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Chitosan/Poly(acrylic acid-*co*-crotonic acid) Semi-IPN의 합성, 분석 및 팽윤거동

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Synthesis, Characterization and Swelling Properties of Chitosan/Poly(acrylic acid-*co*-crotonic acid) Semi-Interpenetrating Polymer Networks

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Abstract: A semi-interpenetrating polymer network (semi-IPN) hydrogel composed of crosslinked chitosan and poly (acrylic acid-*co*-crotonic acid) was prepared in the presence of glutaraldehyde (GA) as a crosslinker. Fourier-transform infrared, thermogravimetric analysis and scanning electron microscopy were employed to confirm the structure of the semi-IPN hydrogel. The swelling capacity of hydrogel was shown to be affected by the monomers weight ratio, chitosan content, initiator and GA concentrations. The results also indicated that the semi-IPN hydrogel had different swelling capacity at various pHs. Additionally, the swelling behavior of the hydrogel was investigated in aqueous solutions of NaCl, $CaCl_2$, and $AlCl_3$.

Keywords: chitosan, acrylic acid, crotonic acid, interpenetrating polymer networks, glutaraldehyde.

Introduction

Synthesizing interpenetrating polymer network (IPN) is a well-known way to force the compatibility of immiscible polymers.[1,2] Such materials are of particular interest when they are made from two components which exhibit highly different properties. In the prepared semi-interpenetrating networks (semi-IPNs) in this work, chitosan is a natural polymer and poly(acrylic acid-*co*-crotonic acid) (poly(AA-*co*-CA)) is a synthetic copolymer.

IPN is an intimate combination of two polymers both in the same network, which is obtained when at least one polymer is synthesized and/or crosslinked independently in the immediate vicinity of the other.[3] In general, chemical bonds do not exist between the constituent networks; if some junctions between components exist, then semi-IPNs are formed. A semi-IPN, which consists of both linear and crosslinked have been used to improved the properties of polymer blends and composites.[1] In fact, materials formed from IPNs share properties characteristic of each network. IPN materials offer great promise for the future in view of the increasing number of applications of IPN materials. Hence, there has been considerable interest in developing IPNs synthesis.[4-12]

Chitosan, a natural poly(aminosaccharide), is non-toxic and easily bioadsorbable.[13] This biopolymer is a weak base with an intrinsic pKa of 6.5 and with gel forming ability at low pH.[14] In acidic solutions, the amine groups of a crosslinked chitosan are protonated and form a cationic hydrogel and result in swelling of the hydrogel network. Both chemical and physical methods have been used to create crosslinked chitosan hydrogels. Chemical crosslinking can be achieved by using glutaraldehyde[15] or formaldehyde.[14,16] Also, chitosan can form gels with non-toxic multivalent counter ions, such as tripolyphosphate, by ionic interaction.[17] Due to its unique properties such as biocompatibility, biodegradability, renewability, antimicrobial activity and wound-healing properties,[18-20] chitosan has its potential applications in wound dressings,[21] wound healing,[22] drug delivery systems[23] and tissue engineering.[24,25]

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The modification of natural polymers is a promising method for the preparation of new materials. Polymeric hydrogels in the form of IPNs are able to absorb large amounts of water without dissolving. They have been proposed for many biomedical applications due to their good biocompatibility and water permeation properties. In recent years, much interest has been shown in the development of the synthesis of natural-based hydrogels.[26-30] These polymers are special soft and flexible materials that can absorb large quantities of water, saline or physiological solutions while the absorbed solutions are not removable even under pressure.

Hydrogels responding to external stimuli such as pH, electric field, and chemical environments are often referred to as "smart" polymers. Among these, pH-sensitive hydrogels have been extensively investigated for potential use in site-specific delivery of drugs to specific regions of the gastrointestinal tract and have been prepared for delivery of low molecular weight drugs. Therefore, these hydrogels have important applications in the field of medicine, pharmacy, and biotechnology.[31-36]

Semi-IPN hydrogels of chitosan have been investigated by researchers. For instance, semi-IPN hydrogels of chitosan with polyether,[37] poly(acrylic acid),[38] poly(ethylene glycol),[39] and poly(*N*-isopropylacrylamide)[40] have been reported.

