Electrical/pH Responsive Properties of Poly(2-acrylamido-2-methylpropane sulfonic acid)/Hyaluronic Acid Hydrogels

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ABSTRACT: Poly(2-acrylamido-2-methylpropane sulfonic acid) (PAMPS)/hyaluronic acid (HA) interpenetrating polymer network (IPN) hydrogels have been prepared by using the sequential-IPN method. The IPN hydrogels exhibited swelling behavior in solutions at various pHs, in NaCl solutions, and under electrical DC stimulation. The IPN hydrogels were highly swollen in water, but lost much of their water capacity when transferred to solutions having a high ionic strength. The IPN hydrogels showed a significant responsive deswelling in an applied electric field. This behavior indicates the potential application of IPN hydrogels as biomaterials. © 2004 Wiley Periodicals, Inc. J Appl Polym Sci 92: 1731–1736, 2004

Key words: poly(2-acrylamido-2-methylpropane sulfonic acid); hyaluronic acid; hydrogel

INTRODUCTION

Smart polymer hydrogels can reversibly change their volume and shape in response to external stimuli, such as temperature, pH, solvent, ionic strength, and electric field.[1,2] Recently, much interest focused on electrically responsive hydrogels actuated by an electrical stimulus, due to their potential scientific and technological importance.[2–5] Electrically responsive hydrogels are usually made of polyelectrolytes, and these are an insoluble, but swellable, interpenetrating polymer network (IPN) that contains both cations and anions.

The swelling properties of polyelectrolyte networks, which can be described in terms of the swelling rate and maximum solution uptake at equilibrium, depend on the physicochemical properties of the polymers and on the composition of the surrounding medium.[6] Several reports have demonstrated alterations in the swelling equilibrium of polyelectrolyte networks by varying the backbone hydrophobicity of the polymer.[7,8] Polyelectrolyte gels change their conformation with the degree of dissociation, which is a function of variables such as the pH value, the polarity of the solvent, the ionic strength, and the external temperature of the gel solution.[9] Recently, much attention has been paid to the equilibrium swelling of polyelectrolyte gels caused by various types of externally applied stimuli, with a view to their possible applications in chemomechanical systems (i.e., for the conversion of electrostatic interaction energy working within a fixed charge into mechanical energy).[10,11] The swelling of polyelectrolyte gels in an applied electric field is of increasing interest.[10,12]

Synthetic polyelectrolytes, such as polyacrylic acid, have shown pH- and electric-responsive volume changes.[13] Stimuli-responsive gels have been studied extensively since Tanaka first analyzed the phase transition of a hydrolyzed polyacrylamide.[10] Of the various mechanisms of stimulus-sensitivity, the most important is the phase separation of gels with both hydrophilic and hydrophobic chemical structures, such as poly(N-isopropylacrylamide), which causes polymer precipitation from a solvent because of desolvation in response to a given stimulus. Another important characteristic is the volume change of polyelectrolytes due to conformational changes caused by ionic interactions between the polymeric ions, or between the polymeric ions and counter ions in the solvent.[14]

The swelling properties of weak polyelectrolyte hydrogels vary greatly depending on the pH of the solution. However, strong electrolyte hydrogels dissociate completely over a wide pH range, and therefore, they exhibit a pH-independent swelling behavior. Sulfonic acid containing hydrogels represent a class of strong polyelectrolyte hydrogels that possess a high degree of ionization. It has been shown that linear polymers containing sulfonate groups derived from 2-acrylamido-2-methylpropane sulfonic acid (AMPS) exhibit an extensive coil-type expansion in aqueous solutions.[15] Karlsson et al.[16] and Melekaslan et al.[17]

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TABLE I
Composition and Designation of the
PAMPS/HA IPN Hydrogels

Sample	AMPS (wt %)	HA (wt %)
AmH81	8	1
AmH61	6	1
AmH41	4	1

observed the swelling behavior of PAMPS hydrogels over a wide pH range in solutions of various salts, and Otake et al.[18] designed a gel robot composed of a PAMPS hydrogel.

The aim of the present study was to make an electro-pH-sensitive hydrogel. For this purpose, AMPS, as a very strong electrolyte hydrogel, and hyaluronic acid (HA), as a highly pH-sensitive polymer, were selected. PAMPS/HA IPN hydrogels were prepared, and their swelling behavior and stimuli-sensitive properties in various environments, such as changing pH, in NaCl solutions and in electric fields, were studied.

