

## Effect of Temperature on the Permeation of Water Through Propylene Glycol Monoacrylate Hydrogel

MIGUEL F. REFOJO, *Cornea Research Unit and Department of Retina Research, Institute of Biological and Medical Sciences, Retina Foundation, Boston, Massachusetts 02114*

### Synopsis

Transparent propylene glycol monoacrylate (PGMA) hydrogels become reversibly opaque when the temperature is rapidly increased to above 30°C. Water permeation, driven by a hydrostatic pressure difference through three PGMA membranes differing in water content and thickness was determined at several temperatures. At room temperature, the permeability to water is relatively low (less than  $10 \times 10^{-16}$  cm.<sup>2</sup>) and is dominated by a diffusion mechanism. When the temperature is suddenly increased, the water permeation rises quickly (up to fifteen times or more depending on the temperature), and viscous flow predominates over diffusive flow. The rapid flow slows down after some time at the same temperature, or on lowering the temperature, and may be interpreted as caused mainly by the reversible transformation of the membrane from the heterogeneous to the homogeneous form. When the temperature is increased gradually, the permeability of the membrane is in the same order of magnitude as that found at room temperature, because no phase separation occurs. The permeation of water decreased in successive measurements made under the same pressure gradient. An increase of the pressure difference also resulted in decreased permeation, indicating that water was pressed out of the gel. Dehydration of the gel caused by increases in temperature (exothermic swelling) and in pressure and changes in the viscosity of water with temperature are some of the factors which are considered in the interpretation of the results.

### INTRODUCTION

It has been found that a transparent propylene glycol monoacrylate (PGMA) hydrogel becomes opaque when its temperature is rapidly increased to 30°C. or higher.<sup>1</sup> It has also been found that the hydrogel maintains its transparency when the temperature is increased slowly. Moreover, a PGMA hydrogel that is transparent at room temperature becomes opaque after a sudden increase in temperature, but it regains its transparency if it is allowed to stand long enough at the higher temperature or if it is allowed to cool. These phenomena are produced by changes in the configuration of the polymer segments as a result of the temperature increase, and they are related to the precipitation of some polymers from solution after an increase in temperature.<sup>2</sup> In PGMA hydrogels, precipitation occurs only after a sudden increase in temperature, indicating that certain changes in configuration occur that are faster than the relaxation time of the polymer segments.

The permeation of water through some PGMA hydrogels under pressure gradients at 25°C. has been determined.<sup>3</sup> It was also found that the average pore radius of a homogeneous PGMA hydrogel, having a water content of 41% or 62% at equilibrium swelling at room temperature, is three to four times the radius of the water molecule. This finding suggests that, at room temperature, the diffusion mechanism plays the most important role in the movement of water through these gels.

The present investigation was undertaken to determine whether a membrane made of a crosslinked polymer possessing the property of inverse temperature dependence (such as PGMA hydrogel) would function as a chemical valve. Under pressure gradients at normal temperature, the membrane would have a relatively low permeability, governed predominantly by a diffusion mechanism, but, on subjecting the membrane to a sudden change in temperature, its permeability would quickly increase, becoming chiefly a viscous flow. The viscous flow would predominate for a time, and then the mechanism would reverse itself.

### EXPERIMENTAL

The nature of the PGMA monomer and the preparation of its hydrogels have been described in an earlier communication.<sup>1</sup>

The membranes (A, B, and C) used in these experiments were prepared as indicated in Table I. After the membranes had been cast, the ethylene glycol in the gel was replaced by distilled water. Some of the characteristics of the water-equilibrated membranes are given in Table I.

Permeability measurements were carried out under essentially the same conditions as those used by other investigators.<sup>4-6</sup> The apparatus used and the methods of operation have already been described.<sup>3,7</sup> In general, the permeability apparatus was placed in a thermostatically controlled water bath at the required temperature just before the determinations were made. The apparatus was kept in the water bath for a few minutes until it reached the temperature of the bath, which was apparent when there was no movement of the meniscus in the capillary tube. Hydrostatic

TABLE I  
Preparation and Properties of PGMA Membranes at Equilibrium Swelling at 25°C.

