Synthesis and Characteristics of Semi-interpenetrating Polymer Network Hydrogels Based on Chitosan and Poly(hydroxy ethyl methacrylate)

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ABSTRACT: Semi-interpenetrating polymer networks (semi-IPNs), composed of chitosan and poly(hydroxy ethyl methacrylate) hydrogels, were prepared and the effects of various pH, temperatures, and an electric-field on the swollen hydrogels were investigated. The swelling kinetics increased rapidly, reaching equilibrium within 60 min. Semi-IPN hydrogels exhibited relatively high swelling ratios, 150~350%. The swelling ratio increased when the pH of the buffer was below pH 7 as a result of the dissociation of ionic bonds. Semi-IPN hydrogels showed electroresponsiveness by shrinking when an electric field was applied. © 2005 Wiley Periodicals, Inc. J Appl Polym Sci 96: 86–92, 2005

Key words: chitosan; poly(hydroxyethyl methacrylate); swelling behavior; pH sensitive

INTRODUCTION

Hydrogels are crosslinked, three-dimensional, hydrophilic polymer networks, which swell, but do not dissolve, when brought into contact with water.[1,2] Many hydrogels are generally formed from water-soluble polymers by their crosslinking with either radiation or chemicals or by polymerizing hydrophilic monomers in the presence of a crosslinker. Crosslinked polymers seem to be one of the candidates for improving the wet strength of hydrogels. Hydrogels have been studied with a particular emphasis on their reversible volume changes in response to external stimuli, such as pH, solvent composition, temperature, ionic concentration, and an electric field.[3–6] They are mainly used in the fields of medicine, pharmacy, biotechnology, and agriculture. In recent years, hydrogels, due to their versatile application in biomedicine and biotechnology, have been used for the immobilization of enzymes, proteins, antibodies, and antigens.[7,8]

Chitosan, obtained from deacetylation of chitin, is one of the most facile chemicals for allowing alteration that gives useful hydrogel derivatives.[9,10] Chitosan appears to be more useful in biomedical applications and for the dehydration of aqueous solutions than chitin, as it has both hydroxyl and amino groups that can be easily modified.[11,12] The key properties of chitosan in this respect are its biocompatibility, nonantigenicity, and nontoxicity (its degradation products are known natural metabolites), the ability to improve wound healing and/or blood clotting, the ability to absorb liquids and to form protective films and coatings, and the selective binding of liquids, which have been used to lower serum cholesterol levels.[13]

Poly(hydroxy ethyl methacrylate) (PHEMA), which has been utilized for biomedical purposes, is a hydrogel that swells, but is insoluble, when placed in contact with water and has the ability to retain water within its structure.[14,15] PHEMA is one of the most frequently used polymers in medicine, and its good performance is well known (nontoxcity, biocompatibility, and high resistance to degradation and hydrolysis under physiological conditions).[16,17] PHEMA hydrogels have been considered for implantable applications, including biohybrid artificial organs, drug delivery devices, and insulin delivery systems.[18] Ethylene glycol dimethacrylate (EGDMA) is a frequently used comonomer in the preparation of PHEMA hydrogels that functions as a crosslinking agent in the thermosetting system. Since the preparation of PHEMA is a free radical chain growth crosslinking polymerization of HEMA and EGDMA, as one may expect, the initial molar ratio of HEMA -C = C- to EGDMA -C = C- double bonds, the concentration of the initiator and the temperatures of curing, would affect the reaction kinetics in different ways.[19]

Chitosan has many useful features, such as hydrophilicity, biocompatibility, and antibacterial properties. PHEMA is a synthetic hydrogel, which possesses

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TABLE I
Compositions and Designations of the Chitosan/PHEMA Semi-IPN Hydrogels

Sample designation	Chitosan (wt%)	Poly(hydroxyethyl methacrylate) (wt %)
CSHM11	0.6	0.6
CSHM13	0.3	0.9
CSHM15	0.2	1.0

high mechanical strength and resistance to significant chemical and microbial degradation. PHEMA hydrogels have gained widespread recognition for their suitability in soft tissue and subcutaneous applications, owing to their good mechanical strength, chemical resistance, and relatively high water content. Much attention has been paid to improving the chemical and physical properties of hydrogels in the swollen state. A new hydrogel, combining the useful properties of the synthetic PHEMA and natural chitosan, can be prepared.