In the present study, semi-IPNs composed of chitosan and poly(AA-*co*-CA) were prepared and their swelling behavior in water, saline and pH solutions were investigated at room temperature. It should be pointed out that to the best of our knowledge based on a precise survey of the Chemical Abstracts, no report was found on semi-IPN hydrogel synthesis composed of chitosan and poly(AA-*co*-CA) in the presence of glutaraldehydev (GA) as a crosslinker. Therefore, following a continuous research, in this paper we attempted the preparation of another chitosan-based semi-IPN.

Experimental

Materials. Chitosan sample (degree of substitution 0.76) was obtained from Sigma-Aldrich Company. Acrylic acid, crotonic acid, and ammonium persulfate (APS) were obtained from Merck, Germany. Glutaraldehyde (GA) was purchased from Panreac, Spain.

Interpenetrating Polymer Networks Preparation. Chitosan-based semi-IPN hydrogels were prepared in two steps. Firstly, the copolymer, poly(AA-*co*-CA), was prepared. In general, 2.90 g of acrylic acid was dissolved in 10 mL distilled water in a two-neck reactor equipped with a mechanical stirrer while stirring. The reactor was immersed in a thermostated water bath at 80 ºC. Then, 0.10 g crotonic acid was transferred in the solution. At this temperature, APS initiator was added to the mixture. After 30 min the viscous copolymer was obtained. At second step, chitosan (0.80 g) was dissolved in 30 mL of distillated degassed 1 wt% acetic acid solution and after homogenizing, 0.75 g of dried poly(AA-*co*-CA) was added to the chitosan solution and it was stirred to achieve a homogenous solution. Finally, 5 mL of the GA solution was added to the mixture. The crosslinking reaction was allowed to proceed for 1 h. The hydrogel was neutralized with NaOH solution (1 N) to pH 7. Ethanol (300 mL) was added to the gelled product while stirring. After complete dewatering for 24 h, the hardened semi-IPN hydrogel product were filtered, washed with fresh ethanol and dried at 50 ºC.

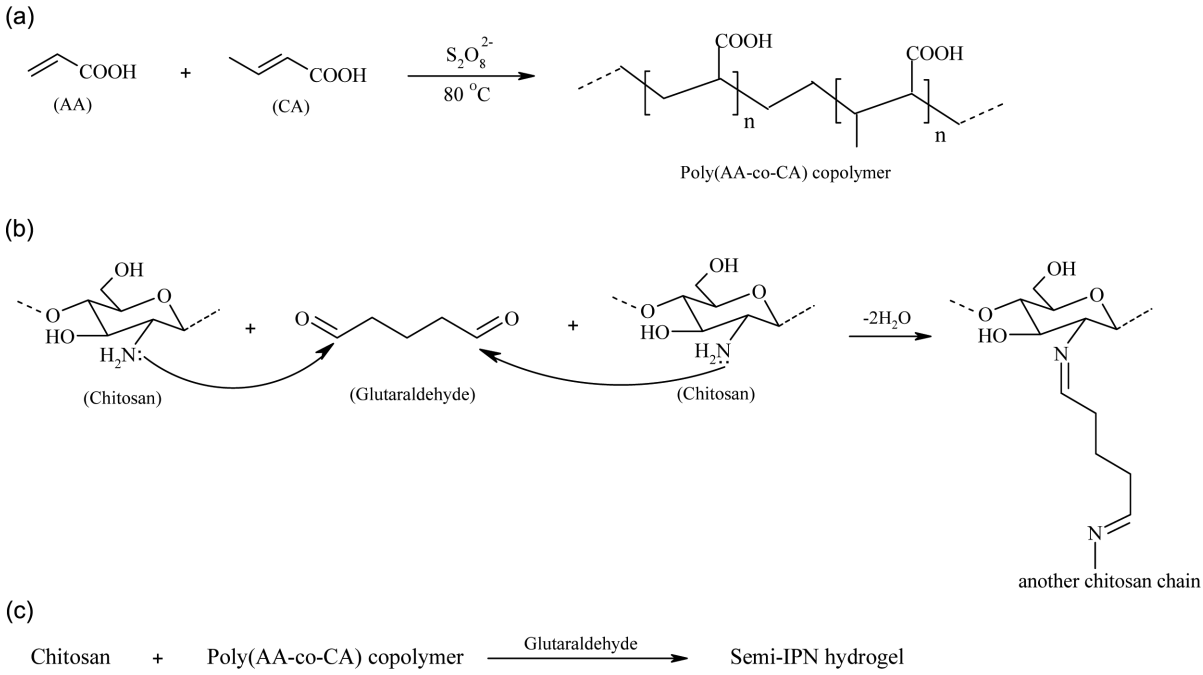
Swelling Measurements. An accurately weighed sample (0.5±0.001 g) of the dried semi-IPN hydrogel was immersed in distilled water (200 mL) and allowed to soak for 30 min at room temperature. The equilibrium swelling (ES) capacity was measured twice at room temperature and using the following formula:

$$ES\ (g/g) = \frac{\text{Weight of swollen hydrogel - Weight of dried hydrogel}}{\text{Weight of dried hydrogel}}$$

Characterization. The Fourier transformation infrared (FTIR) spectra of cotton fabric and grafted fabric samples were recorded on a FTIR spectrophotometer (ABB Bomem MB-100) using KBr. The grafted fabric structural and morphological variations were observed using a scanning electron microscope (SEM). Dried superabsorbent powder were coated with a thin layer of palladium gold alloy and imaged in a SEM instrument (Leo, 1455 VP). Thermogravimetric analyses (TGA) were performed on a Universal V4.1D TA Instruments (SDT Q600) with 8-10 mg samples on a platinum pan under nitrogen atmosphere. Experiments were performed at a heating rate of 10 ºC/min until 600 ºC.

Results and Discussion

Synthesis of semi-IPN. In this study, synthesis and characterization of a chitosan-based semi-IPN hydrogel is investigated. A general reaction mechanism for the poly(AA-*co*-CA) formation, crosslinking of chitosan by GA and semi-IPN hydrogel preparation is shown in Scheme 1. At the first step, the copolymer was formed *via* a simple free radical copo-



Scheme 1. General mechanism for copolymer formation (a); glutaraldehyde-crosslinking of chitosan (b); semi-IPN hydrogel preparation (c).

lymerization. The sulfate anion-radical produced from thermally decomposition of APS radically initiates copolymerization of AA and CA monomers led to a copolymer so called poly(AA-*co*-CA). The mechanism of crosslinking of chitosan with GA was also illustrated in Scheme 1. Many researchers have investigated the crosslinking of chitosan via aldehyde functional group containing reagents.[14,16] As seen in Scheme 1(b), at the first step, the imine bond formation takes place between amine group of chitosan and formyl group of GA. Then the second imine group is formed with the amine group of other chitosan chain and the crosslinks formed result in the semi-IPN hydrogel in the presence of poly(AA-*co*-CA) (Scheme 1(c)).

Structural Characterization. FTIR Analysis: FTIR spectral analyses were carried out to confirm the chemical structure of chitosan-based semi-IPN. The FTIR spectra of pure chitosan, GA-crosslinked chitosan, and the semi-IPN hydrogel are shown in Figure 1. In Figure 1(a) a broad band at 3418 cm^{-1} corresponds to the associated -OH and -NH_2 stretching vibrations of the hydroxyl and amine groups, and the peak at 1615 cm^{-1} corresponds to the N-H deformation bending of chitosan. In the spectrum of the chitosan crosslinked by GA (Figure 1(b)), a new characteristic absorption band is appeared at 1570 cm^{-1} that may be attributed to imine C=N stretching. The semi-IPN hydrogel product comprises a crosslinked chitosan backbone with side chains of poly(AA-*co*-CA) that carry carboxylate functional groups that are evidenced by peak at