Membrane	PGMA monomer, vol.	H <sub>2</sub> O, vol.	Ethylene glycol, vol.	6% (NH <sub>4</sub> ) <sub>2</sub> S <sub>2</sub> O <sub>8</sub> , vol.	5% 2-Dimethylaminoethyl acetate, vol.	H <sub>2</sub> O in gel, %	Membrane thickness, mm.	Appearance
A	3	3	3	1	1	55.3	0.290	Slightly milky
B	4	2	3	0.5	0.5	54.9	0.273	Clear
C	5	10	10	0.5	0.5	50.6	0.680	Clear

pressure was then applied, and the rate of flow was measured in the usual manner.<sup>3</sup>

## RESULTS

The permeability coefficient,  $K$  (in square centimeters), was calculated from the equation:<sup>4,5</sup>

$$K = VL_{\eta}/tA\Delta P$$

where  $V$  is the volume of water (in cubic centimeters) of viscosity  $\eta$  (in poises) flowing through a membrane of thickness  $L$  (in centimeters) and area  $A$  (in square centimeters) in a time  $t$  (in seconds) under a pressure difference of  $\Delta P$  (in dynes/square centimeter).

Since the film thickness  $L$  used in the calculations was measured at equilibrium swelling at normal pressure and temperature (which is larger than the thickness at higher temperatures and pressures), a systematic error occurred in the calculations of the permeability coefficients. The true permeability coefficients should be somewhat lower than those calculated.

To allow better comparison of the permeability coefficients obtained for PGMA membranes at different temperatures, corrections were made for changes in the viscosity of the permeant (water) with temperature. Since the permeability varies inversely with the viscosity of the permeant,<sup>4</sup> the permeability coefficient of a membrane at a given temperature was multiplied by the ratio between the viscosity of water (in poises) at this temperature and that at 25°C. yielding a value,  $K'$  (in square centimeters) which was approximately comparable to the permeability of the membrane to water at 25°C.

### Membrane A

Permeability measurements were carried out on membrane A at 25°C. and at higher temperatures (Tables II–IV). In successive measurements made under the same pressure gradient at constant temperature, the perme-

TABLE II  
Membrane A

$\Delta P$ , mm. Hg	$K \times 10^{16}$ , (25°C.), cm. <sup>2</sup>	Gradual increase of temperature to 66°C.	
		$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>
400	10.25	13.39	6.43
	5.86	13.27	6.37
	3.28	7.27	3.49
500	2.64	13.27	6.37
	2.14	8.01	3.84
		3.75	1.80
600	1.75	6.90	3.31
	1.62	5.83	2.80
		5.38	2.58
700	1.91	5.83	2.80
	1.60	5.59	2.68

TABLE III  
Membrane A

$\Delta P$ , mm. Hg	$K \times 10^{16}$ (25°C.), cm. <sup>2</sup>	Sudden increase to 64°C.		After 1/2 hr. at 64°C.		After 1 1/2 hr. at 64°C.	
		$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>
400	5.96	74.83	36.98	7.91	3.91	9.22	4.59
	5.02			6.81	3.36	3.24	1.60
500	3.46	52.02	25.71	11.29	5.58	2.45	1.21
	2.17			26.90	14.78	1.42	0.69
600	1.58	32.40	16.01	3.21	1.58		
700		19.96	9.86				

ability was found to decrease. Increasing pressure also resulted in a decrease in the permeability.

When the temperature of the permeability apparatus was increased gradually by keeping the apparatus in the water bath until it had reached the desired temperature, the permeability of the membrane was found to be not much higher than that found at room temperature (Table II). Nevertheless, when a sudden temperature change was brought about by placing the apparatus in a hot water bath immediately before the measurements were made and waiting a few minutes to allow the temperature to equilibrate with that of the water bath, the permeability of the membrane

TABLE IV  
Membrane A

$\Delta P$ , mm. Hg	Sudden increase to 41°C.		After 3 hr. at 41°C.	
	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>
400	36.34	26.18	0.71	0.51
			2.47	1.78
500	14.31	10.31	1.58	1.14
			1.18	0.85
600	9.81	7.07		
700	6.29	4.53		

was found to be substantially higher than it was at room temperature (Tables III and IV). The permeability then decreased gradually with time until it approached the value found at room temperature or an even lower value (Tables III and IV). The flow rate used to calculate the permeability coefficient at 64 and at 41°C. was the average of four and three determinations, respectively, for each pressure gradient.

