
Synthesis of superporous hydrogels: Hydrogels with fast swelling and superabsorbent properties

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Abstract: We have been interested in the synthesis of hydrogels with fast swelling kinetics and superabsorbent properties. To increase the water absorption rate, interconnected pores were introduced to the hydrogels. Since the pore size in the dried hydrogels is in the order of hundreds of micrometers, these hydrogels are called "superporous" hydrogels. Superporous hydrogels were synthesized by crosslinking polymerization of various vinyl monomers in the presence of gas bubbles formed by the chemical reaction of acid and NaHCO_3 . The polymerization process was optimized to capture the gas bubbles inside the synthesized hydrogels. The use of the NaHCO_3 /acid system allowed easy control of timing for gelation and foam formation. We found that PF127 was the best foam stabilizer for most of the monomer systems used in our study. Scanning electron microscope (SEM) pictures showed interconnected pores forming capillary channels. The capillary channels, which were critical for fast swelling, were preserved during drying by dehydrating

water-swollen hydrogels with ethanol before drying. The ethanol-dehydrated superporous hydrogels reached equilibrium swelling within minutes. The equilibrium swelling time could be reduced to less than a minute with the use of a wetting agent. In our study, water moisture was used as a wetting agent since the amount of moisture content in the dried hydrogels easily could be controlled. Preparation of superporous hydrogels using the right blowing system, foam stabilizer, drying method, and wetting agent makes it possible to reduce the swelling time to less than a minute regardless of the size of the dried gels. The superporous hydrogels can be used where fast swelling and superabsorbent properties are critical. © 1999 John Wiley & Sons, Inc. *J Biomed Mater Res*, 44, 53–62, 1999.

Key words: superporous hydrogels; swelling kinetics; superabsorbent; wetting; capillary action; hydrogel; foam

INTRODUCTION

A hydrogel is a crosslinked network of a hydrophilic polymer that is insoluble in water. In the presence of abundant water, a hydrogel absorbs water to swell to a size much larger than its original size. A variety of hydrogels have been used in many applications, but their application in the controlled drug delivery area has been most prominent.^{1,2} Drug molecules loaded in a dried hydrogel (i.e., xerogel) are slowly released due to the slow diffusion of water through the glassy matrix of the dried hydrogel. While slow swelling of dried hydrogels has been a useful property for many applications, there are situations where much faster swelling is desirable. We have been

studying the gastric retention property of hydrogels for long-term oral drug delivery. In our previous studies using poly(vinylpyrrolidone) (PVP) hydrogels, we showed that the fully swollen PVP hydrogels were retained in the canine stomach for more than 24 h and up to 60 h.^{3,4} When dried PVP hydrogels were administered, they were emptied from the stomach in less than an hour or so. On the other hand, if the PVP hydrogels were swollen for a few hours before administration, they were retained in the stomach for more than a day even under fasting conditions. Our studies have indicated that dried hydrogel dosage forms have to swell before the arrival of the next interdigestive migrating myoelectric complex (IMMC). Since the timing of the IMMC could not be predicted or controlled, it was necessary to develop hydrogel dosage forms that swelled as fast as possible. To be practical, the swelling had to be completed in less than 30 min, most preferably in less than 5 min.⁵ Thus, our recent efforts have been focused on the synthesis of hydrogels that swell to equilibrium sizes in less than a few minutes regardless of size.

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Since the slow swelling of dried hydrogels is due to the slow diffusion of water into the glassy matrix of the dried hydrogels, we explored the absorption of water into the dried hydrogels by capillary wetting. To make the dried hydrogels with effective capillary action, pores had to be introduced into a hydrogel and the pores had to be connected to provide capillary channels; that is, open channels had to be formed. When a dried hydrogel with the open channel structure is placed in an aqueous solution, water flows through the open channels by capillary effect, instead of diffusion of water through the glassy layer, and this allows extremely fast swelling of the hydrogels. Porous hydrogels can be prepared by a variety of methods, such as the porosigen technique, phase separation technique, crosslinking of individual hydrogel particles, and gas blowing (or foaming) technique. In the porosigen technique, porous hydrogels are made by preparing hydrogels in the presence of dispersed water-soluble porosigens, such as micronized sucrose,⁶ sodium chloride,⁷ and PEG,⁸ which can be removed later by washing with water to leave a meshwork.^{6,9} Water itself can be used as a porosigen if a polymer network is formed in the frozen state.^{6,10} The pore size of hydrogels prepared by the porosigen technique depends on the size of the porosigens. The phase separation technique is based on a decrease in solvent quality for polymers.^{11–17} The major limitation of the phase separation method is that only very limited types of porous hydrogels (such as HEMA and NIPAM) can be prepared, and there is not much control over the porosity of the macroporous hydrogels. Porous hydrogels also can be prepared by crosslinking individual hydrogel particles to form crosslinked aggregates of particles.^{18–21} Pores in such structures are present between hydrogel particles, and the size of pores is much smaller than the size of the particles. This approach is limited to the absorbent particles that have chemically active functional groups on the surface.

In this study, we synthesized porous hydrogels with open channels using the gas blowing (or foaming) technique.^{22–24} The capillary radius in our porous hydrogels are in the range of a few hundreds micrometers. Since this pore size is well beyond the pore sizes described by “microporous” (10–100 nm range) and “macroporous” (100 nm–10 μ m range) hydrogels,^{6,12} we call our hydrogels “superporous” hydrogels. Superporous hydrogels prepared by the gas blowing technique also were called “hydrogel foams” due to the foaming process used in the preparation.^{22,23} This paper describes the synthesis and characterization of superporous hydrogels, drying conditions for maintaining open cell structures, and the improving of swelling kinetics even further using a wetting agent.

