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ARTICLE *in* JOURNAL OF APPLIED POLYMER SCIENCE · APRIL 2012

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Controlled Mechanical and Swelling Properties of Poly(vinyl alcohol)/Sodium Alginate Blend Hydrogels Prepared by Freeze–Thaw Followed by Ca^{2+} Crosslinking

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Received 28 December 2010; accepted 13 June 2011
DOI 10.1002/app.35083
Published online 10 October 2011 in Wiley Online Library (wileyonlinelibrary.com).

ABSTRACT: Poly(vinyl alcohol) (PVA)/sodium alginate (SA) blend hydrogels have immense potential for use as functional biomaterials. Understanding of influences of processing parameters and compositions on mechanical and swelling properties of PVA/SA blend hydrogels is very important. In this work, PVA/SA blend hydrogels with different SA contents were prepared by applying freeze–thaw method first to induce physical crosslinking of PVA chains and then followed by Ca^{2+} crosslinking SA chains to form interpenetrating networks of PVA and SA. The effects of number of freeze–thaw cycles, SA content and Ca^{2+} concentration on mechanical properties, swelling kinetics, and pH-sensitivity of the blend hydrogels were investigated. The results showed that the blend hydrogels have porous sponge structure. Gel fraction, which is related to crosslink density of the blend hydrogels, increased with the increase of freeze–thaw cycles and strongly depended on SA content. The SA content exerts a significant effect on mechanical properties, swelling kinetics, and pH-sensitivity of the blend hydrogels. The number of freeze–thaw cycles has marked impact on mechanical properties, but no obvious effect on the pH-sensitivity of the PVA/SA blend hydrogels. Concentration of $CaCl_2$ aqueous solution also influences mechanical properties and pH-sensitivity of the blend hydrogel. By altering composition and processing parameters such as freeze–thaw cycles and concentration of $CaCl_2$ aqueous solution, the mechanical properties and pH-sensitivity of PVA/SA blend hydrogels can be tightly controlled.
 J Appl Polym Sci 124: 823–831, 2012

Key words: poly(vinyl alcohol); sodium alginate; hydrogel; mechanical properties; pH-sensitivity

INTRODUCTION

Hydrogels were the first biomaterials designed for use in the human body. Hydrogels are more biocompatible than any other class of biomaterials due to their high water content and low interfacial tension with the surrounding biological environment, as well as their similarity to the highly hydrated macromolecular-based materials in the body.[1,2] Over the past few years, important advances have been made in the field of hydrogel biomaterials owing to the technology development and enormous demands in clinical application. However, many hydrogel biomaterials lack the desired functional properties to interface with biological systems and have not been engineered for optimized performance.[3]

Synthetic polymer hydrogels display controlled gelation process, structure, and mechanical properties. While some natural polymers exhibit superior and rare properties, for instance, collagen and hyaluronic acid have been shown to support tissue ingrowth and repair because of their inherent biological properties, and some natural polysaccharides including chitosan and CM-chitosan are suitable for wound dressing materials due to their antibacterial activity.[4,5] Therefore, blending synthetic polymers and natural polymers has been of special interest to develop new hydrogel materials to address the problem that many hydrogel biomaterials lack the desired functional properties.

Poly(vinyl alcohol) (PVA), a water-soluble synthetic polymer, can form stable and crystallizing hydrogel through freezing and thawing method. The hydrogel has been exploited as a biomaterial due to its viscoelastic nature, nontoxic, high-mechanical strength, biocompatibility, economy, and environmental friendly disposal.[6,7] PVA hydrogels have been used in a number of biomedical applications

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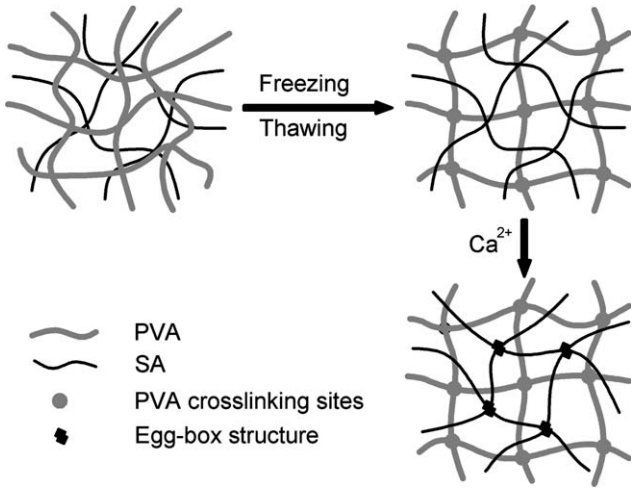
Contract grant sponsor: National Natural Science Foundation of China; contract grant number: 50673037.
Contract grant sponsor: Natural Science Foundation of Jilin Province of China; contract grant number: 20101538.
Contract grant sponsor: Jilin University; contract grant number: 985 Project.