In this study, semi-IPN hydrogels, composed of chitosan and PHEMA, were prepared, and their pH, temperature, and electric field swelling characteristics were studied.

EXPERIMENTAL PROCEDURES

Materials

Chitosan, with an average molecular weight of 2.0×10^5 and a 76% degree of deacetylation, was supplied by Jakwang Co., Korea. The acetic acid was supplied by Duksan Pure Chemical. Co. Ltd., Japan. The HEMA and EGDMA were purchased from Aldrich Chemical Co. and the azobisisobutyronitrile (AIBN) was from Junsel Chemical. Co. Ltd., Japan.

Preparation of semi-interpenetrating polymer network IPN hydrogels

Crosslinked PHEMA hydrogels were prepared by the polymerization of an aqueous reaction mixture containing a monomer, a crosslinking agent, and an initiator. Mixtures of HEMA, AIBN, and EGDMA were dissolved to form an aqueous solution, which was stirred for 4 h at 60°C. The chitosan was dissolved completely in 1 wt % acetic acid. The chitosan and the HEMA solutions were mixed by mechanical stirring for 3 h. The detailed compositions and designations of the chitosan/PHEMA semi-IPN are listed in Table I. The mixed solutions were poured into petri dishes and maintained in an oven at 60°C for 24 h and then dried in an oven at 50°C for 24 h. The obtained products were washed in distilled water for a week to remove any unreacted monomer and acetic acid and then dried in a vacuum oven at 40°C for 24 h.

Preparation of Hank's solution

For a biomedical application, the in vivo tests will be complicated, so the swelling behaviors of semi-IPN hydrogels are performed in Hank's solution[20] to simulate their swelling behavior in a human body fluid system. The composition of Hank's solution used in this paper is listed in Table II.

Characterization

The dried gels were immersed in 50 mL of deionized water at 20°C. The swelling ratios were obtained by weighing the initial and swollen samples at various time intervals.

To measure the swelling ratios, preweighed, dry samples were immersed in deionized water. After the excess surface water had been removed with filter paper, the weights of swollen samples were obtained at various pH and temperatures, and the swelling ratios were determined according to the equation

$$\text{Swelling ratio (\%)} = ((W_s - W_d)/W_d) \times 100 \quad (1)$$

where W_s and W_d represent the weights of swollen and dry state samples, respectively. When swollen, the semi-IPN was placed between a pair of electrodes (noncontact DC electric field in deionized water) [3] and exhibited deswelling on the application of an electric field. The deswelling water ratio of each semi-IPN was evaluated from the equation[21]

$$\text{Deswelling water ratio} = W_t/W_{t0} \quad (2)$$

where W_{t0} and W_t are the initial weight of the fully swollen semi-IPN and that at the deswelling time t, respectively.

TABLE II
Composition of Hank's Solution

Composition	Concentration (g/L)
NaCl	8.00
Glucose	1.00
KCI	0.40
$NaHCO_3$	0.35
$CaCl_2$	0.14
$MgCl_2 \cdot 6H_2O$	0.10
$Na_2HPO_4 \cdot 2H_2O$	0.06
KH_2PO_4	0.06
$MgSO_4 \cdot 7H_2O$	0.06

