Effects of Low Levels of Methacrylic Acid on the Swelling Behavior of Poly(2-hydroxyethyl Methacrylate)

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Synopsis

The effects of low levels of methacrylic acid (MAA) (less than 4 mol %) and a crosslinker (less than 0.3 mol %) on the equilibrium swelling and water content of poly(2-hydroxyethyl methacrylate) (pHEMA) hydrogels were investigated. Numerous pHEMA disks, some of which were doped with small amounts of MAA, were placed in swelling baths simulating possible urological as well as physiological conditions. Several interesting facts are reported, such as, in dilute urea (0.15*M*) or in alkali solution, gels containing 2% MAA are capable of swelling to 3600% their size in mild acid, saline, or distilled water, with associated water contents that range as high as 98%. Also, gels containing small amounts of MAA and finite crosslinker content can be made that are soluble in mild urea or alkali solution. The significance of this study is that gels or gel surfaces can be fabricated that are highly responsive to their environment. In addition, since the levels of MAA that cause this shrink–swell behavior are well within the impurity levels of MAA found in unpurified commercial HEMA, it is conceivable that this shrink–swell behavior may have occurred in early studies of implanted pHEMA gels, thus confusing the subsequent evaluation of its performance as a biomaterial.

INTRODUCTION

Among the most frequently used hydrogels for medical applications are poly(2-hydroxyethyl methacrylate) (pHEMA)[1] and its derivatives. The literature contains many references[2–4] to copolymers of pHEMA and methacrylic acid (MAA); however, none of these references provide details of the effects of low levels of MAA, e.g., less than 4 mol %, on the swelling behavior of gels at crosslinker content less than 0.3%. Our research has shown that gels composed of pHEMA containing less than 3% MAA undergo unexpectedly large swelling, and even dissolution, when placed in different chemical environments in comparison with the much smaller dimensional changes of pure pHEMA. Furthermore, these dramatic swelling changes can be controlled by doping the monomer with the appropriate MAA and crosslinker content. The significance of this information is that not only can gels be fabricated that are highly responsive to local changes in environment, but also the range of MAA required for these transitions to occur is well within the range of impurities normally found in commercial-grade HEMA monomer. Consequently, unless proper purification or analysis of monomer is performed, the presence of impurity levels of MAA

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will affect the swelling behavior of the gel and may confuse subsequent evaluations of its performance.

In most applications of hydrogels, the swelling behavior and water content are important properties that are dependent upon the fraction of ionizable groups and degree of crosslinking as well as the environment in which they are used. In applications where geometric stability is required, such as the artificial ureter[5] or contact lenses,[6] the presence of minute amounts of MAA in the gel lattice causes the gel to swell or shrink in different chemical environments beyond the expected amounts. The subsequent variation in swelling behavior can lead to complications of fit, reduced tensile strength, or variations in flow rates through tubes. In applications where gel permeability is of concern, such as drug release systems,[7] membrane dialyzers,[8] or grafted surfaces,[9] the concentration of ionizable species and crosslinker in the gel structure affects the selectivity and diffusion rates of drugs, metabolites,[3,4] electrolytes through the gel.

The monomer (HEMA) may be purchased from several suppliers and at different purity grades. However, the purity specifications are not sufficient to ensure pure HEMA because the monomer is not stable. Degradation of the monomer during transportation and storage at ambient temperatures may result in increased levels of MAA and the naturally occurring crosslinker ethylene glycol dimethacrylate (EGDMA). As illustrated in Figure 1, HEMA monomer readily undergoes three common reactions[1]: (A) HEMA may hydrolyze at the ester linkage to form MAA and ethylene glycol; (B) two molecules of HEMA may transesterify to form the crosslinker EGDMA and ethylene glycol; (C) monomer may polymerize at the double bond resulting in oligomer or polymer. An inhibitor, such as hydroquinone, is usually added to the monomer to minimize the latter reaction. Some investigators have reported impurity levels as high as 5 mol % MAA and 0.3% EGDMA.[10] In modern practice, careful researchers purify the monomer prior to use to avoid MAA and EGDMA contamination. The