including wound dressing,[8] controlled drug release system for oral use,[9] tissue engineering,[10] and artificial organs such as cartilages.[11] However, like most synthetic hydrogels, the use of PVA hydrogels has been limited by the lack of inherent recognition sites that are required for protein and cell interactions, which is the key point of biocompatibility.[12]

Sodium alginate (SA) is a linear polysaccharide consisting of 1, 4-linked β-D-mannuronic (M) and α-L-guluronic (G) residues in varying proportions, depending on its algal or bacterial origin.[13] Sodium alginate is soluble in aqueous solution and forms stable gels at room temperature in the presence of certain divalent cations (i.e., Ba^{2+}, Ca^{2+}), which can be complexed by carboxylate groups of G residues in a tetradentate structure, then forms the well-known egg-box model.[14,15] Calcium ion crosslinked sodium alginate possesses excellent properties and has been widely used in biomedical applications. SA hydrogel has been explored as a scaffold material for tissue engineering because of its structural similarity to the natural extracellular matrix (ECM), and it can guide cell adhesion, growth, and new tissue formation in 3-D structure when implanted in both animals and humans combined with various cells such as chondrocyte.[16,17] Also, SA hydrogel is beneficial to healing of wound, so it was used as a hemostatic wound dressing material.[18,19] It was reported that SA is nontoxic and biodegradable when given orally.[20] SA hydrogel shrinks at pH 1.2 (gastric environment) and swells at pH 7.4 (intestinal environment), suitable for the intestinal delivery of drugs.[21]

With immense potential for use as functional biomaterials, PVA/SA blend hydrogels have attracted significant interest in recent years. A series of fundamental studies on this blend system have been carried out in parallel with investigations on their biomedical applications. The PVA/SA blend hydrogels were fabricated by Ca^{2+} crosslinking only[22,23] or first Ca^{2+} crosslinking and then followed freeze–thaw cycles[23] and used as controlled release system having pH- and thermosensitivity as well as drug-loaded wound dressing.[24] However, little information is available on the effect of processing parameters and compositions on mechanical and swelling properties of PVA/SA blend hydrogels. Refined control over the mechanical and swelling properties remains necessary not only for designing PVA/SA blend hydrogels with controlled network structure and properties, but also for facilitating their practical applications as controlled release system and wound dressing.

In this work, PVA/SA blend hydrogels were prepared by two steps. First, the freeze–thaw method was applied to induce the physical crosslinking of PVA chains by the hydrogen bonding and crystallite formation; then, SA chains in the PVA-crosslinked mixture gels were chemically crosslinked in $CaCl_2$ aqueous solution to form interpenetrating networks (IPN)[25,26] as showed in Scheme 1. The effects of the number of freeze–thaw cycles, SA content and Ca^{2+} concentration on the mechanical properties, swelling kinetics, and pH-sensitivity of the blend hydrogels were investigated aiming at getting deeper insight of the relationship between properties and composition as well as processing conditions.



Scheme 1 Formation of the IPN of PVA/SA blend hydrogels.

EXPERIMENTAL

Materials

PVA with an average molecular weight of approximately 70,000 was obtained from Sinopharm Chemical Reagent Co. Ltd (Shanghai, China). SA was purchased from Tianjin Guangfu Fine Chemical Research Institute (Tianjin, China). Calcium chloride ($CaCl_2$) was sourced from Xilong Chemical Co. Ltd (Guangdong, China). All the chemicals were analytical grade and used as received without any further purification.

Hydrogel preparation

Both PVA and SA solutions were prepared at concentration of 5% (w/v). The powder materials were dissolved in distilled water, respectively, at 95°C for PVA and at room temperature (20°C) for SA, and continuously stirred for 6 h. The mixture solution was prepared by mixing the two solutions together in mass % ratios (PVA/SA) of 100/0, 75/25, 50/50, and 25/75, and then stirred for 6 h at room temperature. The mixture solution was poured into a stainless steel mold, frozen at −18°C for 22 h and thawed at room temperature for 2 h. The freeze–thaw process was repeated several cycles (*N*) to crosslink PVA. The PVA-crosslinked mixture gels were then immersed in $CaCl_2$ aqueous solution to crosslink SA, and the

PVA/SA hydrogel sheets were obtained. The samples for gel fraction determination and mechanical tests were cut from the obtained hydrogel sheets.

Gel fraction

The hydrogels with a dimension of 25 mm × 20 mm × 4 mm were fully dried in an oven at 50°C and weighted (W_0) in an analytical balance with a precision of 0.1 mg. To remove the soluble and unreacted matters, the dried gels were first soaked in DMSO for 24 h to dissolve unreacted PVA, and then in distilled water for 48 h to dissolve unreacted SA and remove residual DMSO. The insoluble part was filtered out, wiped lightly with filter paper, and fully dried again at 50°C and weighted (W_e). The gel fraction (GF) was calculated by the following equation:

$$\mathrm{GF}(\%) = \frac{W_e}{W_0} \times 100$$

where W_0 is the weight of initial dried gel, and W_e is the dried weight of the sample after extraction of soluble and unreacted matters.