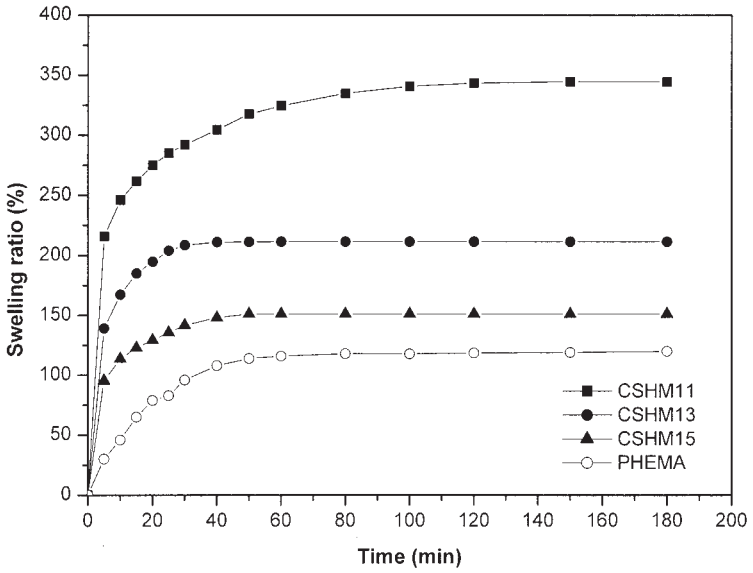

Figure 1 Swelling behavior of the chitosan/PHEMA semi-IPNs at 25°C.

RESULTS AND DISCUSSION

Figure 1 shows the water-swelling behavior of the prepared PHEMA and chitosan/PHEMA semi-IPN hydrogels. As seen from Figure 1, water swelling occurred rapidly, reaching equilibrium in about 60 min. The swelling ratios of the semi-IPNs ranged from 150 to 350% and change in relation to the chitosan content. The swelling ratio of the CSHM11 hydrogel was higher than that of the PHEMA, CSHM13, and CSHM15 hydrogels. Increases in the chitosan content of the semi-IPN hydrogels led to an increase in the equilibrium swelling ratio. This was attributed to the incorporation of the more hydrophilic functional groups the chitosan (i.e., $-NH_2$ and –OH) into the PHEMA network, with the presence of chitosan macromolecules in the polymerization mixture effectively decreasing the molecular mass of the PHEMA, thereby reducing the crystallinity. Therefore, the water molecules penetrate the polymer chains more easily, resulting in an improvement in the semi-IPN hydrogel water-swelling properties in aqueous solution.[22]

Figure 2 shows the swelling ratios of the various samples in various pH buffer solutions at 35°C. They

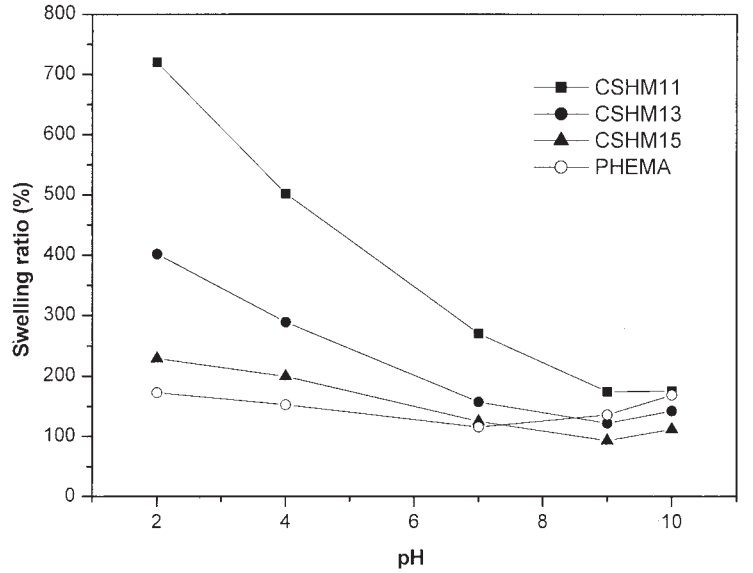

Figure 2 pH-dependent swelling behaviors of the chitosan/PHEMA semi-IPNs at 35°C.

