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Synthesis and characterization of superporous hydrogel composites

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Abstract

Recently, we synthesized superporous hydrogels which swell fast with high swelling ratios for development of gastric retention devices. Due to their superabsorbent nature, superporous hydrogels are too mechanically weak for gastric retention application. The mechanical strength of superporous hydrogels was substantially increased by making superporous hydrogel composites. The composite materials used were hydrophilic particulate materials commonly used as disintegrants in pharmaceutical tablets. In this study, Ac-Di-Sol[®] was used as a model composite material. Addition of Ac-Di-Sol[®] resulted in significant improvement in the properties of superporous hydrogels. The dried superporous hydrogels maintained interconnected channels even after drying in the air. Thus, the swelling kinetics and the swelling ratio were not affected by air drying, which normally would have resulted in partial or total collapse of the interconnected pores. The presence of Ac-Di-Sol[®] also increased the mechanical strength substantially. Scanning electron microscopic examination showed that the composite material increased the physical crosslinking density which provided high mechanical strength and prevented polymer chains from collapsing during air drying. The superporous hydrogel composites possess properties suitable for gastric retention. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Hydrogels; Superporous hydrogels; Composites; Fast swelling; Superabsorbent; Gastric retention

1. Introduction

We have been interested in developing gastric retention devices based on hydrogels. For hydrogels to remain in the stomach, they have to swell fast before all the gastric fluid is emptied. Recently, we synthesized superporous hydrogels which swell in

aqueous solution in a matter of a minute regardless of their size and shape [1]. This is due to the presence of open pores forming capillary channels. Water is taken up into dried hydrogels by capillary rise. Since fully swollen superporous hydrogels are mechanically rather weak, their mechanical strength needs to be increased for effective gastric retention. The maximal stomach contraction pressure in humans is known to be about 50–70 cm water pressure (or 4900–6860 N/m²) [2]. This number, however, reflects only the direct compression pressure, and the presence of other forces, such as abrasion and shear forces, would increase the actual

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pressure on hydrogels. Thus, for a superporous hydrogel to be maintained as an integral dosage form in the stomach, it must be able to withstand a pressure much higher than the 50–70 cm water pressure. While the actual value necessary for hydrogels to remain in the stomach needs to be determined from animal experiments, the above number presents a baseline value to work with.

The mechanical properties of the superporous hydrogels are affected by formulation variables, such as the amount of crosslinking agent, the type of plasticizer, the type of monomer, the amount of blowing agent, and post gelation treatment. The mechanical strength of hydrogels and superporous hydrogels can be enhanced by increasing the concentration of the crosslinking agent. We explored an alternative method of preparing superporous hydrogels with high mechanical strength. Composite materials have been used to prepare materials with new or improved properties. We have examined the swelling and mechanical properties of superporous hydrogel composites. The composite materials tested in our study were hydrophilic particulate materials which have been commonly used as disintegrants in pharmaceutical tablets.

2. Experimental methods

2.1. Synthesis of superporous hydrogel composites

Superporous hydrogels were synthesized as described previously [1] with the exception that composite materials were added before polymerization. The monomers used in our study were acrylamide (AM), 3-sulfopropyl acrylate-potassium salt (SPAK), and acrylic acid (AA). Poly(AM-co-SPAK) and poly(AM-co-AA) superporous hydrogel composites were synthesized using particulate composite materials, such as Ac-Di-Sol[®] (slightly crosslinked sodium carboxymethylcellulose powder), Primojel[®] (slightly crosslinked sodium starch glycolate powder), Explotab[®] (slightly crosslinked sodium starch glycolate powder), and Crospovidone[®] (slightly crosslinked polyvinylpyrrolidone powder). These are superdisintegrants commonly used in pharmaceutical tablets.

Typically, the following procedure was used to

make the poly(AM-co-SPAK) superporous hydrogel composite in a glass test tube (outer diameter of 22 mm, inner diameter of 19 mm, and height of 175 mm). The exact amount of each component can be varied. The following components were added sequentially to the test tube: 1200 μl of 50% AM; 900 μl of 50% SPAK; 450 μl of 2.5% *N,N'*-methylenebisacrylamide (Bis) (Aldrich Chemical); 90 μl of 10% Pluronic[®] F127 (a foam stabilizer); 30 μl of 50% (v/v) acrylic acid; 45 μl of 20% ammonium persulfate (Aldrich Chemical). The solvent used was deionized, distilled water (DDW) unless specified otherwise. The test tube was shaken to mix the solution after each ingredient was added. Then 270 mg Ac-Di-Sol[®] powder was added to the mixture which was stirred using a spatula. Then, 45 μl of 20% *N,N,N',N'*-tetramethylethylenediamine (TEMED) (Bio-Rad Laboratories) was added to the mixture and the test tube was shaken again. Finally, 100 mg of NaHCO_3 powder was added and the mixture was immediately stirred vigorously using a spatula for 10 s. Polymerization is accelerated after adding NaHCO_3 and is complete in a few minutes. The superporous hydrogel was cured at room temperature for 10 min. The superporous hydrogel was retrieved from the test tube, and washed in a 1-l beaker containing 400 ml of simulated gastric fluid (SGF, pH 1.2 based on USP) for 24 h. This step was called acidification. The superporous hydrogel was then dried at room temperature for 5 days.