SEM analysis

Surface and cross-sectional morphologies of the PVA/SA blend hydrogels were examined by using a JEOL (JSM-5600, Japan) SEM operated at an accelerating voltage of 25 kV. The hydrogel SEM samples were freeze-dried, fractured in liquid nitrogen and then coated with a gold-palladium layer using a sputter coater under nitrogen atmosphere.

Mechanical testing

Tensile tests

The tensile tests were carried out on an electronic universal testing machine (Model QJ-210, Shanghai Qingji, China) at a crosshead speed of 50 mm/min using a 100*N* loading cell. The specimens, 50 mm long dumbbells with 4 mm neck width, were cut from the hydrogels. The stress versus strain curve, Young's modulus, ultimate tensile strength, and elongation at break of each specimen were obtained. At least five specimens were measured for each experimental condition and the average values were taken.

Unconfined compression tests

PVA/SA hydrogels were tested in unconfined compression by using an electronic universal testing machine (Model QJ-210, Shanghai Qingji, China) with a 100*N* loading cell and following the procedure described by Joshi et al.[27] Cylindrical hydrogel specimens with a diameter of 55 mm and a thickness of 5 mm were compressed under displacement control at a rate of 5 mm/min until 40% strain was reached. Load and displacement data were recorded by computer and converted to stress–strain curve. Tangent compressive moduli at 15, 20, and 25% strain for each hydrogel specimen were obtained by calculating the slopes of a linear trend line formed with the stress–strain data ranged 10–20%, 15–25%, and 20–30% strain, respectively. At least three measurements for each specimen were recorded and a mean value was calculated.

Swelling characterization

Swelling kinetics

The dried samples with different SA content were immersed in distilled water at 37°C. At specific time intervals, the samples were taken out, blotted with filter paper to absorb excess water on the surface and weighed. The swelling ratio (SR, g/g) was determined according to following equation:

$$\text{Swelling ratio (SR)} = (W_t - W_0)/W_0$$

where W_0 is mass of dried sample and W_t is mass of swollen hydrogels at time t.

pH sensitivity

The pH sensitivity of the PVA/SA hydrogels was investigated by determining swelling ratios of the hydrogels according to the method in literature.[28] The dried samples were first immersed in 20 mL pH 1.2 (HCl - NaCl buffer) solution at 37°C for 6 h and subsequently transferred into 20 mL pH 7.4 medium (phosphate buffer) at 37°C. The swelling ratios (SR) of samples were calculated from the equation expressed in section of Swelling Kinetics.

RESULTS AND DISCUSSIONS

Gel fraction

The changes of gel fraction of PVA/SA blend hydrogels versus the number of freeze–thaw cycle as a function of SA content were shown in Figure 1. The gel fraction increased with the increase of freeze–thaw cycles and strongly depended on the SA content. This is because the increase of freeze–thaw cycles led to a higher crosslink density of PVA network in the hydrogels, and more PVA molecular chains were involved in formation of the network, meanwhile more residual free PVA molecular chains in the hydrogels could be blocked in junction zones. All of these could result in higher gel fraction. As showed in Figure 1, the value of gel fraction

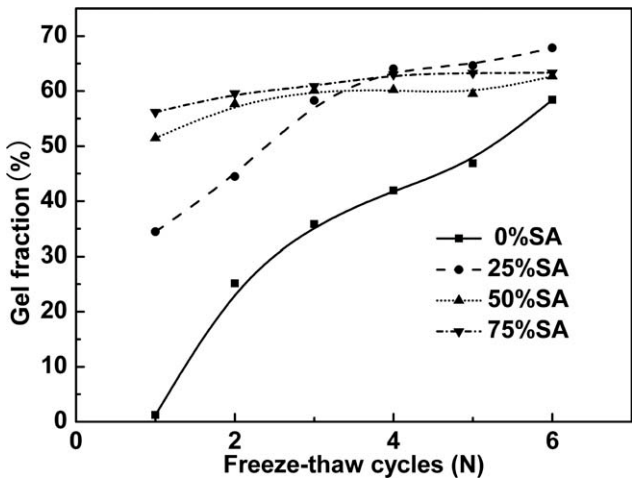


Figure 1 Gel fraction of PVA/SA blend hydrogels as a function of freeze–thaw cycles for different compositions (CaCl2: 2%).

changed rapidly with freeze–thaw cycles for the PVA/SA blend hydrogels containing lower SA contents (i.e., 0%, 25%), while it altered slightly for those with higher SA contents (i.e., 50%, 75%). This can be explained by the fact that the physical crosslinking of PVA occurs easily when the hydrogels possessed a high PVA concentration and less obstacles exist among PVA molecular chains, which could give rise to an increasing number of physical crosslink junction in the hydrogels. It was noted that the gel fraction of the samples with 100% PVA was lower than those containing SA, this is because the samples containing SA were crosslinked not only by freeze–thaw but also by Ca^{2+} crosslinking, which gave rise to much more crosslink junctions in the samples and resulted in a higher gel fraction compared to pure PVA sample.