### Membrane B

The results obtained with membrane B are presented in Table V. At room temperature, the permeability of this membrane was rather low, but it showed a marked increase when the temperature was suddenly raised. When the membrane was maintained at the high temperature for more than  $\frac{1}{2}$  hr., its permeability became too low to be measurable under the conditions of the experiment. After the second series of determinations at 51°C., the pressure was released for  $\frac{1}{2}$  hr. while the apparatus remained at the same temperature. A single determination was then carried out at 400 mm. Hg, and the permeability coefficient was calculated to be  $K = 2.17 \times 10^{-16}$  cm.<sup>2</sup>. After this one determination, the membrane was too impermeable to permit any movement of water through it to be detected. After the series of determinations at 62°C., the apparatus was allowed to remain at this temperature, under normal pressure, for  $1\frac{1}{2}$  hr. Attempts to determine the flow of water afterward were unsuccessful owing to the low permeability of the membrane.

TABLE V  
Membrane B

$\Delta P$ , mm. Hg	$K \times 10^{16}$ cm. <sup>2</sup>	Sudden increase to 41°C.		Sudden increase to 51°C. after 45 min. at room temperature		Sudden increase to 51°C. after overnight at room temperature		Sudden increase to 62°C.	
		$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>
400	6.99	11.31	8.15	32.63	19.73	44.86	27.12	86.11	43.84
		6.78	4.89	20.09	12.15	38.43	23.24	90.51	46.08
		4.24	3.06	18.85	11.39	33.77	20.42	77.13	39.26
		3.32	2.39	17.35	10.49	38.59	23.33	52.79	26.87
500				12.57	7.60	28.23	17.07	41.24	20.99
				16.67	10.08	24.34	14.72	32.87	16.73
				8.97	5.43	12.58	7.41	26.72	13.60
				8.66	5.24	18.85	11.39	29.12	14.82
600				6.13	3.70	15.90	9.61	20.58	10.48
				6.73	4.07	10.10	6.11	23.85	12.14
				3.91	2.37	7.82	4.73	17.49	8.90
				2.24	1.35	5.85	3.54	13.17	6.70
700				0.45	0.27			11.73	5.97
				0.25	0.15			5.40	2.75
800	1.08							8.67	4.41
								7.45	3.79

TABLE VI  
 Membrane C

$\Delta P$ , mm. Hg	Sudden increase to 50.5°C.		Sudden increase to 61°C.	
	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>	$K \times 10^{16}$ , cm. <sup>2</sup>	$K' \times 10^{16}$ , cm. <sup>2</sup>
600			43.59	22.52
			23.27	12.02
			19.42	10.03
			12.04	6.22
700	13.41	8.17	9.41	4.86
	10.03	6.11	10.51	5.43
760	7.79	3.75		
	9.75	5.94		
800	8.61	5.25	10.39	5.32
			13.78	7.12
860	5.61	3.42	10.13	5.23
	3.10	1.89		
900			18.32	9.46
			12.46	6.44
			20.56	10.62

### Membrane C

Membrane C, the thickest and least hydrated of the three, was too impermeable to permit detection of any water movement at 25°C. at hydrostatic pressures of up to 900 mm. Hg. The results obtained at higher temperatures are given in Table VI. The flow rate decreased in each successive measurement. Moreover, in each series of measurements, the higher the pressure applied, the slower was the rate of flow. In the series of experiments carried out at 61°C., the determinations at 700 mm. Hg were made immediately after those at 900 mm. Hg. Because the membrane was already compressed, the flow rate was less than it would have been otherwise.

