

# Preparation and Permeability of Solutes Through Acrylic Acid-*g*-Methylcellulose Copolymer Membranes

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## SYNOPSIS

Graft copolymer membranes from the methylcellulose and the acrylic acid were prepared and their properties and the permeability of four solutes were estimated. Acrylic acid-*g*-methylcellulose (AA-*g*-MC) copolymer dissolved in aqueous acetone solvent was cast to prepare membranes followed by the subsequent crosslinking either with aluminium potassium sulfate or by the thermal-curing method. The equilibrium water content in the membrane increased with the volume fraction of acetone in the aqueous acetone solvent system. Membrane, the ionically crosslinked with the aluminum potassium sulfate, showed the water content in the range of 38.5 and 58.4% and 0.25–0.33 kg/mm<sup>2</sup> of the tensile strength in the wet state. Compared with ionically crosslinked membranes, thermally dried membranes exhibited a more dense structure, resulting in lower water contents and higher mechanical strength. Experimental results on the permeation of four small and midsize solutes through the graft copolymer membranes revealed the molecular weight dependence of the permeability coefficient. The higher the degree of swelling, the greater the permeability coefficient. Ionically crosslinked membranes had higher solute permeability than the commercial Cuprophane membrane had. © 1993 John Wiley & Sons, Inc.

## INTRODUCTION

Among the artificial organs utilizing polymeric membranes, blood dialyzer has been widely used due to its simple process for removing toxic wastes from blood. The materials that need to be removed from blood dialyzer vary from low molecular weight components such as water, wastes, and electrolytes, to high molecular weight components (e.g., low protein immunoglobulin).<sup>1</sup>

One of the most important factors for the selection of biomedical membrane materials is the structure and property relationship of the membrane. Membrane structures have been studied from the viewpoints of micro- and macrostructures. In the former studies the introduction of functional groups onto the polymer and permeating components appear to be important. Qualitatively, permeability is related to diffusivity and solubility, which is governed by the interaction between permeating species

and polymer. According to Cohen and Turnbull,<sup>2</sup> the diffusion coefficient can be expressed by the logarithm of the size of permeating species provided that the free volume of polymer is constant. Meanwhile, Tsujita<sup>3</sup> urged that, in order to enhance the permeability attributed to the solubility coefficient of polymer, it was recommended to use hydrophilic species for hydrophilic polymers and hydrophobic species for hydrophobic polymers. On macrostructural studies, there are reports on the conformational changes due to chemical means such as the change in pH of external solution and on the control of permeability by changing the quantity and distribution of microvoids from thermal treatment or rapid cooling.<sup>4–6</sup>

Water-swallowable polymers have been extensively studied as a possible use in biomedical materials.<sup>7</sup> Polymer surface containing high water content shows an interaction to a small extent with blood being composed largely with water.<sup>8</sup> In these cases, water contents in the membrane and water structure inside of the membrane become important factors influencing the diffusion coefficient of the permeating component.<sup>9–13</sup> However, a lower water content

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contributes the formation of hydrogen bonding between water and polymer chain and thus weakens the chain mobility, resulting in the decrease in the permeability. If the water content is too high, permeability increases and mechanical strength decreases. Therefore, it is necessary to design a polymer containing a proper water content.

The main objective of the present study is the preparation of acrylic acid-*g*-methylcellulose (AA-*g*-MC) and the investigation of permeation behavior of four model solutes through the crosslinked AA-*g*-MC. Crosslinking was carried out by either subsequent ionic crosslinking or thermal drying of the graft copolymer. Methylcellulose was chosen as a base material because it has been known to be chemically stable, physiologically nontoxic, and biologically resistant compared to cellulose. Poly(acrylic acid) is a water-soluble polymer, but is insoluble upon crosslinking. Using the crosslinked graft copolymer membranes, crosslinking conditions, and membrane preparation conditions, properties and solute permeability were accessed for possible application in the blood dialyzer membrane.