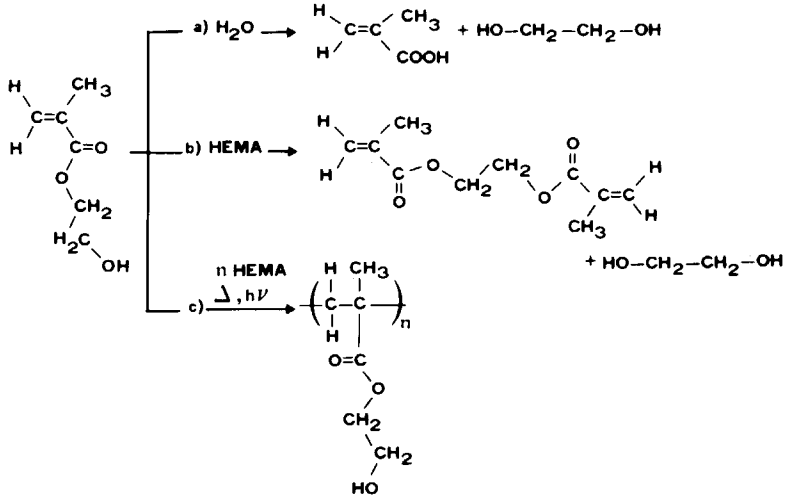

Fig. 1. Degradation of HEMA monomer: (a) hydrolysis to MAA and ethylene glycol; (b) transesterification to form EGDMA and ethylene glycol; (c) polymerization to form oligomer or polymer.

purification process used in this study is similar to the process outlined by Ratner and Miller.[11] With proper care, the levels of impurities may be reduced to insignificant amounts: less than 0.01% MAA and 0.001% EGDMA.

This paper examines the equilibrium swelling and water content of copolymers of pHEMA incorporating small quantities of methacrylic acid and crosslinker. Hydrogel samples containing different fractions of MAA and crosslinker are fabricated by adding known amounts of MAA and crosslinker to ultrapure HEMA monomer. The crosslinker used in this study is tetraethylene glycol dimethacrylate (TEGDMA), rather than ethylene glycol dimethacrylate (EGDMA), due to its better solubility in the aqueous reaction solution.[1] Since our research interests are directed towards the development of urinary tract prostheses, the swelling behavior of the hydrogen samples is monitored in seven different environments that simulate various urologocal as well as physiological conditions. These swelling baths include (1) distilled water, (2) physiological saline, (3) urea, (4) buffered pH 10 solution, (5) buffered pH 4 solution, (6) urea and saline buffered to pH 4, and (7) urea and saline buffered to pH 10.

By controlling the MAA content and the degree of crosslinker, gels may be fabricated that swell in alkali solution to 3600% their volume in acid solution and with water contents that range from 40% to 98%. In addition, gels may be fabricated that are transparent or opaque, sticky or nonsticky, flaccid or firm, and soluble or insoluble in mild alkali or urea. All of the above-named properties can be observed in gels containing less than 3 mol % of MAA.

EXPERIMENTAL METHODS AND MATERIALS

Materials. High purity HEMA monomer was obtained from Alcolac Chemicals under the trade name SIPOMER CL-100. The monomer was further purified prior to use by the procedure discussed in the next section. Methacrylic acid and TEGDMA were purchased from Polysciences, Inc. The inhibitor in MAA, hydroquinone, was removed by passing the MAA through an opaque glass column packed with DEHIBIT-100 (Polysciences). Since only minute amounts of TEGDMA are used in each copolymerization reaction, the impurities contained in the crosslinker are extremely small compared to the reactant concentration. Accordingly, TEGDMA was used as received. HPLC grade methanol and water were purchased from Burdick and Jackson. All other reagents were ACS grade, purchased from Fisher Scientific Co., and were used as received.

Purification of Monomer. The impurity of methacrylic acid (MAA) in HEMA monomer was removed by stirring the monomer with 15% by weight of anhydrous sodium carbonate for 3 h at 24°C, then vacuum filtering through two #50 Whatman filter papers. The yield on an initial volume of 200 mL of SIPOMER CL-100 was 95%.