2.2. Swelling studies

The dry superporous hydrogels were allowed to hydrate in excess DDW at room temperature. The weight of the hydrating samples were measured at timed intervals, after excess water was removed by gentle blotting. 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.

2.3. SEM

Porous structures of superporous hydrogel com-

posites were examined using 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).

2.4. Mechanical characterization of superporous hydrogel composites

A bench comparator was used to test the mechanical properties of the superporous hydrogels and their composites (Fig. 1). A sample swollen in simulated gastric fluid (SGF) was placed longitudinally under the lower touch of the bench comparator that was connected to a micrometer gauge. The superporous hydrogel was supported by a lab jack. Weights were applied to the upper touch of the bench comparator in incremental intervals. The swelling height of the superporous hydrogel under pressure was read from the gauge. The pressure applied to the superporous hydrogel was calculated from the weights and the contact area of the lower touch. Two parameters, swelling height under 100 cm water pressure and ultimate compression pressure (UCP), were determined to characterize the mechanical properties of the superporous hydrogels [3]. The

UCP was determined by applying increasing amounts of weights until a point when the superporous hydrogel started cracking. The pressure at that point was defined as UCP.

3. Results

3.1. Swelling kinetics

The most salient property of a superporous hydrogel is its fast swelling ability. The presence of a composite material is important in fast swelling of dried superporous hydrogels. Poly(AM-co-SPAK) superporous hydrogel composites were prepared using Ac-Di-Sol[®], Primojel[®], Explotab[®], or Crospovidone[®]. Our preliminary study showed that these composite materials provided similar properties in preserving the swelling property and improving the mechanical strength over the control superporous hydrogels. Of these, Ac-Di-Sol[®] was chosen for further study to examine the effect of a composite material on the swelling and mechanical properties in more detail. Table 1 shows the physical characteristics of the poly(AM-co-SPAK) superporous hydrogel composites prepared in our study. When a superporous hydrogel was fully swollen in SGF (pH 1.2), it had diameter of 2.4 cm, length of 3.4 cm, and weight of 13.6 g. Fig. 2A shows the fully swollen superporous hydrogel composite which was freeze-dried for SEM observation. When a fully swollen superporous hydrogel composite was air-dried, it had a diameter of 1.5 cm, length of 2.3 cm, and weight of 1.35 g. As shown in Fig. 2B, the interconnected capillary channels were still intact, which may be the reason that the superporous hydrogel composites could swell rapidly in a minute or so. The dried superporous hydrogels were placed in a moisture chamber to make them flexible [1], and then compressed to be put into a gelatin capsule of a 000 size. The superporous hydrogel composite had a diameter of 0.9 cm, length of 2.4 cm, and weight of 1.35 g. The compressed superporous hydrogels swelled in 6 min (without counting the dissolution time of the gelatin capsule). The slower swelling time (1 min vs. 6 min) may be due to the partial blockage of capillary channels, as shown in Fig. 2C. Since the capillary channels were not completely blocked by compress-

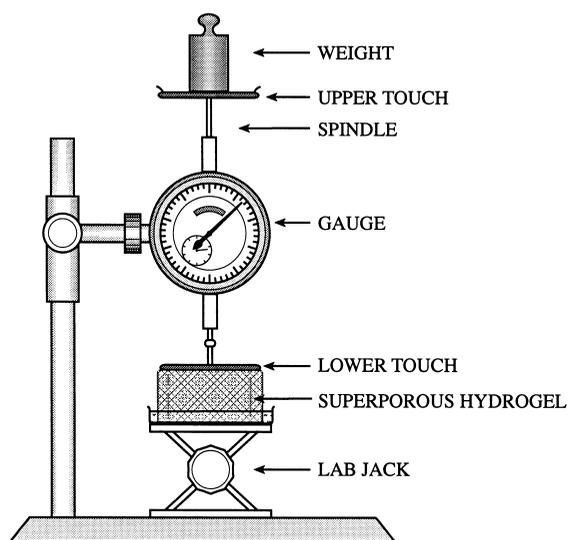


Fig. 1. A bench comparator used to examine the mechanical property of superporous hydrogels.