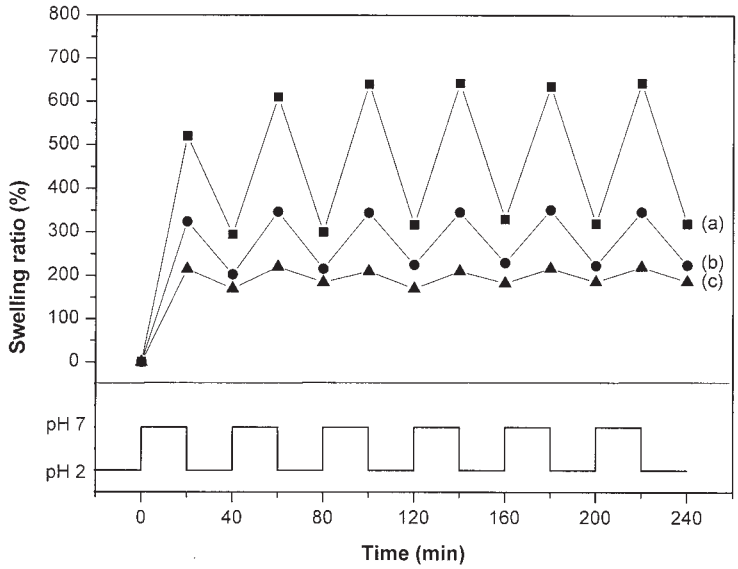

Figure 3 Pulstaile swelling behavior of (a) CSHM11, (b) CSHM13, and (c) CSHM15 in response to pH changes between 2 and 7 at 35°C.

were observed to swell at pH 2 and shrink at pH 7. At pH 2, CSHM11, containing the greatest amount of chitosan among the samples, showed the highest swelling ratio. The positively charged chitosan at a low pH showed a high swelling ratio due to the repulsive force between the like charges of molecules causing a long intermolecular distance and a greater hydrophilic state, which contribute to the network expansion. A high concentration of a charged ionic group in a hydrogel is known to increase the swelling due to osmosis and charge repulsion. On the other hand, alkaline hydrogen bonds tend to associate as the $-NH_3^+$ groups can be changed into $-NH_2$ groups due to the low H^+ concentration. In an acidic solution, the protonation of the amino groups ($-NH_2$) in chitosan hydrogel and the dissociation of the hydrogen bonds, which induces hydrogel swelling, develop an internal ion osmotic pressure.[13] However, Figure 2 shows increases in the swelling ratios in a medium at pH 10. The swelling ratio of the PHEMA was higher than that of the semi-IPN hydrogels. An increase in the PHEMA content in the semi-IPN hydrogels was observed to lead to an increase in the swelling ratio at pH 10.

Figure 3 shows the pulsatile swelling behavior of the semi-IPN hydrogels at 35°C by alternating the solution pHs between 2 and 7. The swelling ratios of the semi-IPNs were measured every 20 min, as the pH was switched, which showed evidence of the reversible pH-sensitive swelling patterns. In summary, the swelling ratios of the semi-IPNs are dependent on the pH and the amount of chitosan.

The swelling behavior of the semi-IPN hydrogels was investigated as a function of temperature. As shown in Figure 4, significant changes in the swelling ratios of all hydrogels occurred over the temperature range 25 to 45°C. As the temperature and chitosan content of the hydrogels in the swelling state increased, the swelling ratio also increased, with that of the CSHM11 sample having the highest temperature-dependent swelling behavior. The enthalpy of the water molecules will increase during an increase of temperature, and the hydrophilic groups in the chitosan will be turned into intramolecular hydrogen bonds under this condition. All chitosan/PHEMA networks

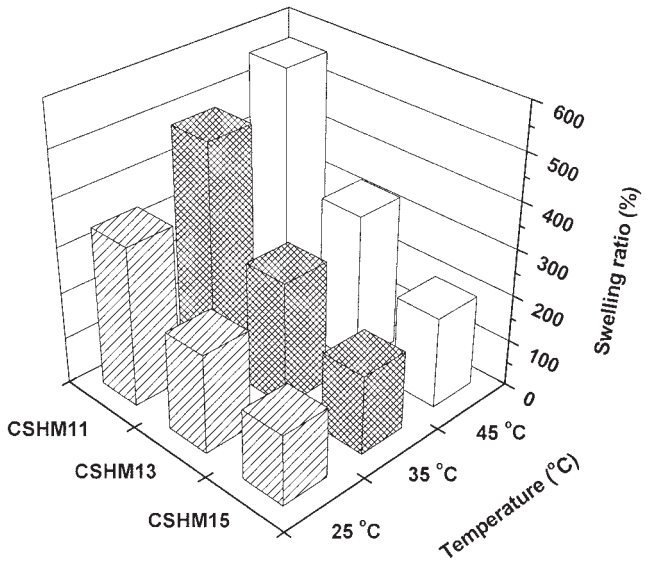

Figure 4 Swelling ratios as a function of temperature of the chitosan/PHEMA semi-IPNs in water.