The impurity of EGDMA was then removed by first dissolving the above-treated monomer in three times its volume of distilled water. Four extractions were performed with 50 mL of a 1/1 (volume) mixture of carbon tetrachloride and cyclohexane, allowing the layers to separate for 30 min between extractions. Usually, two layers are formed in this extraction step; however, three layers may form if the solvent capacity is exceeded due to too high a level of impurities. In this case, increasing the solvent to aqueous phase ratio may be in order. The organic layer containing EGDMA was discarded after each extraction. The

aqueous phase, 760 mL of 25% HEMA, was placed under vacuum to remove any remaining organic solvent. The HEMA was then salted out with 200 g of NaCl, then dried with anhydrous sodium sulfate, and filtered. This purification step had a yield of 93%.

The partially purified HEMA monomer was then vacuum distilled in the presence of 1.8 g of hydroquinone (added to prevent polymerization) at 50–80 μm Hg. The monomer was collected at 38–42°C with the distillation flask being heated in a water bath at 50–55°C. The collection flask was cooled in a dry ice/acetone bath. The distillation process proceeded at a rate of 75 mL/h. The first and last fractions of the distillation product were discarded. When the distillation was terminated, the pure HEMA was transferred to an opaque glass bottle and stored at 0°C until use. The yield from the distillation was approximately 80%. The overall yield was approximately 70%.

Analysis of Products. The purity of the repurified HEMA product was determined by high pressure liquid chromatography (HPLC). A Varian Model 5000 HPLC, equipped with an ultraviolet detector, a 25-cm reverse phase C-18 Ultrasphere-IP column (Altex), and a similar precolumn (Brownlee) were used. The UV detector wavelength was set to 217 nM. The column remained at ambient temperature (24–26°C). HPLC-grade methanol and water were used as the eluent at a constant ratio of 60 parts methanol to 40 parts water. The flow rate was fixed at 0.8 mL/min. All samples were diluted with pure methanol to 1/2000. 10-μL samples were injected for each analysis.

Samples of known concentration of methacrylic acid and EGDMA were injected into the HPLC, and the resultant chromatographs used to construct a standard curve of known concentration vs. area under the curve. The chromatograph showed five distinct peaks. The first peak, 2.5 min, was identified as methacrylic acid (MAA). The following peak, 3.1 min (usually split), was due to pure methanol used as the diluent for the injected samples. The next peak, 4.5 min, was the major peak due to HEMA monomer. This peak routinely had a minor shoulder which was probably due to impurities of diethylene glycol monomethacrylate. The next peak, 13.8 min, which sometimes occurred as a negative peak, was identified as an impurity in the methanol diluent. The final peak, 15.3 min, was due to ethylene glycol dimethacrylate (EGDMA).

All purified HEMA batches were quantitatively analyzed by HPLC. Only HEMA batches containing less that 0.01 mol % MAA and 0.001 mol % EGDMA were used in this study. Analysis of samples from lots of HEMA received from different vendors at different times, and kept refrigerated after receipt for intervals of 1–2 years, showed wide variation of MAA and EGDMA content. It is interesting to note that some batches contained as much as 10% MAA and 3% EGDMA, while other batches contained less than 0.01 mol % contaminants.

Polymerization of PHEMA/MAA Copolymers and Preparation of Samples. Rods of pHEMA/MAA copolymers were prepared by polymerizing the monomeric solution inside as 18.5 mm diameter polypropylene syringe. The initiator and solvent for the polymerization of the gel were similar to those described by Refojo.[12] A 10-mL polypropylene syringe was loaded with 6 mL of repurified HEMA monomer containing the desired mole fraction of MAA and TEGDMA. The mole fractions of MAA that were investigated ranged from 0% to 4% in increments of 0.5%. The TEGDMA concentration was varied between 0% and 0.3% (mol) in increments of 0.06%. All mole fractions were determined

by weighing the appropriate amounts of comonomer, usually from diluted (with HEMA) standard solutions, into the reaction syringe. Ethylene glycol (2 mL) was added to the syringe as a partial solvent. Dissolved oxygen was removed from the reaction solution by purging it with nitrogen for 15 min.

The polymerization reaction commenced upon introduction of 1.0 mL from each of two prepurged aqueous coinitiator solutions, A and B. Solution A consisted of 0.044*M* in ammonium peroxydisulfate, and B, 0.420*M* in sodium metabisulfite. The contents of the syringe was then pressurized to 650 kPa (100 psi) to prevent bubbles from forming in the polymerizing gel.[13] The reaction proceeded under pressure at room temperature for 20 h. The rather long reaction time of 20 h was used due to the acidic environment caused by the presence of MAA as a reactant. In the absence of MAA, the reaction may be completed in less than 15 min. Independent tests performed in our laboratory using a nonpolymerizable acid, such as acetic acid, at molar concentrations equivalent to MAA have demonstrated similar kinetic inhibition effects on the reaction. Our studies have shown that over the range of MAA concentrations examined, the reaction is usually complete in less than 2 h. The reaction was left under pressure overnight for 20 h to insure complete reaction.