Table 1
Physical characteristics of poly(AM-co-SPAK) superporous hydrogel composites under swollen, dried, or squeezed state

Physical state of superporous hydrogel composite	Diameter (cm)	Length (mm)	Weight (g)	Density (g/cm ³)	Swelling time in SGF at 37°C (min)
Fully swollen in SGF	2.4	3.4	13.6		
Completely dried	1.5	2.3	1.35	0.31	1
Compressed to put into a gelatin capsule (size 000)	0.9	2.4	1.35	0.88	6 ^a (>1 h) ^b

^a The swelling time of a squeezed superporous hydrogel was measured after it was taken out from the capsule. When the swelling time of a superporous hydrogel inside a capsule was measured, 3–5 more minutes were needed for the dissolving of the capsule.

^b The swelling time was more than 1 h if the superporous hydrogels did not contain Ac-Di-Sol[®] (i.e., if they were not composites).

sion, the swelling could still occur in 6 min. This swelling time is substantially faster than the swelling of conventional non-porous hydrogels. If Ac-Di-Sol[®] was not added, the compressed superporous hydrogels took more than 1 h to swell. Clearly, Ac-Di-Sol[®] was an important factor in maintaining the capillary structure required for fast swelling.

The effect of the amount of Ac-Di-Sol[®] on the swelling kinetics of superporous hydrogel composites was examined using poly(AM-co-AA) hydrogels, since their large swelling ratios made it easier to differentiate the swelling kinetics. Table 2 shows the effect of the quantity of Ac-Di-Sol on the swelling kinetics. The swelling time of superporous hydrogels (31 min) was reduced to 8 min or less by the addition of Ac-Di-Sol. Addition of 200 mg of Ac-Di-Sol also resulted in a decrease in the density and swelling ratio by a factor of three or four. The swelling time, on the other hand, was reduced by a factor of ten. The reduction in the swelling ratio indicates that the overall crosslinking density is increased. Since Ac-Di-Sol is not expected to participate as a chemical crosslinking agent, it is thought to participate as a physical crosslinking agent. It is highly likely that the polymer chains can physically entangle through Ac-Di-Sol particles. When Ac-Di-Sol[®] was mixed with the monomer solution, it swelled so that monomers (acrylamide and acrylic acid) and crosslinker (Bis) were absorbed into its network. During the synthesis of SPH, the absorbed monomers and crosslinker, along with those that were not absorbed, all participated in the polymerization, leading to the formation of an interpenetrating polymer network (IPN). Fig. 3 shows polymer

layers formed around hollow Ac-Di-Sol particles. Ac-Di-Sol[®] fibers were interlocked with the superporous hydrogel matrix to form an integral unit. This IPN formation was limited to the Ac-Di-Sol[®] particles and thus the localized IPNs in Ac-Di-Sol[®] particles provided additional crosslinking. The decrease in swelling ratios of Ac-Di-Sol[®] incorporated SPH was partially due to the increase in physical crosslinking. During the drying process, the rigid Ac-Di-Sol[®] particles maintained the network structure so that the superporous hydrogels shrank much less and had lower density. SEM pictures of superporous hydrogel composites with different amounts of Ac-Di-Sol[®] showed that the superporous hydrogel composites with higher Ac-Di-Sol[®] content maintained a more porous structure after drying.

3.2. Mechanical strength

One of the most important requirements for a gastric retention superporous hydrogel is its structural integrity. A superporous hydrogel should be able to withstand the pressure expected in the stomach during repeated gastric contractions, especially the housekeeper waves. Formulation variables, such as the amount of crosslinker, amount of Ac-Di-Sol[®], plasticizer, type of monomer, amount of blowing agent as well as process variables such as acidification, all affect the mechanical properties of the superporous hydrogels. In this study, we examined the effect of the concentrations of the crosslinker and Ac-Di-Sol[®] on the mechanical strength of superporous hydrogel composites.