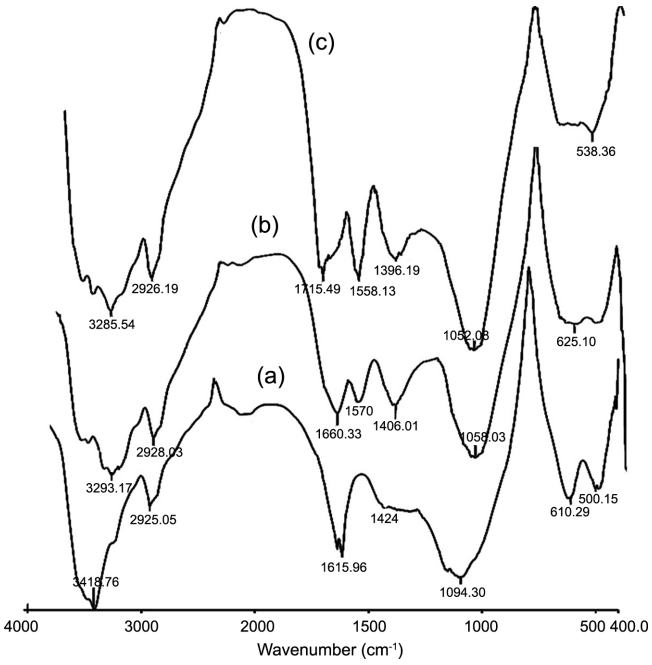


Figure 1. FTIR spectra of chitosan (a); glutaraldehyde-crosslinked chitosan (b); the semi-IPN hydrogel (c).

1715 cm^{-1} (Figure 1(C)). This peak attributed to C=O asymmetric stretching in carboxylate anion that is reconfirmed by another sharp peak at 1396 cm^{-1} which is related to the symmetric stretching mode of the carboxylate group.

TGA Analysis: The semi-IPN formation was also supported

by thermogravimetric analysis (Figure 2). The comparison of TGA curves indicates the structure of chitosan has been changed, which might be due to the crosslinking of chitosan chains. In general, the semi-IPN had lower weight loss than chitosan. This means that the crosslinking increases the thermal stability of chitosan in some extent.

SEM Analysis: The surfaces of the polymeric hydrogels were usually observed by scanning electron microscopy (SEM). The scanning electron micrographs of chitosan (a) and chitosan-based semi-IPN hydrogel (b) are shown in Figure 3. It can be seen that the semi-IPN have a porous structure.

These pores might be induced into the hydrogel by water evaporation. Holes exist between the fine particles, so water can be absorbed easily by the hydrogel because it has a high specific surface area. The characteristic surface morphology is very significant for water absorbency, especially for large particle sizes of hydrogels.

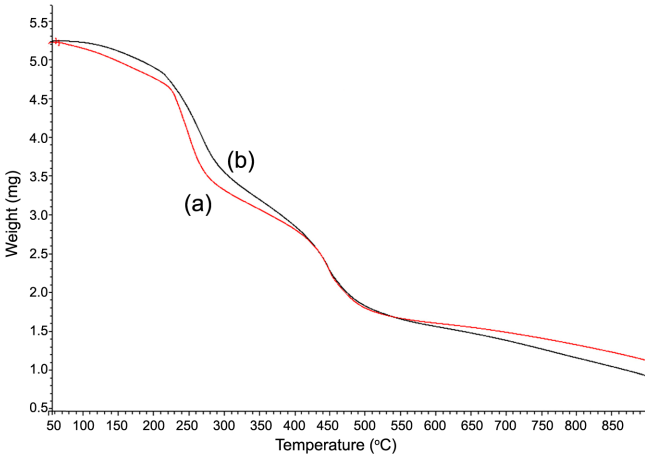


Figure 2. TGA curves of chitosan (a); chitosan/poly(AA-*co*-CA) semi-IPN hydrogel (b).

Optimization of Swelling Capacity. Different variables affecting the ultimate swelling capacity (the monomers weight ratio, chitosan content, initiator and GA concentrations) were optimized to achieve semi-IPN hydrogels with maximum water absorbency.

Effect of Monomers Weight Ratio on Swelling: The effect of monomers weight ratio on water absorbing capacity was studied by varying the amount of AA and CA, while the rest of variables were unchanged (Figure 4). According to the figure, with increasing in AA content the water absorbing capacity is increased, while with increasing in CA concentration the swelling capacity is decreased. This behavior can be originated from the more carboxylate groups generated from AA. On the other hand, the AA content enhanced the hydrophilicity of the hydrogel and caused a greater affinity for water. Although these hydrophilic anionic groups can also be generated from CA, but with increasing the CA amount a higher steric hindrance structure is formed.