MATERIALS AND METHODS

Materials

Acrylic acid (AA), acrylamide (AM), N-isopropyl acrylamide (NIPAM), vinylpyrrolidone (VP), hydroxyethyl methacrylate (HEMA), potassium salt of 3-sulfopropyl acrylate (SPAK), 2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS), (2-(acryloyloxy)ethyl) trimethylammonium methyl sulfate (ATMS), N,N'-methylenebisacrylamide (Bis), ammonium persulfate (APS), and dimethyl sulfoxide (DMSO) were from Aldrich Chemical Company, Inc. (Milwaukee, Wisconsin). Hydroxypropyl methacrylate (HPMA) was from Eastman Kodak Chemical Co. (Rochester, New York). N,N,N',N'-tetramethylethylenediamine (TEMED) was from Bio-Rad Laboratories (Richmond, California). V545 (an azoinitiator) was from Wako Chemicals USA, Inc. (Richmond, Virginia). NaHCO₃ was from Mallinckrodt Specialty Chemical Co. (Paris, Kentucky). Pluronic® F127 (PF127) and Pluronic® P-105 (PP105) were from BASF Corporation (Parsippany, New Jersey). Silwet® L7605 (SL7605) was from OSi Specialties Inc. (Danbury, Connecticut). Voranol_{240–280}® (the subscript numbers are related to the hydroxyl number of a polyol and the molecular weight) was obtained from Dow Chemical Company (Midland, Mississippi).

Synthesis of superporous hydrogels

Superporous hydrogels were synthesized using various vinyl monomers. Table I shows exemplary formulas used in our study. Other variations of the formulas are, of course, possible. Control hydrogels were synthesized following the same formulas used for the synthesis of superporous hydrogels except for the addition of NaHCO₃, acid, and foam stabilizers.

In general, to make a superporous hydrogel, a monomer, crosslinker, water (if necessary), foam stabilizer, acid, polymerization initiator, initiation catalyst (if any), and foaming agent were added sequentially to a test tube (20 mm outer diameter \times 150 mm in length). The test tube was shaken to mix the solution after each ingredient was added. The pH of the monomer solution was adjusted to 5 using acrylic acid (AA) or hydrochloric acid (HCl). For monomers with low pH (such as AA and AMPS), the monomer solution was titrated with NaOH to raise the pH to 5–6. Sodium bicarbonate suspension was added to the monomer solution and mechanically stirred using a spatula for several seconds to evenly distribute the generating gas bubbles. Addition of sodium bicarbonate, which was used as the foaming ingredient, increased the pH of the solution to accelerate the polymerization. The volume of the final superporous hydrogel in the test tube usually expanded to 2–10 times the original solution volume. Synthesized superporous hydrogels were removed from the tube and allowed to swell in water before drying (see “Drying of superporous hydrogels” below). The swelling in water removed most of the water-soluble com-

TABLE I
Exemplary Formulas Used in the Synthesis of Superporous Hydrogels

| Monomer Type | Monomer | Crosslinker (Bis) | Water | Foam Stabilizer | Acid | Initiator | Initiation Catalyst | Foaming Agent (NaHCO ₃) |
|-------------------|---|---------------------------------|-------------|--|------------------------|---------------------------|---------------------------|-------------------------------------|
| AM | 1,000 μ L (50% AM) | 200 μ L (2.5%) | 460 μ L | 100 μ L (10% PF127) | 45 μ L (AA) | 40 μ L (20% APS) | 40 μ L (20% TEMED) | 90 mg |
| AMPS (Na salt) | 1,000 μ L (30% AMPS) | 40 μ L (2.5%) | | 50 μ L (10% PF127) | 25 μ L (AA) | 20 μ L (20% APS) | 20 μ L (20% TEMED) | 90 mg |
| AA | 500 μ L | 200 μ L (2.5%) | 500 μ L | 100 μ L (10% PF127) | | 100 μ L (10% V545) | | 15 mg |
| AA (Na salt) | 1,000 μ L (pH ~6) | 200 μ L (2.5%) | 460 μ L | 100 μ L (10% PF127) | 25 μ L (AA) | 40 μ L (20% APS) | 40 μ L (20% TEMED) | 90 mg |
| ATMS | 1,000 μ L (30% ATMS) | 40 μ L (2.5%) | | 50 μ L (10% PF127) | 30 μ L (AA) | 20 μ L (20% APS) | 20 μ L (20% TEMED) | 90 mg |
| HEMA | 700 μ L | 100 μ L (2.5%) | | 100 μ L (10% PF127) | | 50 μ L (20% APS) | 50 μ L (20% TEMED) | 80 mg |
| HPMA | 500 μ L (in isopropanol) | 200 μ L (10% in DMSO) | | 90 μ L (10% SL 7605 in DMSO) + 30 μ L (5% PP105 in DMSO) | | 180 μ L (10% APS) | 90 μ L (10% TEMED) | 30 mg |
| SPAK | 1,000 μ L (30% SPAK) | 40 μ L (2.5%) | | 50 μ L (10% PF127) | 30 μ L (AA) | 20 μ L (20% APS) | 20 μ L (20% TEMED) | 90 mg |
| VP | 500 μ L | 200 μ L (2.5%) | 100 μ L | 50 μ L (10% PF127) | 20 μ L (AA) | 50 μ L (10% V545) | | 20 mg |
| AM + SPAK | 440 μ L (50% AM) + 300 μ L (50% SPAK) | 250 μ L (2.5%) | | 50 μ L (10% PF127) | 10 μ L (AA) | 30 μ L (20% APS) | 20 μ L (20% TEMED) | 100 mg |
| AM + AA | 300 μ L (50% AM) + 200 μ L (50% AA) | 100 μ L (2.5%) | 330 μ L | 30 μ L (10% PF127) | | 20 μ L (20% APS) | 20 μ L (20% TEMED) | 120 mg |
| NIPAM + AM | 1,000 μ L (25% NIPAM) + 200 μ L (20% AM) | 400 μ L (2.5%) | | 100 μ L (10% PF127) + 30 μ L (10% SL7605 in DMSO) | 50 μ L (6N HCl) | 50 μ L (20% APS) | 50 μ L (20% TEMED) | 60 mg |

ponents, including the foam stabilizer, remaining in the superporous hydrogels.

