Semi-interpenetrating Polymer Network Superporous Hydrogels Based on Poly(3-Sulfopropyl Acrylate, Potassium Salt) and Poly(Vinyl Alcohol): Synthesis and Characterization

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ABSTRACT: Semi-interpenetrating polymer network (semi-IPN) superporous hydrogels (SPHs) based on poly(3-sulfopropyl acrylate, potassium salt) (PSPA) and linear polymers were synthesized using poly(ethylene glycol) diacrylate (PEGDA) or *N*,*N*′-methylenebisacrylamide (BIS) as a crosslinker. The swelling ratio of SPHs was determined by measuring the weight of absorbed water; and the mechanical strength of swollen SPHs was evaluated using texture analyzer. Taguchi orthogonal experimental design [$L_9(3^4)$] was used to evaluate the influence of four factors, consisting of the ratios of 3-sulfopropyl acrylate (SPA) to PEGDA, to initiator, and to acrylic acid (AAc), and acidification of PSPA-SPHs, with each containing three levels on the swelling ratio and mechanical strength of semi-IPN PSPA-SPHs. Analysis of variance (ANOVA) of the experimental design results was carried out using a SAS program. The structure of SPHs was examined using a scanning electron microscope (SEM). Among the polymers evaluated, poly(vinyl alcohol) (PVA) was the best linear polymer to improve the mechanical strength of swollen SPHs. ANOVA indicated that

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0883-9115/04/02 0081–20 $10.00/0 DOI: 10.1177/0883911504042641
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the ratio of SPA to PEGDA and to an initiator, as well as acidification had significant effects on the swelling ratios of PSPA-SPHs. The ratio of SPA to AAc and acidification had significant effects on the mechanical strength, which deceased with increased swelling ratio and time. The optimized semi-IPN PSPA-SPH containing 5% w/w PVA had a swelling ratio 20 times greater within minutes and then up to 40 times. The mechanical strength was over 200 g/cm^2 for a fully swollen gel in a pH 1.2 HCl medium. The optimal PSPA-SPH has swelling and mechanical properties suitable for development of gastro retentive drug delivery systems.

KEY WORDS: superporous hydrogel, semi-interpenetrating polymer network, poly(3-sulfopropyl acrylate, potassium salt), poly(vinyl alcohol).

INTRODUCTION

Superporous hydrogels (SPHs) have been developed for applications as a gastric retention device for oral drug delivery and a chemoembolizing agent for cancer treatment [1–3]. In an effort to overcome the slow swelling property of dried hydrogels, SPHs that can reach a fully swollen state within minutes, regardless of the size of the matrix, have been synthesized [1]. SPHs are hydrogels with numerous pores connected together to form open channel structures. Water is absorbed into the dried SPHs by capillary wetting rather than by diffusion. The dried hydrogels swell extremely fast with the swelling ratio easily reaching more than 100 times within minutes [1,4]. Although these SPHs provided significantly fast swelling kinetics and high swelling ratios, the mechanical strength of the fully swollen SPHs were weak because of the high swelling ratio [1,4].

In order to increase the mechanical strength, composite materials, such as Ac-Di-Sol® (croscarmellose sodium), were added to SPH [4,5]. Semi-interpenetrating polymer networks (semi-IPNs) and IPNs have been used for drug delivery and tissue engineering [6]. IPNs make it possible to combine partially compatible or incompatible polymers and provide unique possibilities for controlling the mechanical and physicochemical properties [7,8]. Chitosan/poly(ethylene oxide) (PEO) semi-IPNs hydrogels display a high capacity to swell, to be adjusted by pH, and elastic properties [9]. A gelatin-PEO semi-IPN was investigated for its swelling behavior and enzyme-induced degradation. By varying the molecular weight and amount of PEO in the semi-IPN, it was possible to design hydrogels for site-specific oral delivery in the stomach and upper intestine [10]. The study of full and semi-IPNs

based on poly(acrylic acid) and gelatin showed that the swelling ratio increased with increasing pH. A significant increase in the swelling was observed when the pH of distilled water was above 10 and a maximum pH was 8.4 in buffer [11]. The study of semi- and full IPNs of poly(acrylamide-co-acrylic acid) and PVA showed that incorporation of acrylic acid increased the swelling ratio several fold. Crosslinked PVA suppresses swelling, therefore, swelling can be effectively varied by adjusting the acrylic acid content and extent of PVA crosslinking [12]. Tensile strength of the swollen semi-interpenetrating NIPA networks of *N*-isopropylacrylamide (NIPA) and BIS in the presence of linear polyacrylamide was higher than that of the swollen NIPA hydrogel alone. Elongation at break was significantly higher for semi-IPN gels compared to the hydrogels, especially, at lower crosslinking densities [13]. A pH-sensitive semi-IPN, composed of crosslinked poly(ethylene glycol) 8000 and Eudragit L100, has been used for control of GI drug delivery [14].

To prepare SPHs with high swelling ratios and good mechanical strengths in acidic medium or a gastric fluid, 3-sulfopropylacrylate potassium salt was used as a monomer and BIS and poly(ethylene glycol) diacrylate (PEGDA) were chosen as crosslinkers. The linear polymers that can be used as pharmaceutical excipients and act as bubble stabilizers in polymerization were added to the polymerization solution to form semi-IPNs. The swelling ratio of SPHs was determined by measuring the weight change, and mechanical strength was measured using a Texture Analyzer. The effect of these factors, such as ratios of PSA to crosslinkers, to initiator and to AAc, as well as acidification, on the swelling ratio and mechanical strength of SPHs were evaluated using a Taguchi orthogonal experimental design to obtain an optimal SPH suitable for application as gastric retention systems.

