

Hydrogels from 2-Hydroxyethyl Methacrylate and Propylene Glycol Monoacrylate*

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Synopsis

Hydrophilic three-dimensional polymer networks (hydrogels) were prepared from 2-hydroxyethyl methacrylate (HEMA) and propylene glycol monoacrylate (PGMA). By wet crosslinking, hydrogels which maintain their original shape and volume relatively well, compared with the dry-cross-linked polymer networks, were obtained. The maximum amount of water which can be maintained in transparent hydrogels depends on the hydrophilicity of the monomers, e.g., about 40% for HEMA gels, about 50% for PGMA gels, and 40–50% for HEMA–PGMA copolymer gels depending on the monomer composition. When the water content exceeds this maximum in transparent gels (homogeneous hydrogels), they become opaque and/or spongy (heterogeneous hydrogels). Effects of the amount of crosslinking agent and the initial dilution of the monomer solution upon the swelling behavior of hydrogels were investigated. The temperature dependence of the swelling of these hydrogels and the water permeation through them were also studied.

INTRODUCTION

Three-dimensional networks of hydrophilic polymers (hydrogels) can be prepared by several methods. For instance, bulk polymerization of a hydrophilic monomer with a crosslinking agent, the introduction of crosslinks to a hydrophilic polymer in solution, and the simultaneous polymerization and crosslinking of monomer–crosslinking agent mixtures, will all produce hydrophilic gels. Among these methods, the last has unique advantages. The polymerization or formation of hydrogels can be achieved very quickly at a low temperature by utilizing redox initiator systems, and also the formation of gels in a given shape can readily be obtained since the starting materials are in a liquid form. Furthermore, the gels can maintain their original shapes without swelling or deswelling in water.

Wichterle and Lim^{1,2} have proposed hydrophilic gels for medical use where the hydrophilicity of polymers plays an important role. In this

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application, hydrogels of hydrophilic methacrylates are of special interest due to the chemical stability of methacrylates. A transparent poly-(hydroxyethyl methacrylate) gel with a water content of less than 30% has been reported by these authors.¹ Polymers from hydroxyethyl methacrylate (HEMA) have been proposed for use as a hydrophilic embedding medium for the preparation of sections for microscopy.^{3,4} According to Rosenberg et al.,⁴ the polymers are transparent with up to 40% water content and beyond that are turbid. Wichterle and Lim¹ also mentioned a porous structure obtained by the rapid polymerization of HEMA.

Although this limited information can be found in literature, little has been reported about the details of swelling properties or the transparency of hydrogels. Since the transparent hydrogels have a potential interest in application to ophthalmology, the study of hydrogels from HEMA and propylene glycol monoacrylate PGMA has been initiated to give more insight into the properties of these hydrogels.

HYDROGELS FROM 2-HYDROXYETHYL METHACRYLATE

HEMA is a commercially available monomer (The Borden Chemical Company, Philadelphia, Pa.). As supplied, it contains about 0.1% dimethacrylate and about 3.0% methacrylic acid. The dimethacrylate content is sufficient to effect some crosslinking. The homopolymer has been reported as an insoluble polymer,^{5,6} although when the pure monomer is polymerized at low conversion (to avoid crosslinking due to chain transfer) a homopolymer soluble in water-ethyl alcohol mixture was found.⁷

When polymerizing both commercial and redistilled HEMA to total conversion, insoluble polymers are obtained. Crosslinks are probably introduced by both residual difunctional monomer and by chain transfer to the polymer. The amount of residual diethylene glycol dimethacrylate in the redistilled HEMA was not determined.

Tetraethyleneglycol dimethacrylate (TEGDMA), being the more hydrophilic diester, was used as a crosslinking agent rather than glycol dimethacrylate. TEGDMA is a commercially available monomer (The Borden Chemical Company, Philadelphia, Pa.), and it was used as such without further purification.