The polymerized hydrogel rod was partially removed from the syringe by applying a positive pressure at the needle port of the syringe. The syringe was mounted on a lathe and the protruding section of the gel was cut into disks with a razor-edged knife mounted on the tool post of the lathe. The disks measured 18.5 mm in diameter and 2.0 mm in thickness or 538 mm^3 in volume. The risks were stored in distilled water.

Swelling and Shrinking Solutions. Numerous disks were cut from each rod of different MAA and crosslinker concentration. Three disks were placed in 50 mL of each of the seven baths described in Table I. The disks were heated for 20 h at 55°C, and then stored for 3 days at room temperature in their respective sealed containers to achieve equilibrium swelling. Disks that were swollen in this accelerated manner were, within experimental error, identical

TABLE I
Swelling and Neutralization Baths

Bath	pH	Aqueous bath composition
1	a	Distilled water
2	a	Saline (9 g/L NaCl)
3	a	0.15*M* urea
4	4	Buffer: 0.100*M* acetic acid 0.018*M* sodium acetate
5	10	Buffer: 0.01*M* sodium carbonate 0.01*M* sodium bicarbonate
6	4	NaCl, 9 g/L Urea, 0.15*M* Buffer: 0.100*M* acetic acid 0.018*M* sodium acetate
7	10	NaCl, 9 g/L Urea, 0.15*M* Buffer: 0.01*M* sodium carbonate 0.01*M* sodium bicarbonate

[a] In nonbuffered distilled water.

to disks that were swollen at room temperature for 30 days. Further exposure to the swelling solution caused no measurable change in volume for either set. Accordingly, both methods were judged to induce the equilibrium swollen state.

Measurements and Equations. The per cent swelling was determined for each hydrogel disk using the following equation:

$$\% \text{ swelling} = (V_s - V_0) \times 100/V_0$$

The swollen volume (V_s) was the volume of the disk at equilibrium swelling as measured with a Vernier calliper. The original volume (V_0) was the volume of the disk that was originally cut on the lathe and is equal to 538 mm^3.

The percent water content was calculated using the following equation:

$$\% \text{ water content} = (W_s - W_d) \times 100/W_s$$

The swollen weight (W_s) was determined for each disk by first blotting the disk with a paper towel to remove excess water, and then weighing the swollen disk. The dry weight (W_d) was measured after drying the sample disk in a convection oven (50°C) overnight. The volume and weights used to determine the percent swelling and percent water were the average values of the three disks used in each swelling bath.

RESULTS

The Effect of MAA on the Swelling Behavior of PHEMA. The swelling behavior of pHEMA gels with different MAA and crosslinker content was explored using disks made and swollen to equilibrium by the procedures described in the previous sections. The degree of swelling was categorized by the water content and physical measurement. The resultant graph of swelling vs. cross-