MATERIALS AND METHODS

Materials

Poly(vinyl alcohol) (PVA) (99% hydrolyzed Mw 124,000–186,000), acrylic acid (AAc), 3-sulfopropyl acrylate, potassium salt (SPA), poly(ethylene glycol) diacrylate (PEGDA), ammonium persulfate (APS), and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMED) were purchased from Aldrich Chemical Company, Inc. (Milwaukee, WI, USA). Hydroxypropyl methylcellulose (HPMC, Methocel K15M) was obtained from the Dow Chemical Company (Midland, Michigan, USA). Poly(ethylene oxide) (Mw 200,000) was bought from Union Carbide

Corporation (Danbury, CT). Propyl glycol alginate (MANUCOL®) was a gift from IPS Alginates Inc. (San Diego, CA). Poloxamer 188 was purchased from BASF Wyandotte Corporation (Parsippany, NJ). *N*,*N*′-methylene-bis-acrylamide (BIS) and carboxymethylcellulose were obtained from Sigma Chemical Co. (St. Louis, MO). Sodium bicarbonate was purchased from Mallinckrodt Baker, Inc. (Paris, Kentucky).

Preparation of Semi-IPN SPHs

PSPA-SPHs were synthesized as previously described [1,4]. The following components were added sequentially to a beaker: SPA (2.60×10^{-3} M); cross-linker (1.30×10^{-5} M); stabilizer (% w/w of SPA); AAc (6.94×10^{-4} M); APS (6.67×10^{-5} M) and mixed using a magnetic stirrer. Then, TMED (6.67×10^{-5} M) was added and, finally, $NaHCO_3$ (2.08×10^{-3} M) powder was added to the mixture and the gelling occurred within 30 s to 1 min. Polymerization was allowed to continue for 10 min. The SPH composite formed was retrieved from the beaker and the SPHs were purified with ethanol. The samples were dried at 60°C in a vacuum oven directly or after being washed in simulated gastric fluid (SGF, pH 1.2) for 24 h which was called acidification of the SPH.

Experimental Design

Based on the preliminary experiments on variables that have effects on the swelling ratio and mechanical strength of resultant SPHs, the ratio of SPA to crosslinker, initiator, and AAc, as well as acidification of SPHs were chosen as the four factors to be studied; each factor had three levels (Table 1). A Taguchi orthogonal experimental design [15] to optimize the combination through 9-run experiment was performed and the experiments were repeated three times. The amount of SPA, PVA (5% w/w) and other variables were maintained constant in the experiments.

The results were analyzed using a SAS® program 8.2e. Because the system can be optimized when the response of swelling ratio or mechanical strength is as large as possible, the ''signal-to-noise ratio'' for the ''Larger the Better'' (SN_L) was calculated using the following equation [15]:

$$SN_L = -10 \log\left(\frac{1}{n}\sum_{i=1}^{n}\frac{1}{y_i^2}\right) \quad (1)$$

Table 1. Independent variables and their correspondence between real and orthogonal values in the orthogonal experimental design.

		Levels		
	Factors	1	2	3
A	SPA:PEGDA (Mole:Mole)	400:1	200:1	100:1
B	SPA:APS (Mole:Mole)	200:1	100:1	50:1
C	SPA:AAc (Mole:Mole)	1:0	8:1	4:1
D	Acidification*	X1	X2	X3

*X1: Acidified in pH 1.2 HCl, purified with ethanol, and then dried.
X2: Purified with ethanol, acidified with pH 1.2 HCl, and dried.
X3: Purified with ethanol and then dried.

Characterization of PSPA-SPHs

Swelling Kinetics

The dried SPHs were used to determine their swelling ratio in pH 1.2 and pH 3.0 HCl solutions and distilled water. To calculate the swelling ratio, the following equation was used:

$$Q = \frac{W_s - W_d}{W_d} \tag{2}$$

where Q is the swelling ratio, W_s the mass in the swollen state, and W_d the mass in the dried state. At the beginning of each experiment, the W_d of each sample of SPH was measured by weight and then immersed into different pH media for swelling, respectively. At predetermined time intervals, the swollen SPHs were removed from the media and weighed. If the swollen SPH appeared to be fragile, it was put on a grid boat with a mesh size of 1 mm. This technique allowed the polymer to be put in water and to weigh it without being broken. Each time, the grid boat with the polymer was removed from the water and gently dried with paper tissue to remove excess water.

Mechanical Strength

A fully swollen SPH was cut into cubic pieces 1 cm in length, width, and height. The mechanical strength of SPH was determined using a Texture Analyzer (TA-XT2, Texture Technologies Corp., Scarsdale, New York). The SPH samples were compressed by 8.0 mm at a pre-test, test, and post-test speed of 2.0, 0.5, and 2.0 mm/s, respectively. The auto trigger compression force was 5.0 g. The maximum peak force during compression was recorded and the mechanical strength of SPH was calculated by dividing the force (g) with the transverse area (cm^2).

Structure of SPHs

The morphology of porous structures of semi-IPN PSPA-SPHs were analyzed using a JSM-840 SEM (JEOL USA, Inc., Peabody, MA). Before analysis, the dried samples were cut to expose their inner structures using a scalpel, coated with a thin layer of palladium gold alloy in Hummer I Sputter Coater (Technics, Alexandria, VA). SEM images were captured using a digital capture card and Digital Scan Generator 1.

RESULTS AND DISCUSSION

Effect of Stabilizers on the Swelling Ratio and Mechanical Strength of SPHs

Linear polymers that can be used as pharmaceutical excipients were chosen as foam stabilizers during the polymerization process. The effect of the stabilizers on the swelling ratio and mechanical strength of SPHs in different pH media are listed in Table 2. The results showed that PVA was the best stabilizer that improved the mechanical strength of SPH with high swelling ratios as compared to other linear polymers. It has been reported that the degree of hydrogen bonding by the hydroxyl groups in PVA govern the elastic behaviors of PVA in water [16].