## EXPERIMENTAL

### Materials

Methylcellulose (MC, 4000 cps) was obtained from Kokusan Chemical Co. Acrylic acid (AA) was from Junsei Chemical and used after vacuum distillation. Potassium persulfate (KPS, Hayashi Pure Chemicals) as an initiator and aluminum potassium sulfate (APS, Junsei Chemical Co.) as a crosslinking agent were all reagent grade and used as received. Urea and sucrose were obtained from Wako Pure Chemicals. Poly(ethylene glycol) (PEG 3400) and vitamin B<sub>12</sub> were purchased from Polyscience and Rhone-Poulenc, respectively.

### Preparation of AA-*g*-MC

Methylcellulose (MC) and acrylic acid (AA) were dissolved in the deionized water and stirred in a flask under nitrogen inflow at 30°C using  $3.7 \times 10^{-4}$  and  $3.7 \times 10^{-3}$  mol dm<sup>-3</sup> of KPS as an initiator. After 3 h, the reaction mixture was heated to 60°C, and the reaction was terminated to obtain the precipitated graft copolymer with poly(acrylic acid) (PAA) homopolymer remaining in an aqueous solution. AA-*g*-MC copolymer was obtained by filtering the reaction mixture, washing several times with hot water, and removing the unreacted initiator followed

by vacuum drying. Infrared spectra for MC and AA-*g*-MC copolymers showed that the peak intensity of  $\nu_{\text{CH}_3}$  at 2940 cm<sup>-1</sup> decreased and  $\nu_{\text{C=O}}$  at 1730 cm<sup>-1</sup> appeared as graft polymerization proceeded.

### Preparation of Crosslinked AA-*g*-MC Membrane

AA-*g*-MC graft copolymer with varying the graft percent was dissolved in 0–40 vol% aqueous acetone to prepare 10 wt % casting solution. The solution was cast on the glass plate and completely dried at 40°C for 1 day under vacuum to obtain the membrane. Since AA-*g*-MC membrane was soluble in water, it was crosslinked for 12 h in a bath and washed with water and dried to obtain the water-insoluble membrane. Aqueous solution of APS in the concentration range of 0.1–1.0 mol dm<sup>-3</sup> was used as a crosslinking agent. The crosslinked membrane was either transparent or opaque, depending upon the concentration of the crosslinking agent and the crosslinking methods. For a comparison, water-insoluble membrane was prepared by the thermal treatment in a convective oven at 70°C without crosslinking agents. The thickness of the dry membrane was about 80  $\mu\text{m}$ .

### Measurements

FTIR (Nicolet, Model 5 DX) was used to determine the structure of the copolymers. Densities of samples were measured by the density gradient column filled with *n*-heptane and CCl<sub>4</sub>. X-ray diffractometer (Rigaku Denkki, Model D/MAX-111 A) was used to estimate the crystallinity of samples at  $2\theta$  ranging from 5° to 50° with 4°/min.

A DuPont 910 thermal analyzer and the cell base was used for all the melting measurements. A membrane sample (~6–15 mg) equilibrated at 37°C was sealed in an aluminum pan and cooled down with the liquid nitrogen to -70°C in DSC. The cell was slowly heated in a stream of nitrogen gas at a program rate of 5°C/min up to 20°C.

Graft percent of PAA in the copolymer was determined by titration, as reported in the literature.<sup>14</sup> Copolymer solution was added with an excess of dilute NaOH solution to react with the carboxylic groups. An excess of NaOH solution was titrated with a dilute HCl solution. Graft percent of PAA was calculated from the known amount of the copolymer and the alkali consumption.

Metal content in the membrane was determined by slowly heating the dry metal-crosslinked membrane in a muffle furnace from 20°C to 850°C and oxidizing the membrane between 850 and 900°C for

1 h. From the amount of the residue, the metal contents were calculated as a percent for a dry membrane.

