Controlled Release of Aspirin from pH-Sensitive Chitosan/Poly(vinyl alcohol) Hydrogel

Atif Islam,[1] Tariq Yasin,[1] Ijaz Bano,[1,2] Muhammad Riaz[3]

[1]*Department of Metallurgy and Materials Engineering, Pakistan Institute of Engineering and Applied Sciences, P. O. Nilore, Islamabad 45650, Pakistan*
[2]*Industrial Biotechnology Division, National Institute for Biotechnology and Genetic Engineering (NIBGE), Pakistan Institute of Engineering and Applied Sciences, P. O. Nilore, Islamabad 45650, Pakistan*
[3]*Chemistry Division, Pakistan Institute of Nuclear Science and Technology (PINSTECH), P. O. Nilore, Islamabad 45650, Pakistan*

Received 25 March 2011; accepted 28 July 2011
DOI 10.1002/app.35392
Published online 29 November 2011 in Wiley Online Library (wileyonlinelibrary.com).

ABSTRACT: The aim of this study was to develop a cheap, pH-sensitive enteric coating of aspirin with biocompatible polymers. A novel approach was used to develop enteric coating from chitosan (CS) and poly(vinyl alcohol) (PVA). Solutions of CS and PVA (5 : 1 mol ratio) were mixed and selectively crosslinked with tetraethoxysilane. IR analysis confirmed the presence of the incorporated components and the existence of siloxane linkages between CS and PVA. The crosslinking percentage and thermal stability increased with increasing amount of crosslinker. The response of the developed coating in different media, such as water, pH (nonbuffer and buffer), and ionic media showed hydrogel properties. All hydrogels showed low swelling in acidic and basic pH media, whereas maximum swelling was exhibited at neutral pH. This pH sensitivity of the hydrogel has been exploited as enteric coating for commercial aspirin tablets. The dissolution test of enteric-coated aspirin tablet in simulated gastric fluid (pH 1.2) showed 7.11% aspirin release over a period of 2 h, whereas a sustained release of remaining aspirin (83.25%) was observed in simulated intestinal fluid (pH 6.8). © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 124: 4184–4192, 2012

Key words: biocompatibility; crosslinking; hydrogels

INTRODUCTION

The development in medical and polymer science is greatly helpful for understanding the functions of biological molecules from renewable sources and makes us realize the importance of hydrogel science and technologies. Polymers from renewable sources contain a variety of functional groups, which can be modified to obtain hydrogel properties. Because of their natural origin, these hydrogels are biocompatible, biodegradable, nontoxic and have similarities with extracellular matrix. Therefore, these materials are particularly useful as biomaterials and in regenerative medicine.[1–4] A hydrogel is a two-component system; it can retain a large amount of water upon swelling and can keep its original shape in the swelling medium.[5,6] Hydrogels are formed by the physical or chemical crosslinking of polymers, a hybrid polymer network, and a semi- or full-interpenetrating polymer network.[7] The properties of hydrogels, such as superabsorbency, hydrophilicity, expandability, selective permeability, softness, and low interfacial tension, can be used in medical, biomedical, and pharmaceutical applications.[7–11] The response of a hydrogel to its biological and environmental media, such as pH, ionic strength, solvent composition, electric field, exposure to light, and temperature, made it attractive in research.[11,12]

Chitosan (CS), a derivative of chitin, has been used to obtain biocompatible and biodegradable hydrogels with low toxicity.[2,13] CS is used as a gel, film, and fiber-forming material.[14] These properties make it an important material, and it has many applications in tissue engineering, pharmaceutical industry, biotechnology, and delivery of drugs, nonviral genes, enzymes, and so on. CS hydrogels are very fragile and can be improved through the incorporation of other monomers and polymers and/or by crosslinking.[15–18] CS/poly(vinyl alcohol) PVA hydrogels have been prepared and have exhibited high swelling in the acidic pH range and low swelling in the basic pH range.[19–21] For drug-delivery applications, these hydrogels need modification because they are not suitable for gastrointestinal delivery because there is a need for negligible drug release at acidic pH (stomach) and controlled release at neutral pH (intestinal).

Aspirin [acetyl salicylic acid (ASA)] is most commonly used as an analgesic, anti-inflammatory, and

Correspondence to: T. Yasin (yasintariq@yahoo.com).

antipyretic drug. It also has an antiplatelet effect by inhibiting the production of thromboxane. The most common side effects of regular aspirin in the stomach are dyspepsia, gastric and duodenal erosions, occult bleeding, and hemorrhage.[22] Generally, aspirin is given with meals or antacids for its buffering in the stomach. To avoid these problems, enteric-coated aspirin has been developed and used. Aspirin tablets contain acetylsalicylic acid, which is absorbed rapidly after oral intake. Aspirin is not released from an enteric-coated tablet in the stomach; rather, it facilitates release in the alkaline medium of the intestine.[22]

The purpose of this work was to develop a pH-sensitive enteric coating for aspirin. CS and PVA were selected and crosslinked with tetraethoxysilane (TEOS). Silane crosslinkers are generally used to bind, and crosslink polymers used in biomaterials.[9,13] This synthetic route was novel, easy, and nontoxic compared to previously reported tripolyphosphate, borate, epichlorhydrine, and glutaraldehyde, which are used as crosslinking agents.[7,8,18,23] The synthesized hydrogels exhibited low swelling at acidic and basic pH value and high swelling at neutral pH. The pH sensitivity and ionic nature of these hydrogels made them suitable carriers for drug delivery. The swelling response in deionized water, pH (nonbuffer and buffer), and ionic media were analyzed. The most suitable hydrogel was used as an enteric coating material for aspirin tablets. The release of aspirin from the enteric-coated tablet was studied at stomach and intestinal pHs with high-performance liquid chromatography (HPLC).