HPMC, Poloxamer 188, and PEO did not increase the mechanical strength of the swollen SPHs. These polymers may have been partially

Table 2. The swelling ratio and mechanical strength of PSPA-SPH containing different stabilizers in various media (n = 3).

Stabilizer (2.0%)	Swelling Ratio (5 h)			Mechanical Strength (5 h)		
	pH 1.2	pH 3.0	Water	pH 1.2	pH 3.0	Water
CMC-Na	34.1 ± 6.2	180.4 ± 20.1	245.6 ± 34.5	+	−	− −
Carbopol 934 P	52.8 ± 5.8	225.9 ± 30.2	306.3 ± 39.4	−	−	− −
HPMC	38.4 ± 6.4	245.3 ± 28.4	257.5 ± 36.5	−	−	− −
Propylglycol alginate	35.6 ± 4.9	120.5 ± 18.9	220.4 ± 29.1	+ −	−	−
Sodium alginate	43.3 ± 5.7	228.6 ± 26.5	298.4 ± 36.4	+	+ −	−
Calcium alginate	41.3 ± 6.8	168.4 ± 15.4	259.7 ± 21.3	+	+ −	−
PEO 200,000	45.2 ± 7.2	268.0 ± 36.7	284.7 ± 40.6	−	−	− −
Poloxamer 188	46.9 ± 5.4	278.6 ± 32.4	301.4 ± 48.2	−	−	− −
PVP K90	46.2 ± 6.1	265.3 ± 28.6	279.4 ± 31.4	−	−	− −
PVA126	46.6 ± 5.6	279.9 ± 26.8	294.1 ± 32.5	+++	++	+

+++ : ≥ 150 g/cm^2
++ : ≥ 100 g/cm^2
+ : 70–100 g/cm^2
+ − : 50–70 g/cm^2
− : ≤ 50 g/cm^2
− − : broken (≤ 50 g/cm^2)

extracted when the SPHs were purified with ethanol since they can dissolve in both water and ethanol [17]. Carbopol 934P is a good stabilizer, but it did not significantly improve the mechanical strength of SPH. Sodium alginate, propyl glycol alginate, and CMC-Na do not dissolve in ethanol, but do form a gel in acidic pH, and thus, the mechanical strength of the SPHs containing these polymers was improved in the acidic media. However, the gels formed were not very elastic in acidic medium and the swelling ratio of SPHs was lowered. When SPHs containing sodium alginate was immersed into calcium chloride solution, calcium alginate SPHs were formed [17]. In an acidic medium, calcium alginate becomes an alginate gel and the SPH obtained had similar properties to that of sodium alginate SPH.

Effect of Crosslinkers on the Swelling Ratio and Mechanical Strength of SPHs

BIS and PEGDA were used as crosslinkers and the ratio of PSA to crosslinker was 200:1. Shown in Figures 1A and 1B are the effects of the crosslinkers on the swelling ratio and mechanical strength of SPHs at 37°C, respectively. The swelling ratios increased following the increase of pH values of media. The swelling ratios of SPHs using BIS as a crosslinker were higher than the corresponding swelling ratios of the SPHs crosslinked by PEGDA in pH 3.0 aqueous solution and in distilled water. However, the mechanical strength significantly decreased as the pH increased due to the high swelling ratios in high pH media. Considering the fact that PEGDA is a commonly used monomer in pharmaceutical field [18], PEGDA was chosen in the preparation of PSPA-SPHs.

Effect of Temperature on the Swelling Ratio of SPHs

Shown in Figure 2 are the swelling kinetics of SPHs at 25°C in various media. The temperature had a significant effect on the swelling kinetics. When the temperature was increased from 25°C (Figure 2) to 37°C (Figure 1A), the swelling ratio and kinetics significantly increased in all the media tested. The temperature effect on the swelling ratio might be due to the association/dissociation of hydrogen bonding between the hydroxyl groups in the PVA and the carboxyl groups and sulfonate groups in the PSPA within the semi-IPN. All the PVA/PAAc IPNs exhibited a temperature-responsive swelling behavior due to the association/dissociation of the hydrogen bonding between the hydroxyl groups in the PVA and the carboxyl groups in the PAAc within the IPN [19,20].