Foam stabilizers

Since stability of the produced foam was essential for the synthesis of homogeneous superporous hydrogels, we examined the foam stabilizing effects of various surfactants, including albumin, gelatin, Pluronic[®] [poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) tri-block copolymers], Silwet[®] [polyalkyleneoxide-modified poly(dimethyl siloxane) surfactants], sodium dodecyl sulfate, Span[®], Triton[®], and Tween[®]. Our preliminary study showed that Pluronic F127 (PF127) had the best foam stabilizing property for most of the hydrophilic monomers; that is, it sustained the foam for the longest period of time. For relatively hydrophobic monomers, such as NIPAM and HPMA, PF127 alone did not provide enough foam stabilizing effect. However, the proper combination of PF127, Pluronic P105 (PF105), and Silwet L7605 provided a satisfactory foam stabilization effect. For this reason, in this study we used only the three foam stabilizers, as shown in

Table I. The surfactant concentration at about 0.5–1.0% of the total solution was found to be adequate.

Drying of superporous hydrogels

Superporous hydrogels were dried under two different conditions. Under Condition I, swollen superporous hydrogels were dried for a day under blowing warm air ($60 \pm 1^\circ\text{C}$) in a food dehydrator (Model FD5, Mr. Coffee, Inc., Bedford Heights, Ohio). Under Condition II, swollen superporous hydrogels were dehydrated first by applying about 5–10 mL of absolute ethanol per each gel. After this initial dehydration step, superporous hydrogels were dehydrated further by placing them in 50 mL of absolute ethanol several times to ensure replacement of all the water by ethanol. During the dehydration process, the soft and flexible superporous hydrogels became hard and brittle. After the dehydration was completed, the excess ethanol in dehydrated superporous hydrogels was removed by draining using paper towel. Then the superporous hydrogels were dried in a 55°C oven for a day.

Wetting agents for superporous hydrogels

To examine the effect of a wetting agent on the swelling kinetics, Voranol® and water (i.e., moisture) were used as wetting agents. Voranol® (1%) was added to ethanol for dehydration of superporous hydrogels during drying under Condition II. To control the amount of water absorbed into the superporous hydrogels dried under Condition II, a simple moistening chamber was built, as shown in Figure 1. A dried superporous hydrogel was placed on a support in a container with a screw cap. A small amount of water was present at the bottom of the container. Constant humidity was maintained with an aqueous solution saturated with appropriate salt. The dried superporous hydrogels were placed on top of the gel support. Hydrogels were removed after 3 days and their weights measured. The salts used for desired humidity were CH_3COOK for 20%, $\text{K}_2\text{CO}_3 \cdot 2\text{H}_2\text{O}$ for 43%, $\text{NaBr} \cdot 2\text{H}_2\text{O}$ for 58%, $\text{NH}_4\text{Cl} + \text{KNO}_3$ for 71.1%, NH_4Cl for 79.3%, $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$ for 88%, and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ for 98% humidity.²⁵

Swelling studies

The dry samples were allowed to hydrate in excess distilled, deionized water (DDW) at room temperature. The weights of the hydrating samples were measured at timed intervals, following removal of excess water by gentle blotting. Some superporous hydrogels swelled to the extent that they became too fragile to handle. Those were placed on a sieve weighing boat. The sieve weighing boat containing the superporous hydrogel was immersed in water for swelling. The weighing boat was taken out to drain the free water from the sieve and a paper towel was used to remove excess water from underneath the sieve. Then the weight of the swollen superporous hydrogels was measured by subtracting the boat weight from the total weight. This method avoided the direct handling of the fragile superporous hydrogels. The swelling ratio (Q) is defined as:

$$Q = (W_s - W_d)/W_d$$

where W_s is the weight of the swollen superporous hydrogel and W_d is the weight of the dried superporous hydrogel.

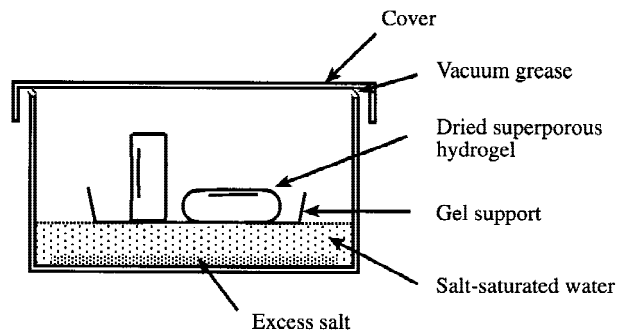


Figure 1. A device used to moisten a dried superporous hydrogel.

