Alginate-Based Biodegradable Superabsorbents as Candidates for Diclofenac Sodium Delivery Systems

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ABSTRACT: Novel types of highly swelling hydrogels were prepared by grafting crosslinked polyacrylamide-*co*-poly-2-acrylamido-2-methylpropane sulfonic acid (PAAm-*co*-PAMPS) chains onto sodium alginate (Na-Alg) through a free radical polymerization method. The superabsorbent formation was confirmed by Fourier transform infrared spectroscopic (FTIR). The controlled release behavior of diclofenac sodium (DS) from superabsorbent polymer was factinvestigated, and shown that the release profiles of DS from superabsorbent polymer were slow in simulated gastric fluid (SGF, pH 1.2) over 3 h, but nearly all of the initial drug content was released in simulated intestinal fluid (SIF, pH 7.4) within 21 h after changing media. Overall the results demonstrated that biodegradable superabsorbent could successfully deliver a drug to the intestine without losing the drug in the stomach, and could be potential candidates as an orally administrated drug delivery system. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 118: 2015–2023, 2010

Key words: control release; diclofenac sodium; polysaccharide; drug delivery system; hydrogels

INTRODUCTION

Loosely crosslinked hydrophilic polymers (hydrogels) being able to absorb and retain hundreds of their own weight of water are known as superabsorbents.[1,2] These hydrogels are suitable candidate for drug delivery system (DDS). Intelligent drug carriers release the right amount of drug at the right time and/or at the right place may enable us to precisely control the delivery of drugs.[3–6] The degree of swelling and dimensions of the superabsorbents can affect and control the release rate of drug. As the dimensions of superabsorbents decrease, the drug release rate increases. The reduction in the swelling degree results in reduction in the path length through which the drug diffuses out of the superabsorbent.[3]

Why hydrogels? Hydrogels are especially interesting as DDSs as they are said to resemble biological tissue due to their hydrophilic nature and tree-dimensional polymeric network which can imbibe large amounts of water or biological fluids.[1,2] Their high water content could contribute to their biocompatibility and their rubbery nature could ensure minimal mechanical irritation to surrounding tissues.[7]

Sodium alginate, widely used in pharmaceutical industries, is water soluble salt of alginic acid, a naturally occurring nontoxic polysaccharide found in all species of brown algae.[8–10]

Diclofenac sodium was frequently used for treating rheumatoid arthritis, which had apparent circadian rhythms and peak symptoms in the early morning. When orally administering DS conventional formulation, it was difficult to achieve the desired clinical effect, because it elicited patients' incompliance of administration in the early morning to coordinate the rhythm of rheumatoid arthritis, due to rapid absorption of the conventional formulation. However, colon-specific DS delivery was not only effective, but also more convenient for administration than the conventional formulation.[11]

The aim of this work is not only to characterize biodegradable polysaccharide-based hydrogel,[4] but also to evaluate the usefulness and feasibility of this polysaccharide-based superabsorbent hydrogel for orally administered DDS. The swelling kinetics was investigated at various surrounding fluid pHs, and ionic strength. The release behavior of DS from these pH-sensitive protein-based superabsorbent was measured to investigate the applicability for intestine DDS.

EXPERIMENTAL

Materials

Sodium alginate (mannuronate/guluronate ratio of the alginate = 1.56, M_w = 270,000) was purchased from Merck Chemical.; *N*,*N*-methylenebisacrylamide

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(MBA, from Merk) as a crosslinker, ammonium persulfate (APS, from Fluka) as a water soluble initiator, acrylamide and 2-acrylamido-2-methylpropane sulfonic acid (AAm, AMPS from Merck) as ionic monomers, Diclofenac sodium was obtained from Hakim Pharmaceuticals (Tehran, Iran). All other chemicals were analytical grade and used without further purification.

Instrumental analysis

Samples were characterized as KBr pellets using an ABB Bomem MB-100 FTIR spectrophotometer. A simultaneous thermal analyzer (STA-625, Reometric Scientific) was used for thermogravimetric analysis of modified alginate hydrogel under nitrogen atmosphere. The heating rate was 208°C/min. The sample weight taken for TG was 10.0 mg.

Graft copolymerization

Water (25 mL) and Na-Alg (1.0 g) were added to a three-neck reactor equipped with a mechanical stirrer (Heidolph RZR 2021) while stirring (200 rpm). The reactor was placed in a thermostat water bath preset at the desired temperature (70–90°C) for 20 min. After dissolving Na-Alg and homogenizing the mixture, APS as a initiator was added and the reaction mixture was stirred for an additional 15 min (delay time) than monomers and crosslinker solutions (AAm, AMPS and MBA) were simultaneously added, gelation was observed within 10–15 min (final volume of solution = 35 mL). The reaction product was allowed to cool to ambient temperature and scissors were used to cut the product into small pieces (diameter $\sim$ 5 mm). The products were then immersed in an excess of deionized water for 7 days to remove the residual unreacted monomers. For dewatering, ethanol (400 mL) was added to the gelled product for 24 h, after which the product was filtered, washed with fresh ethanol and dried at 50°C to constant weight. Next, the product was ground and the resulting powdered superabsorbent hydrogel was stored away from moisture, heat and light.