To measure the water content, samples were immersed either in a distilled water or in pseudo-extracellular fluid (PECF)<sup>15</sup> for 7 days. Then water content of a sample at equilibrium was determined according to the following equation,  $Q_w (\%) = [(W_s - W_d)/W_s] \times 100$ , where  $W_s$  and  $W_d$  denote the weight of wet and dry samples, respectively.

Tensile strength was estimated by an Instron Model 4201 with a crosshead speed of 10 mm/min.

### Permeation Experiment

A permeation cell used in this study has two compartments of equal volume (100 mL).<sup>16</sup> Concentrations of urea, sucrose, vitamin B<sub>12</sub>, and PEG 3400 were 200, 200, 50, and 100 mg/L, respectively. Temperature of the compartment was maintained at 37°C with a constant stirring at 300 rpm to eliminate any concentration polarization. Concentrations in the feed and the permeating compartments were detected using ultraviolet spectrophotometer (Perkin-Elmer, Model 559) and differential refractometer (Waters, Model R 403). Particularly for the vitamin B<sub>12</sub> solution, the light was blocked during the permeation experiments to obtain the precise absorption curves measured at 550 nm.

The solute permeability coefficient  $P$  was calculated from the following equation which was obtained from mass balance equation, i.e.,

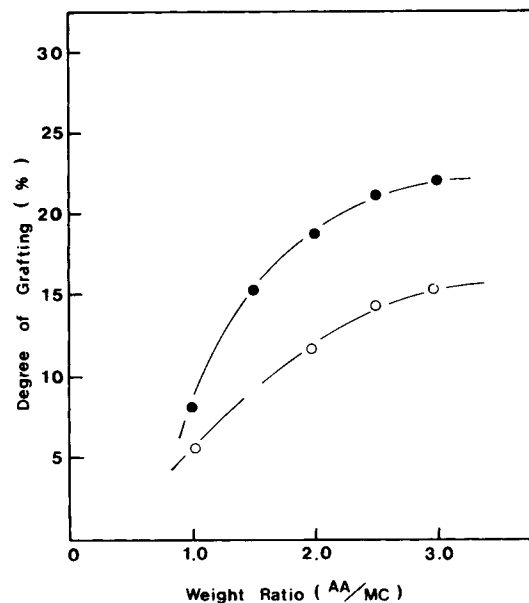
$$P = \frac{-d}{A(1/V_1 + 1/V_2)t} \times \ln \left[ \left( 1 + \frac{V_1}{V_2} \right) \frac{C_t}{C_0} - \frac{V_1}{V_2} \right], \quad (1)$$

where  $V_1$ ,  $V_2$ ,  $A$ ,  $d$ ,  $C_0$ , and  $C_t$  were volumes of the concentrated and the dilute compartment, membrane area (9.62 cm<sup>2</sup>), thickness, and concentrations of the concentrated compartment at times 0 and  $t$ , respectively.

## RESULTS AND DISCUSSION

### Graft Yield of Copolymer

Figure 1 exhibits the change in the degree of grafting as a function of the weight ratio of AA to MC. At the same weight ratio of AA to MC, the high degree of grafting was obtained at the higher concentration

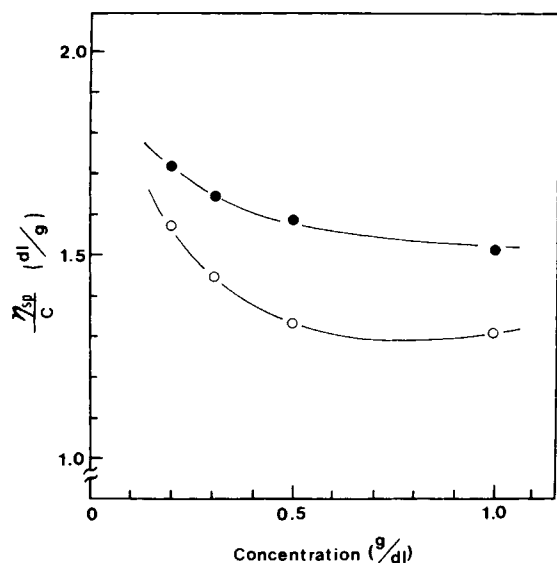


**Figure 1** Effect of the weight ratio of AA to MC on the degree of grafting;  $[K_2S_2O_8]$ : (●)  $3.7 \times 10^{-3}$  mol/dm<sup>3</sup>; (○)  $3.7 \times 10^{-4}$  mol/dm<sup>3</sup>.