Density and morphology of superporous hydrogels

Densities of the dried superporous hydrogels were determined from direct mass and dimensional measurements. The density (d) of a dried superporous hydrogel was calculated by dividing the weight of a dried superporous hydrogel (W_d) with the volume of the dried superporous hydrogel (V_d). The volume (V_d) was calculated by direct measurements of dimensions using a caliper or by a solvent-displacing method. Briefly, with the use of tweezers, a dried superporous hydrogel was submerged underneath the surface of hexane in a graduated cylinder and then quickly was removed from the hexane. The volume change read from the graduated cylinder before and after the removal was the volume of the dried superporous hydrogel. Hexane was used because it is very hydrophobic and superporous hydrogels do not absorb it.

The morphology of porous structures was examined with a scanning electron microscope (SEM). Dried superporous hydrogels were cut to expose their inner structure, coated with a thin layer of palladium gold alloy in a Hummer I Sputter Coater, and imaged in a SEM (JSM-840, JEOL). The pore size was determined from the SEM pictures.

The radius of the pores in a dried superporous hydrogel was calculated from the capillary rise of liquid through open channels. The height of the capillary rise in open channels can be calculated by the Young–Laplace equation:

$$h = (2 \gamma \cos\theta)/(r \rho g)$$

where h is the height in cm, γ is the surface tension of liquid, θ is the contact angle, r is the radius of the capillary tube, ρ is the density of liquid, and g is the acceleration of gravity (981 cm/s^2). We used a 72% ethanol–water mixture since superporous hydrogels do not swell in that solution. The surface tension and density of the 72% ethanol is 26.28 g/s^2 and 0.79 g/cm^3 . A dried cylindrical hydrogel (10 mm in diameter \times 30 mm in length) was placed perpendicularly to the bottom of a petri dish containing 72% ethanol–water solution. The solution contained 0.01% coomassie blue so that the rise in liquid level easily could be visualized and measured. The contact angle of the 72% ethanol–water mixture on dried hydrogels was measured using a goniometer. Due to the fast absorption of the solution into the dried hydrogel, immediately after placing a drop on the surface the contact angle was measured.

RESULTS

Selection of monomers, crosslinker, and initiators

In this study, superporous hydrogels were prepared by crosslinking polymerization of monomers in the presence of gas bubbles. Carbon dioxide gas bubbles were generated by reaction of sodium bicarbonate with acid. The foam size was determined by the amount of released gas bubbles, which, in turn, was determined by the amount of acid and NaHCO_3 . We used excess amounts of NaHCO_3 so that the foam size

was controlled by the amount of the added acid, which was either AA or HCl. To make superporous hydrogels with homogeneously distributed gas bubbles, polymerization and foaming processes had to occur simultaneously. Thus, control of timing of the two processes was critical. Since stabilizing a foam longer than a few minutes was difficult, the gelling had to start within a few minutes after the beginning of foaming (e.g., after addition of NaHCO_3 to the monomer mixture). The fast gelling could be achieved by a careful choice of monomers (type and concentration), initiators (type and concentration), temperature, and solvent. Examples of how superporous hydrogels of various monomers were made are shown in Table I.

Typically, AM, sodium salt of AMPS, sodium salt of AA, ATMS, NIPAM, SPAK, and their copolymers gelled quite fast in aqueous solution when the APS/TEMED pair was used as the initiator. The monomer concentrations used in our study were higher than 10% to ensure fast gelling. Some monomers (such as HEMA, HPMA, and VP) polymerized too slowly without increasing the temperature to 60°C (for HEMA) or 80°C (HPMA and VP). The APS/TEMED redox-initiator pair was effective for polymerization of most of the monomers listed in Table I. They initiated the gelling process within 1–2 min when used at a concentration of about 1–2% (w/w) of the monomer. APS/TEMED was not suitable for gelling of VP monomer due to the reaction of persulfate with VP monomer. In the synthesis of poly(*N*-vinylpyrrolidinone) (PVP) superporous hydrogels, an azo-initiator, V545, was chosen since it could initiate the gelling of VP monomer in less than a minute at 60°C and above. APS/TEMED also failed to initiate the polymerization of AA (in acid form) because the initiation mechanism was inhibited under acidic conditions. Unlike the redox APS/TEMED pair, the radical generation of V545 is based on thermo-decomposition. Thus, it was used successfully in the synthesis of superporous hydrogel from AA.

Once we synthesized superporous hydrogels from various vinyl monomers, as shown in Table I, we examined the effects of the amount of NaHCO_3 , dehydration method, wetting agent, and moistening on the swelling kinetics. For these studies, we used mainly superporous hydrogels made of poly(acrylamide-co-acrylic acid [P(AM-co-AA)]).

Polymerization and foaming processes

For making homogeneous superporous hydrogels, the timing of foam formation and polymerization processes was very important. Figure 2 shows the two processes involved in the superporous hydrogel preparation. When the APS/TEMED pair was used as

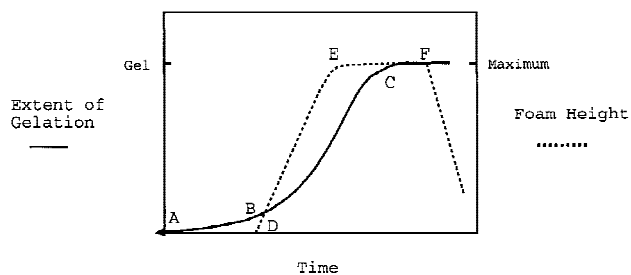


Figure 2. Relative kinetics of gel formation by crosslinking polymerization and the foam formation. The solid line A-B-C represents the polymerization process while the dashed line D-E-F represents the foaming process.

an initiator, the polymerization rate was pH dependent. The optimal pH for the initiator was around 7–8. Under this pH, the polymerization proceeded rapidly after the addition of initiators, and the gelling usually started within 1–2 min. If the foaming started too early or the polymerization proceeded too slowly, the foam rose and subsided before the onset of gelling. The result was a poorly porous or sometimes nonporous hydrogel. If the foaming started too late, the solution became too viscous for the even distribution of gas bubbles. This resulted in a porous but nonhomogeneous hydrogel. To make a homogeneous superporous hydrogel, the timing for the addition of the foaming agent and the onset of gelling had to be controlled carefully. The NaHCO_3 /acid system used in our study provided a special trigger system that made controlling the timing rather easy.