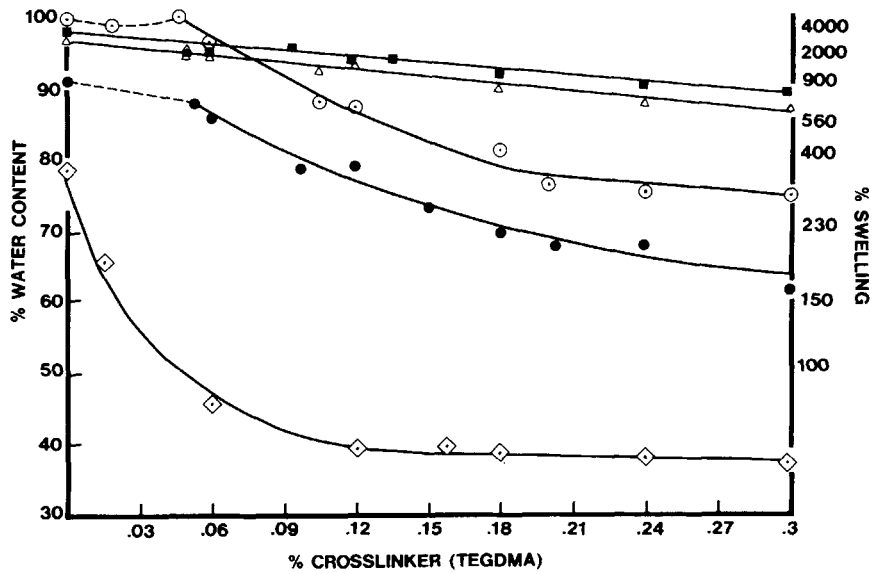

Fig. 2. Water content and swollen volume of gels having various MAA contents vs. percentage of crosslinker (TEGDMA) in the gel. The MAA mole fractions include: (◈) 0%; (●) 1%; (⊙) 2%; (△) 3%; (■) 4%. All gels were equilibrated in 0.15*M* urea.

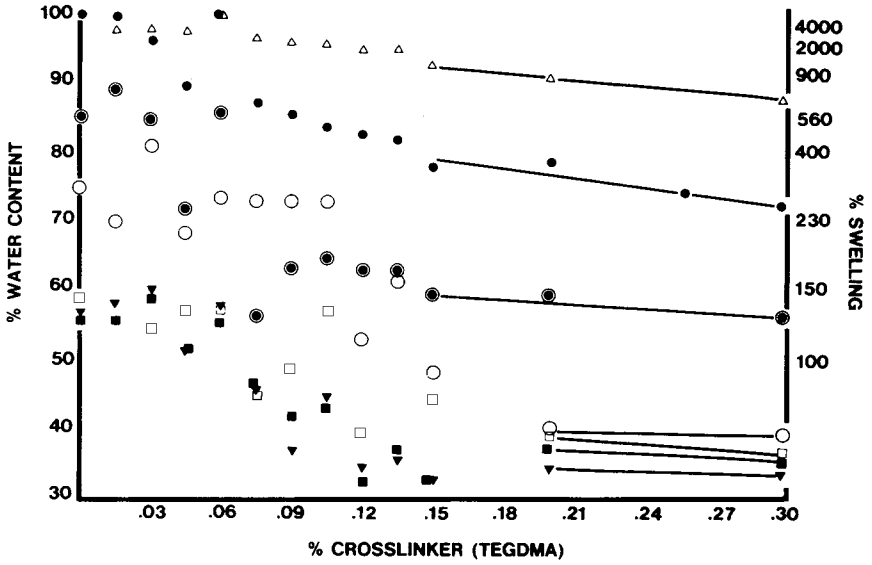

Fig. 3. Water content and swollen volumes of gels containing 2.5% MAA vs. crosslinker (TEGDMA) in different swelling solutions. The swelling solutions include: (△) urea; (●) pH 10; (⊙) urea and NaCl buffered to pH 10; (○) distilled water; (□) pH 4; (■) NaCl; (▼) urea and NaCl buffered to pH 4 (for composition of solutions see Table I).

linker (TEGDMA) at different MAA content is presented in Figure 2 for gels that were equilibrated in 0.15*M* urea. The crosslinker content range illustrated is from 0.00% to 0.30% (all percent units refer to mol %). Other tests performed at crosslinker content of 0.5% and 1.0% indicate that the water content of the gels are virtually the same as gels with 0.30% crosslinker.

As illustrated in Figure 2, without MAA (0% MAA) in the polymer lattice, the gels swelled considerably at low crosslinker concentration. At TEGDMA levels above 0.12%, the gels behaved in an orderly fashion, showing only a slight decrease in swelling with increased crosslinker. Gels containing 1% MAA behaved somewhat linearly throughout the crosslinker range investigated. Similarly, gels containing 3% and 4% MAA swelled linearly in respect to crosslinker; however, the effect of crosslinker on the water content of the gels were not so great for 3% and 4% as it was for 1% MAA.

The behavior of gels containing 2% MAA was distinctly different than the other gels investigated. Repeated tests of HEMA monomer from different purification batches show dissolution of 2% MAA disks in 0.15*M* urea solution at two different TEGDMA concentrations. These points were 0.00% and 0.05% TEGDMA crosslinker. The swelling behavior of the gels at other crosslinker concentrations in the vicinity of the 0.05% dissolution point was extremely erratic.