SM observations

SEM observations showed that the PVA/SA blend hydrogels with different SA contents have porous sponge structure. Surface and cross-sectional SEM photographs of the blend hydrogel containing 50% SA were given in Figure 2. The observations of the SEM photographs also indicated blend homogeneity between PVA and SA networks. The porous texture of PVA/SA blend hydrogels could have excellent adhesion and growth for seeded cells.[26]

Mechanical properties

Tensile properties

For the blend hydrogel system in this work, the tensile properties were affected by SA content, number of freeze–thaw cycles and concentration of $CaCl_2$ aqueous solution because these parameters determine nature and crosslink density of IPN. Table I presented the tensile properties of the hydrogels prepared in various conditions. The samples in Table I were coded as A-B-C, where A is the SA content (%), B is the freeze–thaw cycles and C is the concentration (w/v) of calcium chloride aqueous solution. For instance, the 75-4-2 sample contained 75% SA and were prepared by four freeze–thaw cycles and then put into 2% (w/v) $CaCl_2$ aqueous solution. As shown in Table I, the tensile strength decreased with increasing of SA content. However, the elongation at break of the hydrogels increased with increasing of SA content up to a certain level then dropped rapidly when SA content was 75%. The change of Young's modulus showed a reversed tendency to that of elongation at break. It is known that PVA gels are soft and elastic, whereas SA gels are rigid and brittle.[29] For the blend hydrogels in this study, the PVA network was first formed and this network would restrict the formation of SA network. When PVA content was high, the blend hydrogels were PVA dominant and showed good flexibility and

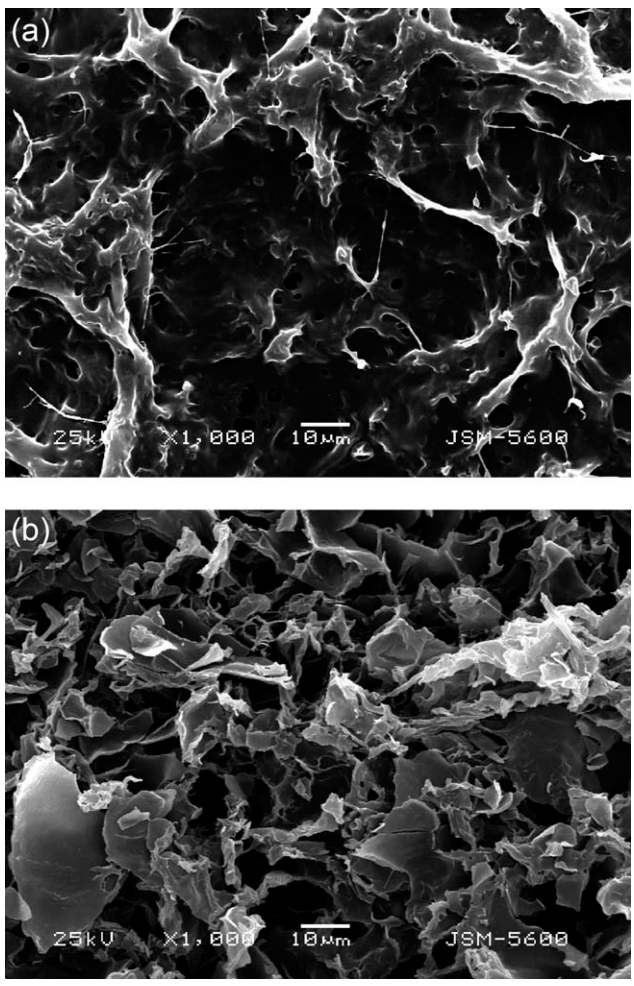


Figure 2 SEM micrographs of PVA/SA blend hydrogel (SA: 50%; $N = 4$; CaCl2: 2%), (a) surface; (b) cross section.