In the beginning of polymerization (Point A in Fig. 2), all the ingredients except NaHCO_3 were mixed. The presence of acid reduced the pH to an acidic level (pH 5–6). Thus the TEMED-catalyzed free radical generation from APS was inhibited because TEMED was protonated under this pH. This resulted in a very slow polymerization (A → B). At point D, NaHCO_3 was added to the monomer solution, and it reacted with acid to start the foaming process (D → E). In the meantime, the pH of the solution increased to 7–8 because an excess amount of NaHCO_3 had been used. At this pH, TEMED (in its free-base form) could catalyze the free radical generation from APS and start the accelerated polymerization.²⁶ Consequently, the polymerization proceeded rapidly (B → C) and the solution gelled at point C. This resulted in the inclusion of gas bubbles and gas channels in the polymer matrix. Here, NaHCO_3 acted as a trigger for polymerization so that the foaming and polymerization could proceed in parallel. Therefore no special timing control was necessary. The foam stayed at its maximum height (E → F) in the presence of a suitable foam stabilizer. After point F the foam would subside if gelling did not occur. Acrylate monomers polymerized relatively fast (within a few minutes after addition of NaHCO_3) with the APS/TEMED redox pair so that the foam re-

mained stabilized until the gelling started. We used an excess amount of NaHCO_3 to make the trigger system work because it ensured the final pH above neutral. The foam volume was controlled by the amount of acid in the monomer solution.

Pore size of superporous hydrogels

Structures of conventional and superporous hydrogels were examined under SEM. Figure 3(A) shows the inside of an air-dried conventional P(AM-co-AA) hydrogel that was fractured after it was cooled in liquid nitrogen. Figure 3(B,C) shows the inner surfaces of superporous P(AM-co-AA) hydrogels at different magnifications. After synthesis, superporous hydrogels were washed in water, dehydrated with ethanol, and then air dried in a 60°C oven, as described above. The average diameter of the pores in Figure 3(B) is

approximately $150\ \mu\text{m}$, and some pores are as large as $300\ \mu\text{m}$. As clearly shown in Figure 3(B,C), the pores are connected to each other to form extensive capillary channels, which help the dried gels swell to near equilibrium size in a matter of minutes. Conventional and superporous hydrogels made of other monomers also showed similar images. For all the monomers tested, conventional hydrogels showed no pores while superporous hydrogels showed interconnected pores with sizes in the order of a few hundred micrometers. The porosity increased as the amount of NaHCO_3 , acid, and foam stabilizer increased.

The largest pore size of superporous hydrogels was calculated from the Young–Laplace equation. Since the extent of capillary rise is expected to be determined by the largest pores in superporous hydrogels, the height of capillary rise was used to estimate the largest radius of the capillary channels. The contact angle of the dried conventional [P(AM-co-AA) hydrogel was $15 \pm 2^\circ$, and the height of the capillary rise in the superporous hydrogel was $3.8 \pm 0.5\ \text{cm}$. Thus the effective capillary radius (r) in the superporous hydrogel is:

$$\begin{aligned} r &= (2 \gamma \cos\theta) / (h \rho g) \\ &= \{2 (26.28\ \text{g}/\text{sec}^2) \cos 15\} / \{(3.8\ \text{cm}) (0.79\ \text{g}/\text{cm}^3) \\ &\quad (981\ \text{cm}/\text{sec}^2)\} \\ &\approx 170\ \mu\text{m} \end{aligned}$$

Thus, the largest diameter of the capillary channels in superporous hydrogel is estimated to be approximately $340\ \mu\text{m}$. As shown in Figure 3(B), the largest pore size observed by SEM was close to this value.

Swelling kinetics and extent

For the study of kinetics and extent of gel swelling, superporous P(AM-co-AA) hydrogels were synthesized under various conditions. As mentioned in the experimental section, our preliminary study showed that PF127 is the best foam stabilizer at the concentration of 0.05% or higher. We used 0.3% PF127 for making superporous P(AM-co-AA) hydrogels for the swelling studies. Figure 4 shows the swelling kinetics of P(AM-co-AA) hydrogels synthesized using different amounts of NaHCO_3 . A conventional hydrogel made in the absence of added NaHCO_3 did not swell to a measurable extent during the 30 min time period. When only 10 mg of NaHCO_3 was added to the monomer mixture, no open channels were formed, and thus the swelling of the dried hydrogels was similar to that of the control. As the amount of NaHCO_3 increased to 20 mg, the swelling of the dried hydrogels was faster than the control, but it still took more than 25 min to swell. When the amount of NaHCO_3 was 50 mg and above, superporous hydrogels swelled to their equilibrium sizes in less than 10 min. This was due to the