Bulk Polymerization

Bulk polymerization of HEMA proceeds in a similar fashion to the bulk polymerization of methyl methacrylate. The resulting polymer resembles poly(methyl methacrylate), although poly-HEMA is much harder and more brittle than PMMA. When bulk-polymerized HEMA is immersed in water, it gradually swells and becomes soft.

Distilled HEMA (n_D^{25} 1.4498) was polymerized at 65°C, with 0.03% benzoyl peroxide as initiator and the polymer allowed to swell in water at

room temperature for about one year. The water in the gel was then found to be 37.5%.

Heterogeneous Hydrogels

When HEMA is polymerized in aqueous solution with high water content or in water alone with a redox initiator system, polymers precipitate out of the monomer solution as the polymerization proceeds and yield opaque gels or porous sponges, depending on the polymerization conditions. The swelling of the sponge is proportional to the amount of water added to polymerization mixture. With 1% ammonium persulfate and 2% sodium metabisulfite initiator in the monomer and a variable amount of water in

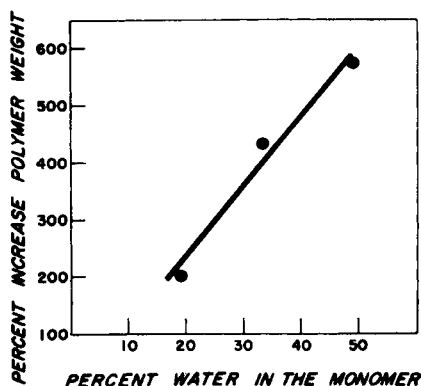


Fig. 1. Swelling of heterogeneous HEMA hydrogels in water.

the solution, the polymerization was allowed to proceed at room temperature and completed overnight at 55°C. The resulting polymers were kept in water for five weeks, and the increase in weight was determined. In mixtures of monomer with 20, 33, and 50% water, the increase in weight of the polymer in water is two, four, and five and a half times, respectively. (Fig. 1).

Homogeneous Hydrogels

HEMA can be polymerized in solution with a redox initiator in a homogeneous system. In this case, the polymerization medium must be a good solvent system for both the monomer and the polymer. Such a solvent system is ethylene glycol-water solutions. By polymerizing HEMA in an aqueous solution of ethylene glycol with persulfate-bisulfite initiator, a transparent gel is obtained. The gel is converted to transparent hydrogel upon equilibration in water. During the exchange of the glycol by water the gel becomes opaque, but becomes completely transparent again after equilibrium is reached. The hydrogel is transparent from freezing to boiling temperature in water and has a remarkable shape and volume stability.

The refractive index of the equilibrated hydrogel was found to be n_D^{25} 1.431. If allowed to dry out completely, the polymer is hard, brittle, and transparent.

Of course, when the water in the hydrogel is exchanged for another solvent, the final effect on the gel is dependent upon the nature of the solvent. Allyl alcohol and dioxane, for example, seem to be very good solvents for HEMA polymers. The gel swells markedly when the water is exchanged for either of these solvents. In the same way, when the chemical activity of water in the hydrogel is modified by some solute, a different amount of water will be found in the gel at equilibrium. Sodium chloride

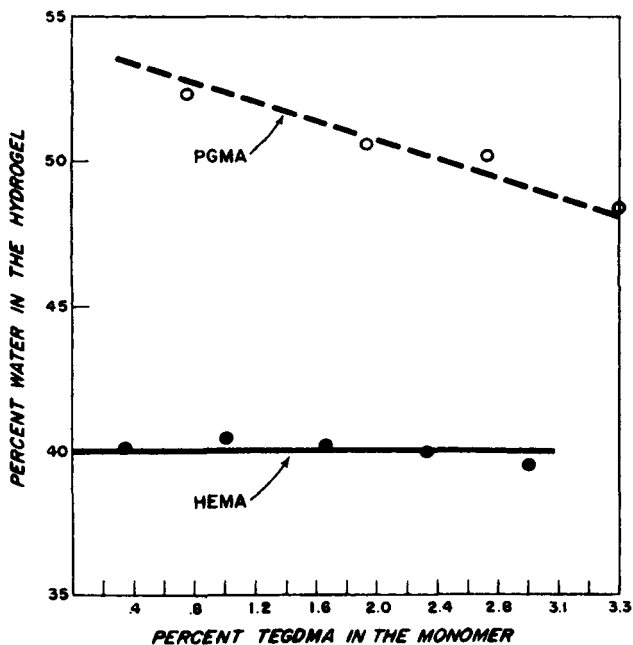


Fig. 2. Effect of crosslinking on the water content in HEMA and PGMA hydrogels.