Swelling measurements using the tea bag method

A tea bag (i.e., a 100 mesh nylon screen) with average particle size between 40 and 60 mesh (250–420 μm) and containing an accurately weighed powdered sample (0.1 ± 0.0001 g) was immersed in distilled water (250 mL) or desired salt solution (100 mL) and allowed to soak for 3 h at room temperature. The tea bag was suspended for 15 min to remove the excess fluid. To measure swelling kinetics or the rate of absorption, the water-absorbed samples were taken from the solution at various time points and swelling measurements were taken following the above procedure. The equilibrated swelling (ES) was calculated twice using the following equation:

$$\mathrm{ES(g/g)} = (\mathrm{W_s} - \mathrm{W_d})/\mathrm{W_d} \quad (1)$$

where W_s and W_d are the weights of the swollen gel and the dry sample, respectively. Thus, absorbency was calculated as gram of water per gram of resin (g/g). The accuracy of the measurements was found to be ±3%.

Absorbency at various buffer solutions

To investigate the swelling behavior of Na-Alg based hydrogels at various pHs, buffer solutions (ranging from 1 to 12) were used. The pH values were precisely checked by a pH meter (Metrohm/620, accuracy ±0.1). Then, 0.1 ± 0.0001 g of the dried hydrogel was used for the steady state swelling measurements according to eq. (1).

pH sensitivity and reversibility

Two buffer solutions with pH 1.2 and 7.4 were used to study pH sensitivity of the hydrogel. The pH values were precisely checked by a pH meter and then 0.1 ± 0.0001 g of dried sample was used for the swelling measurements in both buffers according to aforementioned method.

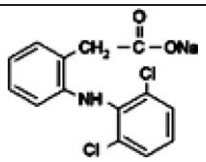
Model drug selection

The model drug used in preparing the drug loaded biodegradeble superabsorbent hydrogel for this study was diclofenac sodium salt (DS), which is nonsteroidal anti-inflammatory drugs (NSAIDs); NSAIDs act as nonselective inhibitors of the enzyme cyclooxygenases, required for the production of prostaglandins, which are involved in the inflammation process The physical and chemical properties of this model drug are summarized in Table I.[12]

Drug loading efficiency and *in vitro* drug release

An accurately weight powdered sample (optimized sample, 1 ± 0.0001 g) with average particle size between 40 and 60 mesh (250–420 μm) was immersed entirely in solution of DS (0.29 g drug dissolved in 50cc distilled water), and were incubated at 0°C for 13 h in refrigerator, later the completely swollen hydrogels loaded with drug were placed in vacuum oven and dried under vacuum at 37°C, the water absorbency of optimized sample was obtained 42 g/g in above drug solutions. The loading amount of drug in the hydrogel was calculated from the decrease in the concentration of DS solution which

TABLE I
The Physical and Chemical Properties of Diclofenac Sodium (Model Drug)

Structure	M_w (g/mL)	pK_a	UV_{max}	Solubility
 Diclofenac sodium	318.13	4	276 (water)	Water (pH 5.2) >9 mg/mL Methanol >24 mg/mL Acetone 6 mg/mL Phosphate buffer (7.2) 6 mg/mL

was determined using UV spectrophotometer (UV-1201, Shimadzu, Kyoto, Japan). The loading efficiency of the Na-Alg based hydrogel was calculated as the ratio of the final to initial DS concentration.

In vitro release was carried out by incubating 0.01 ± 0.0001 g of DS-loaded hydrogel using a cellophane membrane dialysis bag (D_{9402}, SIGMA-ALDRICH) in 50 mL of buffer solution (either pH 1.2 or 7.4) at 37°C. The medium was periodically replaced, and the amount of drug released into the medium was quantified by measuring the absorbance of the drug at 276 nm by UV spectrophotometer. The drug release percent was calculated tree times using the following eq. (2)

$$\text{Drug release } (\%) = R_t/L*100 \quad (2)$$

where L and R_t represent the initial amount of drug loaded and the cumulative amount of drug released at time t.

RESULTS AND DISCUSSION

Mechanism of hydrogel formation

Crosslinking graft copolymerization of acrylamide and 2-acrylamido-2-methylpropansulfonic acids onto sodium alginate was carried out using APS as a free radical initiator and MBA as a hydrophilic crosslinker. The persulfate initiator is decomposed under heating to generate sulfate anion-radicals. The radical abstracts hydrogen from the backbone of the alginate to form radicals on the substrate. So this persulfate-saccharide redox system results in active centers on the substrate to radically initiate polymerization of AAm-*co*-AMPS leading to a graft copolymer. As a crosslinking agent, e.g., MBA, is present in the system, the copolymer is comprised of a crosslinked structure.