Poly(AM-co-SPAK) superporous hydrogels con-

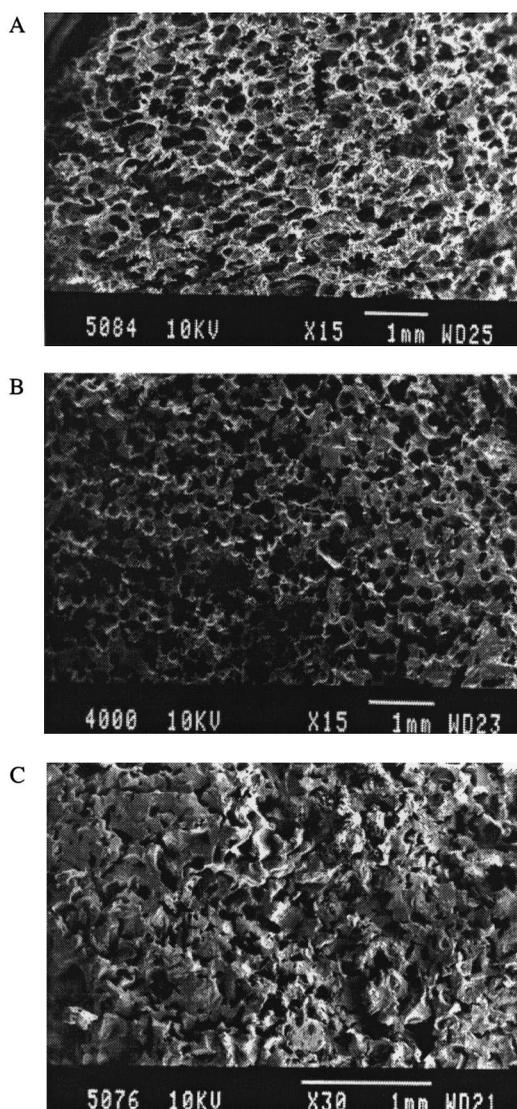


Fig. 2. SEM pictures of poly(AM-co-SPAK) superporous hydrogel composites. (A) Freeze-dried after fully swollen in SGF. (B) Air-dried at room temperature. (C) Air-dried at room temperature, moistened, and then compressed into a 000 gelatin capsule.

taining different amounts of Bis (0.22 mol% to 0.86 mol% of the monomer content) were prepared as described above, except that all these superporous hydrogels were not subjected to the acidification step. The mechanical properties of these superporous hydrogels were studied on a bench comparator after they swelled to equilibrium size in SGF. As shown in Fig. 4, the increase in the crosslinker (Bis)

Table 2
Swelling ratio and swelling time of P(AM-co-AA) superporous hydrogel^a composites with different amounts of Ac-Di-Sol

Ac-Di-Sol (mg)	Size ^b (mm×mm)	Density (g/cm ³)	Swelling ratio	Swelling time (min)
1.00 ^c	5.0×2.0	1.30±0.08	173±7	720±110
2.00	6.0×3.0	0.76±0.08	328±40	31±6
3.50	7.0×3.0	0.48±0.05	294±44	8.5±6.1
4.10	7.0×3.5	0.39±0.02	192±18	1.2±0.6
5.15	7.5×4.0	0.33±0.04	120±23	0.6±0.2
6.20	8.0×4.0	0.28±0.01	91±22	0.3±0.1

^a All superporous hydrogels were dried at 60°C overnight. The amount of NaHCO₃ used for making superporous hydrogels was 120 mg (*n*=4).

^b Diameter×height.

^c Conventional hydrogel without porous structure.

concentration did not change the height of the superporous hydrogels very much when they were swollen in the absence of pressure. In addition, the UCP was not affected very much. The UCP varied from 150 to 200 cm water pressure. However, the height of the swollen superporous hydrogels under 100 cm water pressure increased with the increase of Bis when the concentration of Bis was less than 0.66 mol% of the monomers. This implies that when the Bis concentration increased, the resulting superporous hydrogels would deform less under the stomach pressure. The size under pressure is thought to better represent the actual size in the stomach because it reflects the more realistic situation in the stomach. According to previous studies in our laboratory, hydrogels that deformed less were more likely to be retained in the stomach [4]. A Bis concentration of 0.66 mol% of the monomer content (equivalent to 450 μl of 2.5% Bis) was found to be the best among the conditions studied for the improvement of the mechanical strength.

Superporous hydrogels containing different amounts of Ac-Di-Sol[®] (0 to 300 mg) were prepared and their mechanical properties were examined. Fig. 5 shows that the incorporation of Ac-Di-Sol[®] slightly decreases the swelling size of the superporous hydrogels under pressure. On the other hand, it considerably increases the UCP value of the superporous hydrogels. The possible reason for the improved structural integrity is that the addition of Ac-Di-Sol[®] increases the physical cross-linking density of the superporous hydrogel. However, if too