Effect of Chitosan Content on Swelling: The swelling dependency on chitosan amount is shown in Figure 5. Maximum swelling (215 g/g) has been observed at 2.2 wt% of chitosan, while other factors were kept constant. Swelling of hydrogel is considerably increased with increasing of chitosan

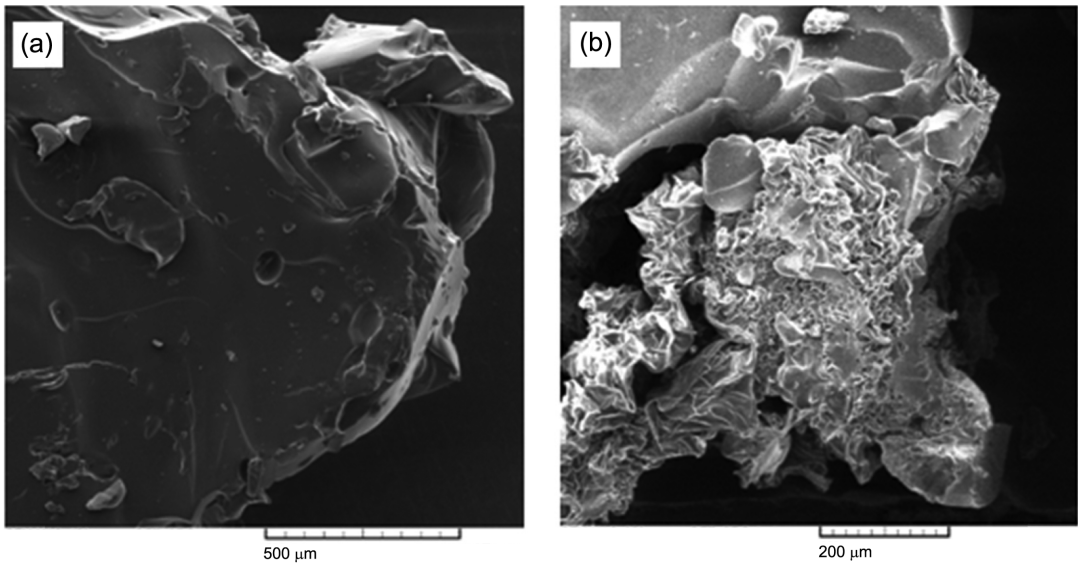


Figure 3. SEM photographs of chitosan (a); chitosan/poly(AA-*co*-CA) semi-IPN hydrogel (b).

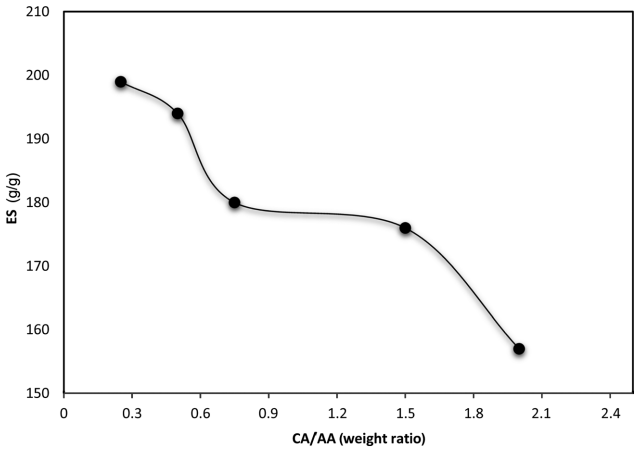


Figure 4. Swelling dependency of the semi-IPN on monomers weight ratio.

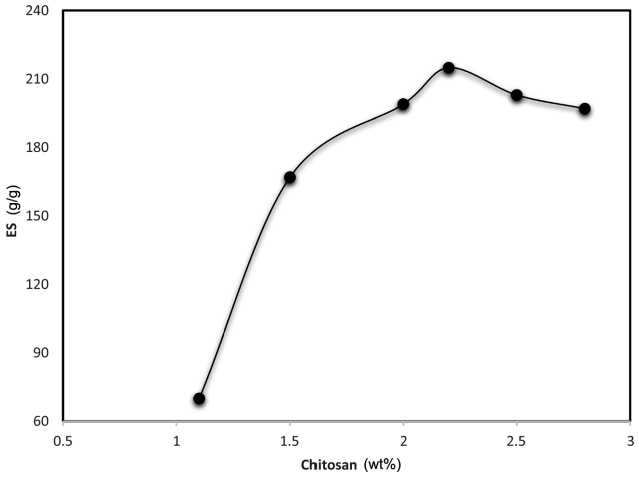


Figure 5. Swelling dependency of the semi-IPN on chitosan content.

value from 1.1 to 2.2 wt%. This behavior is attributed to the availability of more -NH_2 sites for reaction with GA to form semi-IPN network at higher chitosan concentration. However, upon further increase in the substrate concentration, increase in the crosslinking points decreases the space between the copolymer and chitosan chains and, consequently, the resulted highly crosslinked rigid structure cannot be expanded and hold a large quantity of water.