Thermal characterization and FTIR analysis

The grafting was confirmed by comparing the T_g value of polysaccharide (260°C)[13] and AAm-*co*-AMPS (162°C),[14] with the grafted hydrogel (356°C, Fig. 1). The grafted alginate and AAm-*co*-AMPS copolymer have shown improvement in thermal stability as clear from T_g value. These observations have clearly confirmed the grafting of poly(AAm-*co*-AMPS) onto alginate backbone. The drug loading was confirmed by comparing the FTIR spectra of the polysaccharide substrate with that of the grafted products. Figure 2 shows the FTIR spectra of (a) sodium alginate, (b) diclofenac sodium, (c) sodium alginate-*g*-poly(AAm-*co*-AMPS), and (d) diclofenac sodium loaded in sodium alginate-*g*-poly(AAm-*co*-AMPS). The FTIR spectrum of the sodium alginate-*g*-poly(AAm-*co*-AMPS) [Fig. 2(c)] shows four new characteristic absorption bands at 1664, 1606, 1206, and 3188 cm^{-1} verifying the formation of graft copolymer product. These peaks are attributed to carbonyl stretching of the amide (AAm, AMPS) groups, R_2CH_2-SO_3^- (AMPS) and NH groups, respectively also the FTIR spectrum of the diclofenac sodium loaded in sodium alginate-*g*-poly(AAm-*co*-AMPS) [Fig. 2(d)] shows six new characteristic absorption bands at 765, 1300, 1450, 1506, 1689, and 3354 cm^{-1} verifying the loading of drug into superabsorbents.

Optimizing the parameters affecting the swelling capacity

Effect of crosslinker concentration

Figure 3, demonstrates the effect of MBA concentration on water absorbency of the synthesized hydrogels. Different amount of MBA (5.4×10^{-3}, 9.1×10^{-3}, 1.8×10^{-2}, 2.7×10^{-2} mol/L) was used and the maximum of swelling was achieved at 5.4×10^{-3} mol/L of MBA concentration. In lower amount of MBA concentration $<5.4 \times 10^{-3}$, a slimy gel is formed so that the swollen gel strength is not sufficient to be referred to as a real "superabsorbent hydrogel." It is well-known that a higher crosslinker

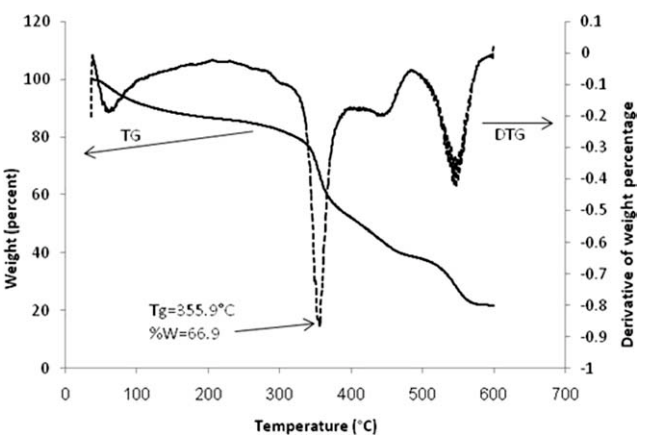


Figure 1 TG&DTG thermograms of Alg-*g*-(AAm-*co*-AMPS) hydrogel, heating rate 20°C/min, under N2.

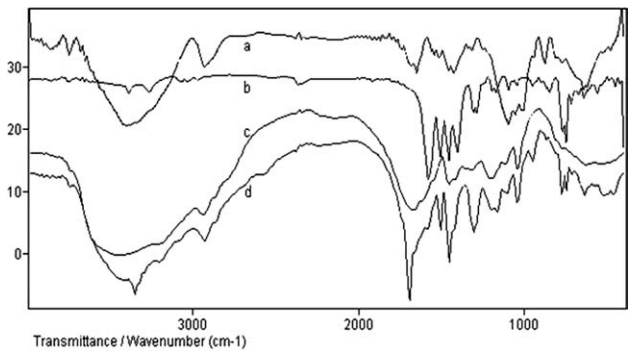


Figure 2 FTIR spectra of (a) sodium alginate (b) diclofenac sodium (c) sodium alginate-*g*-poly(AAm-*co*-AMPS) and (d) diclofenac sodium loaded in sodium alginate-*g*-poly(AAm-*co*-AMPS).

concentration increases the extent of crosslinking of the polymeric chains and decreases the free spaces between them; consequently the swelling capacity is decreased after maximum point.