EXPERIMENTAL

Materials

CS (viscosity = 200–799 centipoise, degree of deacetylation >75%, bulk density = 0.15–0.30 g/cm^3), PVA (weight-average molecular weight = 146,000–186,000, 98–99% hydrolyzed), acetic acid, TEOS, sodium hydroxide, hydrochloric acid, sodium chloride, and calcium chloride were purchased from Sigma Aldrich (Milwaukee, WI) and were used as received. All other chemicals were analytical grade and were purchased from Sigma Aldrich.

Synthesis of the hydrogels

CS (1 g) was dissolved in 50 mL of acetic acid (0.5*M*) in a glass reactor fitted with a magnetic stirrer. An appropriate amount of PVA was dissolved separately in deionized water (80°C) and added to CS solution; this was followed by the addition of different quantities of TEOS under constant stirring. After 1 h, the resulting mixture was transferred into a plastic container to dry at room temperature. After drying, the films were washed and vacuum-dried at 60°C. The hydrogels were coded as HG2, HG4, HG6, HG8, and HG10, where HG stands for the CS/PVA hydrogel, and the digits represent the percentage crosslinking. All formulations contained fixed mol ratio of CS to PVA of 5 : 1.

The structural analysis was performed with a Fourier transform infrared (FTIR) spectrophotometer (Thermo Electron Corp., Nicolet 6700, Waltham, Massachusetts, USA). The spectra were recorded with an attenuated reflectance technique with a diamond crystal; samples were scanned from 4000 to 400 cm^{-1} with a resolution of 6.0 cm^{-1} and were averaged over 200 scans.

The surface morphology of the samples was imaged with the contact mode of an atomic force microscopy (AFM) system (JPK NanoWizardIIs, Berlin, Germany). A silicon cantilever was used with a force constant of 0.2 N/m. The samples were swelled in distilled water before imaging. The images were obtained from top-view optics at a scan size of 10 μm.

The gel contents of the samples were determined according to ASTM 2765.[24] The samples were cut into small pieces, and a known weight was placed into a stainless steel cloth. Extraction was carried out with distilled water for 8 h in a Soxhlet extractor. After extraction, the samples were vacuum-dried at 60°C to a constant weight. The gel fraction was measured by weighing the insoluble part of samples using the following equation:

$$\text{Gel fraction } (\%) = (W_g/(W_o) \times 100$$

where W_g (g) is the weight of extracted sample and W_o (g) is the initial weight of the sample.

The thermal stability was studied with thermogravimetric analysis (TGA). The experiments were performed on a Mettler Toledo (TGA/SDTA851^e) instrument (Schwerzenbach, Switzerland) under a nitrogen flow of 50 mL/min. Approximately 6–8 mg of sample was placed in the alumina pan at a heating rate of 20°C/min from room temperature to 600°C.

Swelling studies

Swelling in water

The following procedure was used in all of the swelling experiments.[9,13] The dried sample (~ 50.0 mg) was placed in vial filled with solutions (100 mL), and the vials were set in a temperature-controlled bath at a desired temperature. At different time intervals, the weight of the swollen sample was determined after removal of the excess surface solution. The sample was placed again in the same solution. The swelling ratio of the sample was determined gravimetrically with the following equation:

$$\text{Swelling (g/g)} = (W_s - W_d)/W_d$$

where W_d is the dry weight and W_s is the swollen weight of the sample at time t.[25]

Swelling in nonbuffer, buffer, and salt solutions

The swelling response of the hydrogels at pH 1–13 was studied in nonbuffer and buffer solutions. Nonbuffer solutions were prepared from the dilution of stock solutions of HCl (0.1*M*) and NaOH (0.1*M*) with distilled water. Buffer solutions were prepared with a standard method, and the pH values were rechecked by a pH meter. The swelling of the hydrogels was also studied in sodium chloride and calcium chloride solutions having different concentrations ranging from 0.05 to 1.0 mol/L.

Aspirin-release behavior

Preparation of the buffer solutions

Simulated gastric fluid (SGF; pH = 1.2) was prepared by the mixture of 1 g of NaCl in 3.5 mL of HCl (37%); this was diluted up to 500 mL with distilled water. Simulated intestinal fluid (SIF; pH = 6.8) was prepared by the mixture of 250 mL of KH_2PO_4 (0.2*M*) with 118 mL of NaOH (0.2*M*).[26]

Aspirin-coating and -release behavior

Commercial aspirin tablets (Disprin from Reckitt & Colman, Karachi, Pakistan) containing 300 mg of ASA were taken and coated with HG2 solution. A dry nitrogen atmosphere was maintained in the glovebox to minimize moisture absorption and acid hydrolysis. The coated tablets were air-dried in the glovebox for 1 day. The enteric-coated tablets were placed for 2 h in a beaker containing SGF solution and then transferred to the SIF solution. Aliquots of 3 mL were taken from the vial every 30 min; 3 mL of fresh solution was added back to the vial to make up the liquid volume. The amount of released aspirin was analyzed with HPLC instrument.