TABLE I
Tensile Properties of the PVA/SA Hydrogels

Samples No.	Tensile strength (kPa)	Elongation at break (%)	Young's modulus (kPa)
0–4–2	263 ± 33	275 ± 44	100 ± 5
25–4–2	192 ± 11	309 ± 30	64 ± 4
50–4–2	102 ± 9	380 ± 20	23 ± 1
75–4–2	50 ± 2	106 ± 1	44 ± 3
50–2–2	65 ± 5	278 ± 17	20 ± 1
50–4–2	102 ± 9	380 ± 20	23 ± 1
50–6–2	111 ± 5	426 ± 22	24 ± 1
50–4–1	61 ± 2	248 ± 20	21 ± 1
50–4–2	102 ± 9	380 ± 20	23 ± 1
50–4–3	95 ± 6	346 ± 24	25 ± 1
50–4–4	116 ± 8	339 ± 20	31 ± 1

high tensile strength. However, when SA content was up to higher level (i.e., 75%), formation of PVA network was influenced and meanwhile the effect of PVA on the formation of SA network declined, the blend hydrogels were SA dominant and possessed rigid and brittle characteristics.

The data in Table I indicated that the number of freeze–thaw cycles correlated positively with tensile strength and elongation at break. For the hydrogels containing 50% SA and immersed in 2% $CaCl_2$ aqueous solution, the tensile strength increased rapidly from 65 kPa to 111.2 kPa, elongation at break increased from 278 to 426%, when freeze–thaw cycles rose from 2 to 6. These results are consistent with the reported ones for pure PVA hydrogels.[30] From the data of Young's modulus, it can be seen that the Young's modulus of the blend hydrogels increased slightly with increment of freeze–thaw cycles. The above results suggested that, when the freeze–thaw treatment was repeated, the tensile strength and elongation at break of the blend hydrogels could increase substantially while flexibility of the hydrogel would only change slightly. This characteristic could be of great significance when the PVA/SA blend hydrogels is recommended as wound dressing material, as its strength and elongation at break can be improved by controlling freeze–thaw cycles, while its ability to conform to body surface would not be affected dramatically.

As illustrated in Table I, the tensile strength and Young's modulus of the blend hydrogels increased with increasing of the concentration of $CaCl_2$ aqueous solution, this is because more Ca^{2+} bonded to the SA chains when higher concentration $CaCl_2$ aqueous solution was used, which gave rise to a highly crosslinked SA network. The high crosslink density enhanced the strength of SA network and resulted in a decrease in the flexibility of the blend hydrogels. In addition, the elongation at break increased with concentration of $CaCl_2$ aqueous solution first, but decreased when the concentration exceeded 2% (w/v). This is because the treatment by using 1% $CaCl_2$ solution may not be able to form a sufficiently crosslinked SA network in the hydrogel, while the higher crosslink density resulted from the treatments by using $CaCl_2$ aqueous solution with concentration exceeded 2% (w/v) lead to a decrease in the elongation at break.

Unconfined compression properties

The effects of SA content, freeze–thaw cycles and concentration of $CaCl_2$ aqueous solution on the compressive properties of the PVA/SA blend hydrogels were studied. Compressive modulus determined at 15, 20, and 25% strain for the blend hydrogels with different SA contents were summarized in Table II. The data in Table II showed that the compressive modulus increased with increasing of SA content. Compared with pure PVA samples, the increasing amount of compressive modulus at 20% strain for the samples containing 25, 50, and 75% SA were 15, 85, and 322%, respectively. These results indicated that the blend hydrogels became stiff after incorporating a high SA content into the system. As presented in Table II, under unconfined compression, compressive modulus of PVA/SA hydrogels increased with increasing strain magnitude, suggesting a nonlinear stress–strain response.

The changes of compressive modulus of the blend hydrogels with the number of freeze–thaw cycles was also presented in Table II. The compressive moduli at 15, 20, and 25% strain increased when increasing freeze–thaw cycles. The changes of compressive modulus versus concentration of $CaCl_2$ aqueous solution were similar to that of freeze–thaw cycles. Since crosslink density of the blend hydrogels increased with increasing of freeze–thaw cycles and concentration of $CaCl_2$ aqueous solution, it may conclude that the blend hydrogels with higher crosslink density possess higher compressive modulus, i.e., more excellent compression resistance capability.

TABLE II
Compressive Modulus (kPa) of the PVA/SA Hydrogels at Various Strains

Samples no.	15% strain	20% strain	25% strain
0–4–2	16 ± 2	20 ± 1	24 ± 1
25–4–2	17 ± 2	23 ± 1	29 ± 4
50–4–2	31 ± 6	37 ± 5	41 ± 1
75–4–2	67 ± 3	84 ± 3	95 ± 4
50–2–2	18 ± 1	29 ± 2	40 ± 4
50–4–2	31 ± 6	37 ± 5	41 ± 1
50–6–2	68 ± 1	76 ± 5	91 ± 2
50–4–1	15 ± 7	20 ± 7	25 ± 7
50–4–2	31 ± 6	37 ± 5	41 ± 1
50–4–3	54 ± 2	77 ± 2	89 ± 3
50–4–4	65 ± 5	94 ± 4	107 ± 2