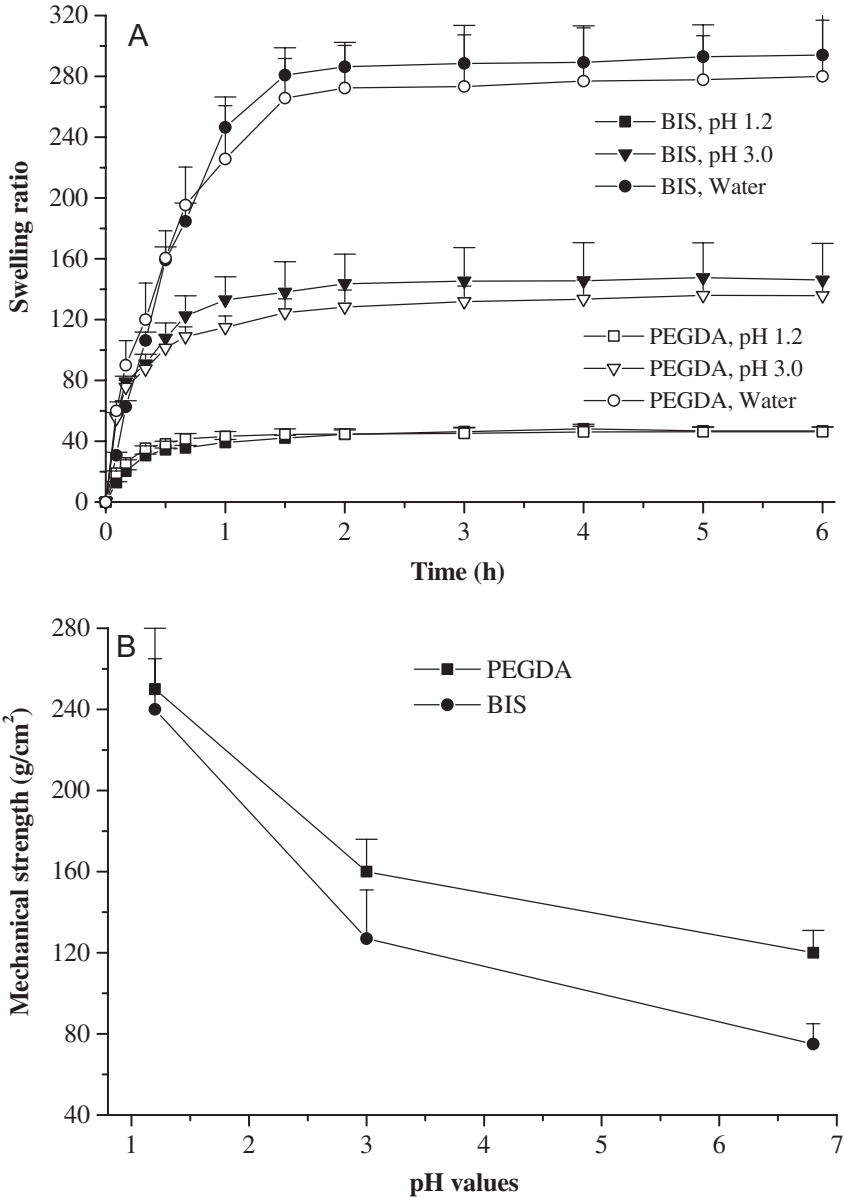

Figure 1. The swelling ratio (A) and mechanical strength (B) of PSPA-SPHs containing 2.0% PVA cross-linked with *N*,*N*′-methylenebisacrylamide (BIS) and poly(ethylene glycol) diacrylate (PEGDA) at 37°C. Data are means ± SD ($n = 3$).

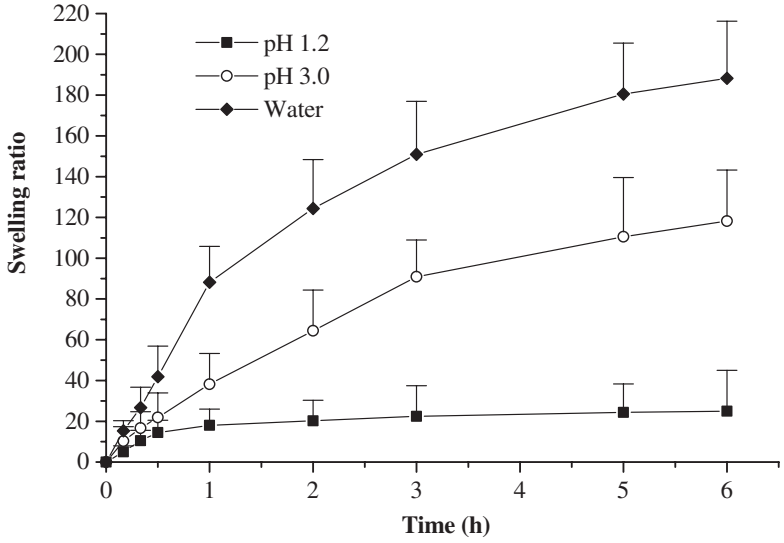

Figure 2. Swelling kinetics of PSPA-SPHs containing 2.0% PVA at 25°C. Data are means ± SD ($n = 3$).

The bound water, which is involved in the hydrogen bonding with the polymer, is known to decrease with temperature, while the free water, which has no interaction with polymer chains, is known to increase with the increase in temperature [21].

Effect of PVA Content on the Swelling Ratio and Mechanical Strength of SPHs

Shown in Figure 3 are the swelling kinetics of PSPA-SPHs containing different amounts of PVA. The swelling ratios and rates decreased with the increase of PVA content in the SPHs (Figures 3A, 3B, and 3C). As the PVA content increases in the semi-IPN, the degree of the hydrogen bonding between the hydroxyl groups of PVA and the carboxyl and sulfonate groups of PSPA-SPHs became higher. The swelling ratio of the semi-IPN drastically decreased as the content of PVA in PAAc network increased [22]. The mechanical strength increased following the increase of the PVA content in SPHs (Figure 3D). In the wet state, the tensile strength of PVA/PAAc IPN greatly increased with increase of the PVA content in the IPNs [22]. When PSPA-SPH contained 5% w/w PVA, the swelling ratio was high and the mechanical strength was high enough to withstand the stomach contraction pressure of 100–130 g/cm^2 in humans [23,24].