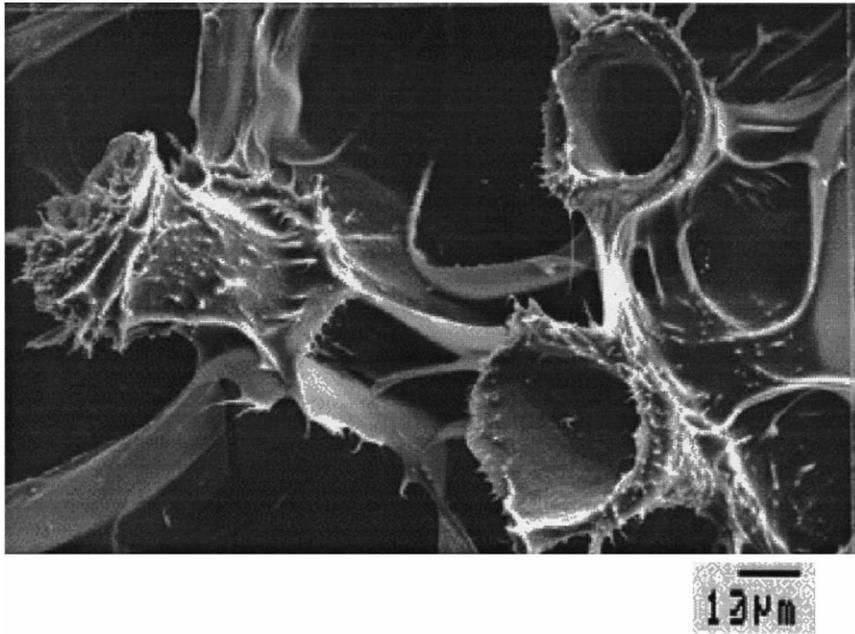


Fig. 3. SEM picture of a freeze-dried poly(AM-co-AA) hydrogel composite containing Ac-Di-Sol[®] fibers. The Ac-Di-Sol[®] fibers showed hollow lumen structure.

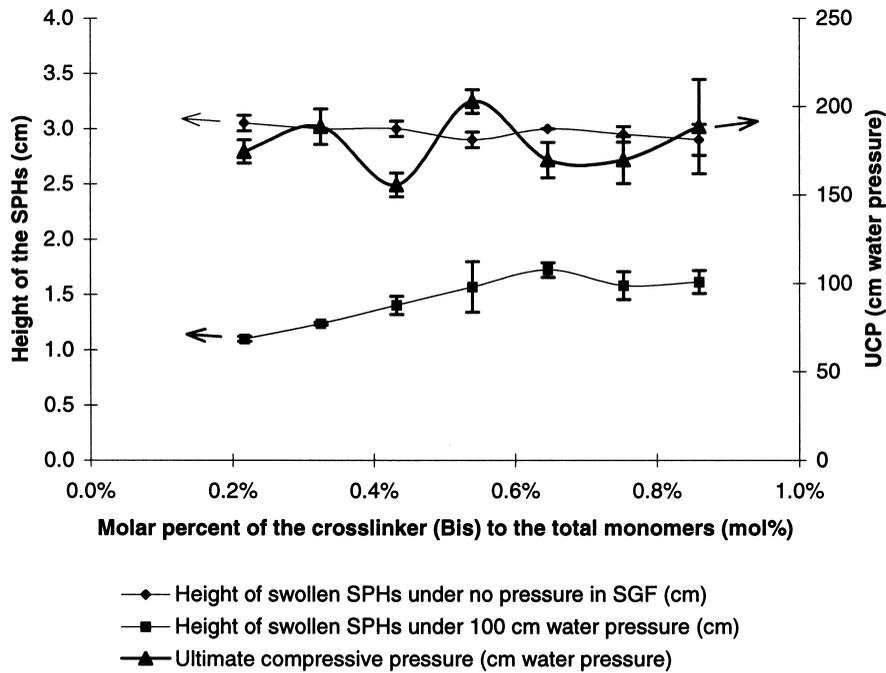


Fig. 4. The effect of crosslinker (Bis) concentration on the swollen size under no pressure (◆), the swollen size under 100 cm water pressure (■), and the ultimate compression pressure (▲) of the poly(AM-co-SPAK) superporous hydrogel composites. The amount of Ac-Di-Sol[®] was 100 mg.