and fluorescein, for example, in dilute solution in water affect the amount of water in the hydrogel. When HEMA hydrogel was kept in $2 \times 10^{-4}\%$ aqueous fluorescein solution, the water found in the equilibrated hydrogel at room temperature was 40%; when the concentration of fluorescein was increased to $2 \times 10^{-2}\%$, the equilibrated hydrogel contained 49% water. With equilibration at room temperature in 0.9% sodium chloride solution, the amount of water in HEMA hydrogel decreased to 38%, but when the concentration of sodium chloride was increased to 1.4%, the amount of water in the hydrogel also increased markedly to 46%.

The effect of the amount of crosslinking agent upon the water content in the hydrogel is shown in Figure 2. The amount of water in the equilibrated hydrogel is 0.6% less in the gel with 3.0% TEGDMA than in the gel with

0.3% crosslinking agent. The same variation in the cross-linking agent added to a hydrogel of propylene glycol monoacrylate (PGMA) produces a change in the amount of water in the equilibrated PGMA hydrogel in the order of 4%.

The water found in the equilibrated HEMA hydrogels is not dependent upon the amount of water or the amount of glycol added to the poly-

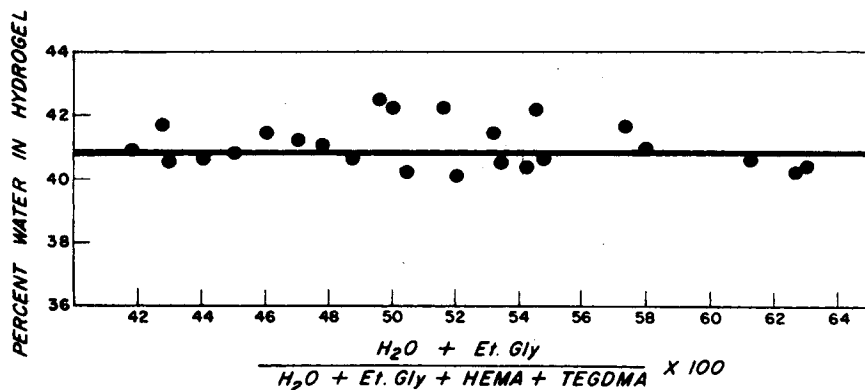


Fig. 3. Effect of the amount of solvent in the monomer solution upon the amount of water in HEMA hydrogel.

merizing mixture. A series of experiments was carried out in which the water and the ethylene glycol in the monomer mixture varied widely and the amount of the crosslinking agent TEGDMA varied from 0.3 to 1.6%. The crosslinking agent under limits was shown to influence slightly the amount of water in the equilibrated hydrogel. The amount of initiator in this series also was variable, but this did not seem to influence the amount of water in the hydrogel. The amount of water in the equilibrated hydrogel varies slightly under these experimental conditions (Fig. 3).

HYDROGELS FROM PROPYLENE GLYCOL MONOACRYLATE

The propylene glycol monoacrylate (PGMA) (kindly supplied by the Celanese Chemical Company) used in these experiments was a mixture of two isomers, 2-hydroxy-1-propyl acrylate and 1-hydroxy-2-propyl acrylate, in concentrations of approximately 70 and 30%, respectively. It contains hydroquinone monomethyl ether, 200 ppm, as the inhibitor.⁸ In this work, PGMA was used as supplied, without further purification.