The Effect of Urologically or Physiologically Similar Swelling Solutions on the Water Content of PHEMA/MAA Gels. The water contents of pHEMA/MAA gels (2.5% ± 0.1% MAA) in seven different solutions vs. crosslinker (TEGDMA) content are shown in Figure 3. The solutions, whose compositions are listed in Table I, simulate aspects of urological or physiological conditions. Examination of the crosslinker dependence on the water content, for a given solution, shows a large variation in water content for low levels of crosslinking. Because the swelling points are reproducible within ±5% of the swollen volume, the large variation in swelling implies a complex and sensitive

behavior. A smooth curve was not fitted to the data points on the left side of Figure 3 due to insufficient data between the points.

There are three general aspects of swelling behavior illustrated by the data in Figure 3. The first apsect concerns the overall extent of swelling of the gel disks at crosslinker concentration greater than 0.15% TEGDMA. Hydrogel disks that were equilibrated in the swelling baths composed of urea (0.15*M*) and pH 10 swelled to a much greater extent than any of the other baths. For example, a gel at 0.2% TEGDMA was approximately 1000% larger in volume in urea solution than in distilled water. Gels that were placed in distilled water, pH 4, NaCl, and a combination of NaCl and urea buffered to pH 4 swelled to approximately 40%, which is consistent with commonly quoted literature values for the swelling of pHEMA hydrogels in water or saline.[1,14] The swelling baths containing NaCl and urea buffered to pH 10 swelled the gels intermediately.

The second aspect describes the behavior of the gel at low crosslinker content. The swelling curve of the gel is very erratic but generally starts off with higher water content, remains about the same until approximately 0.075% TEGDMA, and then decreases to an asymptotic value by 0.15%.

The third aspect involves the presence of a maximum near the TEGDMA concentration of 0.06%. Both pH 10 and urea actually dissolve such polymer compositions. Gels swollen in the bath containing urea and NaCl buffered to pH 10 do not dissolve; however, they do swell about 500% with water contents of 81% at this point. The other swelling solvents do not demonstrate any unusual behavior at this unique concentration point.

Physical Observations of HEMA/MAA Gels in Different Solvents. When the hydrogel copolymer disks of pHEMA/MAA were first placed in the swelling bath described in Table I, they were totally transparent. After a few minutes, the gels became cloudy and then eventually opaque. After further time, which varied from minutes to days, depending upon the fraction of MAA and crosslinker in the gel, some of the gels regained their transparency and at the same time, began to deform and swell dramatically. The time required for the hydrogel copolymers to reach their apparent swollen equilibrium state was much less than the time allotted for equilibrium swelling. Once swelling equilibrium of the gel was achieved, the physical appearance of the gel was often markedly different from the original clear disk. For example, the clarity of the gel may have changed, the gel may have become sticky and fused to other gels in its vicinity, or the physical integrity of the polymeric structure may have been severely affected. Some of the more drastic changes in physical properties that occur repeatedly at specific chemical compositions or within certain chemical ranges are described below for gels containing 2.5% (±0.1%) MAA.

At equilibrium, all gels that were swollen in urea and pH 10 were clear and nonsticky throughtout the range investigated (0.00–1.0 mol % TEGDMA). At crosslinker ranges less than 0.15%, the gel disks had so little integrity that they could not be lifted by an edge, with a forcep, without damage.

Gels that swelled to a lesser extent such as those swollen in water, NaCl, pH 4, and the combination of NaCl and urea buffered to pH 4, remained opaque (white) at crosslinker concentrations less than 0.15%. These gels were easily handled with no apparent damage. At TEGDMA concentrations greater than 0.15%, the gels became totally transparent.

Stickiness of the gel was observed only at low degree of crosslinking (less than

0.02%) in the swelling baths consisting of distilled water, NaCl, and pH 4 buffer. These hydrogel disks fused to each other in their swelling baths and could not be separated from each other without tearing the disks.

The gels in the bath containing NaCl and urea buffered to pH 10 behaved somewhat differently than those equilibrated in the other swelling media. These gels were sticky below 0.015% crosslinker, were opaque until 0.075%, and had little physical integrity below 0.015% and at the crosslinker point of 0.065% ± 0.005% TEGDMA. At the points between 0.015% and 0.06%, and at TEGDMA concentration greater than 0.07%, the gels were much firmer and could be easily handled.