of initiator. Potassium persulfate (KPS) has been known to form free radicals by the dissociation in an aqueous media and macroradicals by taking an unstable hydrogen from the main chain in MC.<sup>17</sup> At the low initiator concentration, a relatively small number of large chains are formed, while, at the high initiator concentration, many short chains are generated, resulting in a high degree of grafting.

The degree of grafting was increased with the growing monomer concentration. As the monomer ratio was higher than 2.5, the increase in the degree of grafting dropped due primarily to the limited number of radical sites in the main chain in MC. Graft copolymers having up to 15% degree of grafting were soluble in cold water, insoluble in acetone, and soluble in a mixed solution of water and acetone. Solubility of copolymer was particularly excellent when the volume fraction of acetone was 0.2.

The reduced viscosity was plotted as a function of solution viscosity of the graft copolymer prepared at 30 and 40°C, as shown in Figure 2.  $\eta_{sp}/C$  of the graft copolymer rises with decreasing concentration, indicating the polyelectrolytic character of the copolymer due to the presence of the acrylic acid moiety, a weak electrolyte. Ordinarily, the reduced viscosity increases with the concentration. The anomalous shape of the curve of  $\eta_{sp}/C$  versus concentration of electrolytes, in the absence of added salt, was typified by polyvinylbutylpyridinium bromide, a strong electrolyte.<sup>18</sup>



**Figure 2** Dependence of the reduced viscosity on the concentration of AA-*g*-MC copolymers in water; AA/MC = 3 (weight ratio),  $[K_2S_2O_8] = 3.7 \times 10^{-3} \text{ mol/dm}^3$ ; reaction temperature: (●) 30°C; (○) 40°C.

### Crosslinked AA-*g*-MC

Aluminium potassium sulfate (APS) was chosen as a crosslinking agent because of its notable solubility in water. It did not dissociate easily after crosslinking. We obtained the water-insoluble membrane by heat treatment as well. IR spectra for AA-*g*-MC, crosslinked with APS, and after thermal treatment showed that  $\nu_{C=O}$  at  $1721 \text{ cm}^{-1}$  due to carboxylic acid decreased and  $\nu_{C=O}$  at  $1638 \text{ cm}^{-1}$  due to carboxylate ion appeared for samples crosslinked with

APS. The crosslinking density grows apparently with the concentration of crosslinking agent.

### Properties and Morphology of Crosslinked AA-*g*-MC

Table I lists the characteristics of the crosslinked AA-*g*-MC graft copolymer which contains 15% degree of grafting and is designated as AMC-13. The AMC-13 was chosen because it had a very good solubility in water and mechanical properties among the samples investigated. Casting solvent was 20 vol % acetone in water. As can be seen in the table, the concentration of crosslinking agent influences to a great extent on physical properties of the resultant membrane.

Equilibrium water content in the thermally dried membrane is much smaller than that in membranes crosslinked with APS. Water contents inside of the membranes show higher than 50% for APS crosslinked membranes and decrease with growing crosslinking density.

Mechanical properties of samples in the dry state are regarded as excellent. However, in wet state, only AMC-1307 and -1308 show higher tensile strength than that of commercially available Cuprophane membrane,<sup>19</sup> that is, about  $0.3 \text{ kg/mm}^2$ . Densities of samples are greater than 1.3, which is typical for cellulose. Graft copolymer thermally dried at 70°C, AMC-13TD, has tensile strength about 2.5-fold higher than that of Cuprophane, and shows the lowest density among the series of AMC-13, indicating that the evaporation of solvent at high temperature causes the membrane dense in structure.