PGMA hydrogels were made according to the procedure of homogeneous solution polymerization used to prepare homogeneous HEMA hydrogels. Ethylene glycol-water was used as the solvent of polymerization, persulfate-bisulfite redox as the initiators, and TEGDMA as the crosslinking agent. As did the HEMA gels, the PGMA gels became opaque during the exchange of solvent for water during the equilibration step.

The amount of water found in PGMA hydrogels at equilibrium is more dependent on the amount of crosslinking agent added to the polymerizing mixture and more dependent on the temperature of the hydrogel-water system.

The refractive index of a PGMA hydrogel having a water content of 50.6% at 25°C. was found to be n_D^{25} 1.411.

Homogeneous solution polymerization of commercial PGMA, in which there is 0.4% residual propylene glycol diacrylate, gives a very soft and sticky gel. The physical properties of the gel improve greatly with the use of TEGDMA as a crosslinking agent, although PGMA hydrogels with TEGDMA crosslinks do not have as good mechanical properties as do HEMA hydrogels. If allowed to dry out completely, PGMA polymer is flexible and transparent.

The effect of the number of crosslinks upon the water contained in PGMA hydrogels is more marked than in HEMA hydrogels (Fig. 2). Since TEGDMA is more soluble in the PGMA-glycol-water system than in the HEMA solution, it is possible to introduce more crosslinks in the PGMA polymer than there are in the HEMA polymers.

HYDROGELS FROM HEMA-PGMA COPOLYMERS

The amount of water in the copolymer hydrogels is dependent upon the proportion of each monomer in the copolymer (Fig. 4).

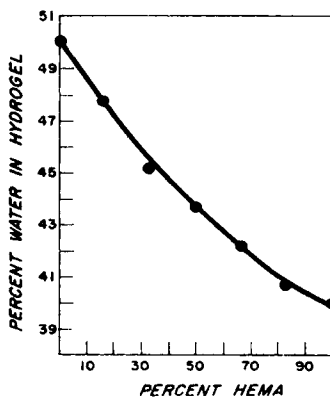


Fig. 4. Effect of HEMA-PGMA copolymer composition upon water content.

The copolymer hydrogels exhibit the inverse temperature dependence shown in PGMA homopolymers, which will be discussed in the following section. Of course, this property is more marked when the proportion of PGMA in the copolymer is larger.

TEMPERATURE DEPENDENCE OF THE SWELLING OF HYDROGELS

The amount of water in HEMA hydrogels is dependent upon the temperature of the hydrogel-water system. Changes in the amount of water in the gel ranging from 3 to 4% are observed by equilibrating the gel in water at different temperatures. A minimum in the amount of water in the hydrogel is found in the neighborhood of 60°C. and increases up to the freezing and boiling temperatures (Fig. 5). The minimum found in the curve in HEMA hydrogels is independent of the temperature at which the polymerization was carried out.

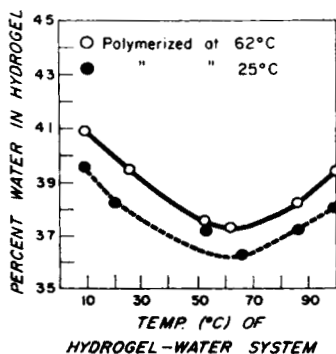


Fig. 5. Effect of temperature on water content in HEMA hydrogels.

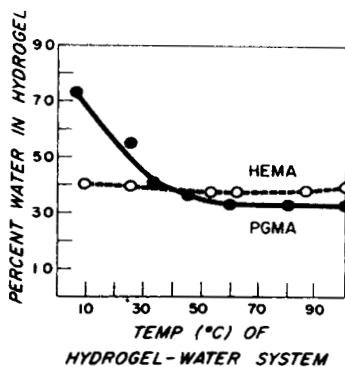


Fig. 6. Effect of the temperature of the hydrogel-water system upon the amount of water in HEMA and in PGMA hydrogels.