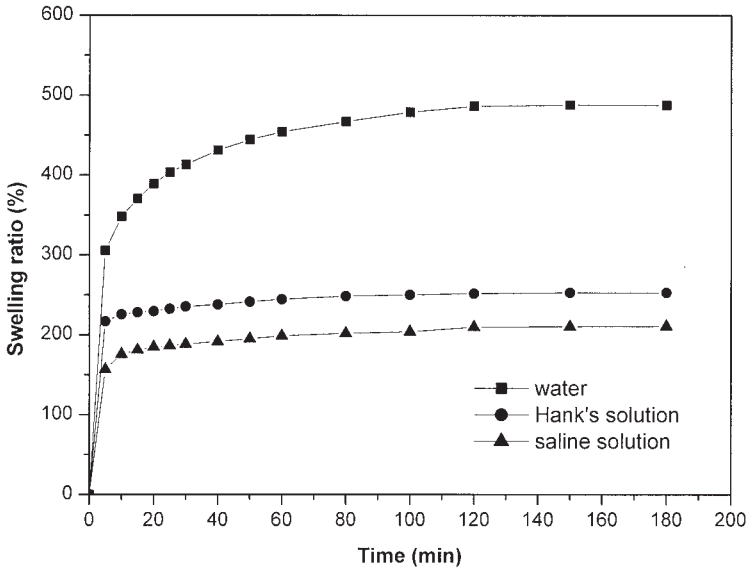

Figure 5 Swelling behaviors of the CSHM11 chitosan/PHEMA semi-IPN in water, Hank's solution, and saline solution at 35°C.

exhibited temperature-responsive swelling behavior due to the association/dissociation of the hydrogen bonding by the amine groups on the chitosan.[23]

The swelling behaviors in water, Hank's solution, and an aqueous saline solution (NaCl 0.86%) are shown in Figure 5. The water absorbencies of the samples in water alone are higher than those of the corresponding swelling in the saline solution. This behavior is well known, and the semi-IPNs can expand as follows: in the presence of NaCl, the osmotic pressure inducing the penetration of water into the hydrogel structure decreases, leading to a reduction in the swelling. Generally, the swelling ratio of a semi-IPN hydrogel depends on the association state of the ionic group within the polymer and the affinity of the complex for water. According to the Donnan osmotic pressure equilibrium,[24] an increase in the movable counterions of a solution leads to a decrease in the osmotic pressure within the hydrogel, causing the hydrogel to shrink. The swelling kinetics of a semi-IPN in Hank's solution and saline solution are shown in Figure 5. The swelling ratios of semi-IPNs in the Hank's solution were similar to those in the saline solution. As shown in Table II, the main component of

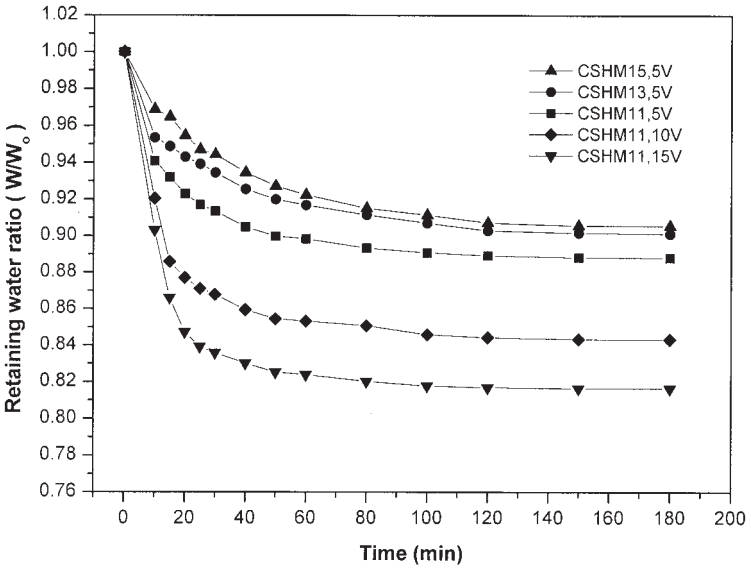

Figure 6 Deswelling behavior of the chitosan/PHEMA semi-IPNs in direct contact with a pair of electrodes in water at 35°C.