The known relationship between swelling and concentration of crosslinking agent is stated as eq. (3).

$$S = kC_c^{-n} \tag{3}$$

where k and n are constant values for an individual hydrogels. Figure 3 exhibits a power low behavior of absorbency Cc, with $k = 12.58$ and $n = 0.6157$, which was obtained from the fitted curve. Such behaviors are also reported by others.[15]

Effect of initiator concentration

The swelling ratios of the sodium alginate-*g*-poly (AAm-*co*-AMPS) for various initiator concentrations are shown in Figure 4. According to this figure, the absorbency is increased by increasing the APS concentration from 0.0037 up to 0.0062 mol/L and then is decreased considerably with a further increase in the amount of initiator. The maximum absorbency

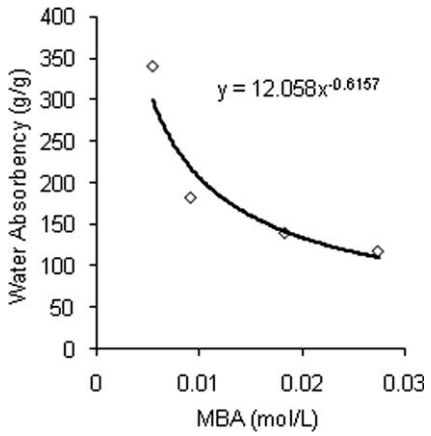


Figure 3 Effect of crosslinker concentration on water absorbency.

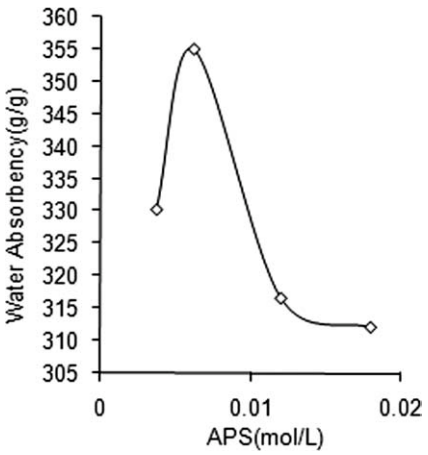


Figure 4 Effect of initiator concentration on swelling.

(355 g/g) is obtained at APS 0.0062 mol/L. The initiator concentration is increased which, in turn, results in higher graft polymerization extent and consequently higher final water absorbency. APS concentrations higher than the optimum value, however, lead to low-swelling superabsorbent. This swelling loss may be attributed to an increase in terminating step reaction via bimolecular collision, which, in turn, enhances the crosslinking density. Chen et al.[15] refer to this possible phenomenon as ''self-crosslinking.'' A subsequent decrease in water absorbency is expected since crosslinking prevents the network from expanding to its fullest extent. In addition, a decrease in molecular weight (M_w) of grafted poly(AAm-*co*-AMPS) of the hydrogel causes a decrease in the swelling value. The latter reasons are due to the inverse relationship between M_w and initiator concentration.[16]

Effect of delay time on water absorbency

Delay time is defined as a time distance between the addition of initiator and addition of monomers in to reaction mixture. According to Figure 5, the

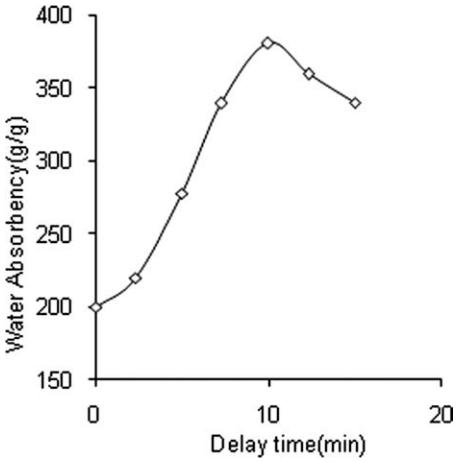


Figure 5 Effect of delay time on swelling.

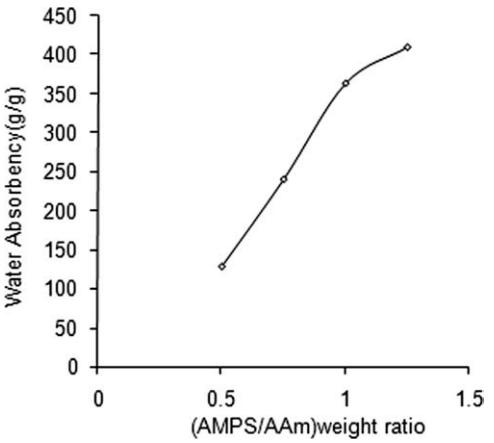


Figure 6 Effect of AMPS/AAm weight ratios on swelling.

absorbency is increased by increasing the delay time from 0 up to 10 min and then is decreased considerably with a further increase in the delay time. The maximum absorbency (380.7 g/g) is obtained at delay time 10 min. The increase of water absorbency with increasing delay time may be ascribed to an increasing number of active sites on the polysaccharide backbone arising from the attack of sulfate radical-anions. Delay time higher than the optimum value, however, lead to low-swelling superabsorbent. A relatively high delay time may cause a reduction of the grafting yields due to the termination of growing grafted chains by excess of primary radicals formed from the initiator. In addition, the free radical degradation of Na-Alg backbones by sulfate radical-anions is an additional reason for reducing of swelling at higher delay time.[17]