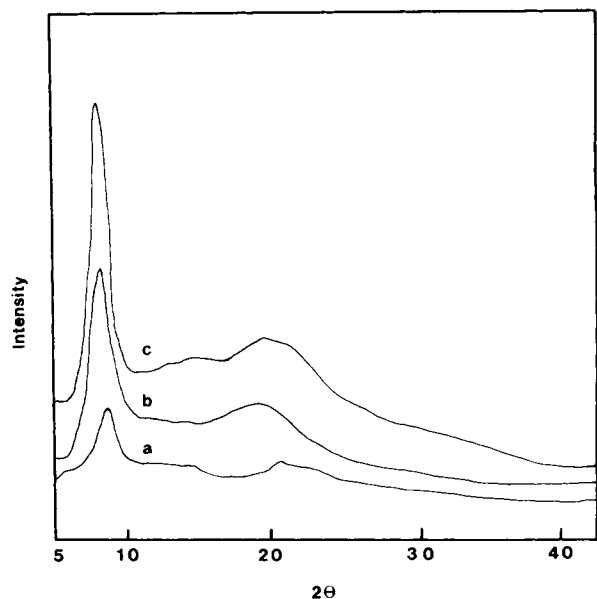
Figure 3 illustrates the X-ray diffraction patterns

**Table I** Characteristics of AA-*g*-MC Copolymer Membranes After Crosslinking With APS

Membrane	Concentration of Crosslinking Agent ( $\text{mol dm}^{-3}$ )	$Al^{3+}$ Content (wt %) <sup>a</sup>	Degree of Swelling (%)		Tensile Strength ( $\text{kg/mm}^2$ )		Density ( $\text{g m}^{-3}$ )
			In Water	In PECF	Dry	Wet	
AMC-1301	0.1	2.25	86.5	92.3	2.01	0.09	1.3590
AMC-1305	0.5	2.42	67.0	69.6	3.45	0.18	1.3696
AMC-1306	0.6	2.46	56.8	60.3	3.60	0.22	1.3607
AMC-1307	0.7	2.51	55.3	57.7	3.81	0.31	1.3536
AMC-1308	0.8	2.55	51.3	55.1	4.13	0.34	1.3607
AMC-1309	0.9	2.52	59.7	64.4	3.72	0.29	1.3592
AMC-1310	1.0	2.46	62.4	67.3	3.56	0.27	1.3529
AMC-13TD <sup>b</sup>	—	—	23.8	24.2	3.89	0.75	1.3206

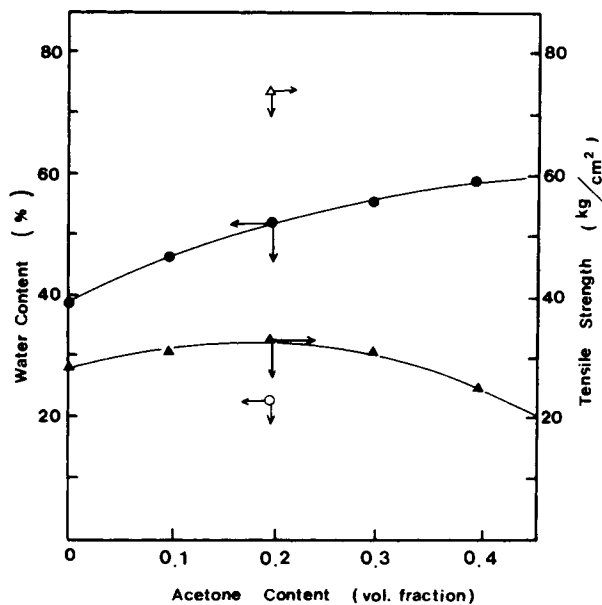
<sup>a</sup> g Al/g dry membrane.