Effect of Initiator Concentration on Swelling: For studying the initiator concentration effect on absorbency, amount of APS was varied from 0.13 to 0.44 mol/L (Figure 6). The absorbency is increased versus increasing the APS concentration from 0.13 up to 0.22 mol/L and then, it is decreased considerably with a further increase in the amount of APS. The number of active free radicals is increased in terms of the initiator levels lower than 0.22 mol/L. This accounts for the initial increment in swelling up to a certain amount of APS. The swelling decrease after the maximum may be attributed to increased number of produced radicals led to terminating step via bimolecular collision resulting in enhanced crosslink density. This possible phenomenon is referred to as "self crosslinking" by other workers.[41] An additional reason for decreasing the absorbency can be related to decreasing molecular weight (MW) of the copolymer at high levels of APS concentration. Since MW inversely depends on initiator concentration, [I], higher [I] results in lower MW and, in turn, lower swelling capacity of the hydrogel.[42]

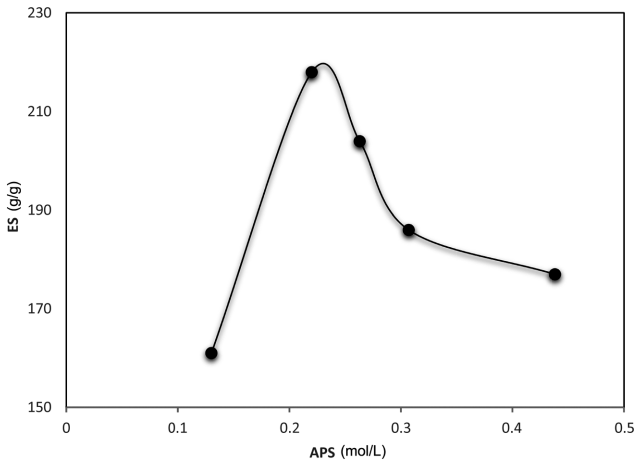


Figure 6. Swelling dependency of the semi-IPN on initiator concentration.

Effect of Glutaraldehyde Concentration on Swelling: The swelling ratio as a function of GA concentration was also investigated (Figure 7). Crosslinks is necessary to form a semi-IPN in order to prevent dissolution of the hydrophilic polymer chains in an aqueous environment. As the concentration of GA was increased, the water absorbency of the semi-IPNs is gradually increased and then, it is intensely decreased. Initial increment in water absorbency can be attributed to formation of a stable semi-IPN network. A further increase of GA concentration, however, results in decreased absorbency. It is due to decrease in the space between the copolymer and chitosan chains as the crosslinker concentration is increased.

Effect of pH of Solution on Swelling: Since it has been reported that the swelling properties of polybasic gels are influenced by buffer composition and pKa,[43] no additional ions (through buffer solution) were added to the medium for setting pH. Therefore, stock NaOH (pH 10.0) and HCl (pH 1.0) solutions were diluted with distilled water to reach desired basic and acidic pHs, respectively. Ionic hydrogels exhibit swelling

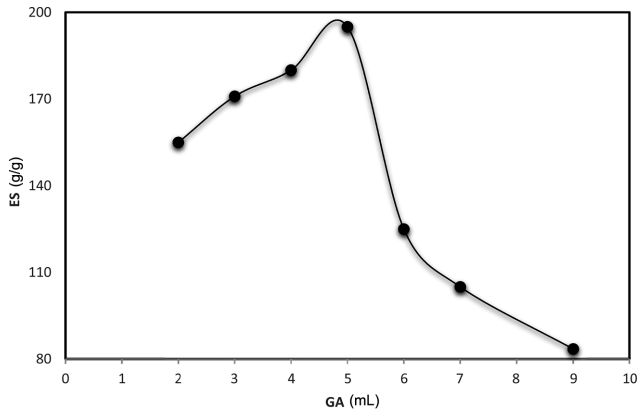


Figure 7. Swelling dependency of the semi-IPN on crosslinker concentration.