A PerkinElmer series-10 solvent delivery system (Massachusetts, USA) was fitted with a 20-μL loop and a Rheodyne 7120 sample injector (Wilmington, Delaware). A variable UV detector (DuPont, Tokyo, Japan) and a data processor (D-2500, Hitachi, Japan) were used. The HPLC column was a Eurosphere C18 (25 cm × 4.6 mm) from Knauer (Berlin, Germany). The mobile phase contained 70% methanol and 30% NaH_2PO_4/H_3PO_4 buffer at pH 3.0 and was used at a flow rate of 0.8 mL/min; the UV wavelength was 230 nm. The phosphate buffer was used to keep the ASA in nonionized form. A reference of 300 mg of aspirin in SGF and SIF was prepared. The amount of released aspirin was calculated by the peak heights of each aliquot from the HPLC data.

RESULTS AND DISCUSSION

The blend of CS with PVA and its crosslinking with different amount of TEOS gave hydrogels with different crosslinking densities. The possible chemical reactions between CS, PVA, and TEOS are presented in Scheme 1.

Structural analysis

Infrared spectroscopy was performed to analyze the chemical changes between the incorporated components. The IR spectra of CS, PVA, and crosslinked CS/PVA hydrogels are shown in Figure 1. The spectrum of CS showed absorption peaks at 1653 and 1322 cm^{-1}, which were characteristic of chitin and CS moieties, respectively. The peaks at 893 and 1155 cm^{-1} confirmed the pyranose ring and saccharine structure of CS, respectively.[27,28]

The IR spectrum of PVA showed a broad band between 3500 to 3250 cm^{-1}, which showed O—H stretching of intermolecular and intramolecular hydrogen bonds. The vibrational band of alkyl groups (C—H stretching) was observed from 3000 to 2840 cm^{-1}. The peaks at 1750 and 1730 cm^{-1} were attributed to the unhydrolyzed acetate group from poly(vinyl acetate) during PVA synthesis.[27,28]

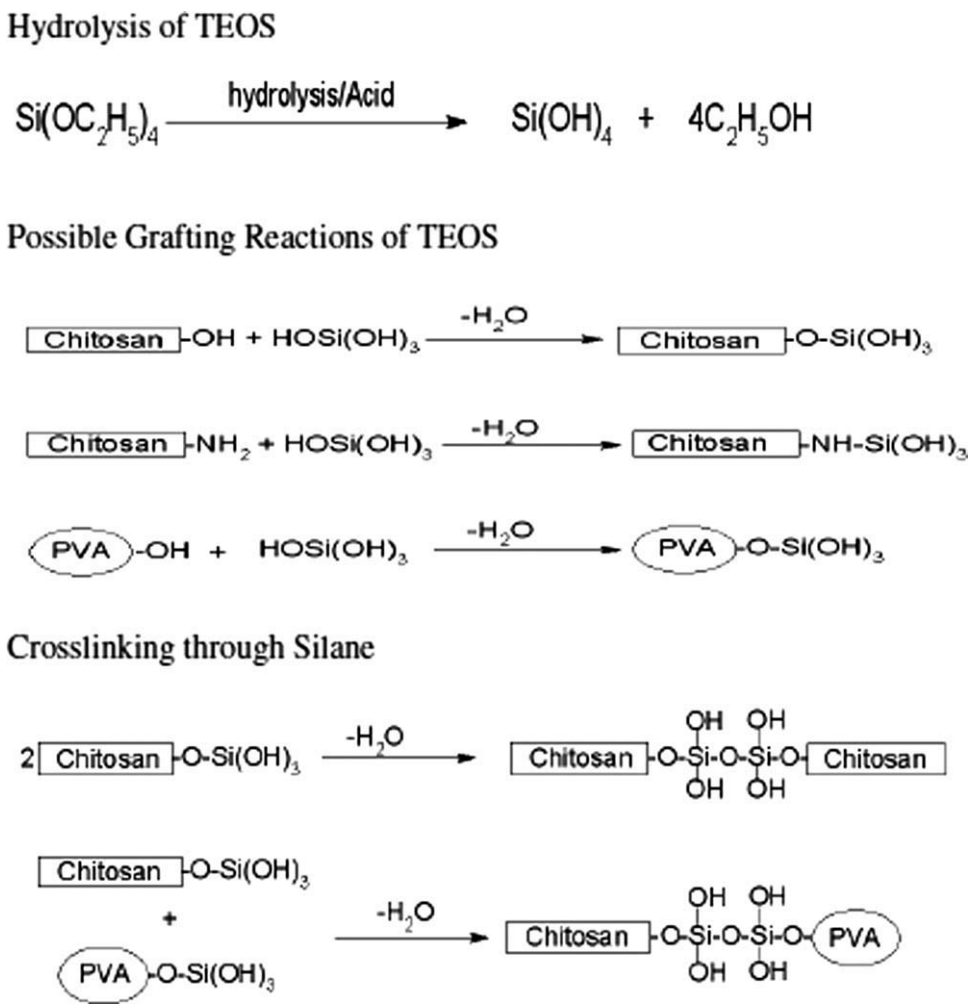
The IR spectrum of the CS/PVA hydrogels revealed peaks in the range 1100–1020 cm^{-1}; this indicated the presence of Si—O—Si and Si—O—C linkages.[13] The existence of siloxane linkages confirmed the reaction of TEOS with CS and PVA, as already discussed in the scheme. Moreover, the intensity of siloxane increased from 10 to 21% as the crosslinker amount was increased from 2 to 10% during the crosslinking reactions.