Effect of AAm/AMPS ratio on water absorbency

The effect of APMS/AAm weight ratio on the swelling capacity of the hydrogel was studied by varying the AMPS/AAm ratio from 0.5 to 1.25 (WAAm +WAMPS = 4 g) as shown in Figure 6. Maximum swelling (410 g/g) was obtained at WAMPS/WAAm = 1.25. According to this figure, increasing the AMPS concentration at monomer feed composition, increased the swelling capacity, since AMPS have polar groups like —CONH and —$SO3^-$, according to eq. (4) (Flory 1953).

$$q_m^{5/3} \cong \frac{(i/2v_u S^{*1/2}) + (1/2 - \chi_1)/v_1}{v_e/V_0} \qquad (4)$$

where q_m is swelling ratio, i/ν_u is the concentration of the fixed charge of the unswelling networks, S^* is the ionic strength of the swollen solution, and ν_e/V_0 is the crosslinking density that refers to the number of effectively crosslinked density which refers to the number of effectively crosslinked chains in unit volume. The expression $(1/2 - \chi_1)/v_1$ represents the network-medium affinity. Increasing the network-medium affinity, swelling capacity will also be increased.

Effect of sodium-alginate concentration

The effect of Na-Alg weight on hydrogel swelling is shown in Figure 7. Maximum swelling (438.35 g/g) has been observed at 0.75 g of Na-Alg, whiles other factors including monomers ratio, initiator, MBA concentration, reaction delay time, were kept constant. Swelling capacity increased by increasing the Na-Alg weight from 0.5 to 0.75 g from 238.85 to 438.35 g/g. As the Na-Alg weight was increased in the polymerization feed (0.5 up to 0.75 g), the active sites can react easily with monomers. Increasing Na-Alg content more than 0.75 g, results in a high viscosity of the medium is high and a decrease in the diffusion of monomers to active sites to produce crosslinked hydrogels.

Effect of reaction temperature

Figure 8 demonstrates the effect of the reaction temperature on swelling of Na-Alg-*g*-poly(AAm-*co*-AMPS) product. Increasing the reaction temperature from 70 to 80°C increases the water absorbency until it is considerably decreased with a further increase in the temperature. The maximum absorbency (477.5 g/g) was obtained at 80°C. As APS is a thermal initiator, it efficiently dissociated at the temperatures higher than its dissociation temperature, i.e., about 70°C.[16] Thus, the higher initiating radicals increased the extent of polymerization reaction. In addition, the rate of diffusion of AAm and AMPS onto Na-Alg macroradicals as well as the kinetic energy of radical centers is increased at higher temperatures which, in turn, result in higher graft polymerization

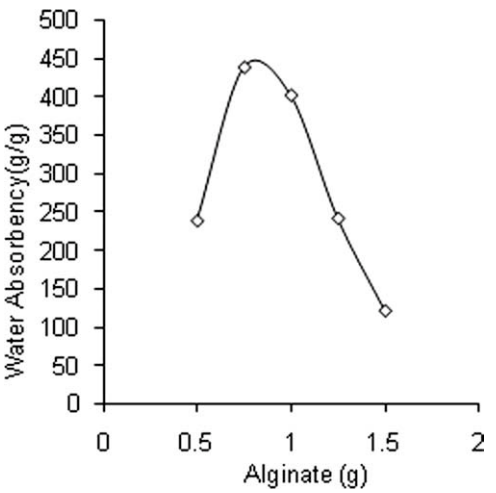


Figure 7 Effect of Na-Alg concentrations on swelling.

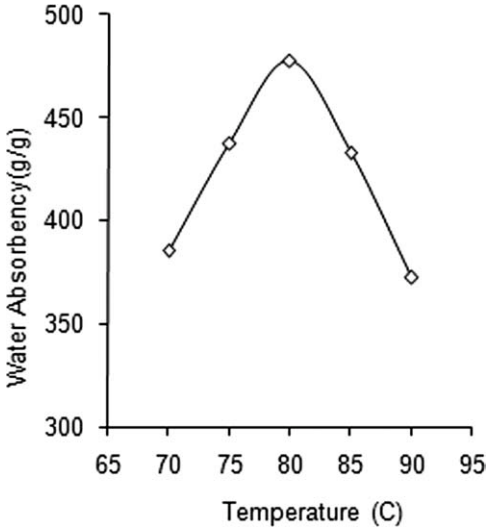


Figure 8 Effect of temperature concentrations on swelling.

and consequently higher final water absorbency of the produced hydrogel. The absorbency loss after 80°C can be ascribed to (a) oxidative degradation of Na-Alg chains by sulfate radical-anions generated from thermally dissociation of APS,[18] and (b) increasing the rate of termination and chain transfer reactions.