EXPERIMENTAL

Materials

The AMPS monomer, N,N′-methylene-bis-acrylamide crosslinker (BIS, crosslinker I), and potassium persulfate (KPS) initiator used were purchased from the Aldrich Chemical Co. (Milwaukee, WI). The hyaluronic acid (HA sodium salt, $M_v = 1.7 \times 10^6$) was provided by the Pacific Chemical Co. Ltd. (Seoul, Korea). The 1-ethyl-(3–3-dimethylaminopropyl) carbodiimide hydrochloride crosslinker (EDC, crosslinker II) used was purchased from the Sigma Chemical Co. (St. Louis, Mo). All other chemicals were of reagent grade and were used without any further purification.

Preparation of the PAMPS/HA hydrogels

The PAMPS/HA IPN hydrogels were prepared by using the sequential-IPN method, employing the following two steps. The first step was to dissolve HA and AMPS powders in deionized water at room temperature over 12 h. Each solution was mixed by using specific weight ratios and stirred at room temperature for 12 h. The crosslinking polymerization reaction of the AMPS was carried out in water at 40°C for 1 day in the presence of HA, using BIS (5 wt % of the AMPS) and KPS (1 wt % of the AMPS) as the crosslinking agent and initiator, respectively. The detailed compositions and designations of the PAMPS/HA IPN hydrogels are listed in Table I. The polymerized solution was poured into a petri dish and dried at 30°C for 2 days.

The second step was to crosslink the HA with EDC. The prepared films were immersed in an acetone/water mixture (9 : 1 by volume), containing a given concentration of EDC (20 wt % of the HA in each sample). To ensure adequate crosslinking, the samples were shaken slowly at room temperature for 48 h. The dried films were washed with distilled water to remove any unreacted materials that were not incorporated into the network. The films were then dried in a convection oven at 30°C for 1 week.

Measurements

Swelling behavior

To measure the swelling ratios, preweighed, dried samples were immersed in deionized water, and in various buffered and NaCl solutions. After the excess surface solution had been removed with filter paper, the swollen samples were weighed at various time intervals. This procedure was repeated until there was no further weight increase, and then for a further five times. The swelling ratio was determined according to the equation

$$\text{Swelling Ratio } (\text{---}) = [(W_s - W_d)/W_d] \qquad (1)$$

where W_s and W_d denote the weights of the swollen and dry samples, respectively. The equilibrium water content (EWC) was calculated from the equation:

$$\text{EWC } (\text{---}) = [(W_e - W_d)/W_e] \qquad (2)$$

where W_e represents the weight of the swollen gel at equilibrium.

Effect of electric fields

The technique used to carry out the electric field effect measurements in a noncontact DC electric field has been described in previous work.[13] Deionized water was poured into a petri dish equipped with two parallel carbon electrodes spaced 30 mm apart. The PAMPS/HA IPN hydrogels were swollen in deionized water at room temperature and then cut into 30 × 30 mm² strips. When an electric stimulus was applied, the EWC values were measured.

RESULTS AND DISCUSSION

The swelling ratios of the IPN hydrogels were calculated by using eq. (1), with the swelling kinetics of the IPN hydrogels in deionized water at room temperature being shown in Figure 1. All the IPN hydrogels initially swelled rapidly and reached equilibrium within 12 h. Because HA reaches equilibrium in about 1 h, the initial swelling behavior was due to the swell-
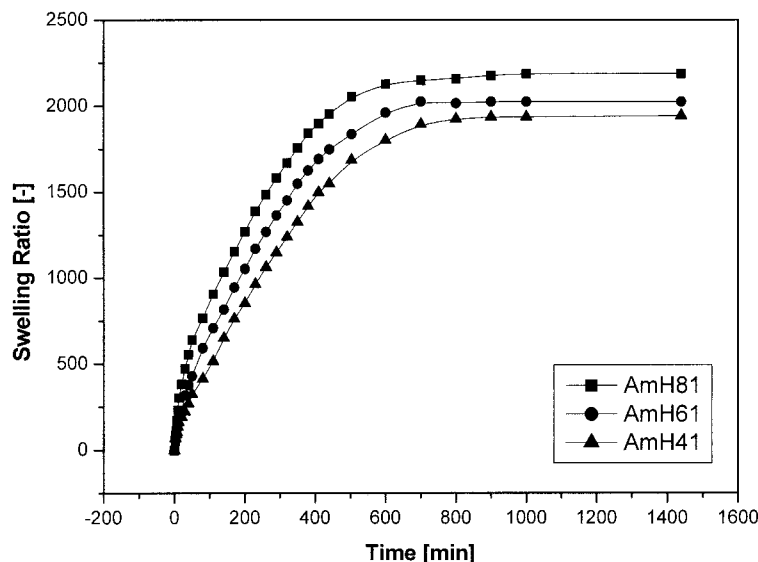
Figure 1 Swelling kinetics of the PAMPS/HA IPN hydrogels in water.