The swelling behavior of the pHEMA/MAA hydrogel disks was found to be reversible. A gel that was swollen at pH 10 or in urea, would shrink, or collapse, when placed in baths containing NaCl or pH 4 or water. Similarly, gels that collapsed at pH 4, etc., would swell to larger volumes when subsequently equilibrated in urea or pH 10 solution. The repetition of this shrink–swell cyclic behavior was not investigated for more than several cycles, however; the cycling should only be limited by chemical degradation of the polymer.

It was also observed that the extent of swelling could differ depending upon the quantity of ionic species or urea in the swelling baths. Baths buffered to pH 10 with a high ionic strength would result in reduced swelling. Similarly, baths containing large concentrations of urea also caused decreased overall swelling of the gel. The decrease in swelling of the gel at high levels of urea is well documented in the literature.[11,12]

DISCUSSION

The presence of methacrylic acid (MAA) as an impurity in gels fabricated from commercial HEMA is sufficient to cause the gel to distort by swelling or shrinking, depending upon the present stage of the gel and the chemical environment in which it is placed. The effect of MAA contamination is most apparent at low degrees of crosslinker. The phenomenon of polymer deformation by swelling or shrinking, or the more dramatic volume change, termed polymer collapse, is not new. The physical chemistry of such polymer transitions has been studied intensively.[15,16] In a recent article, Tanaka[16] models the swelling and collapse phenomenon of gels as a critical-point event involving three opposing forces, namely, rubberlike elasticity, polymer–polymer/solvent affinity and electrostatic interactions. The sum of these three forces sets the osmotic pressure of the gel, which determines whether the gel expands or collapses when placed in a different environment.

The rubberlike elasticity is reflected in the resilience of the polymer strand toward deformation. The degree of crosslinking sets the effective free length of polymer segments that exhibit rubberlike elasticity. As illustrated in Figures 2 and 3, the overall swelling of the gel disks increases with decreasing crosslinker content, thus showing the importance of the effective free length of polymer segments. In environments that favor swelling, the extent of swelling is limited by the rubberlike elasticity. When the gel is compressed, the rubber elasticity tends to expand it to a position at equilibrium with the other forces acting upon it.

The polymer–polymer affinity can be traced to an interaction between the

polymer strands, while the polymer–solvent affinity is that of the polymer strands with the solvent. Such interactions can be either repulsive or attractive, depending mainly upon the electrical properties of the molecule. Where the interaction is attractive, the polymer can reduce its total energy by surrounding its individual chains with solvent molecules; where the interaction is repulsive, the solvent is excluded, i.e., sections of the polymer chains prefer to lay next to one another. The points of polymer dissolution shown in Figures 2 and 3 may be explained by these forces and are discussed below.

Tanaka quantifies the effects of electrostatic interactions due to ionization of the polymer network by the concept of "hydrogen ion pressure." In his model, effects due to negatively charged species in the polymer lattice are reflected by the behavior of a hydrogen ion gas. The thermodynamic activity of the ion gas represents the activity of ionized species on the polymer. However, the relationship between the ion gas and pH of the ambient solution is not a simple proportionality, but rather a more complex association involving shielding and coupling effects. Key facts explained by his model are that increased ionization or temperature tend to expand the gel network.

Rearrangement of the polymer network when the gels are immersed in different solvents is coupled to the three forces described above. The polymer strands reorient themselves to compensate for the change in solvent. Reorientation involves new spatial distribution of the "monomeric links" and, in general, a different state of stress (rubber elasticity) and electrostatic interaction. The subsequent change in clarity observed when reorientation of the gel begins is presumably due to the relative changes in droplet size accociated with the inbibed solvent. Droplet sizes exceeding the wavelength of light (about 1 μm) cause scattering, rendering the gel opaque. Over a period of time, the solvent redistributes to regions smaller than the wavelength of light eliminating scattering and producing a transparent material.

In alkali solutions the MAA incorporated in the gel lattice is fully ionized. The repulsive forces of the ions tend to swell the gel to the large dimensions recorded in Figure 2. In acidic solutions, the acid comonomer groups are not dissociated. The large ion-pressure is not present and the gel is collapsed to an equilibrium state governed by the rubberlike elasticity and the polymer–polymer/solvent affinity of the gel. In a similar manner, significant amounts of dissolved salt, such as sodium chloride, results in collapsed gels.

