the range M=6000—170000 g mol^{-1}, and as shown in Fig. 8 log D_0 showed a linear relation with log M. The values of D_0 in the ranges of $M<$ 6000 and $M>$170000 g mol^{-1} showed the results reported by Kambe et al.[26,27] and Rossi et al.[28] The diffusion coefficients are reported to be proportional to M to the $-\nu$ power.

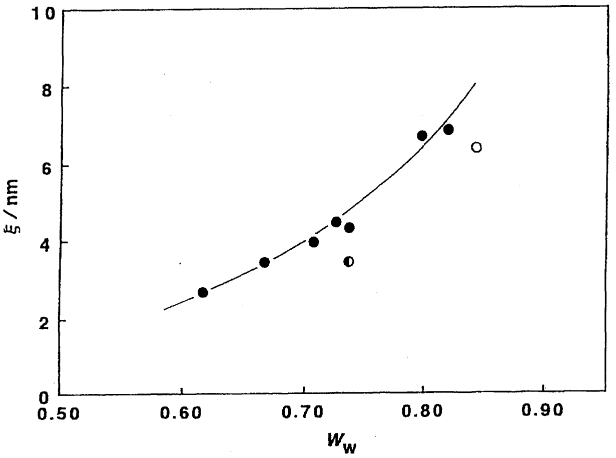

Fig. 6. Mesh size ξ of PVA gel membrane as a function of water content W_w. PVA(FD): ●, PVA(FT)-84: ○, PVA(B)-74: ◐

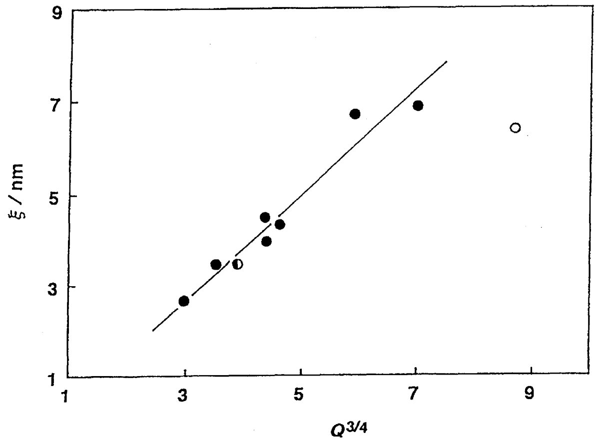

Fig. 7. Mesh size ξ of PVA gel membrane as a function of swelling ratio to 3/4th power $Q^{3/4}$. PVA(FD): ●, PVA(FT): ○, PVA(B): ◐.

$$D_0 \propto M^{-\nu}. \tag{20}$$

The value of ν of PEG in water at 25 °C was found to be 0.54.

From the diffusion coefficients, the hydrodynamic sizes of solutes can be estimated. At this stage, by assuming that molecules of PEG are spherical, the hydrodynamic diameters (d_0) were obtained from Einstein–Stokes's equation, and are shown in Fig. 8. The values of ξ of PVA gels shown in Table 2 are also plotted by arrows in Fig. 8. When the values of d_0 of PEG are greater than the values of ξ of PVA gel membranes, PEG should not permeate through them. Then, the molar mass of PEG, whose diameter is equal to ξ, can be defined by the cut-off molar mass (M_{cutoff}) of PVA gel membranes. The values of M_{cutoff} of PVA(FD)-62, PVA(B)-74, and PVA(FT)-84 were estimated to be 2500, 7000, and 15000 g mol^{-1}, respectively. These values are also indicated in Fig. 5 by arrows. The values of P/D_0 of PEG were found to abruptly decrease when approaching M=M_{cutoff}.