<sup>b</sup> TD = thermally dried.



**Figure 3** X-ray diffraction patterns of crosslinked AA-g-MC copolymer membranes: (a) AMC-1308; (b) AMC-13; (c) AMC-13TC.

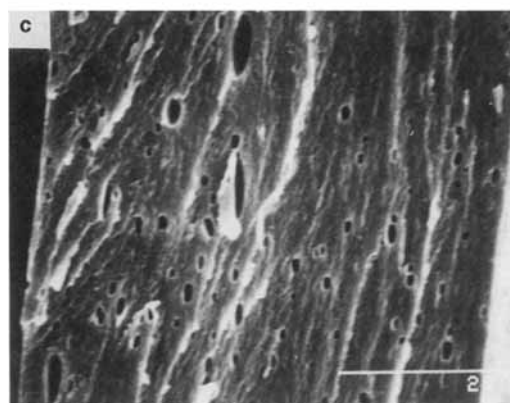
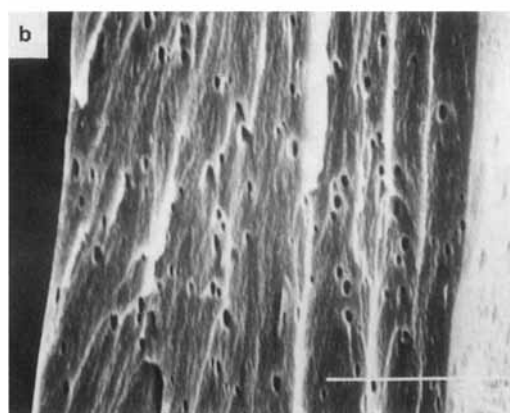
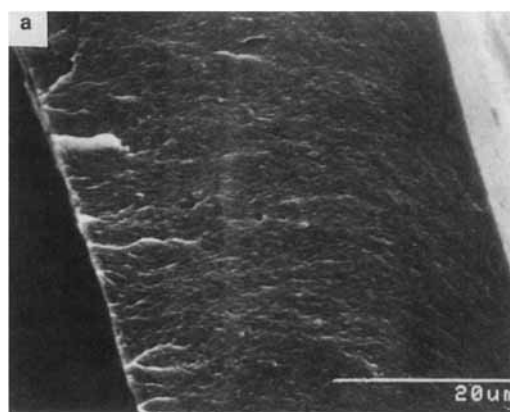
for AA-g-MCs. Maximum peak intensity appeared at  $2\theta = 8-9^\circ$ . Compared with samples AMC-13 and AMC-1308 (curves a and b in Fig. 3), the peak intensity decreases with the growing crosslinking density. Thermally dried dense membrane (AMC-13TD, curve c) show more crystalline character due



**Figure 4** Effect of the solvent composition for preparing crosslinked AMC copolymer membrane on water content and tensile strength in wet state: (●) and (▲) for AMC-1308; (○) and (△) for AMC-13TC.

to the compactness of the chain packing in the polymer membrane.

Since the AMC-1308 showed the best mechanical properties, it was cast from the different composition in casting solvents. Membranes were designated as AMC-1308-A-E, depending upon the volume fraction of acetone in aqueous solvent, varying from 0.0 to 0.4 by the increment of 0.1.



**Figure 5** Scanning electron micrographs of AMC membranes: (a) AMC-1308-A; (b) AMC-1308-C; (c) AMC-1308-E.

Figure 4 illustrates the change in equilibrium water content in the membrane and tensile strength in the wet state as a function of composition of acetone in a mixed solvent. Equilibrium water content increases with the amount of acetone in a solvent system. Tensile strength increases at lower concentration of acetone, but then shifts to decrease at higher volume fraction of acetone in the solvent mixture. This trend can be explained by the observation of cross sections of the membranes, as shown in Figure 5, where the membrane becomes more porous as the volume fraction of acetone, which acts as a nonsolvent, in a mixed solvent system increases. Meanwhile, the thermally dried membrane shows low water content and high tensile strength in the wet state because of the dense structure.