### DISCUSSION

At constant temperature and pressure, crosslinked polymers attain equilibrium swelling. The degree of swelling is, of course, dependent on the solvent or the solvent mixture. Inasmuch as the same solvent was used through these experiments, it may be assumed that only the temperature and the pressure affected the swelling of the PGMA membranes. It was found previously that, in PGMA hydrogels, the degree of equilibrium swelling decreases when the temperature is raised.<sup>1</sup> Moreover, it is well known that when the pressure exerted on a gel is greater than the equilibrium swelling pressure, the solvent is pressed out of the gel. Since it has been reported that the permeability of a hydrophilic gel decreases as the water content of the gel decreases,<sup>3,5</sup> both the dehydration that occurred under hydrostatic pressure and the dehydration resulting from the increase in temperature should contribute to a substantial decrease in the permeability of the PGMA membranes.

At a fixed degree of swelling, the permeability of a membrane varies inversely with the viscosity of the permeant.<sup>4</sup> Inasmuch as the viscosity of water decreases with increasing temperature, it is possible that the increase in temperature contributes to the increase in the water permeability of PGMA membranes.

We have, then, two opposing effects counteracting each other, namely, the dehydration of the gel caused by the increasing temperature and pressure, which should decrease the flow of water through the membrane, and the lowering of the viscosity of the permeant, which should increase its flow. In addition, the reversible transformation of PGMA hydrogels from the homogeneous to the heterogeneous form brings into play the pore size of the membrane at different temperatures. The size of the pores determines whether the flow within the membrane will be predominantly viscous or whether it will be diffusive.<sup>8</sup> The pressure gradient leads to a viscous flow, and the gradient in the chemical potential, resulting from the gradient in hydrostatic pressure, leads to a diffusive flow. Viscous flow across a hydrophilic membrane predominates when the pore radius is much larger than the radius of the water molecule.



In the transparent form of the PGMA hydrogel, the polymer and the water are in a homogeneous state, and the pore size is in an ultramicroscopic order of magnitude. In the opaque form of the hydrogel, the structure is spongelike, with macroscopic holes. These forms are related, respectively, to the ultragel and the microgel structures distinguished by Elford.<sup>9</sup> A faster flow may be expected to occur through the macroscopic holes of the opaque form than through the ultramicroscopic pores of the transparent form. The rapid decrease in the permeability of the PGMA membranes found at higher temperatures can be related both to the compression of the membrane by the pressure and the temperature and to the reversal transformation of the gel from the heterogeneous to the dehydrated, homogeneous form.

The permeability coefficient of a PGMA membrane containing 41% water at equilibrium swelling was previously reported to be  $K = 0.87 \pm 0.24 \times 10^{-16}$  cm.<sup>2</sup>; a second membrane, containing 62% water at equilibrium swelling, was found to have a permeability coefficient of  $K = 2.83 \pm 0.33 \times 10^{-16}$  cm.<sup>2</sup>.<sup>3</sup> It was therefore calculated, by the Ticknor method,<sup>8</sup> that, in these hydrogels, diffusion is the predominant factor in the water transport. It was also found that the net water transport in hydrogel membranes with a permeability coefficient in the order of  $40 \times 10^{-16}$  cm.<sup>2</sup> and higher is primarily one of viscous flow. Judged from the magnitude of the permeability coefficients, it can be stated that, when the temperature of a PGMA membrane is suddenly increased to above 30°C., the movement of water through the membrane is initially dominated by a viscous flow, which changes with time and increasing pressure, until the diffusion mechanism assumes control.

There are, however, additional factors which contribute to the difficulties in the interpretation of the results; for example, when permeation occurs by the diffusion mechanism, the rate of flow increases with the temperature and is essentially independent of the hydrostatic pressure.<sup>10</sup> Inasmuch as the flow of water through transparent PGMA is dominated by a diffusion mechanism, the flow rate should increase with the temperature. Nevertheless, when the dehydration of PGMA by increased temperature and pressure is taken into account, a clearcut interpretation of the results cannot be made.

This investigation was supported by a PHS research grant (NB-6456) from the National Institute of Neurological Diseases and Blindness, U.S. Public Health Service.