The permeability coefficients of solutes through the gel membranes depend on the hydrodynamic radius of solutes (d_0) and the mesh size of the network (ξ). When interactions between the matrixes and the solutes can be negligible, the diffusion should be a function of the ratio of mesh size ξ to d_0.[29]

$$P/D_0 = f(x) \tag{21}$$

and

$$x = \xi/d_0. \tag{22}$$

The values of P/D_0 of PVA gels shown in Fig. 5 are replotted as a function of x in the log–log form. As shown in Fig. 9,

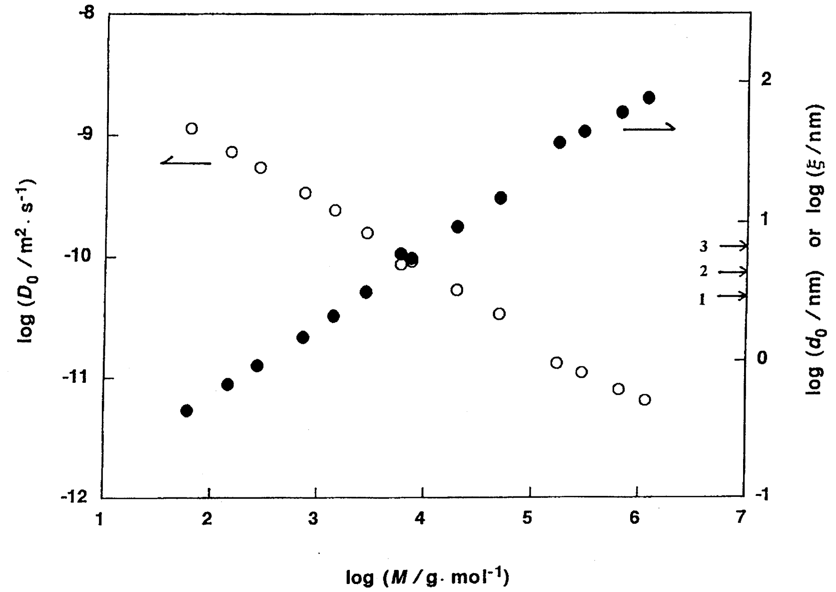

Fig. 8. Diffusion coefficient D_0 and hydrodynamic diameter d_0 of PEG as a function of molar mass M. ○: diffusion coefficient of PEG D_0, ●: hydrodynamic diameter of PEG d_0. Arrows show the values of mesh sizes ξ of PVA membranes. Numbers: 1; PVA(FD)-62, 2; PVA(B)-74, 3; PVA(FT)-84.

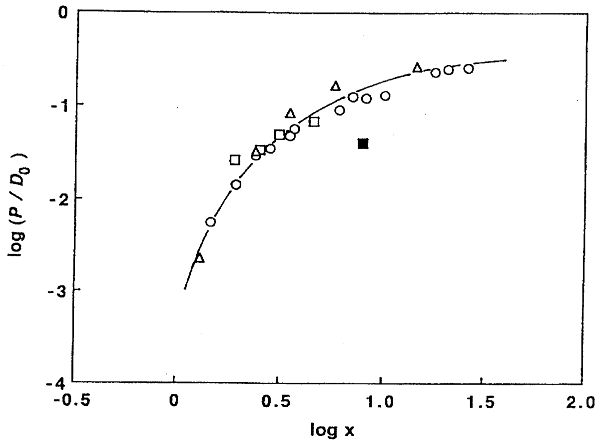

Fig. 9. Normalized permeability coefficient P/D_0 as a function of $x(=\xi/d_0)$ PVA(FD)-62: ○, PVA(FT)-84: △, PVA-(B)-74: □. The mark ■ shows the result of NaBA through PVA(B)-74 membrane.

the results of PVA(FD), PVA(B), and PVA(FT) were found to be on a curve, except for the result of NaBA through PVA(B)-74. This deviation results from an electrostatic interaction between negative charges of the boratecrosslinks and benzoate. Taking the electrostatc interaction term into consideration, the result of NaBA through PVA(B)-74 should be on the same curve. The electrostatic term will be studied more. From these results, when the interaction between the matrix and the solute can be negligible, ξ/d_0 is found to be the main factor of the permeability through gel membranes.

Conclusions

1) The permeability coefficients (P) of PVA gel membranes are proportional to the diffusion coefficients (D) of solutes, only when the mesh sizes of the gel membranes are much larger than that of the solute, and the interaction between the matrix and the solute can be negligible.