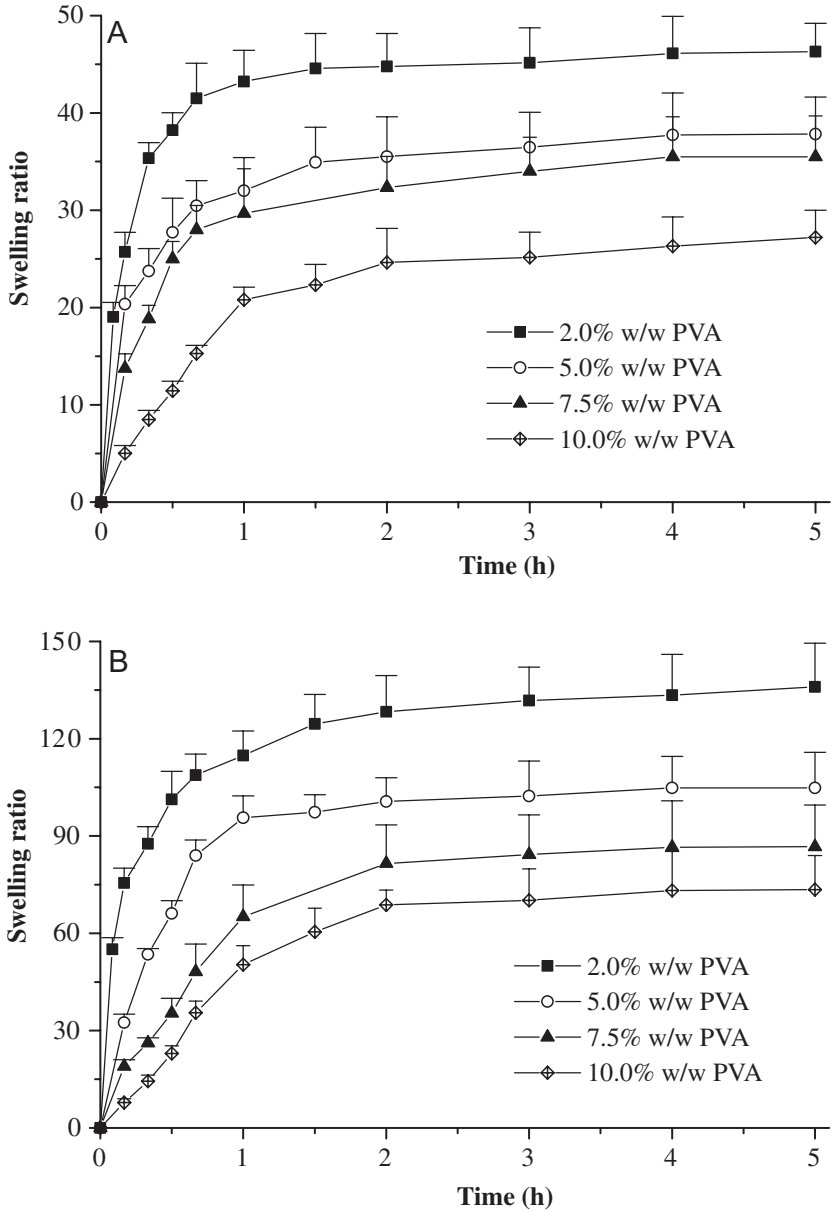

Figure 3. Swelling kinetics of PSPA-SPHs containing various amounts of PVA at 37°C in pH 1.2 (A), pH 3.0 (B), and distilled water (C), and the corresponding mechanical strengths (D). Data are means ± SD ($n = 3$).

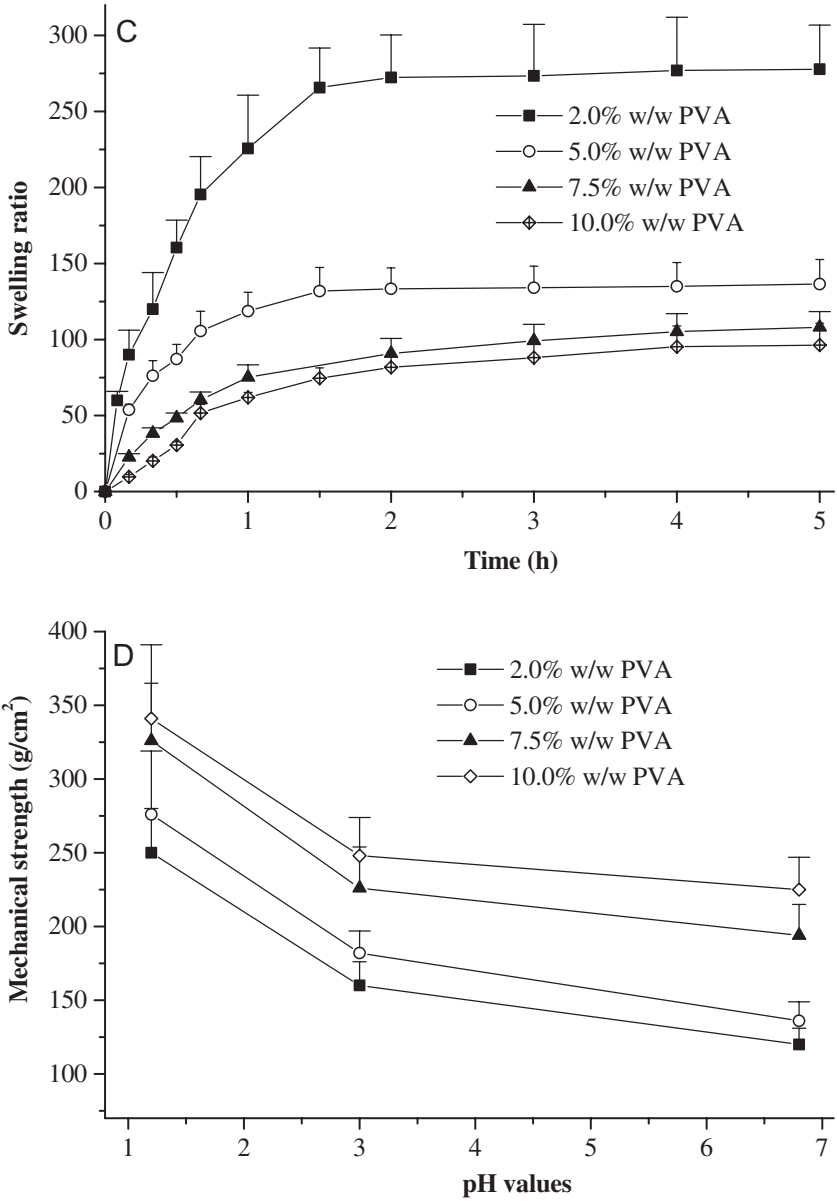

Figure 3. Continued.