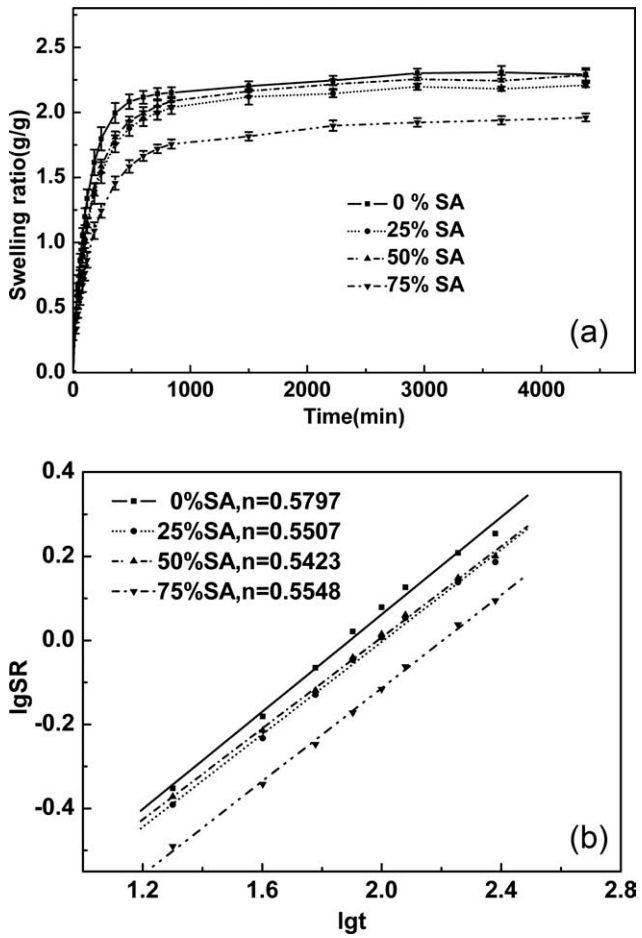


Figure 3 (a) Swelling ratio of PVA/SA blend hydrogels with different SA contents in distilled water at 37°C; (b) lg SR as a function of lg t ($N = 4$; CaCl2: 2%).

This is because a highly crosslinked structure could not only increase stiffness of the hydrogels but also prevent water release from the hydrogels during the compressive testing, while the water in the hydrogel behaves as an incompressible fluid to resist compression.[31]

Swelling characteristics

Swelling kinetics

To investigate the effect of SA content and crosslink density on swelling behavior of PVA/SA blend hydrogels, dried samples with different SA contents were immersed in distilled water to avoid the influence of pH, and swelling ratio of these samples were measured, the results were shown in Figure 3(a). It can be seen that all the samples have similar swelling tendency, the swelling ratio grew quickly in the first 8 h conditioning, afterwards the curves turned into level. The equilibrium swelling ratio for samples with 0, 25, 50, and 75% SA were 2.30, 2.20, 2.25, and 1.93, respectively. It is known that an increased crosslink density will result in a more compact network structure and less space in the polymeric matrix to accommodate water. Thereby, the swelling ratio negatively related to crosslink density. However, since PVA is more hydrophilic than SA, and hence, equilibrium swellings ratio of PVA/SA blend hydrogels will also increase with increasing of PVA content in the hydrogels.[32]

A critical analysis of the swelling of hydrogel reveals three continuous processes: (1) penetration of the solvent molecules to the inside of hydrogel network, (2) relaxation of polymer chains, and (3) stretch of whole hydrogel network in solution.[33] Swelling kinetics of the blend hydrogels was analyzed by using the initial swelling data to fit a rate equation:[34]

$$\mathrm{SR} = kt^n$$

where SR is the swelling ratio of the hydrogels at time t, k is a characteristic constant of the hydrogel, and n is the kinetic exponent. For a slab-based delivery system, a value of $n = 0.5$ indicates Fickian kinetics in which the rate of penetrating diffusion is rate-limiting; when the value of n is between 0.5 and 1, the swelling follows a non-Fickian process, $n = 1$ implies relaxation-controlled diffusion. The constants n were calculated from the slopes of the graph of lgSR against lg$t$ shown in Figure 3(b), the values of n were 0.5797, 0.5507, 0.5423, and 0.5548 for the PVA/SA blend hydrogels with 0, 25, 50, and 75% SA, respectively. These results indicated that the swelling of all the blend hydrogels follows non-Fickian mechanism. The value of n decreased with increasing SA content when the SA content was below 50%, and increased when SA content up to 75%, which meant the swelling of the hydrogel containing 50% SA was closest to Fickian kinetics. This phenomenon was attributed to that the swelling process is depending on water diffusion and group ionization. If the ionization rate is much slower than the diffusion, the ionization process is rate limiting and the swelling kinetics will be non-Fickian.[35] With the increase of SA content, more —COOH or —COONa groups are ionized, the ionization rate increased and the exponent n decreased. The blend hydrogel containing 75% SA possessed a higher n value may be attributed to the great crosslink density of the SA network and most —COOH or —COONa groups could be blocked in a compact structure after drying, which restricts the ionization rate of these groups.