### Solute Permeabilities of Crosslinked AA-g-MC Membranes

Table II lists permeabilities of solutes through membranes AMC-1308 and -TD. When the volume fraction of acetone is over 0.1, solute permeabilities of a series of AMC-1308 membranes were higher than that of Cuprophane.<sup>19</sup> In general, membranes (AMC-1308-B, -C, and -D) show higher permeability of solutes than and comparable mechanical properties to Cuprophane. Solute permeabilities decrease as the molecular weight of solutes increases. All the crosslinked membranes show the similar molecular weight dependency.

In Figure 6, the solute permeability increases with the equilibrium water content, and the change in the solute permeability drops beyond 50% of water content in the membrane. This was mainly attributed to the water structure in the membrane. Since

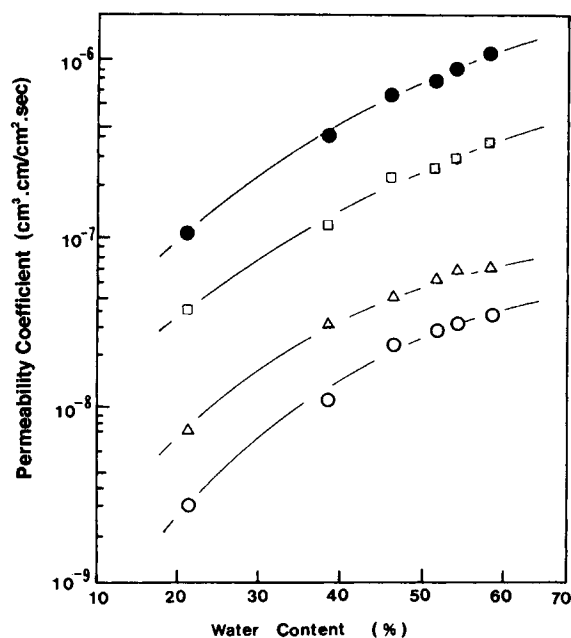


Figure 6 Dependence of permeability coefficients on the water content for AMC membranes: (●) urea; (□) sucrose; (△) vitamin B<sub>12</sub>; (○) PEG 3400.

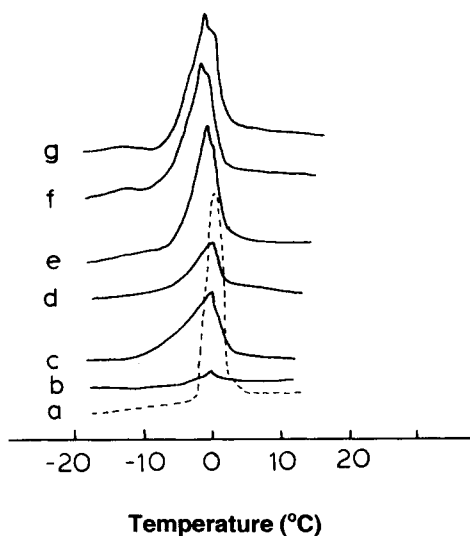
solutes are permeated only into the water region in hydrophilic polymer, the structure of water in the swollen polymer matrix may play a significant role in the permeation of solutes.