AFM

The surface topographies of the HG2 and HG10 hydrogels in swollen form are shown in Figure 2(a,b). Both the hydrogels showed macromolecule aggregation, but the aggregation pattern and its size were different from each other. The dark portion in the images was due to the presence of water in the hydrogel network. The low swelling of HG10 showed the effect of crosslinking on its swelling response compared to HG2. These macropores in the hydrogel were responsible for the higher degree of swelling and allowed interaction with surrounding hydrophilic groups.[29]

TGA

The thermal decomposition data of CS, PVA, HG2, and HG10 at various percentage weight losses are shown in Figure 3. This figure shows that the



Scheme 1 Proposed chemical reactions during the synthesis of the CS/PVA hydrogel.

degradation of PVA started from 260°C and that nearly 90% of the polymer was degraded up to 600°C. The thermal degradation of CS took place in steps, which involved the removal of moisture and dehydration of CS from 50 to 280°C. Above 280°C, the main backbone of the polymer degraded. Both HG2 and HG10 showed similar weight loss patterns up to 600°C. The 10% weight loss of HG2 was at 190.6°C, whereas that of HG10 was at 194.9°C. This higher temperature stability of HG10 was the result of increased crosslinking.

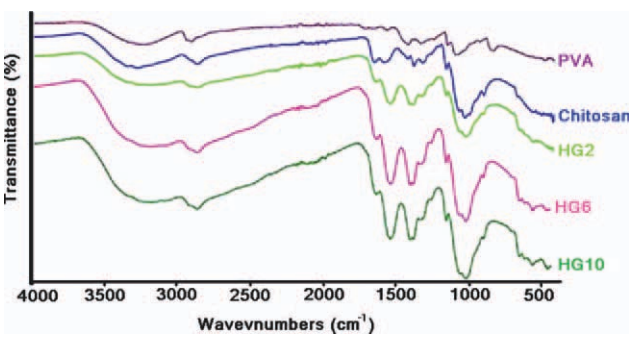


Figure 1 FTIR spectra of the PVA, CS, and crosslinked CS/PVA hydrogels. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

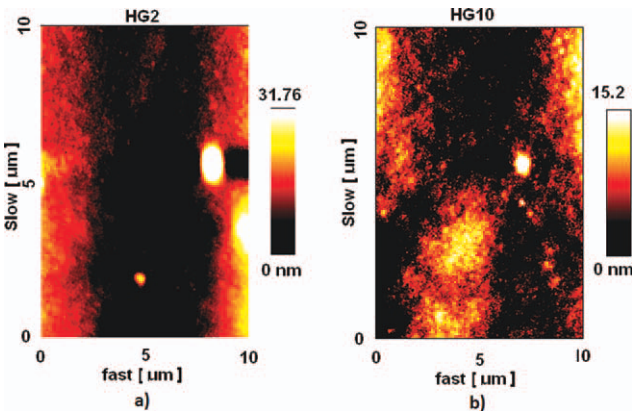


Figure 2 AFM images of the swollen (a) HG2 and (b) HG10 hydrogels. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

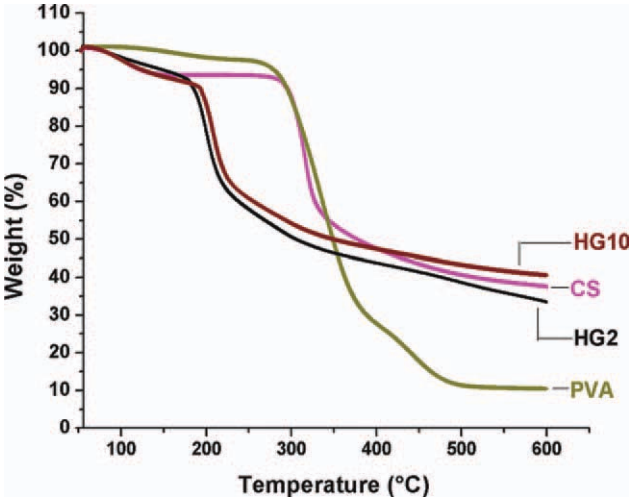


Figure 3 Thermograms of the CS, PVA, HG2, and HG10 hydrogels. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

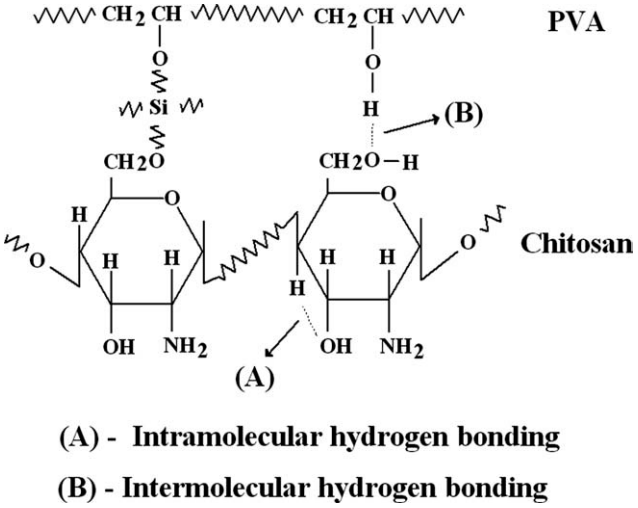


Figure 4 Intermolecular and intramolecular hydrogen bonding between the CS/PVA hydrogels.

Gel content analysis

The extraction of the CS/PVA crosslinked samples with water left behind the crosslinked polymer network, which gave the percentage crosslinking. The gel contents of the crosslinked CS/PVA hydrogel are shown in Table I. The gel content increased linearly as the concentration of crosslinker increased from 2 to 10%. The gel content of HG2 was 66.7%; this increased by 13.6% with an increase in the concentration of TEOS crosslinker from 2 to 10%.