changes at a wide range of pHs. Therefore, in this series of experiments, equilibrium swelling for the synthesized semi-IPN hydrogels was measured in different pH solutions ranged from 1 to 13. According to Figure 8, the two sharp swelling capacity changes can be attributed to high repulsion of $-NH_3^+$ groups in acidic media and $-COO^-$ groups in basic media. However, at very acidic conditions (pH 3), a screening effect of the counter ions, i.e. Cl^-, shields the charge of the ammonium cations and prevents an efficient repulsion. As a result, a remarkable decreasing in equilibrium swelling is observed (gel collapsing). Around pH 5, the carboxylic acid component comes in to action as well. Since the pK of the weak polyacid is about 6.4, its ionization occurring above this value, may favour enhanced absorbency. But under pH 6.4, at a certain pH range 4-6, the majority of the base and acid groups are as non-ionized forms, so hydrogen bonding between amine and carboxylic acid may lead to a kind of crosslinking followed by a decreased swelling. At pHs 4-6 the protonated amine groups are decreased and consequently swelling capacity is diminished. At higher pHs, the carboxylic acid groups become ionized and the electrostatic repulsive force between the charged sites (COO^-) causes increasing in swelling. Again, a screening effect of the counter ions (Na^+) limits the swelling at pH 8-13.

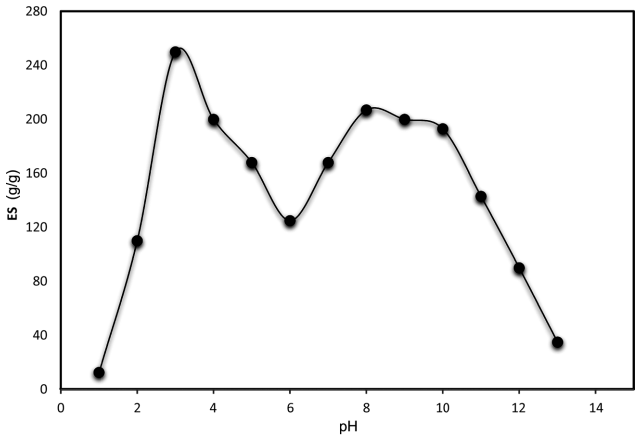


Figure 8. Effect of pH of buffer solutions on swelling capacity of semi-IPN hydrogel.

Effect of Salinity on Swelling: To study various saline effects on the swelling behavior of the synthesized chitosan-based semi-IPNs, equilibrium swelling was measured in solutions of NaCl, $CaCl_2$ and $AlCl_3$ (Figure 9). In general, all swelling values in saline media are expectedly decreased. The reason is usually attributed to the reduction of osmotic pressure between the gel and the aqueous phase. Osmotic pressure, the driving force for swelling, is originated from anion-anion repulsion. In the presence of excess cations, they can shield the anions and prevent efficient electrostatic repulsion. This phenomenon is often referred to as charge "screening effect". An additional reason is increasing electrostatic attraction between anionic sites of chains and multi-valent cations leading to increased ionic crosslinking degree and consequent loss of swelling. However, the swelling in NaCl is yet considerable (190 g/g).

The swelling values for some chitosan-based semi-IPNs are comparatively given in Table 1. As seen from the data in Table 1, the ultimate swelling capacity of the chitosan/poly(AA-*co*-CA) semi-IPN hydrogels is higher than most of its counterparts.

Table 2 also shows a comparison between the equilibrium swelling capacity of the chitosan-based semi-IPN prepared in

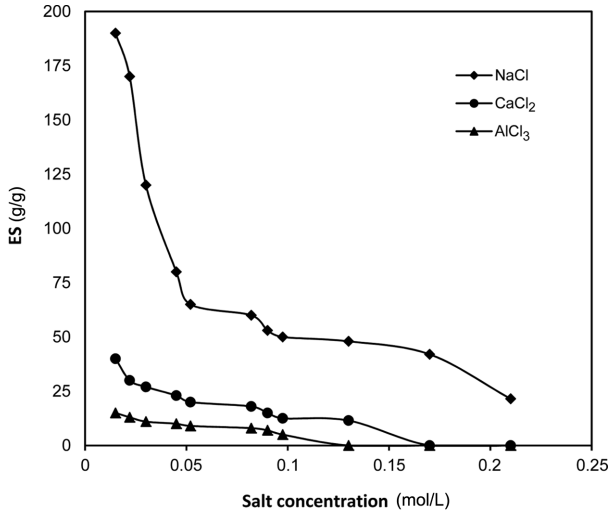


Figure 9. Swelling capacity of chitosan-based semi-IPN hydrogels in different salt solutions with various concentrations.