Effect of pH on the Swelling Ratio and Mechanical Strength of SPHs

The pH values of swelling media showed a significant effect on the swelling ratios of PSPA-SPHs (Figures 1A, 2, and 3). The swelling ratios increased significantly with increasing pH values. PSPA-SPH is an ionic hydrogel containing sulfonic acid group, which showed either sudden or gradual changes in their dynamic and equilibrium swelling behavior as a result of changing the external pH [18,22]. As the pH increases, the degree of ionization of fixed charges increases, resulting in increased electrostatic repulsion between the chains. This leads to an increased hydrophilicity of the polymeric network and greater swelling ratios [18]. The pKa value of PSPA is 3.97 in a non-salt solution and it is decreased with the addition of salts, such as NaCl, and KCl [25]. As the salt concentration increased, the pKa greatly decreased. An increase of ionic strength from 0.1 to 1.0 M caused the pKa to decrease from 3.51 to 3.2 at the half-neutralization point [25]. Increase in ionic strength suppressed the swelling ratio of PSPA. The pKa value of poly(acrylic acid) is 4.28, and thus, at a pH less than 4, poly(acrylic acid) chains are in the collapsed state, reducing the swelling ratio. However, as the pH increases above 6, the poly(acrylic acid) forms carboxylate ions, which cause repulsion between the network, resulting in rapid increase in the swelling ratio. Electrostatic repulsion between the carboxylic acid in the polymer chains, the ions present in the buffer solution, and the ionic osmotic pressure generated by mobile counter ions to charged ions in the network may also be responsible for the increase in swelling [11].

The strength of SPHs decreased with increasing pH values (Figures 1B and 3D). As the pH increased, the swelling ratios increased and the mechanical strength decreased. The mechanical properties of the PVA/PAAc IPN were influenced more by the degree of swelling rather than by the crosslinking density with the IPN in a fully swollen state [22].

Experimental Design

Taguchi orthogonal experimental design [$L_9(3^4)$] provided an investigation of four independent variables at three levels after performing only a 9-run experiment. Selection of factors and levels in the design was based on the results of preliminary data. Shown in Table 3 are the variables and results of the Taguchi orthogonal experimental design. Listed in Tables 4 and 5 are the ANOVA results of the swelling ratio in the enzyme-free simulated gastric fluid (pH 1.2) at 20 min and the

Table 3. Variables and results of Taguchi orthogonal experimental design [$L9(3^4)$].

	Independent Variables				Swelling Ratio at 20 min					Mechanical Strength at 5 h (g/cm^2)				
Run	A	B	C	D	1	2	3	Mean (SD)	SN_L	1	2	3	Mean (SD)	SN_L
1	1	1	1	1	14	17.2	16.4	15.9 ± 1.7	23.91	307.0	330.0	298.0	311.7 ± 16.5	49.85
2	1	2	2	2	15.9	20.4	19.6	18.6 ± 2.4	25.25	188.0	230.0	180.0	199.3 ± 26.9	45.85
3	1	3	3	3	12.7	16.5	15.6	14.9 ± 2.0	23.32	210.0	280.0	285.0	258.3 ± 41.9	47.98
4	2	1	2	3	10.2	10.2	8.4	9.6 ± 1.0	19.53	124.0	155.0	110.0	129.7 ± 23.0	42.00
5	2	2	3	1	10.5	11	12.4	11.3 ± 1.0	21.00	320.0	220.0	260.0	266.7 ± 50.3	48.22
6	2	3	1	2	17.4	19.2	21.4	19.3 ± 2.0	25.63	330.0	360.0	310.0	333.3 ± 25.2	50.41
7	3	1	3	2	9.5	8.4	10.8	9.6 ± 1.2	19.48	480.0	450.0	440.0	456.7 ± 20.8	53.17
8	3	2	1	3	6.4	7	7.2	6.9 ± 0.4	16.70	226.0	260.0	195.0	227.0 ± 32.5	46.94
9	3	3	2	1	14.3	16.9	13.3	14.8 ± 1.9	23.30	250.0	220.0	220.0	230.0 ± 17.3	47.19

Table 4. ANOVA of the swelling ratio of PSPA-SPHs in enzyme-free simulated gastric fluid (pH 1.2) at 20 min.

Source	Degree of Freedom	Sum of Squares	Mean Square	F Value	Pr > F
A	2	165.02	82.51	31.45	< 0.0001
B	2	117.43	58.71	22.38	< 0.0001
C	2	31.03	15.51	5.91	0.0106
D	2	134.42	67.21	25.62	< 0.0001
Error	18	47.23	2.62		
Total	26	495.12			

Table 5. ANOVA of mechanical strength of PSPA-SPHs at the fully swollen state.

Source	Degree of Freedom	Sum of Squares	Mean Square	F Value	Pr > F
A	2	18753.85	9376.93	10.24	0.0011
B	2	21468.96	10734.48	11.73	0.0005
C	2	96214.3	48107.15	52.55	< 0.0001
D	2	70088.07	35044.14	38.28	< 0.0001
Error	18	16478.67	915.48		
Total	26	223003.85			

mechanical strength at equilibrium swelling, respectively. The factors *A*, *B*, and *D* had significant effects on the swelling ratio of semi-IPN SPH. But, the factors *C* and *D* had significant effects on the mechanical strength.