Swelling studies

Swelling in water

The swelling response of a hydrogel in water is attributed to the absorption mechanism caused by the diffusion process. This diffusion process is controlled by the affinity between the polymer chains and the external media.[30] Swelling affects the physical properties of a hydrogel, which can be controlled by changes in the crosslinking density, charge, pK_a values of the ionizable groups, and nature of polymer.[13,31] The blends of CS and PVA were miscible and interacted through intermolecular and intramolecular hydrogen bonding.[32] The possible structure of the crosslinked CS/PVA hydrogel is shown in Figure 4.

The time-dependent swelling of the CS/PVA hydrogel in deionized water is shown in Figure 5. All of the reported results are the average of three readings with a relative standard deviation of 5%. All of the hydrogels exhibited a rapid increased in absorbed water content and reached their equilibrium state around 5 h. It is evident from the figure that the swelling increased with increasing time, and HG2 showed a maximum swelling of 752 g/g after 6 h.

The increase of crosslinker amount from 2 to 10% decreased the swelling of hydrogel. This decrease in swelling might have been to a decrease in the hydrophilicity of the hydrogel through the incorporation of more —OH groups of CS and PVA for crosslinking, as

TABLE I
Diffusion Parameters and Gel Contents of the Crosslinked CS/PVA Hydrogels

	Hydrogel				
	HG2	HG4	HG6	HG8	HG10
n	0.85	0.80	0.78	0.70	0.65
k	0.14	0.15	0.16	0.17	0.21
Gel content (%)	66.7	69.5	73.7	77.6	80.2

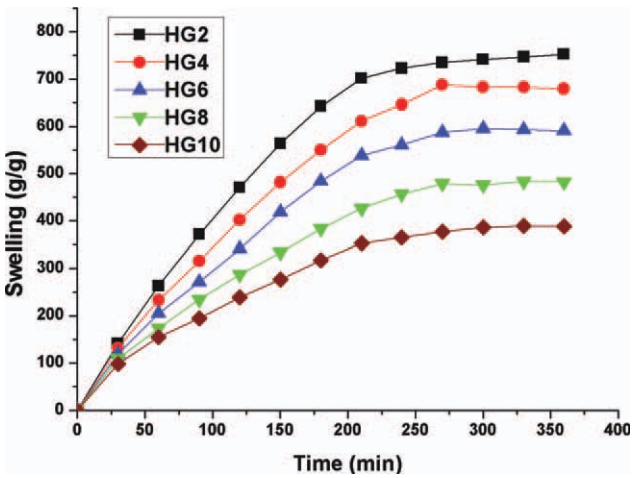


Figure 5 Swelling responses of the crosslinked CS/PVA hydrogels in water. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

shown in the scheme. These reactions also decreased the pore size of the CS/PVA hydrogels, and the increased gel contents with increasing TEOS concentration further confirmed this argument. These factors retarded the diffusion process of water molecules into the hydrogel. Rasool et al.[9] also observed similar behavior in carrageenan/acrylic acid hydrogels for insulin delivery.

As discussed earlier, the crosslinking density affected the hydrophilic/hydrophobic nature of the CS/PVA hydrogels. Therefore, it was very important to investigate the mechanism and kinetics of the swelling behavior.

The mechanism of water diffusion could be determined with the following equation:

$$M = kt^n$$

where M is the fractional swelling ratio at time t (min) and k is the rate constant that is characteristics of the polymer network and water, and n is the diffusion exponent, which indicates the mechanism of diffusion. The value of n is used to characterize the transport or release mechanism.[33] When n is equal to 0.5 or 1, diffusion is defined as Fickian and case II diffusion, respectively. When it is between 0.5 and 1, it is non-Fickian (anomalous diffusion). If the value of n is greater than 1, it is super-case II diffusion.[30] The values of n and k obtained from Figure 5 are shown in Table I. This table shows non-Fickian diffusion in all hydrogels because the value of n was above 0.5 in all cases. The increase in the crosslinker concentration from 2 to 10% lowered the value of n from 0.85 in HG2 to 0.65 in HG10.

Effect of the pH on swelling

The response of the molecular interactions (e.g., hydrogen bonding, Van der Waals and electrostatic interactions) present in the hydrogel was greatly affected by the pH of the external media. This change in the pH of the external media affected the penetration of solvent molecules into the hydrogel network.[30] This response of swelling and deswelling of hydrogels at different pHs plays an important role in biomedical and pharmaceutical applications. In this study, the swelling response of the hydrogels against pH (from 1 to 13) in nonbuffer and buffer media was investigated.

Swelling in nonbuffer pH

The effect of nonbuffer pH on the swelling of the hydrogel is shown in Figure 6. This figure shows low swelling at acidic and basic pHs, and maximum swelling was observed at neutral pH. The crosslinking percentage also affected the swelling response,

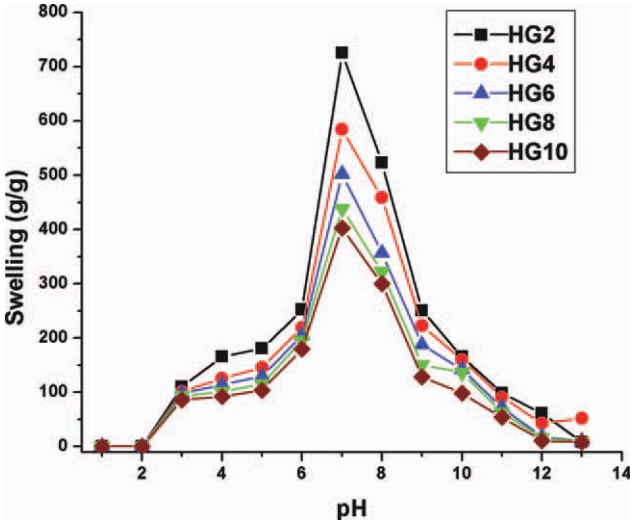


Figure 6 Swelling behaviors of the crosslinked CS/PVA hydrogels in nonbuffer. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