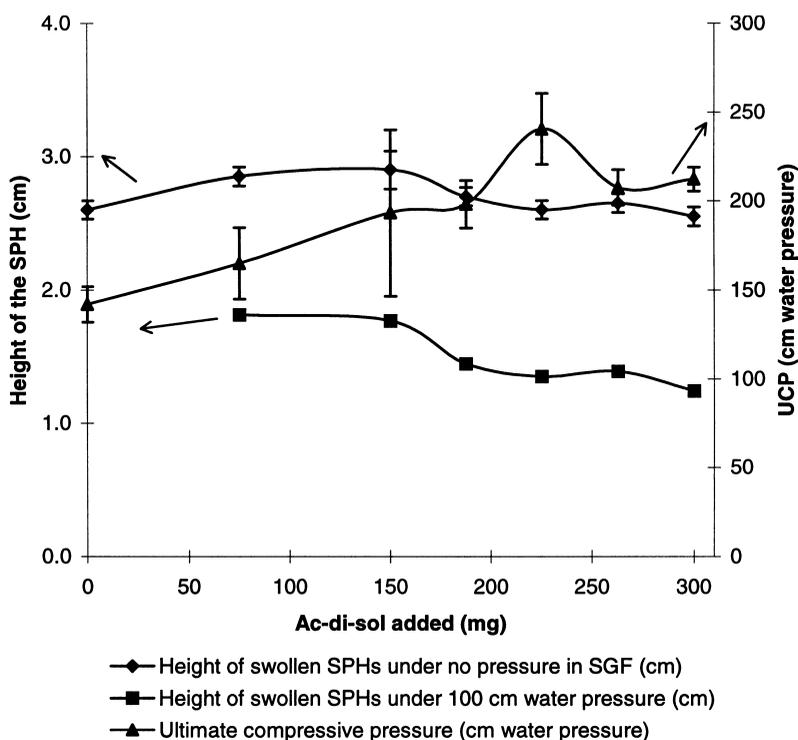


Fig. 5. The effect of the Ac-Di-Sol[®] amount on the swollen size under no pressure, the swollen size under 100 cm water pressure (■), and the UCP of the poly(AM-co-SPAK) superporous hydrogel composites (▲).

much Ac-Di-Sol[®] is incorporated, due to the increase of solution viscosity, good mixing of all the ingredients becomes difficult. In most of the studies, 270 mg Ac-Di-Sol[®] was used.

3.3. Effects of acidification on the mechanical properties

Mechanical properties of superporous hydrogels with three different post-treatments were measured: (A) superporous hydrogels without washing in SGF; (B) superporous hydrogels washed in SGF and then oven dried at 60°C for 24 h; and (C) superporous hydrogels washed in SGF and then air dried at room temperature for 5 days. The washing step partially converted the anionic SO_3^- group into the unionized SO_3H group, and it substantially changed the properties of the superporous hydrogels. The UCP value for the three samples A, B, and C were 189, 284, and 368 cm water pressure, respectively. The acidification of the superporous hydrogels made them much

stronger than the superporous hydrogels prepared without acidification. Moreover, the UCP of the acidified superporous hydrogels that were dried at room temperature were even stronger than those dried in a 60°C oven. It is clear that acidification provided a significant improvement in the mechanical properties of superporous hydrogels.

3.4. The role of Ac-Di-Sol[®] in foam stabilization

As mentioned above, Ac-Di-Sol[®] has the function of increasing the swelling rate and improving the superporous hydrogel strength. Another important role of Ac-Di-Sol[®] is to stabilize the foam during the synthesis. Since it is desirable to have superporous hydrogels with a well-connected and uniformly distributed intercellular capillary channel system (which is essential for fast swelling), the limited amount of gas bubbles should be well preserved during the preparation. To examine the effect of Ac-Di-Sol[®] on the foam stabilization, four types of

superporous hydrogels were prepared with the following changes: (A) no Pluronic® F127 was added; (B) no Ac-Di-Sol® was added; (C) both Pluronic® F127 and Ac-Di-Sol® were added; (D) no Ac-Di-Sol® was added but twice as much acrylic acid (i.e. 60 μ l instead of 30 μ l of 50% AA) was added. After the synthesis, all samples were dried in a 60°C oven. In order to take the SEM pictures, sample C and D were cut using a razor blade to expose the inner structures, while sample A and B, being difficult to cut with a razor blade, were fractured in liquid nitrogen to expose the inner structures. Fig. 6 shows SEM pictures of these superporous hydrogels.

To make superporous hydrogels with uniform and interconnected pores, the monomer solution must have good foaming and foam stabilizing mechanisms. The cell–air interfacial tension must be lowered and the cell film viscosity must be raised.

Sample A in Fig. 6A had a large pore size but the total gas volume was small. The large pores were the result of the high air–film interfacial tension in the absence of PF127. Its swollen size was also small and the swelling speed was slow. The rough surface on the picture shows the presence of Ac-Di-Sol®. The pore sizes in sample B which contained PF127 were smaller than those in sample A, as shown in Fig. 6B. However, most of the cells in sample B were closed-cells, and no interconnected capillary channels were formed. During the preparation, many of the gas bubbles escaped from the solution because the viscosity of the solution was not high enough in the absence of Ac-Di-Sol®. The retained gas bubbles were not enough to form connected channels. Thus, the total gas volume was small and the swelling rate was also very slow. Sample C contained both PF127 and Ac-Di-Sol® which worked together to retain