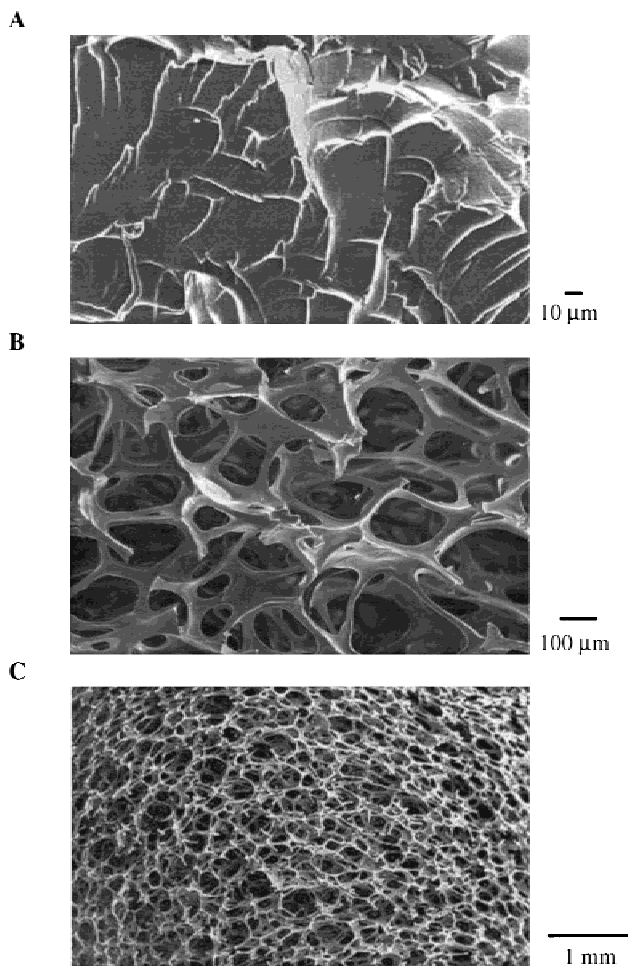


Figure 3. SEM pictures showing (A) a poly(acrylamide-co-acrylic acid) conventional hydrogel and (B and C) superporous hydrogels at different magnifications. The gels were dried and fractured after cooling in liquid nitrogen to expose the structures inside the gels. P(AM-co-AA) superporous hydrogels were made according to the recipe in Table I.

formation of homogeneous open channels throughout the hydrogels. The equilibrium swelling occurred within 6 min as the amount of NaHCO_3 increased to 90 mg. This is rather fast swelling for a cylindrical gel with a dimension of 10 mm in diameter and 25 mm in height. For all monomers tested, the equilibrium swelling occurred faster as the amount of NaHCO_3 increased. The faster swelling was accompanied with a higher degree of swelling. As shown in Figure 4, the equilibrium swelling ratio reached 300 when the amount of NaHCO_3 was 50 mg or higher.

Effect of drying condition and wetting agent on swelling

To find the optimum drying condition that did not alter the swelling ratio of dried superporous hydrogels, we examined a few drying conditions. Table II lists the swelling ratios and swelling times of conventional and superporous P(AM-co-AA) hydrogels dried under two different conditions. The density of dried conventional hydrogels was $1.30 \pm 0.08 \text{ g/cm}^3$ while the densities of superporous hydrogels were less than 1 and as low as 0.13. There was little difference in the equilibrium swelling ratios among superporous hydrogels resulting from changes in drying conditions or the wetting agent used. However, depending on the drying condition, the superporous hydrogels showed dramatic differences in the time it took them to reach equilibrium swelling (swelling time). When the swollen superporous hydrogels were dried at 60°C overnight (Condition I), the swelling time was close to an hour. Although this swelling time was much faster than that of the conventional hydrogels, the swelling was still too slow to be useful for our intended appli-

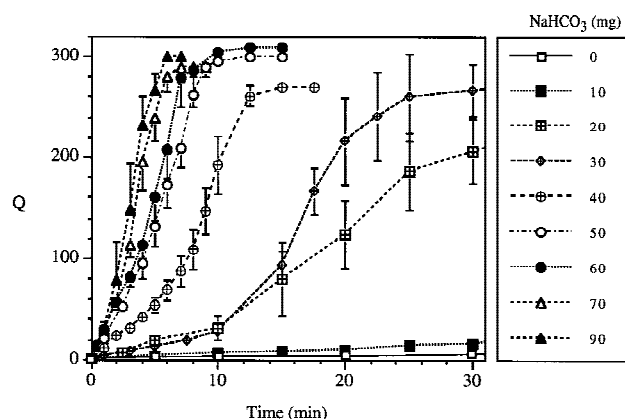


Figure 4. Effect of the amount of NaHCO_3 on swelling kinetics of poly(acrylamide-co-acrylic acid) conventional and superporous hydrogels. Each hydrogel was prepared from 1.0 mL of monomer mix in a 15 mm \times 85 mm glass tube ($n \geq 4$). Superporous hydrogels were dehydrated in ethanol before drying to constant weights.

cations. When a superporous hydrogel dried under Condition I was placed in water, the outer region swelled to equilibrium only seconds after contact with water. This swelling changed the outer region from opaque to clear. With the penetration of water, the clear region gradually expanded towards the center. This penetration step was quite slow and took most of the swelling time. The center part remained opaque until water penetrated through. Once water reached the center, the central region became clear and swelled to the fully swollen state in just a few seconds. The slow penetration into the center of the dried superporous hydrogels indicated that the drying under Condition I somehow disrupted the capillary channels. The inner structure of the superporous hydrogels under SEM showed that many of the capillary channels were closed or partially blocked, forming "dead end" structures [Fig. 5(A)]. Since a small percentage of closed pores can result in overall poor capillary action, the slow swelling of the superporous hydrogels was understandable. It is likely that the removal of water during drying resulted in collapse of polymer chains and the pores due to the high surface tension of water. Such a collapse brought substantial shrinkage of the gel, as indicated by a rather high density of 0.80 g/cm^3 . For this reason, we examined a method of drying in the absence of water to maintain intact capillary channels even after drying. When the superporous hydrogels were dried under Condition II (i.e., dehydrated in ethanol first before drying), the swelling time was reduced to about 4 min. This is an order of magnitude reduction in the swelling time. As shown in Figure 5(B), pores remained intact and no signs of pore collapses were seen. During ethanol dehydration, the superporous hydrogel became rigid, probably due to precipitation of polymer chains in a poor solvent. This rigid structure might have contributed to better maintenance of the pore structures during drying in ethanol, which has low surface tension. This resulted in less shrinkage of the gel during drying, as indicated by the low density of 0.13 g/cm^3 . Dehydration by other water-miscible organic solvents, such as acetone, methanol, and isopropanol, had the similar results.