and it decreased with increasing crosslinking percentage. The swelling of HG2 was negligible up to pH 2, and it increased steadily with a sharp increase at pH 6. The maximum swelling was observed at pH 7 (725.3 g/g). Above this pH, swelling again decreased and reached 8.3 g/g at pH 13. This interesting pH sensitivity of the prepared hydrogels could be explained as follows: the CS chains exhibited amino groups ($-NH_2$), which ionized to $-NH_3^+$ in acidic pH and deionized at basic pH. At low pH, it exhibited strong repulsive interactions between the polymer chains. Because the free movement of $-NH_3^+$ groups was not allowed as they were fixed on the polymer chain, the mobile counter ion (Cl^-) present in the media moved and localized near the $-NH_3^+$ present in the polymer chains to keep the electroneutrality. This, in turn, increased the osmotic pressure within the hydrogel and decreased swelling. Mitsuhiro et al.[34] already discussed this in the volume-phase transition and related phenomenon of polymer gels.

At neutral pH, the polymers chains present in the hydrogels were no more ionized and exhibited optimized chain interaction within the sequence of a polymer (intrachain hydrogen bonding) and sequence of polymers (interchain hydrogen bonding). The chain associations via hydrogen bonding of amino and hydroxyl groups of CS and the hydroxyl group of PVA and crosslinking stabilized the configuration of the swollen structure. As a result, the hydrogel incorporated more water in different forms around hydrogen-bonded groups, capillary pores, and so on, which in turn, gave the highest swelling. At basic pH (>7), because of the complete deprotonation of $-NH_3^+$ groups, the degree of ionization of

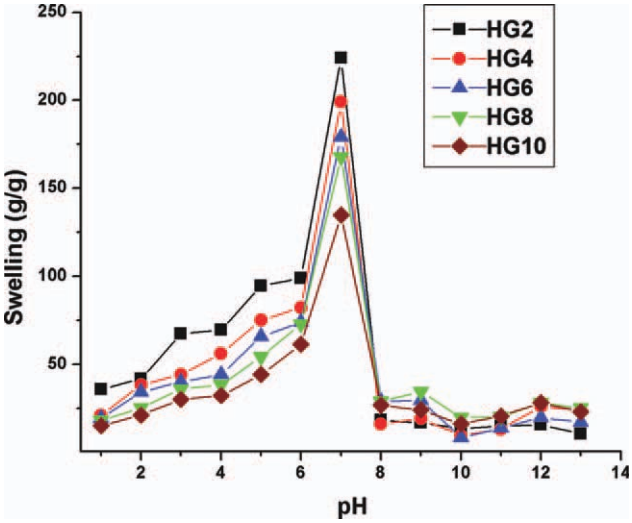


Figure 7 Swelling of the crosslinked CS/PVA hydrogels in buffer. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

the hydrogel was lowered; this, in turn, lowered its swelling.

Swelling in buffer pH

The swelling behavior of the CS/PVA hydrogels as a function of buffer pH was also studied, and the results are shown in Figure 7. This figure shows similar swelling behavior against pH, as observed in nonbuffer media. All of the hydrogels showed low swelling at acidic and basic pH, and maximum swelling was exhibited at neutral pH. However, at the same pH, these hydrogels showed three times less swelling compared to those in the nonbuffer media. The swelling ratio of HG2 was 224.0 g/g at pH 7, whereas at same pH in nonbuffer media, it was 725.3 g/g. This possible reduction in swelling might have been due to the high ionic strength of the buffer media compared to the nonbuffer media.

Swelling in electrolytes

The influence of the type and concentration of two electrolytes, namely, NaCl and $CaCl_2$ were studied, and the swelling response of the hydrogel is shown in Figure 8. This figure shows that as the concentration of NaCl and $CaCl_2$ increased in the solution, the swelling decreased. This behavior might be have been due to the increased ionic strength of the swelling media; this reduced the osmotic pressure between the external media and hydrogel network.

All hydrogels showed higher swelling at concentration of 0.05 mol/L of $CaCl_2$ as compared to NaCl. In HG2, the swelling at 0.05 mol/L $CaCl_2$ was 94.0 g/g, whereas, at same NaCl concentration, it was 65.2 g/g. This increase in swelling at low concentration was a consequence of Ca^{2+} complexation with the polymer network, which increased its pore size.

Release analysis of enteric-coated aspirin

A commercially available Disprin tablet was coated, and its release in SGF and SIF for different time periods was studied. The HG2 formulation was selected for enteric coating because of its high swelling. The HPLC technique was used to measure aspirin release at a 230-nm wavelength. The retention times of ASA in methanol were at 4.07 min. This retention time was increased to 4.23 and 4.25 min for standard ASA in SGF and SIF, respectively.