The interaction of urea with the polymer network has puzzled researchers for many years.[11,12] Our findings have shown that it is the decomposition of urea to ammonium ion, cyanate ion, and carbon dioxide and the subsequent rise in pH that causes the gel to swell in urea solution.[17] The reason the water contents of gels equilibrated in pH 10 solution are lower than the same gels equilibrated in 0.15M urea, as reported in Figure 3, is due to the comparatively small electrolyte content associated with the urea solution. Urea acts as a replenishable reservoir of ammonium ion that eventually buffers the solution to pH 9.2. Increased electrolytes, such as the sodium ions, prevalent in the carbonate buffer system, tend to shield the resultant ions that form in the gel lattice and limit the extent of swelling of the gel.[16] Other tests performed in our laboratory with increased buffering indices confirm the fact that the gels tends to shrink in higher electrolyte environments.

A gel that is swollen in alkali solution has an extended or porous lattice. The

spaces between the neighboring polymer strands are sufficiently large such that the attractive forces holding the lattice together, such as Van derWaal's or hydrogen bonding forces, are severely reduced. The reduction in attractive forces and reduced polymer overlap decreases the tensile strength of the swollen gel tremendously. At high water content the gels are flaccid and easily fractured; at low water content the gels remain firm with much superior mechanical properties.

In the swelling environments examined here, the balance among the three forces composing the osmotic pressure of the gel is very delicate at certain fractions of MAA and crosslinker. An increase in MAA concentration in the gel not only provides ionization sites that can increase the ion pressure within the gel, but it also changes the nature of the polymeric strand, which changes the polymer–polymer/solvent affinity. The change in primary properties of the monomer system, by introducing both MAA and crosslinker, affects both secondary and tertiary properties of the resultant gel. For small changes of gel composition, the affinity of the polymer backbone for a certain solvent or for itself need not be the same, and the gel may not orient the same way. The combination of physiochemical events described above may account for the unusual behavior of the 2.0% MAA curve in Figure 2.

When a level of crosslinker is selected, a working region of rubber elasticity is effectively set. Large changes such as the 2% MAA dissolution, at finite crosslinker, are then controlled in the main by polymer–polymer/solvent affinity and ionic pressure. Polymer–polymer affinity and polymer–solvent affinity may be manipulated separately from ionization by addition of another comonomer. Polymers designed from two or more monomers could be optimized to exhibit critical-point phenomenon, where the gel exhibits discontinuous, large changes of dimension associated with small perturbations of environment. The wide range of ways to cause excursions through the critical point include variation of temperature, pH, electrolytes, solvents, and even electrical fields.[18]

CONCLUSION

The most dramatic effects on the swelling behavior and water content of hydrogel copolymers of pHEMA/MAA occur when the mol % of MAA in the gel is between 1% and 3% and the crosslinker content is less than 0.3%. The incorporation of ionizable groups in the polymer lattice causes the gel to swell differently than pure pHEMA structures in the same environment. The gel will remain collapsed in saline or acid solutions and swell extensively in alkali environments. At certain specific mole fractions of MAA and crosslinker and in certain favorable environments, the gel may exhibit dramatically different equilibrium volumes and may even go into solution.

The concentration of MAA impurities in unpurified commercially available HEMA monomer can be sufficiently high as to fall into the range of dramatic swelling behavior described above, and seriously affect the nature of the gel. This problem may be avoided by purifying the monomer to remove the MAA and crosslinker, and then adding the crosslinker back into the reaction bath at levels above the critical value of 0.3%. Unless proper quality control is applied to the monomer before polymerization, the physiochemical properties of the gel may be unpredictable, and, if implanted, the biocompatibility or the reproducibility

of the gel are jeopardized. On the other hand, with adequate understanding of the chemistry and physiochemical events of the gel and its environment, it is possible to design highly responsive gels for use as biomaterials. Such gels will exhibit reversible motions due to perturbations in the local environment. Further, such gels need not be bulk gels; grafted surfaces may show similar events. Biomaterials of this nature may prove to be very useful in areas of dynamic chemical environment, for example, as materials for use in the urinary tract.

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