ing of the HA content of the IPN hydrogel. The swelling ratios of IPN hydrogels increased in the range 1940–2190 [—] with increasing PAMPS content.

Figure 2 shows the pH-dependent swelling behavior of the PAMPS/HA IPN hydrogels. The pH-sensitive characteristics of the IPN hydrogels were studied by using swelling tests in the pH range 2–11. PAMPS hydrogels are strongly acidic and dissociate completely over this pH range, and therefore, they exhibit pH-independent swelling behavior. However, as can be seen from Figure 2, the swelling ratios of the IPN hydrogels increased with increasing pH. This swelling behavior was due to the HA content of the IPN hydrogels. When the carboxylic acid groups of the HA are below a pK_a value of about 3.3, they exist in the —COOH form. As the pH of the solution increases, the —COOH groups become ionized to —COO$^-$ groups, and the IPN hydrogels swell to a large volume, because of the development of a large osmotic swelling force in the presence of these ions.

Figure 3 shows the equilibrium swelling ratios of the PAMPS/HA IPN hydrogels in aqueous sodium chloride solutions at room temperature as semilog plots of the swelling ratio versus NaCl concentration. The swelling ratio was highly dependent on the association state of the ionic groups within the polymer, and the affinity of the complex for water because of the ionic strength of the solution. As the ionic strength
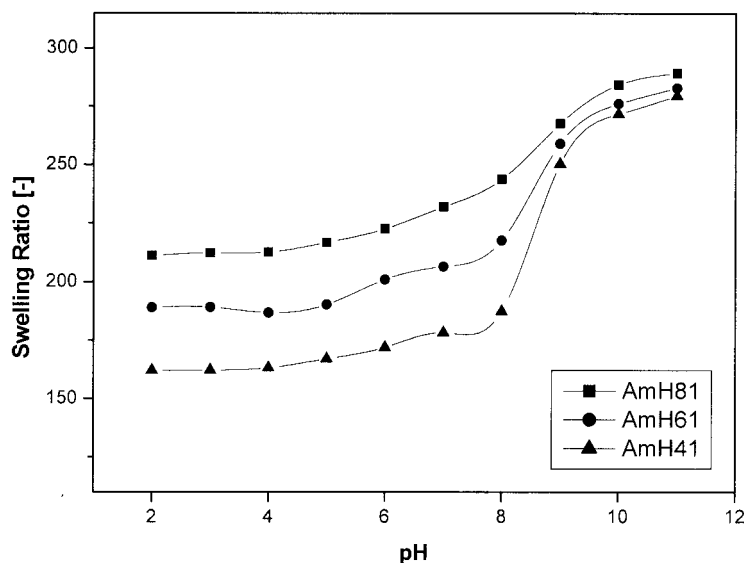

Figure 2 pH-dependent swelling behavior of the PAMPS/HA IPN hydrogels in various buffer solutions.
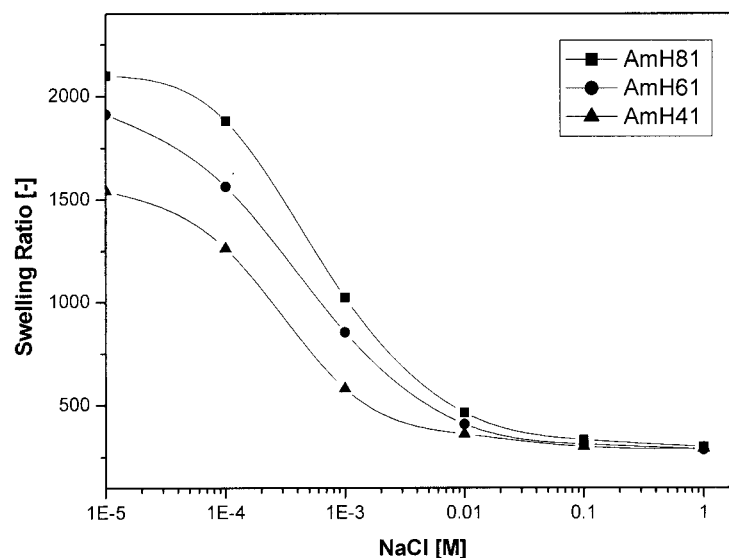
Figure 3   Swelling behavior of the PAMPS/HA IPN hydrogels as a function of the ionic strength.