Effect of neutralization percentage

In this series of experiments, sulfonic acid groups of grafted and nongrafted PAMPS were neutralized to sulfonate anions by NaOH solution after completion of the reaction. Without the neutralization stage, the sulfonate anions are protonated, eliminating the main anion–anion repulsive forces and consequently decreasing the water absorbency. According to Figure 9, the best neutralization percentage was found to be 40%. In high neutralization percents of the sulfonic acid groups, reduced swelling is observed due to different phenomena that are related to the ''charge screening effect''[19] of excess Na^+ ions in the swelling media and negative interactions of sulfonate anions. The excess cations shield the sulfonate anions (as well as the carboxylate groups of the polysaccharide backbone) and prevent effective anion–anion repulsion (screening/shielding effect).

Effect of mixing rate on water absorbency

The effect of mechanical mixer rate on water absorption of the hydrogel was investigated by varying the mixing rate from 100 to 400 rpm. As a shown in Figure 10, maximum absorption was achieved at 300 rpm. Under the 200 rpm, a slimy gel is formed so that the swollen gel strength is not sufficient to be referred to as a real "superabsorbent hydrogel." As well-known, relatively high mechanical mixer rate in

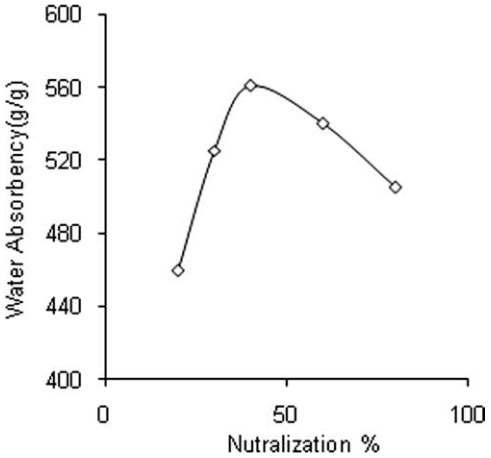


Figure 9 Effect of neutralization percentage on swelling.

high viscosity of Na-Alg solution, cause to better mixing and increased propagation of Na-Alg grafts, increased mobility and diffusion of monomer molecules and their collision with backbone macroradicals, therefore increased grafting yield and swelling ratio, but above the 300 rpm swelling ratio decreased, This can be attributed to high mixing rate that cause to degradation of polymer backbone by cutting forces.

Effect of salt solution on the water absorbency

According to Figure 11 the ultimate swelling capacity of hydrogel in salt solution are decreased comparing with the value measured in distilled water (600 g/g). Generally, swelling values for all "anionic" hydrogels in saline media are expectedly decreased.[20] This undesired swelling-loss has been attributed to the ''charge screening effect'' of the cations led to the reduction of osmotic pressure, the driving force for swelling, between the gel and the aqueous phases. An additional reason is increasing

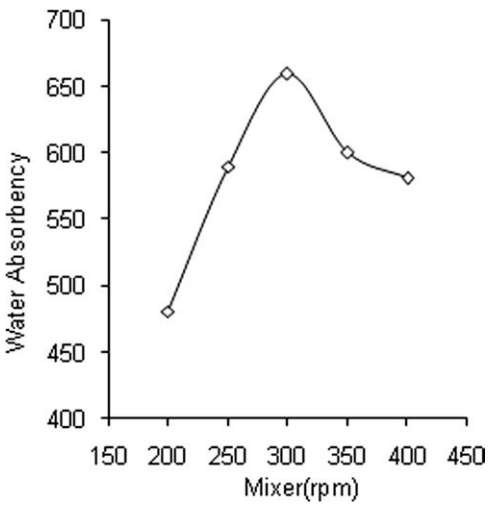


Figure 10 Effect of mixing rate on water absorbency.

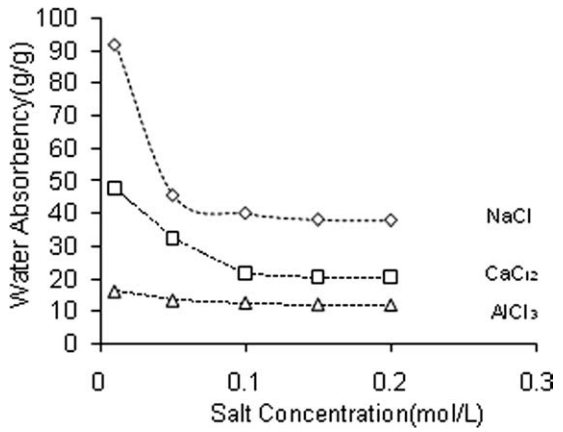


Figure 11 The swelling capacity variation of Na-Alg-*g*-poly(AAm-*co*-AMPS) hydrogel.

electrostatic attraction between anionic sites of chains and multivalent cations (Ca^{2+} and Al^{3+}) leading to increased "ionic crosslinking" degree and consequently loss of swelling. The effect of charge of cation on swelling can be concluded from Figure 11. As shown in the figure, the absorbency of hydrogel in the studied salt solutions is in the order of monovalent >divalent >trivalent cations. With increasing the charge of cation, degree of crosslinking increased and swelling is consequently decreased.