Since good capillary action requires surfaces with good wettability, the effects of wetting agents on swelling kinetics were examined to see whether the swelling time could be further shortened. Voranol[®] was used in the literature as a wetting agent to increase the swelling rate of polyacrylate hydrogel particles.²⁷ When superporous hydrogels were dehydrated with ethanol containing 1% Voranol[®] before drying (Sample #4 in Table II), the swelling time was reduced even further to less than 3 min. While there was some advantage to using Voranol[®], the decrease in the swelling time was not as dramatic as expected. It was reasoned that the best wetting agent would be water itself, and so moisture was absorbed into the

TABLE II
Effects of Drying Condition and Wetting Agent on the Swelling of P(AM-co-AA) Superporous Hydrogels

| Gel | Drying Condition* | Wetting Agent | Size in the Dried State (Diameter × Height (mm)) | Density of Dried Gels (g/cm ³) | Swelling Ratio (Q) | Swelling Time (min) |
|----------------|-------------------|---------------|--|--|--------------------|---------------------|
| 1. Control | I | | 5 × 2 | 1.30 ± 0.08 | 173 ± 7 | 720 ± 110 |
| 2. Superporous | I | | 6 × 3 | 0.80 ± 0.06 | 307 ± 29 | 51 ± 22 |
| 3. Superporous | II | | 11 × 5.5 | 0.13 ± 0.02 | 337 ± 76 | 4.1 ± 0.3 |
| 4. Superporous | II | Voranol | 8 × 4 | 0.25 ± 0.02 | 368 ± 34 | 2.8 ± 0.7 |

P(AM-co-AA) superporous hydrogels used here were made according to the recipe in Table I. The amount of NaHCO₃ used was 120 mg. *Drying Condition I: swelling in water and drying at 60°C overnight; drying Condition II: swelling in water, dehydration in ethanol, and drying at 60°C overnight. *n* = 4.

dried superporous hydrogels in a controlled manner using a moistening chamber. Figure 6 shows the equilibrium swelling time of superporous hydrogels as a function of the moisture content in the dried hydrogel. In this particular experiment, superporous hydrogels were prepared using 50 mg of NaHCO₃ instead of the 120 mg used for making the hydrogels tested in Table II. This was done to make the effect of moisture on swelling kinetics more prominent. When the moisture content in the superporous hydrogel was 20% of the total weight or less, a moderate decrease in swelling time was observed. When the moisture content reached 25%, the superporous hydrogel became soft

and the swelling time was reduced dramatically to about 2 min. The swelling time decreased further to less than 1 min as the moisture content increased. For the matrix with 10 mm in diameter and 25 mm in length, this is a pretty fast swelling time. This is almost instantaneous compared to the days taken to swell the conventional hydrogels of the same size. In summary, our study has shown that fast swelling can be achieved by preserving the capillary channels during drying and by making the surface of pores more wettable.

DISCUSSION

Hydrogels with different pore sizes

Bulk polymerization of vinyl monomers, such as those listed in Table I, leads to a production of a

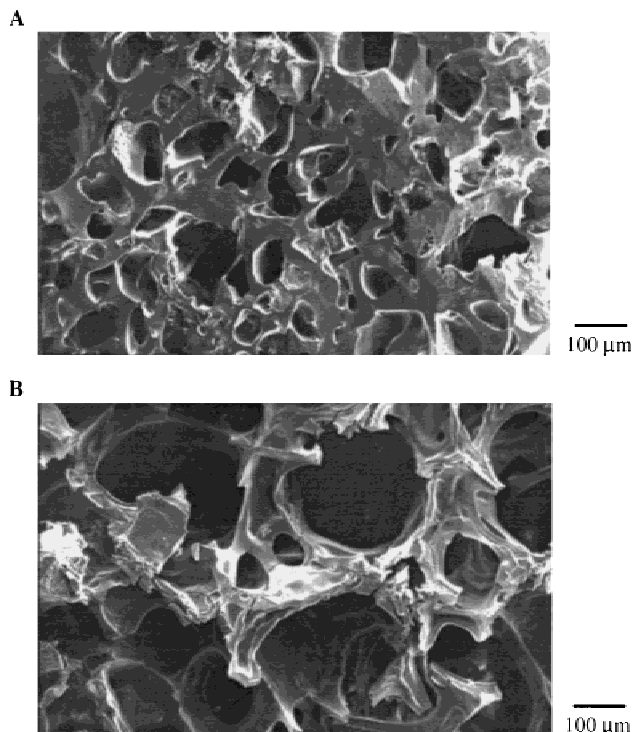


Figure 5. SEM pictures showing superporous poly(acrylamide-co-acrylic acid) hydrogels dried under two different conditions: (A) superporous hydrogel was swollen in water and dried in an oven (Sample #2 in Table II); (B) superporous hydrogel was swollen in water, dehydrated in ethanol, and dried in an oven (Sample #3 in Table II).