Figure 7 shows DSC heating curves of water-swollen AA-g-MC membranes. With the increase in swelling ratio of membrane, it was found that an endothermic peak appearing at around 0°C due to the presence of free water was growing and separated into two peaks, one remaining at close to 0°C and the other shifting toward -4°C. These endothermic

Table II Solute Permeability Coefficients and Calculated Bound Water and Free Water in Crosslinked AA-g-MC Copolymer Membranes

Membrane	Permeability Coefficient $\times 10^7$ ( $\text{cm}^3 \text{ cm/cm}^2 \text{ s}$ )				$W_t$ , Water Content (%)	$W_b$ , Fraction of Bound Water	$W_f$ , Fraction of Free Water
	Urea	Sucrose	Vitamin B <sub>12</sub>	PEG 3400			
AMC-1308-A	4.0	1.3	0.32	0.10	38.5	0.54	0.46
AMC-1308-B	6.8	2.2	0.51	0.23	46.3	0.48	0.52
AMC-1308-C	7.6	2.6	0.62	0.28	52.6	0.42	0.58
AMC-1308-D	8.6	2.9	0.67	0.32	54.1	0.42	0.58
AMC-1308-E	10.9	3.6	0.71	0.37	58.4	0.41	0.59
AMC-13TD	1.2	0.4	0.07	0.03	21.3	0.99	0.01
Cuprophane <sup>a</sup>	4.8	2.0	0.57	—	50.0	—	—

<sup>a</sup> Data were taken from Ref. 19.



**Figure 7** DSC melting endotherms of pure water (a) and free water in AMC membranes: Water contents in the membrane are 21.3% (b), 38.5% (c), 46.3% (d), 52.6% (e), 54.1% (f), and 58.4% (g).

peaks confirm the existence of two types of water in the membrane,<sup>7,16</sup> i.e., a free water and a freezing bound water. The former has a melting temperature comparable with that of bulk water (curve a in Fig. 7), whereas the latter shows a lower temperature peak presumably by a weak interaction between water and the polymer chain.

The amounts of free, freezing bound, and non-freezing water in the membrane are estimated and listed in Table II for different polymer membranes. The values were calculated from enthalpies given by the area of peaks appearing at  $-4$  and  $0^{\circ}\text{C}$ . The amount of bound water in the membrane is approximately estimated from the following equation:

$$W_b = W_t - (W_f + W_{fb}) \quad (2)$$

$$= W_t - Q_{\text{endo}}/Q_f \quad (3)$$

where  $W_b$  and  $W_t$  are the weight of bound and total water in the membrane, respectively.  $W_f$  and  $W_{fb}$  are the weight fraction of free water and freezing bound water, respectively. The sum of  $W_f$  and  $W_{fb}$  is the ratio of  $Q_{\text{endo}}/Q_f$ , where  $Q_{\text{endo}}$  is the observed endothermic heat (cal/g) originating from bound and freezing bound water from water-swollen membrane and  $Q_f$  is the heat fusion of ice (79.7 cal/g). It can be seen that the total water content increases as the membrane becomes crosslinked and porous. The amount of free water increases while the fraction of bound water becomes less as the membranes

become crosslinked and porous. The more the increase in the amount of total water, the greater the permeability of solutes through the membrane. Free and freezing bound water may form water cluster by hydrogen bonding between themselves. The strength in hydrogen bonding between free and freezing bound water is obviously weaker than that between bound water. Bound water is difficult to move because it strongly combines with polymer chains. Therefore, solutes find difficulty in diffusing through this region and may rather transport through the region of free and freezing bound water. Note that the permeability coefficients increases with the amount of free water. Greater amount of free water coupled with porosity in the membrane contributed to the permeation of solutes through the membrane.

## CONCLUSION

Membrane was prepared from the methylcellulose grafted with the acrylic acid by crosslinking either with aluminium potassium sulfate or after the thermal-treatment. AA-g-MC copolymer was dissolved well in 20 vol % aqueous acetone. Tensile strength in wet state of membrane crosslinked with APS ranged from 0.25 to 0.33 kg/mm<sup>2</sup>, while the water content was about 38.5–58.4%. The permeabilities of urea and sucrose through the crosslinked membrane was superior to that of Cuprophane. The thermally crosslinked membrane was dense in structure and thus showed the lower water content and about 2.5-fold higher tensile strength compared to Cuprophane. The water structure inside of the membrane was investigated from the DSC results. The permeability of solutes correlated well with the amount of water content or free water in the membrane.

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