PGMA hydrogels show inverse temperature dependence. They are transparent up to about 30°C., regardless of the temperature experience of the gel. The water content of gels at equilibrium increases steadily with decreasing temperature below 30°C. (Fig. 6). However, some physical properties, such as optical transparency and the water content at equilibrium, are quite different at temperatures higher than the critical

temperature of approximately 30°C. For example, PGMA hydrogel becomes opaque at temperatures above 30°C. if the change in temperature is rapid. On the other hand, if the rate of temperature change is very slow, the hydrogels maintain their transparency up to 100°C. A hydrogel opaque at any temperature above 30°C. which was transparent below this temperature, regains its transparency if allowed to stand long enough at the higher temperature. The transparent hydrogel at higher temperatures will maintain its transparency if it is cooled slowly. Above 30°C. the water content of the hydrogels is much less dependent on the temperature and approaches the constant value of 33% (Fig. 6).

The opacification of PGMA hydrogels upon rapid changes in temperature may be interpreted as a microphase separation or the introduction of optical heterogeneity due to uneven configurational changes of polymer segments caused by temperature changes which are faster than the relaxation time for the configurational change of polymer segments.

PERMEABILITY OF HYDROGELS

The permeability or rather the pervaporation rate of the hydrogels to water was determined by the inverted cup procedure. Under experimental conditions, no difference was found between the permeability of HEMA and PGMA hydrogels. The relative permeability of the hydrogels and some other materials are shown in Table I.

TABLE I
Water Permeability of Polymers

Polymer	Water transmission rate at 27°C., g.-mil/m. ² -24 hr.
Polyethylene	5
Nylon 66	280
HEMA hydrogel	30,000
PGMA hydrogel	30,000
Polyelectrolytes complex*	170,000

* Poly(vinyl-trimethylammonium)-Poly(styrene sulfonate), water content 35% (Amicon Inc., Cambridge, Massachusetts).

The pervaporation process under the conditions of measurement consisted of two consecutive processes: (1) permeation through the polymer matrix and (2) evaporation from the surface of the polymer. This method of measurement may not be a sufficiently accurate means of estimating the permeability of some highly permeable materials, since the effect of the air layer which exists between the out-flowing surface of the polymer film and the desiccant becomes as great as the permeation process. A study of the permeability of these highly permeable membranes is under progress and will be presented elsewhere.

DISCUSSION

The swelling properties of hydrogels are, in principle, similar to those of hydrophobic network polymers in organic solvents which have appeared in the literature.⁹⁻¹¹ The swelling of the network depends on at least three important parameters: (a) the interaction parameter between polymer and solvent, (b) the number of crosslinks or the molecular weight of the polymer chain between crosslinks, and (c) the reference degree of swelling in which state the polymer chains have their unrestrained end-to-end distance, and/or the initial dilution of monomer in the case where crosslinks are introduced simultaneously with the chain growth of the main chain. However, the main limitation in the study of the hydrogels is the fact that most of their properties are measured only in a particular solvent, i.e., water. On the other hand, the two monomers studied in this work do not yield water-soluble polymers. In other words, water is not a solvent for either of these polymers even when no crosslinks exist. Consequently, in order to obtain homogeneous network polymers it is necessary to add to the polymerization mixture an organic solvent which is miscible with both water and monomer. Therefore, the polymer-solvent interaction and also the reference degree of swelling of the polymer at the time of polymerization differ from those of polymer-water at the final state of the gels.

The fact that water is a rather poor solvent for these polymers is the predominant factor which tends to overshadow some other controlling factors of gel properties, such as the initial dilution and number of crosslinks. Similar trends were also observed with the vinyltoluene-divinylbenzene polymer network and methyl methacrylate-ethylene dimethacrylate polymer network in poor solvents.¹¹ Undoubtedly this is the main reason why homogeneous HEMA gels exhibit relatively constant swelling in water regardless of the initial dilution and the number of crosslinks. By the same token, the dependence of the swelling of PGMA gels, to which water has higher solvent power than to HEMA gels, upon the initial dilution and the crosslinks density can be explained. With better solvents, the effect of the initial dilution and the crosslinks density upon the swelling of gels becomes more evident.