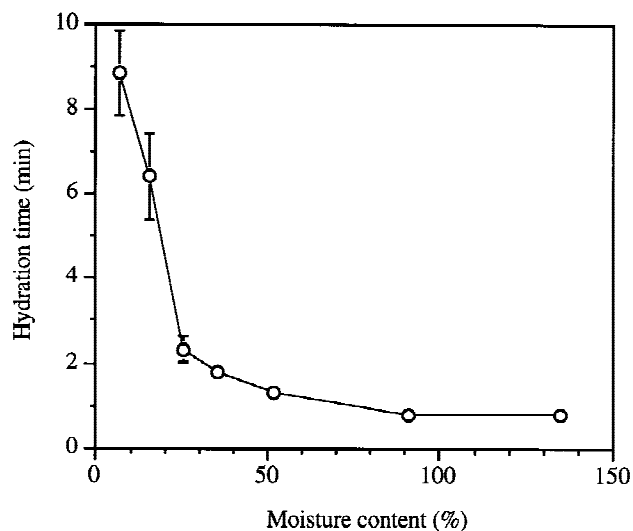


Figure 6. Equilibrium swelling time of superporous hydrogels as a function of moisture content. P(AM-co-AA) superporous hydrogels used here were made according to the recipe in Table I using 50 mg of NaHCO₃. The size of superporous hydrogels was 10 mm in diameter × 25 mm in length. *n* = 4.

glassy, transparent polymer matrices that are very hard. When immersed in water, such glassy matrices swell to become soft and flexible. Although they allow transfer of water and some low molecular weight solutes, this kind of swollen polymer matrices (i.e., hydrogels) is considered nonporous. The pores between polymer chains are in fact the only spaces available for the mass transfer, and the pore size is within the range of molecular dimensions (a few nanometers or less).¹² Under SEM, the surface of the dried hydrogels appears completely nonporous. In this case, the transfer of water or other solutes is achieved by a diffusional mechanism.¹² This restricts the rate of absorption and the size of species that are absorbed as well as released.²⁸ This type of homogeneous hydrogel has been used widely in various applications, especially in the controlled drug delivery area where limited diffusional characteristics are required.¹ Hydrogels usually are prepared by solution polymerization. The nature of a synthesized hydrogel, whether a compact gel or a loose polymer network, depends on the type of monomers, the amount of diluent in the monomer mixture (i.e., monomer–diluent ratio), and the amount of crosslinking agent.¹³ As the amount of diluent (usually water) in the monomer mixture increases, the pore size also increases up to the micrometer (μm) range.¹² Although attempts have been made to distinguish hydrogels with different pore size ranges using the terms “microporous” (10–100 nm range) and “macroporous” (100 nm–10 μm), the two terms usually are used interchangeably. Recently, superporous hydrogels were made by a gas blowing method.^{22,23} The size of pores in superporous hydrogels is larger than 100 μm , usually in the range of several hundred micrometers, and can be up to the millimeter range. Most of the pores inside of the superporous hydrogel are connected to form the open channel system. The size and number of the pores can be controlled by adjusting the type and amount of surfactant and gas-forming agent during crosslinking polymerization. The size of the largest pores, which determines the extent of capillary rise, easily can be determined using the Young–Laplace equation of capillary wetting.

Fast swelling of superporous hydrogels

In the swelling of conventional hydrogels (without any pores), the characteristic swelling time (τ) is described by the following equation:

$$\tau = L^2/D$$

where L is the characteristic length of the gel and D is the diffusion coefficient of the gel network in the solvent.²⁹ The characteristic length for a spherical or cylindrical hydrogel is the radius, and for a hydrogel

sheet it is the half thickness. The diffusion coefficient of hydrogel networks is in the order of 10^{-7} cm^2/s .^{15,29} Thus, swelling of a conventional hydrogel with L of 1 mm will take about a day.^{15,30} It took 12 h to swell for a 2 mm thick P(AM-co-AA) hydrogel, as shown in Table II. To reduce the characteristic length, and thus the swelling time, dried hydrogels of submillimeter size in a powder form commonly are used in making fast swelling, superabsorbent polymers. An alternative approach has been to make porous hydrogels in order to reduce the characteristic length for diffusive processes.¹⁵ Since the thickness of the cell walls and struts in porous hydrogels, especially superporous hydrogels, is in the micrometer range, the swelling time will be in the second range. Thus the factor that really determines the swelling time of the dried porous hydrogels is the time it takes for water to enter into the gel matrix and cover most of the surface of the pores. This is determined by the effectiveness of the capillary action and the wettability of the pore surface. As shown in Table II, superporous hydrogels with well maintained capillary structures and good wetting property will swell to equilibrium in less than a minute regardless of the size of the total mass.

Potential applications of superporous hydrogels

Our initial goal for developing superporous hydrogels was to be able to use them as a gastric retention device. Animal experiments currently are being conducted to find out whether or not superporous hydrogels possess all the properties necessary for gastric retention and, if not, what other properties are necessary. Currently available superabsorbents usually are made of conventional hydrogels in the micrometer range. The restriction on the size of the gels, however, limits the useful application of these fast swelling, superabsorbent polymers, and certainly superabsorbent polymers of larger dimension are highly desirable.³¹ Since the fast swelling of superporous hydrogels is size independent, they will be useful in applications where large surface area and fast mass transfer are beneficial. If superporous hydrogels are made of stimuli-sensitive polymers (e.g., pH-sensitive or temperature-sensitive polymers), the response to environmental stimuli is faster than that of conventional hydrogels by orders of magnitude.^{15,32} Such a fast response may be highly useful in the design of new controlled release drug delivery systems.

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