increased, the ionized hydrogels shank. At an NaCl concentration of 1 mol %, the samples had approximately the same swelling capacities, regardless of the PAMPS content in the hydrogels. This type of behavior with polyelectrolyte hydrogels is well known and can easily be explained by the Donnan equilibrium[19] or the repulsion between opposite charges on the polymer chains. According to the Donnan osmotic pressure equilibrium, an increase in the movable counterions of a solution leads to a decrease in the osmotic pressure within the hydrogel, which causes it to shrink.

Figure 4 shows the shrinking behavior of the IPN hydrogels when exposed to an electric field with in-creasing voltage. The relative weight change of the IPN hydrogels were calculated by using eq. (2). A small movement of the hydrogel toward the anode was observed. The electric field causes the migration of positively charged counterions in the hydrogel toward the cathode, which results in a partial shielding of the sulfonate and carboxylate groups, thus reducing the extent of hydration of the gel. Generally, the swelling ratios of the PAMPS/HA IPN hydrogels increased with increasing PAMPS content in the IPN hydrogels. However, the hydrogels shrank with increasing PAMPS content, and with increasing applied voltage. All the hydrogel samples exhibited equilibrium swelling capacities at 10 V. This indicates that the voltage
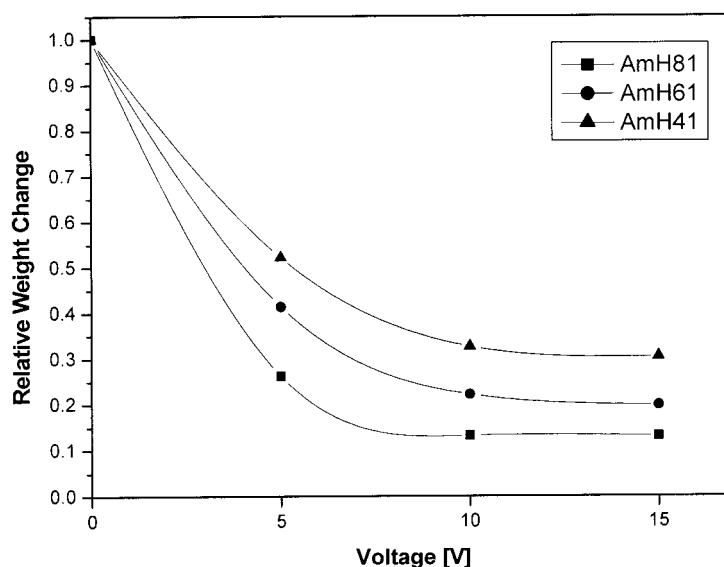

Figure 4   Shrinking of the PAMPS/HA IPN hydrogels on the application of an electric field.
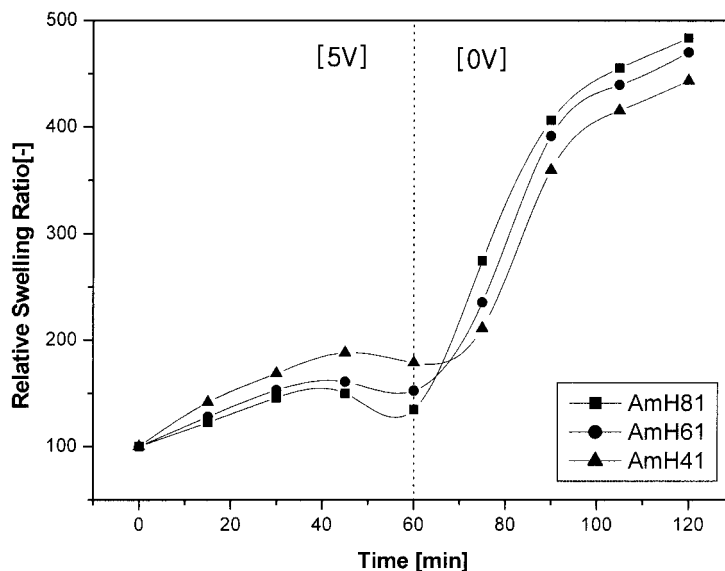
Figure 5 Relative swelling of the PAMPS/HA IPN hydrogels when an electric field of 5 V was switched off.

necessary to reach the equilibrium deswelling is about 10 V. The theories of electrodiffusion, electrophoresis, electroosmosis, and local pH profiles, involving the electrolysis of water, can be used to explain the mechanism of the stimuli response of normal polyelectrolyte gels in DC electric fields.