The maximum amount of water which can be maintained in homogeneous hydrogels depends on the hydrophilicity of the monomer, consequently on the hydrophilicity of the polymer. A rough test indicates that water is only about 45% miscible in HEMA monomer at room temperature; however, the value seems to increase up to about 55% at 60°C. The change in solubility is reflected in the water content in hydrogels polymerized at two different temperatures (Fig. 5), presumably due to the difference in the reference degree of swelling at the two temperatures.

PGMA monomer is miscible with water at any ratio. The miscibility of the monomer with water gives another limitation in the practical range of the experiments, i.e., the amount of crosslinking agent which can be added to the polymerization mixture depends largely on the water mis-

cibility of the monomer, since the solubilities of crosslinking agents (difunctional methacrylates) are generally much less than those of monofunctional hydrophilic monomers.

The transparency of hydrogels seems to depend entirely on the randomness of the polymer network-water (solvent) system. This can be demonstrated by the inverse temperature dependence of PGMA gels transparency and also by the opacification of hydrogels in the solvent exchange process. On the other hand, this will give an interesting comparison with the transparency of the cornea in the eye. The cornea consists of microfibrils which exist in an extremely regular and high order, yet existing heterogeneously. The small size of the fibrils and the order of arrangement give the extremely high transparency of the cornea. This may give us an interesting hint for the structure of hydrogels which could be highly transparent, highly permeable, yet have high mechanical strength.

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Résumé

On a préparé des réseaux tridimensionnels de polymères hydrophiles (hydrogels) à partir de méthacrylate de 2-hydroxyéthyle (HEMA), et de nonacrylate de propylène glycol (PGMA). Par pontage à l'état mouillé on a obtenu des hydrogels qui conservaient relativement bien leurs dimensions et volume d'origine si on les compare avec les réseaux de polymères pontés à sec. La quantité maximum d'eau qui peut être maintenue dans les hydrogels transparents dépend du pouvoir hydrophile des monomères, par exemple elle est de 40% pour les gels HEMA, d'environ 50% pour les gels PGMA, et de 40 à 50% pour les gels formés de copolymère HEMA-PGMA suivant la composition en monomère. Lorsque la teneur en eau dépasse ce maximum dans les gels transparents (hydrogels homogènes), ils deviennent opaques et/ou spongieux (hydrogels hétérogènes). On a étudié l'influence de la quantité d'agent de pontage et de la dilution initiale de la solution de monomère sur le gonflement des hydrogels. On a également étudié la dépendance vis-à-vis de la température du gonflement de ces hydrogels et de la pénétration d'eau.

Zusammenfassung

Hydrophile dreidimensionale Polymernetzwerke (Hydrogele) wurden aus 2-Hydroxy-äthylmethacrylat (HEMA) und Propylenglycolmonacrylat (PGMA) dargestellt. Durch die nasse Vernetzung wurden Hydrogele erhalten, welche im Vergleich zu den trockenvernetzten Polymernetzwerken ihre ursprüngliche Gestalt und ihr Volumen relativ gut beibehalten. Die maximale Wassermenge, die transparente Hydrogele enthalten können, hängt von der Hydrophilie der Monomeren ab, z.B. etwa 40% für HEMA-Gele, etwa 50% PGMA-Gele und 40–50% für HEMA-PGMA-Copolymergele je nach der Monomerzusammensetzung. Wenn der Wassergehalt in transparenten Gelen (homogenen Hydrogelen) dieses Maximum übersteigt, wird sie opak oder schwammartig (heterogene Hydrogele). Der Einfluss der Vernetzungsmittelmenge und der Anfangsverdickung der Monomerlösung auf das Quellungsverhalten der Hydrogele wurde untersucht. Weiters wurde die Temperaturabhängigkeit der Quellung der Hydrogele und die Wasserpermeation durch dieselben gemessen.

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