2) The mesh sizes (ξ) of PVA(FD) gel membranes showed a good linear relation as a function of $Q^{3/4}$. The result of PVA(FT) having heterogeneous network structures deviated from the line.

3) The permeability coefficients of solutes through gel membranes (P) depend on the hydrodynamic radius of the solute (d_0) and the mesh size of the network (ξ). When the interaction between the matrix and the solute can be negligible, the normalized permeability coefficients (P/D_0) were found to be the scaling function of ξ/d_0.

References

1) M. Yonese, *Pharm Tech Jpn.*, **6**, 391 (1990).
2) I. Oomime and T. Tanaka, *J. Chem. Phys.*, **77**, 5725 (1982).
3) Y. Osada and M. Hasabe, *Chem. Lett.*, **1985**, 1285.
4) K. Baba, M. Yonese, and H. Kishimoto, *Bull. Chem. Soc. Jpn.*, **65**, 121 (1992).
5) H. Tanzawa, *Kobunshi*, **37**, 750 (1988).
6) M. Yonese and M. Nakagaki, *Yakugaku Zasshi*, **92**, 1521 (1972).
7) M. Nanbu, *Koubunshi Kakou*, **32**, 523 (1983).
8) C. T. Reinhart and N. A. Peppas, *J. Membr. Sci.*, **18**, 227 (1984).
9) A. T. Y. Cheng and F. Rodriquez, *J. Appl. Polym. Sci.*, **26**, 3895 (1981).
10) I. Sakurada and Y. Ikada, *Bull. Inst. Chem. Res. Kyoto Univ.*, **42**, 22 (1964).
11) K. Kaji, T. Kanaya, and M. Ookura, *Koubunshi Kakou*, **38**, 54 (1989).
12) M. Makkee, A. P. G. Kieboom, and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, **104**, 230 (1985).
13) R. K. Schultz and R. M. Raymond, *Macromolecules*, **2**, 281 (1969).

14) M. Yonese, K. Baba, M. Kondo, and H. Kishimoto, *Chem. Lett.*, **1992**, 199.

15) R. F. Chen, *J. Biol. Chem.*, **242**, 173 (1967).

16) M. Yonese, K. Sato, and H. Kishimoto, *J. Membr. Sci.*, **26**, 179 (1986).

17) M. Yonese, K. Baba, and H. Kishimoto, *Bull. Chem. Soc. Jpn.*, **61**, 1857 (1988).

18) K. Baba, M. Yonese, and H. Kishimoto, *Bull. Chem. Soc. Jpn.*, **65**, 121 (1992).

19) A. Katchalsky and P. F. Curran, "Nonequilibrium Thermodynamics in Biophysics," University of Tokyo Press, Tokyo (1965), Chap. X.

20) M. Yonese, K. Baba, M. Kondo, and H. Kishimoto, *Chem. Lett.*, **1992**, 199.

21) P. J. Flory "Principles of Polymer Chemistry," Cornell University Press, New York (1963), Chap. XI.

22) D. L. Meadows and N. A. Peppas, *Chem. Eng. Commun.*, **31**, 101 (1984).

23) C. T. Reinhart and N. A. Peppas, *J. Membr. Sci.*, **18**, 227 (1984).

24) P.-J. de Gennes, "Scalling Concepts in Polymer Physics," Cornell University Press, New York (1979).

25) S. R. Lustig and N. A. Peppas, *J. Appl. Polym. Sci.*, **36**, 735 (1988).

26) Y. Kambe and C. Honda, *Polym. Commun.*, **24**, 208 (1983).

27) Y. Kambe and C. Honda, *Polym. Commun.*, **25**, 154 (1984).

28) C. Rossi, E. Bianchi, and G. Conio, *Chim. Ind.* (*Milan*), **45**, 1498 (1963).

29) M. Tokita, T. Miyoshi, K. Takegoshi, and K. Hikichi, *Jpn. J. Appl. Phys.*, in press.