Water absorbency for the hydrogel in various concentrations of salts solutions (0.01, 0.05, 0.1, 0.15, and 0.2 mol/L NaCl, $CaCl_2$, and $AlCl_3$) decreases with increasing ionic strength of salt solutions as shown in the Figure 11. These results are due to the fact that the osmotic pressure difference between the hydrogel and the external solution is reduced with increasing of external solution concentration. Also the results show (Table II) that the swelling degree of alginate based superabsorbent is higher than PAA superabsorbent.

pH sensitivity and pulsatile behavior

Ionic superabsorbent hydrogels exhibit swelling changes at a wide range of pHs. Therefore, in this series of experiments, equilibrium swelling for the synthesized hydrogel was studied at various buffer solutions ranged from 1.0 to 12.0 (Fig. 12). Maximum swelling 190 (g/g) was obtained at pH 5. Under acidic pHs (pH < 3), most of the carboxylate (Na-Alg backbone) and sulfonate anions are protonated, so the main anion–anion repulsive forces are eliminated and consequently swelling values are decreased. At higher pHs (pH > 3), some of the carboxylate and sulfonate groups are ionized and the electrostatic repulsion between $-COO^-$ and $-SO_{3-}$ groups causes an enhancement of the swelling capacity. The reason of the swelling-loss for the highly basic solutions (pH > 10) is "Charge Screening effect" of

TABLE II
Swelling Data in Water and Saline Solutions (0.15 mol/L) for Crosslinked Na-Alg-*g*-poly(AAm-*co*-AMPS) Superabsorbent Hydrogel (Optimum Condition), and Full Synthetic Superabsorbent Based on 40% Neutralized Acrylic Acid

Swelling medium	Na-Alg-*g*-poly (AAm-*co*-AMPS) ES (g/g)	Crosslinked PAA ES (g/g)
H_2O	660	226
NaCl	38.1	18
$CaCl_2$	20.5	4
$AlCl_3$	12.2	1

excess Na^+ in the swelling media, which shields the carboxylate (Na-Alg backbone) and sulfonate anions and prevents effective anion–anion repulsion. Similar swelling-pH dependencies have been reported in the case of other hydrogel systems.[21]

The pH-dependent swelling reversibility of the hydrogels was examined in buffered solutions (Fig. 13). The figure demonstrates the hydrogel reversibility to absorb water upon changing the pH in acidic and basic region (pH 1.2 and 7.4). At pH 7.4, the hydrogel swells up to 180 g/g due to anion–anion repulsive electrostatic force, while at pH 1.2 it shrinks within a few minutes due to the protonation of carboxylate and sulfonate groups. This sudden and sharp swelling–deswelling behavior at different pH values makes the system highly pH-sensitive and suitable for tailoring pulsatile (on–off swelling) drug-delivery systems. Similar swelling-pH dependencies have been reported in the case of other hydrogel systems.[22]

Swelling kinetics

The swelling kinetics of the SAP hydrogel hybrids was studied by means of a previously reported Voigtbased viscoelastic model.[23]

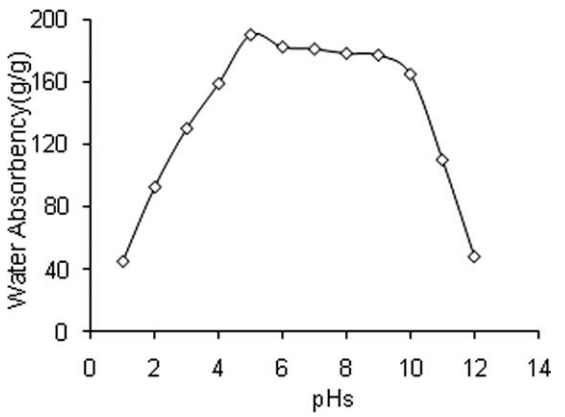


Figure 12 Water-absorbency dependence of crosslinked Na-Alg-*g*-poly(AAm-*co*-AMPS) hydrogel on pH.

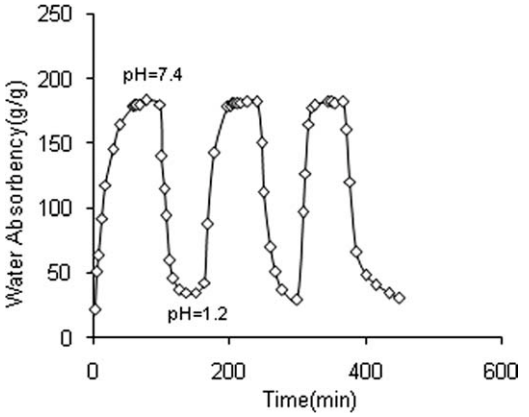


Figure 13 On–off switching behavior as reversible swelling (pH 7.4) and deswelling (pH 1.2) of the pH-responsive superabsorbent hydrogel.

$$S_t = S_e(1 - e^{\frac{-t}{r}}) \quad (6)$$

where S_t is amount of swelling (g/g) at any moment, S_e, the equilibrium swelling, is swelling at infinite time or maximum water-holding capacity, t is the swelling time (s), and r, the rate parameter (s), is the time required to reach 0.63 of the equilibrium swelling. The swelling rate increases with decreasing rate parameter. The rate parameter for the superabsorbent hydrogel is found to be 2.6 min in distilled water (Fig. 14).