Figure 9 shows the chromatograms obtained during the release of aspirin from the enteric-coated tablet at different time intervals. The *in vitro* release

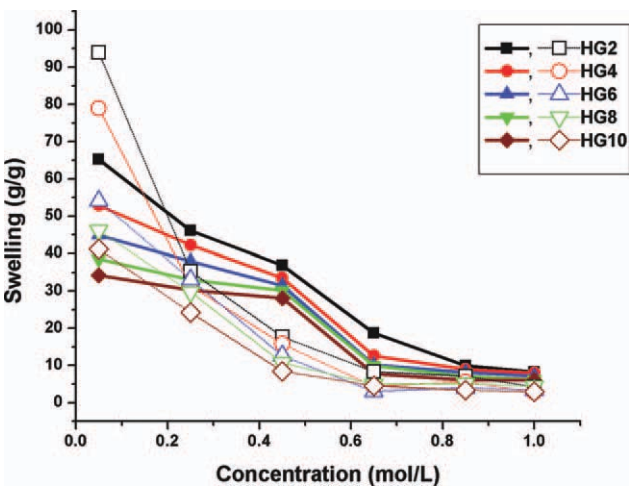


Figure 8 Swelling behaviors of the crosslinked CS/PVA hydrogels in electrolytes. [NaCl (—) and $CaCl_2$ (. . .)]. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

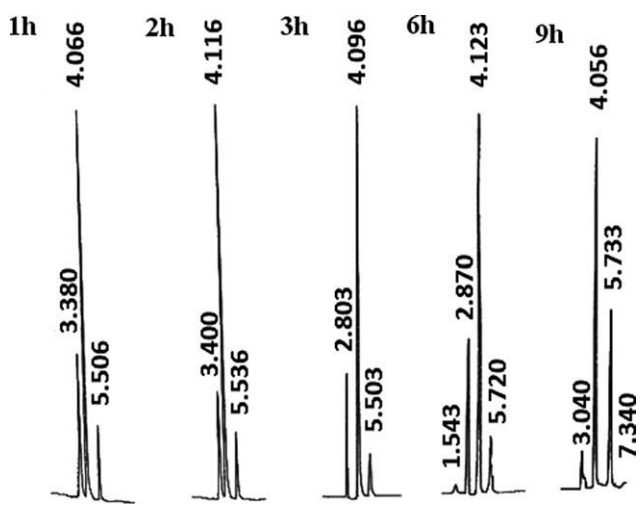


Figure 9 Chromatograms showing the response of ASA and SA after 1, 2, 3, 6, and 9 h from HG2.

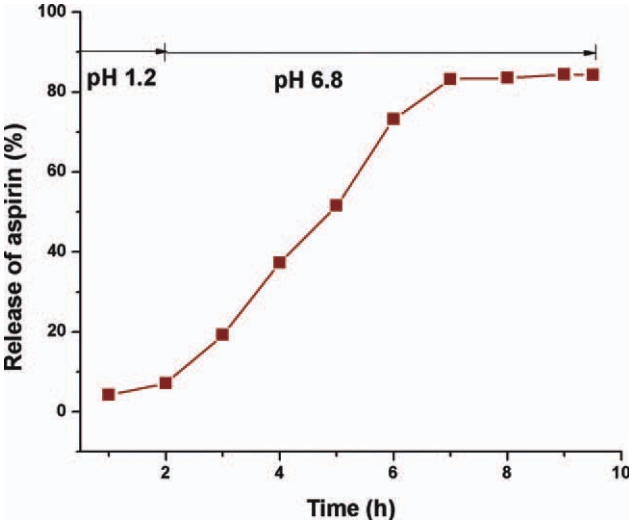


Figure 10 Release behaviors of aspirin from the HG2 hydrogel at pH 1.2 and 6.8. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

data obtained from these chromatograms after every 0.5 h are shown in Figure 10. This figure shows a negligible release of aspirin from HG2 in SGF for 2 h, and 7.11% aspirin was released during this time. This might have been due to the presence of aspirin in nonionized form, which was trapped within the ionized hydrogel.

After 2 h, the tablet was placed in SIF, and its release was monitored for a further 7 h. When the hydrogel was transferred into SIF, it swelled gradually into its fully swollen form. The neutral pH of the SIF converted the aspirin into ionized form. Both the swollen structure and the ionized aspirin facilitated its removal from the hydrogel. A sustained amount of aspirin was released during 7 h, and a total amount of 83.25% of the aspirin was released during this time. This release profile of the enteric-coated aspirin in SGF and SIF fulfilled the U.S. Pharmacopeia specification (USP XXIV).[22] According to this; a maximum release of 10% is acceptable at the acidic stage (SGF), and a minimum of 80% is acceptable at buffer stage (SIF). The presence of a peak at 5.53 min was due to the hydrolysis of ASA into salicylic acid during tablet drying. After 9 h, the remaining aspirin was difficult to measure because of the crumbling of the hydrogel into large fragments and the entrapment of aspirin in the hydrogel.

CONCLUSIONS

A novel pH-sensitive hydrogel was prepared from CS and PVA and selectively crosslinked with TEOS. The presence of incorporated components and the development of siloxane linkages was confirmed by FTIR spectroscopy. The gel content analysis confirmed the presence of three-dimensional network structures in the hydrogel. The swelling of the hydrogel in deionized water was affected by crosslinking, and low swelling was observed in the highly crosslinked hydrogel. The hydrogel (HG2) having a 66.7% gel content showed a maximum swelling of 752 g/g in water. The large swelling of the hydrogel in water could be understood by diffusional process. The value of n ranged from 0.65 in HG10 to 0.85 in HG2; this demonstrated that the water transport mechanism was non-Fickian in nature. The pH of the surrounding media significantly affected the swelling process of the CS/PVA hydrogel. The response against pH revealed high swelling in nonbuffer media and low swelling in buffer media. This pH sensitivity and low swelling in acidic and basic pH media and maximum swelling at neutral pH makes this hydrogel suitable for drug-delivery applications. HG2 was used as an enteric coating, and commercial aspirin tablets were coated. The dissolution test of the enteric-coated aspirin tablet in SGF (pH 1.2) showed a 7.11% aspirin release over a period of 2 h, whereas a sustained release (83.25%) of aspirin was observed in SIF (pH 6.8).