The crosslinking ratio is one of the most important factors affecting the swelling of hydrogels. With a change in the degree of crosslinking, the degree of swelling of IPNs was also different [26]. The high ratio of initiator to SPA should provide low molecular weight PSPA. When the molar ratio of SPA to initiator was 50:1, there was a high swelling ratio and a good mechanical strength (Figure 4).

A small amount of AAc significantly increased the mechanical strength, but had little effect on the swelling property of PSPA-SPHs. However, acidification had a great effect on the swelling property and mechanical strength (Figure 4). When the PSPA-SPH was put into absolute ethanol first to extract the water in SPH, dried, and then acidified with pH 1.2 HCl, the resulting SPH had a good swelling property and high mechanical strength. It has been reported that the ionic strength can affect the swelling ratio of hydrogels and IPNs [18,22].

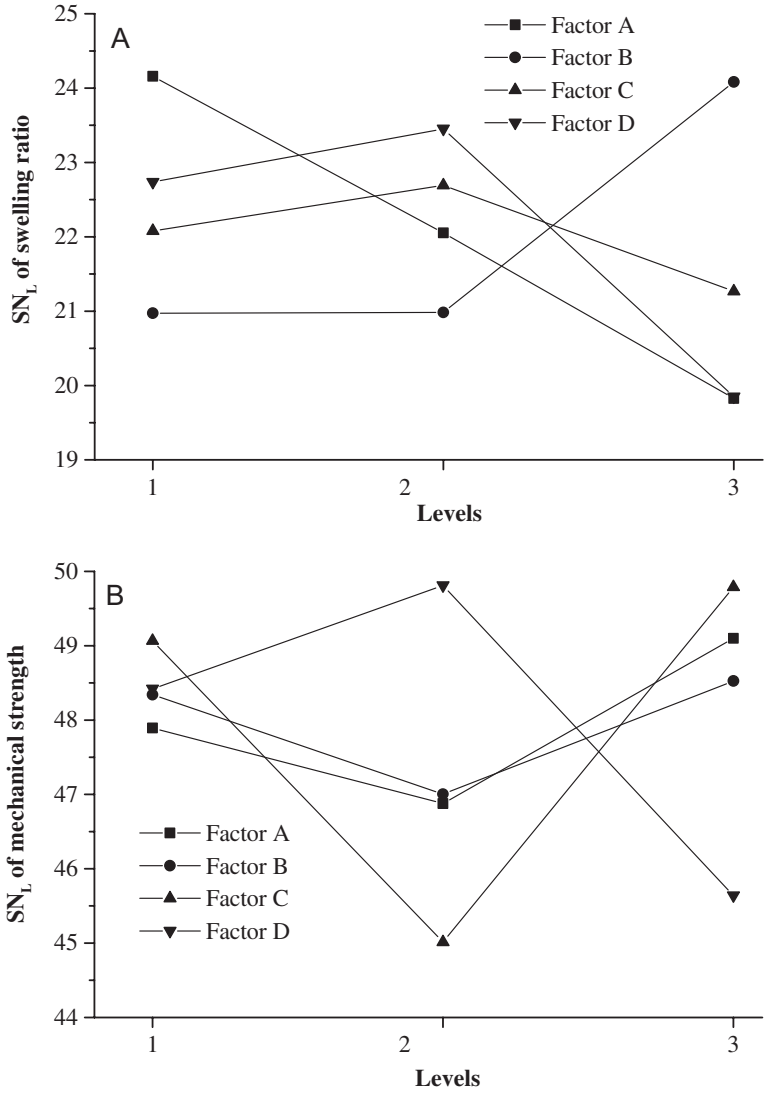

Figure 4. Effects of controllable factors on SN_L of swelling ratio (A) and mechanical strength (B).

The mechanical strength was improved by acidification of the SPAK residues. The acidification process partially protonated the anionic $-SO_3^-$ group to form the $-SO_3H$ group. The decrease in overall negative charges is expected to increase interactions between polymer chains and thus increase in mechanical strength [27].

The SN_L was used to optimize the semi-INP PSPA-SPHs because the use of the SN ratio generally eliminates the need for examining specific interactions between the controllable and noise factors [15]. Shown in Figure 4 are the effects of controllable factors on SN_L of swelling ratio and mechanical strength.

The maximal stomach contraction pressure in the fasted and fed states is known to range from 100 to 130 g/cm^2 in humans [23,24]. The results (Table 3) indicate that the mechanical strength of PSPA-SPH in enzyme-free simulated gastric fluid (pH 1.2) was higher than the maximal stomach contraction pressure for all samples in a full swollen state; this indicated that all the samples had enough strength to withstand the gastric peristaltic contraction. The swelling ratio was the only considered response in the optimization for the use of PSPA SPH in gastric retention drug delivery systems. According to the data in Figure 4 and Table 3, the optimal setting with the highest swelling ratio was $A_1B_3C_2D_2$. The molar ratios of SPA : PEGDA, SPA : initiator, and SPA : AAc were 400 : 1, 50 : 1, and 8 : 1, respectively. The acidification of the synthesized PSPA-SPH was first extracted using alcohol and then acidified using pH 1.2 HCl, washed with distilled water and the SPH was dried in an oven at 60°C. The optimal experimental setting was performed three times. The optimal PSPA-SPH had a swelling ratio of 24.3 ± 2.1 at 20 min and 37.8 ± 3.8 at full swollen state in pH 1.2 medium with a mechanical strength of 206.7 ± 26.8 g/cm^2 in the fully swollen state (5 h).