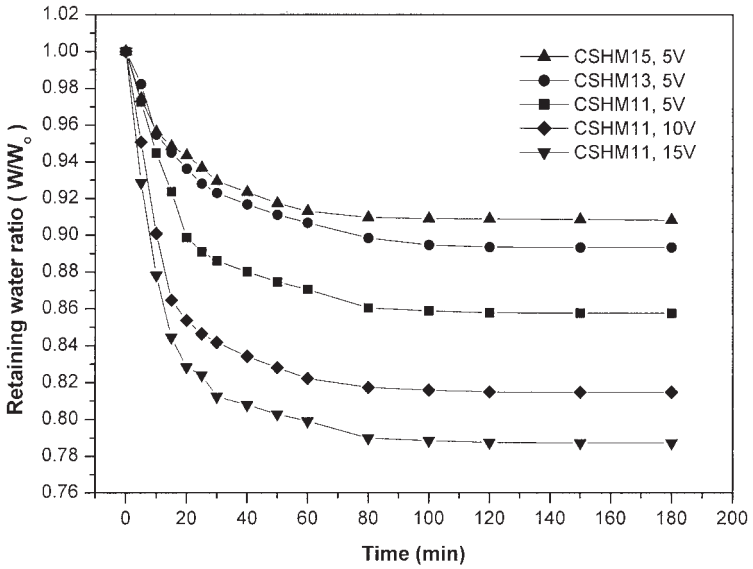

Figure 7 Deswelling behavior of the chitosan/PHEMA semi-IPNs in direct contact with a pair of electrodes in saline solution at 35°C.

Hank's solution is NaCl, which plays a dominant role during swelling.

The deswelling water ratios of the IPNs were measured using Eq. (2) to quantify the degree of deswelling. Figure 6 shows the remaining water ratio as a function of the voltage applied to the semi-IPN. As shown in Figure 6, the deswelling of the semi-IPNs was enhanced in proportion to the applied voltage. In particular, the fully swollen CSHM11 showed about an 18% reduction from its original weight within 60 min, under 15 V of applied voltage. To examine the effect of the ionic groups in the semi-IPN, the remaining water ratio in the different semi-IPNs, CSHM15, CSHM13, and CSHM11, was measured. This also showed that increasing the deswelling water ratio in the semi-IPNs increased with increasing ionic group content. Generally, the shrinking deformation under a stimulus increased with the larger molecular mobilities within a hydrogel with a smaller crosslinking density.

Figure 7 exhibits the remaining water ratio, as a function of time, depending on the voltage applied, and the chitosan content to the semi-IPN in saline solution. The deswelling of the semi-IPNs was enhanced in proportion to the applied voltage. The deswelling ratio increased with increases in the chitosan content. In particular, the fully swollen CSHM11 showed about a 22% reduction from its original weight within 80 min, under 15 V of applied voltage. When exposed to an electric field, the relative deswelling ratios of the semi-IPNs in the saline solution were larger than in water.

CONCLUSIONS

Semi-IPN hydrogels, composed of various ratios of chitosan and PHEMA, were prepared by crosslinking with EGDMA. The semi-IPN hydrogels exhibited pH-sensitive and electro-responsive properties. The semi-IPN hydrogels exhibited relatively high swelling ratios as the chitosan content was increased. The semi-IPN hydrogels swelled rapidly, within 60 min, with equilibrium swelling from 150 to 350%, at 25°C. The CSHM11 sample, containing the highest chitosan content among the samples, showed the highest pH-, temperature-, and electric-stimuli-dependent swelling behaviors. The semi-IPN hydrogels showed electroresponsiveness by their shrinking. The relative deswelling ratios of the semi-IPNs in saline solution were larger than in water. The CSHM11 semi-IPN hydrogel showed the greatest electroresponsiveness swelling change.

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