### References

1. M. F. Refojo and H. Yasuda, *J. Appl. Polymer Sci.*, **9**, 2425 (1965).
2. H. Morawetz, *Macromolecules in Solution*, Interscience, New York, 1965, p. 77.
3. M. F. Refojo, *J. Appl. Polymer Sci.*, **9**, 3417 (1965).
4. S. Madras, R. L. McIntosh, and S. G. Mason, *Can. J. Res.*, **27B**, 764 (1949).
5. M. L. White, *J. Phys. Chem.*, **64**, 1563 (1960).
6. B. O. Hedbys and S. Mishima, *Exptl. Eye Res.*, **1**, 262 (1962).
7. M. F. Refojo, *J. Appl. Polymer Sci.*, **10**, 185 (1966).

8. L. B. Ticknor, *J. Phys. Chem.*, **62**, 1483 (1958).
9. W. Elford, *Proc. Roy. Soc. (London)*, **B106**, 216 (1930).
10. A. Lebovits, *Mod. Plastics*, **43**, No. 7, 139 (1966).

### Résumé

Des hydrogels transparents de propylène glycol monoacrylate (PGMA) deviennent réversiblement opaques lorsque la température est rapidement accrue au-dessus de 30°C. La perméation à l'eau exercée par une différence de pression hydrostatique, à travers trois membranes PGMA différentes en teneur eau et épaisseur, a été déterminée à de nombreuses températures. A température de chambre, la perméabilité à l'eau est relativement basse (moins que  $10 \times 10^{-16}$  cm<sup>2</sup>) et elle est dominée par un mécanisme de diffusion. Lorsque la température est subitement accrue la perméabilité à l'eau croît rapidement (jusque 15 fois ou plus suivant la température) et l'écoulement visqueux prédomine jusque au-dessus de l'écoulement par diffusion. L'écoulement rapide ralentit après quelque temps à la même température ou en abaissant la température, et peut être interprété comme causé principalement par la transformation réversible de la membrane d'une forme hétérogène à une forme homogène. Lorsque la température est accrue graduellement la perméabilité de la membrane est du même ordre de grandeur que celle trouvée à température de chambre, parce que il n'y a plus de séparation de phase. La perméation d'eau décroît au cours des mesures excessives effectuées sous même gradient de pression. Une augmentation de la différence de pression entraîne également une diminution de perméation ce qui indique que l'eau a été pressée hors du gel. La déshydratation du gel causée par l'augmentation de la température (gonflement exothermique) et de la pression, et des changements de viscosité de l'eau en fonction de la température sont certains des facteurs qui sont considérés pour l'interprétation des résultats.

### Zusammenfassung

Transparente Propylenglykolmonoacrylat-(PGMA)-hydrogele werden bei rascher Erhöhung der Temperatur über 30°C reversibel undurchsichtig. Die Wasserpermeation unter einem hydrostatischen Überdruck durch PGMA-Membrane mit verschiedenem Wassergehalt und verschiedener Dicke wurde bei mehreren Temperaturen gemessen. Raumtemperatur ist die Permeabilität für Wasser relativ niedrig (weniger als  $10 \times 10^{-16}$  cm<sup>2</sup>) und durch einen Diffusionsmechanismus bestimmt. Bei plötzlicher Temperaturerhöhung steigt die Wasserpermeation rasch an (je nach Temperatur bis zum fünfzehnfachen und mehr) und das Diffusionsfließen wird von viskosem Fließen überdeckt. Das schnelle Fließen verlangsamt sich nach einiger Zeit bei der gleichen Temperatur und kann als hauptsächlich durch die reversible Umwandlung der Membran von der heterogenen in die homogene Form verursacht betrachtet werden. Bei graduller Temperaturerhöhung bleibt die Permeabilität der Membrane in der gleichen Größenordnung wie bei Raumtemperatur, da keine Phasenänderung eintritt. Die Wasserpermeation nahm bei aufeinanderfolgenden Messungen unter gleichem Druckgradienten ab. Auch eine Zunahme der Druckdifferenz führte zu einer Herabsetzung der Permeation, was zeigt, dass Wasser aus dem Gel ausgepresst wurde. Dehydration des Gels durch Temperatur-(exotherme Quellung) und Druckzunahme sowie die Viskositätsänderung des Wassers mit der Temperatur sind Faktoren die zur Interpretierung der Ergebnisse herangezogen werden.

Received July 19, 1966

Prod. No. 1467