In Figure 5, the phenomenon of relative swelling is shown more clearly by switching the electric field on and off. For a clearer comparison, the weights of the swollen samples are expressed relatively. When exposed to an electric field, the relative swelling ratio of Sample AmH41 was larger than that of the other hydrogel samples. However, the swelling ratio of Sample AmH81 was found to be rapidly restored in the ab-

sence of an electric field. This result agrees with the data shown in Figures 1 and 4.

Figure 6 shows the electroresponse of the PAMPS/HA IPN hydrogels due to an input voltage of 5 V, with an on–off interval of 1 h. By switching the voltage on and off, the PAMPS/HA IPN hydrogels showed clear relative weight changes. Sample AmH81 showed a relatively large electroresponsive volume and weight change. The IPN hydrogels with low HA content were softer than high HA content and the electroresponsiveness increased with decreasing HA content. Generally, the shrinkage deformation under a stimulus increases with higher molecular mobility in a gel with a smaller crosslinking density. However, after
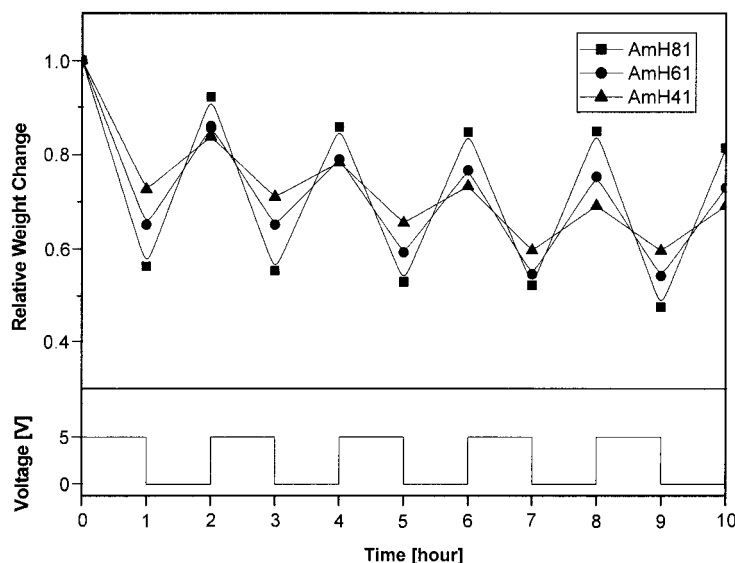

Figure 6 Electroresponsiveness of the PAMPS/HA IPN hydrogels due to switching the electric field (5 V) on and off.

removal of the stimulus, volume recovery (expansion) occurs because of the relaxation of the gel, and this is also increased with a lower crosslinking density. Therefore, there should be an optimum viscoelasticity for a given crosslinking density. The crosslinked HA and PAMPS compounds have different chemical end groups. These structural differences determine the crosslinking density, the mobility, and the flexibility of the network, and the viscosity of the gel. They may also affect the deformation (shrinkage) and relaxation (swelling) properties of a gel when the stimulus is switched on and off. Accordingly, the most responsive sample was the 8 : 1 composition of AMPS monomer to HA (Sample AmH81).

CONCLUSION

IPN hydrogels that exhibit pH-sensitive properties and electroresponsiveness, such as a reversible shrinkage and expansion when an electric field is switched on and off, have been fabricated. The PAMPS/HA IPN hydrogel showing the greatest electroresponsive volume change was Sample AmH81. The PAMPS dissociates completely over a wide pH range, and therefore, PAMPS hydrogels are expected to exhibit pH-independent swelling behavior. However, our PAMPS/HA IPN hydrogels exhibited a pH-dependent swelling behavior. The IPN hydrogels prepared in this study swelled reversibly under the influence of a DC electric field, making them useful for electric-field-driven actuators.[20]

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