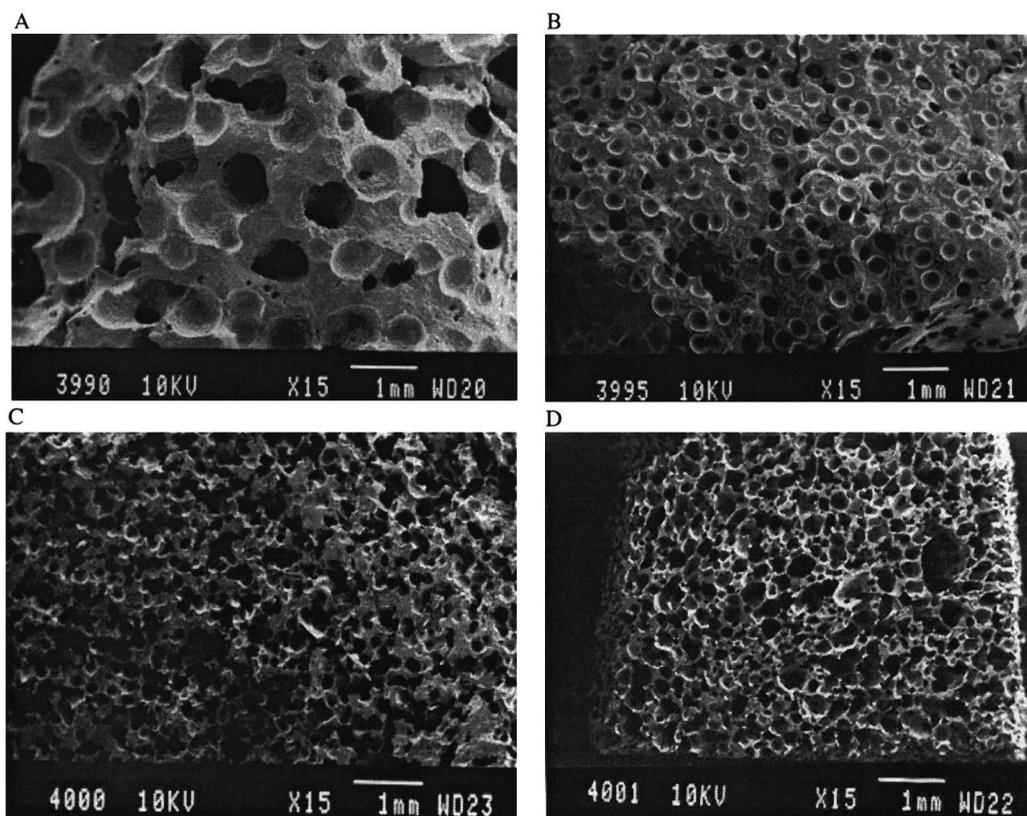


Fig. 6. SEM pictures of poly(AM-co-SPAK) superporous hydrogels containing (A) no PF127, (B) no Ac-Di-Sol®, (C) both PF127 and Ac-Di-Sol®, (D) no Ac-Di-Sol® but 60 μ l of 50% AA. All samples were dried in a 60°C oven. Sample C and D were cut using a razor blade to expose the inner structures. Sample A and B were fractured in liquid nitrogen to expose the inner structures.

most of the gas bubbles, and resulted in the production of superporous hydrogel composites with fine pores and uniform pore distribution. The pore size in sample C was smaller than that in sample A, and most of the pores were connected to each other to form capillary channels (Fig. 6C). This superporous hydrogel composite showed high swelling ratio with very fast swelling kinetics. Sample D contained two-fold more acid than the other three samples. Even though many gas bubbles escaped, the retaining gas bubbles were still enough to form interconnected capillary channels. Sample D had a small pore size, open-cells, large gas volume, and a fast swelling rate (Fig. 6D). Even though both samples C and D had interconnected capillary channels, only sample C had a fast swelling rate and good mechanical strength, both of which are the most important properties for gastric retention. Using Ac-Di-Sol[®] as a composite material resulted in pores interconnected to each other even when only a small amount of blowing agent was used. Ac-Di-Sol[®] appears to have multiple useful functions in making superporous hydrogels with well structured channels.

4. Discussion

A variety of vinyl monomers can be used to make superporous hydrogels utilizing the gas blowing technique [1]. Superporous hydrogels swell rapidly to large sizes. Since most of the weight of a fully swollen superporous hydrogel is due to water, the gels are mechanically very weak. For gastric retention applications, the mechanical strength must be high. This is, first of all, necessary to maintain the fully swollen superporous hydrogels in the solid form. If the fully swollen hydrogels behave like a highly viscous solution, they may be emptied from the stomach as liquid would be emptied. High mechanical strength is also required for maintaining the superporous hydrogels intact in the stomach by withstanding the pressure exerted by the gastric contractions. The mechanical strength of superporous hydrogels was improved substantially by making composites. Since dried superporous hydrogel composites should swell rapidly, it would be ideal if the composite materials were also highly hydrophilic. For this reason, we used several superdisintegrants

commonly used in tablets and capsules to promote their fast disintegration. The composite materials used were Ac-Di-Sol[®], Primojel[®], Explotab[®], and Crospovidone[®]. Of these, Ac-Di-Sol[®] was the best in promoting the swelling speed.