pH-sensitivity

The PVA/SA hydrogels with different SA contents were allowed to swell in a solution with pH 1.2 for 6 h and subsequently in another solution with pH 7.4 for additional 14 h at 37°C, and their swelling ratios were monitored. The results, as depicted in

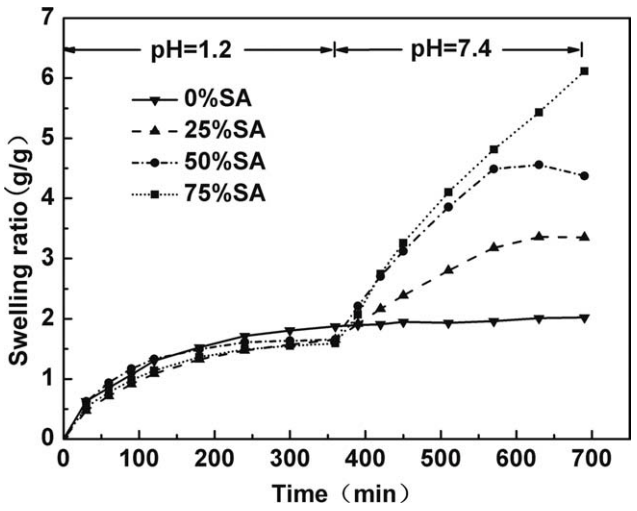


Figure 4 Swelling characteristics of PVA/SA hydrogels with different SA contents in a solution at pH 1.2 for 6 h and subsequently in another solution at pH 7.4 at 37°C ($N = 4$; CaCl2: 2%)..

Figure 4, clearly indicated that the swelling ratios of pure PVA reached an ultimate value about 2.00 and varied little with the pH. This is because there was no any ionic group in pure PVA hydrogel. The swelling ratios of all the samples containing SA were approximately the same at pH 1.2, but at pH 7.4, the swelling ratio of the hydrogels increased significantly with increasing of SA content (i.e., concentration of —COO^-). This is because most —COO^- groups of SA transformed into —COOH groups in the medium of pH 1.2,[28] which may provide a compact structure in the hydrogels due to the decrease of the electrostatic repulsion between —COO^- groups. While in the physiological pH (7.4), the —COOH groups of SA tended to ionize and form —COO^- groups,[28] which will ultimately cause the stretch of whole hydrogel network and enhance the gel swelling since the electrostatic repulsion among negatively charged —COO^- groups increased. As a result, the water uptake ability increased with increasing of SA content. After the attainment of equilibrium water uptake, the highly hydrated hydrogels containing SA began to disintegrate. This is because the Na^+ and K^+ ions in solution exchanged the Ca^{2+} ions in the polymannuronate and polyguluronate blocks of alginate chains, led to removal of Ca^{2+} ions and decrease in crosslinking of SA,[36] which resulted in the disintegration of network structure, and hence the hydrogels started to loose their weight. The results in Figure 4 showed that the sample with 50% SA began to disintegrate after about 630 min immersion in the media, while the hydrogel with 25% SA was found still stable. This is because higher PVA content would increase the stability of blend hydrogels.[23] The continuous increase of swelling ratio in the hydrogel with 75% SA is probably due to its higher pH sensitivity which could lead to the mass of absorbed water was larger than the mass of lost polymer. In conclusion, the swell and stability of the blend hydrogels are strongly depending on SA content.

For the IPN structure formed by two steps method in this study, the SA network formation could be influenced by the presence of the PVA network, while the degree of crosslinking of PVA network may affect the expansion and swelling of SA network. To investigate this, we prepared blend hydrogels by repeating different freeze–thaw cycles and examined the swelling behavior of the obtained hydrogels in the media of varying pH. The influences of freeze–thaw cycles on swelling ratio of the hydrogels were depicted in Figure 5, which clearly indicated that all the three samples exhibited a swelling ratio approach 1.66 after the samples were soaked in the solution of pH 1.2 for 6 h. After transferring into phosphate buffer medium of pH 7.4, all the samples showed similar swelling tendency at the initial stage and they began to disintegrate after approximately 10 h. These results suggested that the number of freeze–thaw cycles have no obvious effect on the pH-sensitivity of the hydrogels. It is known that increasing the number of freeze–thaw cycles will increase crosslink density of PVA network, while a higher crosslinked PVA network will not only restrict the swelling of blend hydrogels, but it may also decrease the crosslink density of SA network which in turn give rise to higher swelling ratio. Thus, the blend hydrogels prepared with different freeze–thaw cycles could have similar swelling ratio.