In vitro DS release in the simulated human gastrointestinal system

Drug delivery to the colon has implications in a number of therapeutic areas, particularly in the treatment of colonic diseases such as ulcerative colitis and Chron's disease and in the oral delivery of peptides and other drugs degraded in the upper gastrointestinal tracts.[5,6] To study potential application of alginate based superabsorbent containing DS as a pharmaceutically active compound, we have studied the drug releases behavior of the polymers under physiological conditions. The percent of released drug from polymeric carriers as a function of time is shown in Figure 15. The concentration of DS released at selected time intervals was determined by UV spectrophotometry. The results from the present study indicate that DS-loaded hydrogel with high degrees of drug loading (loading efficiency 70%) can be prepared by a swelling-diffusion method. The amount of DS released in a specified time from the alginate based hydrogel decreased when the pH of the dissolution medium was lowered (Fig. 15), suggesting final release in a medium with pH much higher than that of the stomach. At low pH values, electrostatic repulsion between the carboxylic acid and sulfonic acid groups of backbone is low, thus decreasing gel swelling and minimizing release of DS via diffusion. However, in alkaline media the presence of excess OH^- increases the electrostatic repulsion between carboxylate and sulfonate ions groups of chains, thus increasing the gels swelling degree, so the release of DS increased.

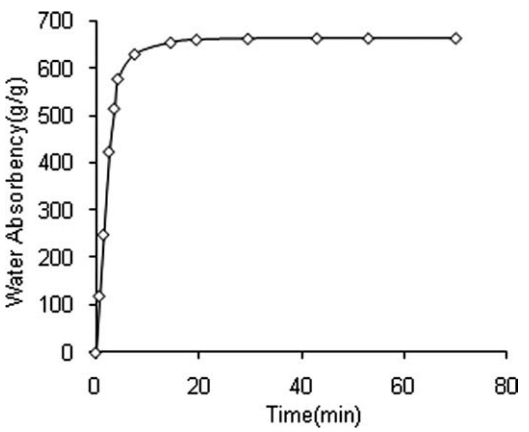


Figure 14 The swelling behavior of Na-Alg based superabsorbent hydrogel at distilled water.

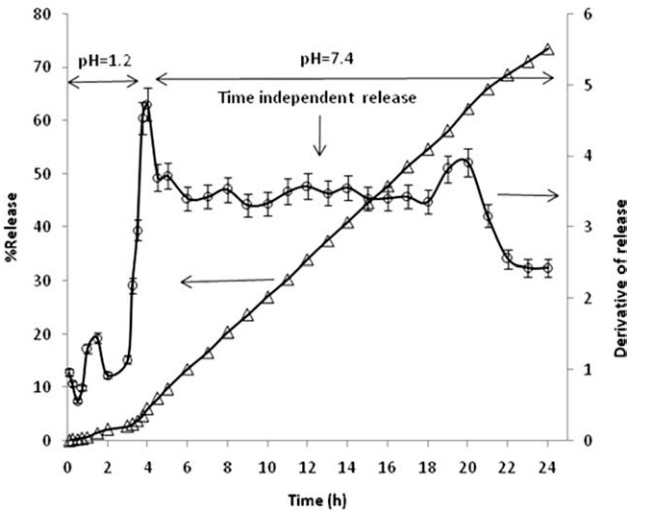


Figure 15 Release of DS from superabsorbent carrier as a function of time and pH at 37°C.

CONCLUSION

The synthesis and swelling characteristics of a new superabsorbent hydrogel based on natural polysaccharide is described. The maximum water absorbency for the sample in optimize condition was around 660 g/g which is a high swelling capacity for a hydrogel. Studying the surface morphology of hydrogels using scanning electron microscopy (SEM) showed a highly porous and cellular structure for the sample. This special morphology can explain the high water absorbency in our system. Furthermore several factors affecting the swelling behavior of hydrogel including pH of medium, and sensitivity

to the salt solution were studied and a normal behavior was observed. The drug-release profiles indicated that the drug entrapped in hydrogels is released faster in SIF than in SGF as a result of the pH sensitivity. These preliminary investigations also revealed that alginate based hydrogels could be applied for the oral drug delivery by virtue of both the bioadhesive and pH-sensitive nature of the protein-based polymeric systems.

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