The function of Ac-Di-Sol[®] in promoting the swelling kinetics was threefold. First, it helped retain the capillary channels even after air drying of the superporous hydrogels. Ac-Di-Sol[®] exists as stiff fibers in the dry state with diameters of 10–20 μm and lengths of 100–200 μm . It is insoluble but swells in aqueous solution. When a compressed tablet containing Ac-Di-Sol[®] is placed in aqueous solution, Ac-Di-Sol[®] can quickly absorb water, swell, and break apart the tablet [5]. Our swelling study showed that the superporous hydrogel composites indeed swelled faster than those without the composite material and the effect was related to the quantity of the composite material added. In addition, the swelling action of Ac-Di-Sol[®] can expand and open up closed capillary channels. This action is similar to that in tablet disintegration. Ac-Di-Sol[®] exists as long fibers with a hollow lumen [6]. Similar to its action in tablet disintegration, Ac-Di-Sol[®] not only made a superporous hydrogel more hydrophilic (therefore better wettability), but also provided intrafibrous capillary channels (the hollow lumen of each fiber) that caused a strong wicking effect. The strong relaxation of cellulose fibers may also facilitate water penetration by expanding the closed capillary channels [7]. These effects, causing fast disintegration of tablets, decreased the swelling time of squeezed superporous hydrogel from 1 h (with no Ac-Di-Sol[®]) to just 5–6 min (with Ac-Di-Sol[®]). Superporous hydrogels without composite materials had to be dehydrated with ethanol before drying in the air to preserve their interconnected capillary structures. The superporous hydrogel composites, however, could be dried in the air with their porous structures intact even though they were not washed with ethanol. It was also noticed that the presence of Ac-Di-Sol[®] resulted in better stabilization of foams, presumably due to the increase in viscosity, resulting in easier control of the synthetic process.

In addition to the above mentioned superdisintegrants, other materials, such as poly(ethylene glycol) (MW=8000) (PEG 8000), Voranol_{240–800}, Voranol_{250–473}, PVP (MW=10 000), Pluronic[®]

P103, and microcrystalline cellulose (Avicel PH101), were also tested for promoting the swelling rate of compressed superporous hydrogel composites. The use of PEG 8000, Voranol_{240–800}, Voranol_{250–473} (which were used as wetting agents in other experiments), and Pluronic® P103 did not enhance the swelling kinetics of the compressed, dried superporous hydrogels. This may be due to the fact that all of these materials, upon contact with water, became viscous gel-like liquids that blocked the passages of water through the capillary channels and impeded the further penetration of water into the superporous hydrogels. This blockage effect was overwhelming even though some of these materials improved the wettability of the superporous hydrogels [8]. Microcrystalline cellulose accelerated the swelling of the squeezed superporous hydrogels, even though the acceleration was not as great as the superdisintegrants. The mechanism by which microcrystalline cellulose promotes the swelling is believed to be similar to that of the superdisintegrants. It appears that the best composite materials for fast swelling are those which are strong enough to prevent collapse of polymer chains during drying by high water surface tension and at the same time hydrophilic enough to wet very easily.

The compressibility of dried superporous hydrogel composites without compromising their fast swelling property is an important property for many applications. Compression increases the overall swelling ratio. The presence of composite materials makes compression easier without breaking interconnected capillary channels. This particular property makes it possible to compress, or even fold, a superporous hydrogel composite and place it inside gelatin capsules. Our gastric retention study in dogs showed that the superporous hydrogel composites made of poly(AM-co-SPAK) swelled fast enough to remain in the stomach for extended periods of time [9]. The gastric retention time ranged from 3 h to 5 h in the fasted condition, and it increased to more than 24 h in the fed condition (if food is given only in the beginning of the experiment). There is no doubt that further improvement is necessary for developing clinically useful gastric retention devices based on

superporous hydrogel composites. At the same time, however, it is very promising that the superporous hydrogel composites prepared in our laboratory possess several features necessary for effective gastric retention.

The nature of the composite material is expected to alter the overall property of the superporous hydrogel composites. Since there are numerous candidates for composite materials, it is quite possible to develop superporous hydrogel composites with improved properties. The nature of further improvement of superporous hydrogel composites depends on specific applications, but one of the most important properties to develop is the elasticity of the fully swollen superporous hydrogel composite. If the fully swollen superporous hydrogel composites have elasticity resembling rubber, they could find a wide variety of applications. We are currently working on optimizing this particular property of superporous hydrogel composites.

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