Table 1. Comparsion between the Equilibrium Swelling (ES) Capacity of the Semi-IPN Prepared in the Present Work and Some Chitosan-based Semi-IPNs Prepared by Other Researchers

Chitosan-based semi-IPN	ES (g/g)
Chitosan-PEGM[a]	74-97
CECS-HEMA[b]	82
Chitosan-PVA[c]	210-350
Chitosan-PEO[d]	245
Chitosan-SPH-IPNs[e]	17-24
Chitosan-PAAm[f]	298
Chitosan-PNIPAAm[g]	246
CS-CM[h]	23
Chitosan-P(AA-*co*-CA)[i]	212

[a]Poly(ethylene glycol), in the presence of glutaraldehyde as a crosslinking agent.[44] [b]*N*-carboxylethyl chitosan (CECS) and 2-hydroxyethyl methacrylate (HEMA).[45] [c]Poly(vinyl alcohol).[46] [d]Poly (ethylene oxide).[47] [e]Superporous IPN hydrogels of chitosan and poly(acrylamide) and poly(acrylamide-*co*-acrylic acid).[48] [f]Poly(acrylamide), prepared via UV irradiation.[49] [g]Poly(*N*-isopropylacrylamide).[50] [h]Chitosan (CS) and carboxymethyl chitosan (CM) complex film.[51] [i]Prepared in this work.

Table 2. Comparsion between the Equilibrium Swelling (ES) Capacity of the Chitosan/Poly(AA-*co*-CA) Semi-IPN Prepared in the Present Work and Some Known Commercial/Reported Superabsorbing Hydrogels

Superabsorbent hydrogel	ES (g/g)	
	Water	0.9 wt% NaCl
Stockosorb AGRO[a]	222	35
SuperAB A200[b]	176	30
Sanwet IM-815A[c]	304	51
GS-3000H[d]	310	50
PAA[e]	85	27
P(AA-*co*-AM)[f]	134	83
Alg-CMC[g]	48	30
Chitosan-P(AA-*co*-CA)[h]	212	52

[a]An agricultural superabsorbent purchased from Stockhausen Co., Germany. [b]An agricultural superabsorbent purchased from Rahab Resin Co., Iran. [c]A hygienic superabsorbent purchased from Sanyo Chemical Co., Japan. [d]A hygienic superabsorbent purchased from Kolon Co., Korea. [e]Partially neutralized poly(acrylic acid) prepared by photoinduced surface crosslinking.[52] [f]Poly(acrylic acid-*co*-acrylamide).[53] [g]Full-polysaccharide hydrogels based on carboxymethylcellulose (CMC) and sodium alginate (Alg).[54] [h]Semi-IPN prepared in this work.

the present work and some known commercial/reported superabsorbing hydrogels. On the contrary, the semi-IPNs synthesized in this work had acceptable water and saline absorbency.

Conclusions

In this work, we prepared a semi-IPN hydrogel composed of chitosan and poly(AA-*co*-CA) using glutaraldehyde as crosslinking agent. The maximum swelling capacity was achieved under the optimum conditions that found to be CA/AA weight ratio 0.25, chitosan 2.2 wt% , APS 0.22 mol/L, and GA 5 mL. The effect of glutaraldehyde concentration showed that with increasing of this parameter, the water absorbency of the semi-IPN hydrogels decreased. The swelling of hydrogels in solutions with various pHs also exhibited a high sensitivity to pH. Investigation of swelling in different salt solutions showed a known swelling-loss in the presence of multi-valent metal cations. Very low salt sensitivity of swelling of the chitosan-based semi-IPNs is another feature of this new hydrogels. On the other hand, due to highly swelling characteristics of these hydrogels, they may be categorized in *superabsorbents* family. So, this semi-IPN hydrogel may be considered as an excellent candidate to applications such as pharmaceuticals, agriculture, and drug delivery systems.

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