To investigate the pH sensitivities of the PVA/SA blend hydrogels as a function of concentration of $CaCl_2$ solution, the swelling ratio of blend hydrogels

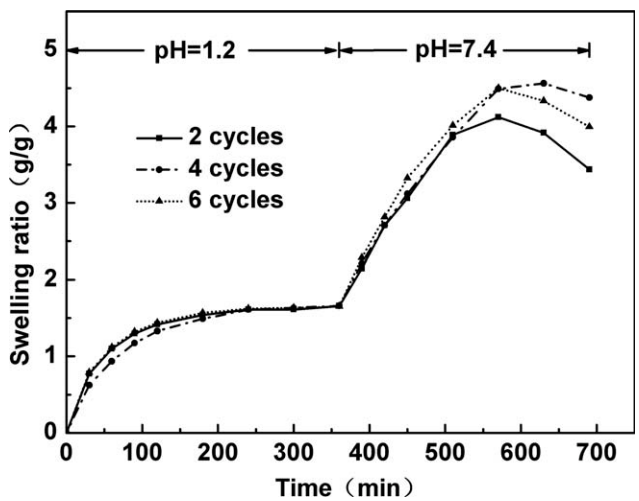


Figure 5 Swelling characteristics of PVA/SA hydrogels with different freeze–thaw cycles in a solution at pH 1.2 for 6 h and subsequently in another solution at pH 7.4 at 37°C (SA: 50%; CaCl2: 2%)..

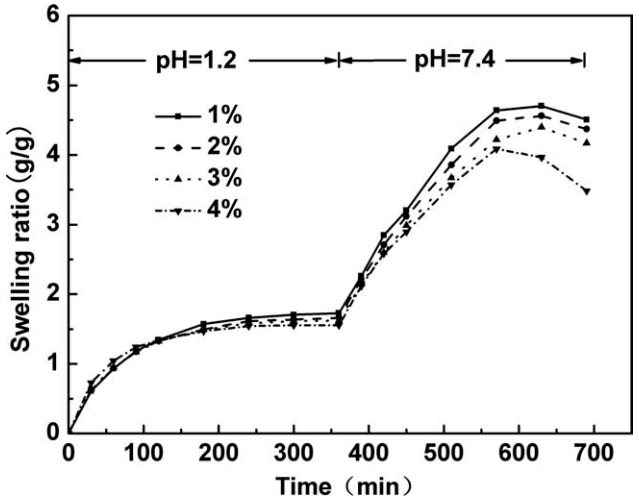


Figure 6 Swelling characteristics of PVA/SA hydrogels treated with different concentrations of CaCl2 in a solution at pH 1.2 for 6 h and subsequently in another solution at pH 7.4 at 37°C (SA: 50%; $N = 4$).

crosslinked in 1, 2, 3, and 4% $CaCl_2$ solutions were measured. The results, as presented in Figure 6, showed that the swelling ratio of the PVA/SA blend hydrogels decreased with the increase of concentration of $CaCl_2$ solution, and similar behavior has already been reported for pure SA beads.[37] It is known that with increasing concentration of $CaCl_2$ solution, the amount of Ca^{2+} per unit volume of the liquid increases and more Ca^{2+} will bond to the SA chains. This will result in a diminished network space, so less water can enter the hydrogels. On the other hand, the number of $-COO^-$ groups decreased with increasing concentration of $CaCl_2$ solution due to the combination of Ca^{2+} and —COOH groups of SA. Therefore, the electrostatic repulsion between $-COO^-$ groups becomes weak, and this also gave rise to decreasing of swelling ratio of the hydrogels.

CONCLUSIONS

PVA/SA blend hydrogels with different SA contents were prepared with two steps, first through freeze–thaw cycles to crosslink PVA and then followed by Ca^{2+} crosslinking SA to form PVA/SA interpenetrating networks. Gel fraction of the blend hydrogels, which is related to crosslink density, increased with the increase of freeze–thaw cycles and strongly depended on the SA content. The obtained blend hydrogels possessed a porous structure. Compared to pure PVA hydrogel, the PVA/SA blend hydrogels have typical pH-sensitivity due to the electrostatic repulsion among the introduced $-COO^-$ groups after incorporated SA. This pH-sensitivity can be enhanced by increasing SA content and decreasing Ca^{2+} concentration. The mechanical properties of the blend hydrogels were influenced by composition and processing conditions significantly. The PVA dominant blend hydrogels showed good flexibility and high tensile strength, while higher SA content gave rise to the blend hydrogels rigid and brittle characteristics. At fixed SA content, the tensile strength and elongation at break of the blend hydrogels could increase substantially with slight change of flexibility when increasing number of freeze–thaw cycles. In the investigated range of concentration of $CaCl_2$ aqueous solution, 1–4% (w/v), higher concentration would yield stiffer blend hydrogels, but 2% $CaCl_2$ aqueous solution gave rise to highest values of tensile strength and elongation at break.

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