Two of the authors (A.I. and I.B.) are highly obliged to Higher Education Commission of Pakistan for granting them Ph.D. fellowships to work at the Department of Chemical and Materials Engineering at PIEAS (Pakistan Institute of Engineering and Applied Sciences).

References

1. Piyakulawat, P.; Praphairaksit, N.; Chantarasiri, N.; Muangsin, N. AAPS Pharm SciTech 2007, 4, E1.
2. Chen, S. C.; Wu, Y. C.; Mi, F. L.; Lin, Y. H.; Yu, L. C.; Sung. H. W. J Controlled Release 2004, 96, 285.
3. Reis, A. V.; Guilherme, M. R.; Moia, T. A.; Mattoso, L. C.; Muniz, E. C. J Polym Sci Part A: Polym Chem 2008, 46, 2567.
4. Dusek, K.; Toyoichi, T. Advances in Polymer Science; Springer-Verlag: Berlin, 1993; p 109.
5. Park, K. P.; Nho, Y. C. Radiat Phys Chem 2003, 67, 361.
6. Bajpai, A. K.; Shukla, S. K.; Bhanu, S.; Kankane, S. Prog Polym Sci 2008, 33, 1088.
7. Rodrigues, I. R.; Forte, M. M. C.; Azambuja, D. S.; Castagno, K. R. L. React Funct Polym 2007, 67, 708.
8. Lorenzo, C. A.; Concheiro, A. J Controlled Release 2002, 80, 247.
9. Rasool, N.; Yasin, T.; Heng, J. Y. Y.; Akhter, Z. Polymer 2010, 51, 1687.
10. Sokker, H. H.; Ghaffar, A. M. A.; Gad, Y. H.; Aly, A. S. Carbohydr Polym 2009, 75, 222.
11. Wang, T.; Turhan, M.; Gunasekara, S. Polym Int 2004, 53, 911.
12. Chen, H.; Hsieh, Y. L. J Polym Sci Part A: Polym Chem 2004, 42, 6331.
13. Rasool, N.; Yasin, T.; Akhter, Z. e-Polymers 2008, 142, 1.
14. Wang, M.; Qiang, J.; Fang, Y.; Hu, D.; Cui, Y.; Fu, X. J Polym Sci Part A: Polym Chem 2000, 38, 474.
15. Jin, R.; Teixeira, L. S. M.; Dijkstra, P. J.; Karperien, M.; Van Blitterswijk, C. A.; Zhong, Z. Y.; Feijen, J. Biomaterials 2009, 30, 2544.

16. Zhao, L.; Mitomoa, H.; Zhaib, M.; Yoshiic, F.; Nagasawac, N.; Kumec, T. Carbohydr Polym 2003, 53, 439.
17. Yang, X.; Yang, K.; Wu, S.; Chen, X.; Yu, F.; Li, J.; Ma, M.; Zhu, Z. Radiat Phys Chem 2010, 79, 606.
18. Tang, Y.; Du, Y.; Li, Y.; Wang, X.; Hu, X. J Biomed Mater Res Part A 2009, 91, 953.
19. Singh, A.; Narvi, S. S.; Dutta, P. K.; Pandey, N. D. Bull Mater Sci 2006, 29, 233.
20. Kim, S. J.; Park, S. J.; Kim, S. I. React Funct Polym 2003, 55, 53.
21. Kim, S. J.; Lee, K. J.; Kim, I. Y.; Kim, S. I. J. Macromol Sci Part A: Pure Appl Chem 2003, 40, 501.
22. Zeitoun, A. A.; Dib, J. G.; Mroueh, M. J Appl Res 2003, 3, 242.
23. Liang, S.; Liu, L.; Huang, Q.; Yam, K. L. Carbohydr Polym 2009, 77, 718.
24. Mir, S.; Yasin, T.; Halley, P. J.; Siddiqi, H. M.; Nicholson, T. Carbohydr Polym 2011, 83, 414.
25. Paradossi, G.; Lisi, R.; Paci, M.; Crescenzi, V. J Polym Sci Part A: Polym Chem 1996, 34, 3417.
26. Nho, Y. C.; Park, S. E.; Kim, H. I.; Hwang, T. S. Nucl Instrum Methods Phys Res B 2005, 236, 283.
27. Costa-Junior, E. S.; Barbosa-Stancioli, E. F.; Mansur, A. A. P.; Vasconcelos, W. L.; Mansur, H. S. Carbohydr Polym 2009, 76, 472.
28. Mansur, H. S.; Costa, E. S., Jr.; Mansur, A. A. P.; Barbosa-Stancioli, E. F. Mater Sci Eng C 2009, 29, 1574.
29. Salimi, H.; Pourjavadi, A.; Seidi, F.; Jahromi, P. E.; Soleyman, R. J Appl Polym Sci 2010, 117, 3228.
30. Swarnalatha, S.; Gopi, R.; Kumar, A. G.; Selvi, P. K.; Sekaran, G. J Mater Sci Mater Med 2008, 19, 3005.
31. Francisa, S.; Kumarb, M.; Varshney, L. Radiat Phys Chem 2004, 69, 481.
32. Jin, L.; Bai, R. Langmuir 2002, 18, 9765.
33. Brannon-Peppas, L.; Peppas, N. A. Biomaterials 1990, 11, 635.
34. Shibayama, M.; Tanaka, T. In Advances in Polymer Science; Duesk, K., Tanaka, T., Eds.; Springer-Verlag: Berlin, 1993; p 109.