Structure of Optimal PSPA-SPH

The structures of the optimized PSPA-SPHs were examined under SEM. Shown in Figure 5A are superpore structures with diameters ranging from 100 to 2000 μm in the optimal PSPA-SPH. Along the walls and ridges of these superpores, there are many capillaries and/or micropores with the diameters ranging from 1.0 to 100 μm (Figure 5B). The superpores and/or micropores are connected to one another forming extensive capillary channels; these cause the dried SPHs to reach their fully swollen size in only a few minutes [1]. Seen in Figure 5, the capillaries have an orientation due to the gas generated rising from the bottom to the top of the container while the pores were being formed. The orientation of capillaries in SPH has been recognized and the direction of compression had a significant effect on the swelling kinetics of SPHs [28]. When SPHs were compressed radially, the interconnected porous structure was retained and the swelling equilibrium was reached within minutes regardless of the compression pressure

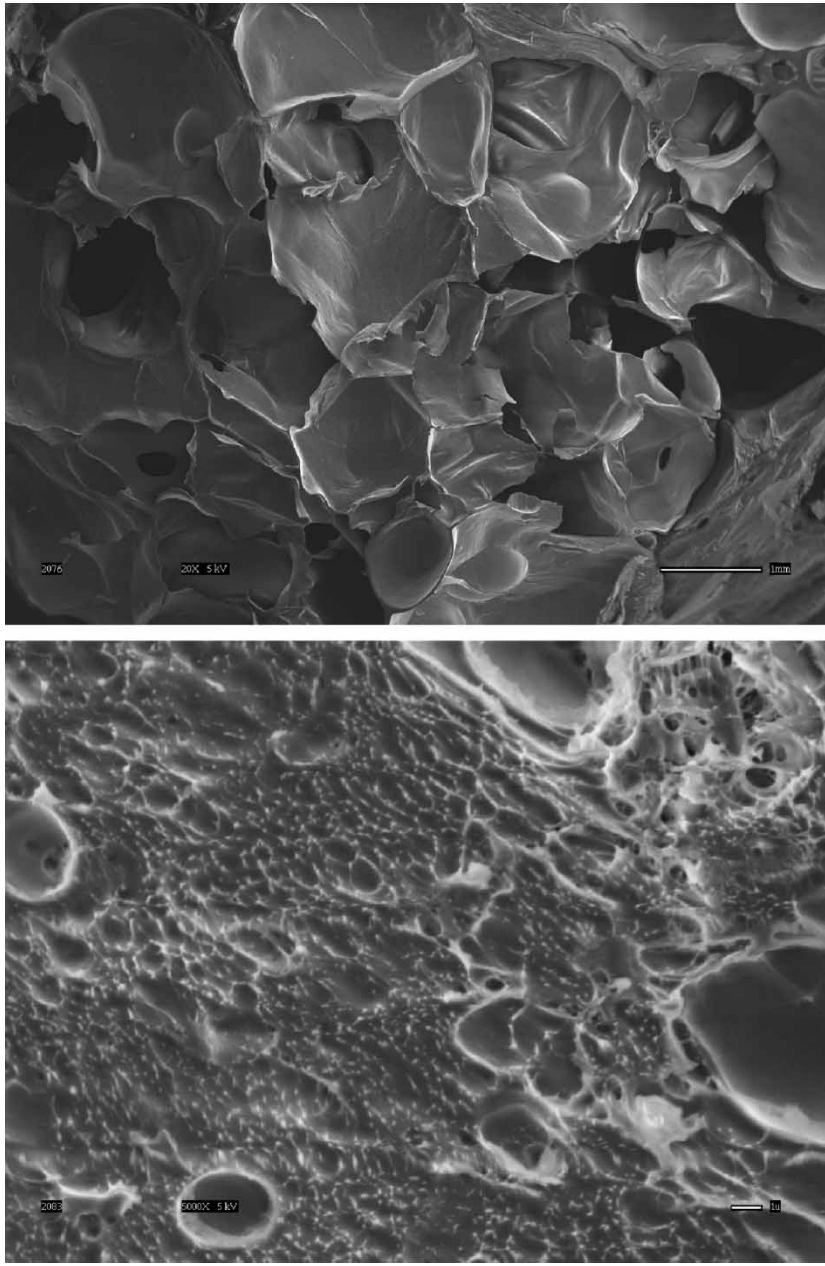

Figure 5. Scanning electron micrographs of an optimal superporous hydrogel (A: $\times$ 20; B: $\times$ 5000).

used. When the SPHs were compressed axially, the interior porous SPH structure was nearly closed after compression, thus, resulting in a decreased swelling rate [28].

CONCLUSIONS

PSPA-SPHs were prepared by crosslinking SPA with PEGDA or BIS to form a network. Among the polymers used, PVA was the best linear polymer to form semi-IPNs for improving the mechanical strength of swollen PSPA-SPHs as well as a very effective foam stabilizer in the polymerization. The swelling ratios of PSPA-SPHs were significantly influenced by the ratio of SPA to PEGDA and to initiator, and acidification. The ratio of SPA to AAc and acidification had significant effects on the mechanical strength. Based on the Taguchi orthogonal experimental design, the optimal setting was generated as $A_1B_3C_2D_2$: SPA : PEGDA (400 : 1), SPA : APS (50 : 1), SPA : AAc (8 : 1) and acidification. The optimal PSPA-SPH contained superpores with diameters from 100 to 2000 μm and capillaries (and/or micropores) with diameters ranging from 1.0 to 100 μm along the walls and ridges of the superpores to form extensive capillary channels. The optimal PSPA-SPH has a high swelling ratio and good mechanical strength making it suitable as a platform in the development of gastric retention drug delivery systems.

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