

Swelling Behavior of Polyelectrolyte Complex Hydrogels Composed of Chitosan and Hyaluronic Acid

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ABSTRACT: Polyelectrolyte complex (PEC) hydrogels composed of various weight ratios of chitosan and hyaluronic acid were prepared. The PEC hydrogels were formed by the reaction of the oppositely charged chitosan polymers. The PEC films swelled in water rapidly, reaching equilibrium within 30 min, and exhibited relatively high swelling ratios, 243–322%, at 25°C. The swelling ratio increased with increasing temperature. The transport phenomena of all PEC samples were non-Fickian and diffusion and relaxation

controlled. The diffusion coefficients of the PEC films ranged from 2.22×10^{-6} to 10.05×10^{-6} cm²/s. The activation energy of the polyelectrolyte complexes ranged from 37.14 to 54.58 kJ/mol and proved to be hydrophilic. © 2004 Wiley Periodicals, Inc. *J Appl Polym Sci* 93: 1097–1101, 2004

Key words: chitosan; hyaluronic acid; hydrogel; swelling; kinetics

INTRODUCTION

Generally, a polymer complex can be classified as a hydrogen-bonding complex, a polyelectrolyte complex (PECs), a stereocomplex, or a charged-transfer complex.¹ In particular, PECs are formed by a reaction of oppositely charged polymers. The formation and properties of polymer complexes depend on the charge ratio of anionic-to-cationic polymers, the degree of neutralization, the ionic strength, and the valence of simple ions in the electrolyte solution.^{2,3} Therefore, a strong polyelectrolyte complex is obtained if anions and cations in the polymers contain strong acids and bases or if polyions attain their fully ionized forms. On the other hand, weak polyelectrolyte complexes are formed in each weak acid and base.⁴ PECs are an important class of polymer materials that are widely used in many applications, such as membranes, medical prosthetic, antistatic coatings, environmental signals to the sensors, drug delivery systems, and protein separation.^{5,6} PECs with a high tendency of aggregation usually result when both polyions have strong ionic groups, with compatible match charges. The PECs prepared from natural polymers, such as polysaccharides, have the additional advantages of being nontoxic and bioabsorbable.⁷

Hyaluronic acid (HA) is a naturally occurring linear polysaccharide with a high molecular weight. It has a repeating disaccharide structure, consisting of 2-acet-

amide-2-deoxy- β -D-glucose and β -D-glucuronic acid residues, linked by alternating (1–3) and (1–4) glycoside bonding.^{8,9} HA is a weak polyacid with a very low charge density, because only one charge can be present for every two residues.⁴ HA, a component of the extracellular matrix of all higher animals, has high capacities for lubrication, water sorption, and water retention and influences several cellular functions, such as migration, adhesion, and proliferation.^{10,11} Recent biomedical applications of HA have included ophthalmic surgery, arthritis treatment, scaffolds for wound healing, tissue engineering, and use as a component of implant materials.^{12–14}

Chitosan, obtained from deacetylation of chitin, appears to be more useful in biomedical applications and for the dehydration of aqueous solutions than chitin because it has both hydroxyl and amino groups that can be easily modified.^{15,16} For its uses, key properties of chitosan are biocompatibility, bioactivity, nonantigenicity, nontoxicity (its degradation products are known natural metabolites), the ability to improve wound healing and/or blood clotting, the ability to absorb liquids and form protective films and coatings, and its selective binding of liquids, which has been used to lower serum cholesterol levels.^{17,18} Chitosan is a weak base, with an intrinsic pK_a near 6.5, and has a low charge density.⁴

Chitosan has a cationic characteristic and is likely to impart hydrophilicity to the PECs prepared by the formation of its composites with anionic characteristics, such as HA. Therefore, it was of interest to investigate the formation of PEC films utilizing the unique properties of chitosan and HA.

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Many researchers have studied the swelling kinetics of PECs. Chen and Yi reported on the swelling kinetics and stimuli-responsiveness of poly(dimethylaminoethyl methacrylate) hydrogel and showed them to be pH-sensitive, with the swelling process tending to be Fickian kinetics in relation to the pH.¹⁹ Issa and Fabio studied the swelling kinetics and the releases of theophylline and aminophylline from acrylic acid/*n*-alkylmethacrylate hydrogel.²⁰ Murat and Olgun studied the dynamic deswelling of poly(*N*-ninyl-2-pyrrolidone/itaconic acid) hydrogels.²¹ Blanca and Julio studied polymeric hydrophilic hydrogels with flexible hydrophobic chains and showed their swelling kinetics and surface properties.²²

In this paper, the study of the water uptake behavior of HA/chitosan PECs is reported. The degree of complexation between the oppositely charged ionic groups was also estimated. The purpose of this work was to investigate the water uptake properties of insoluble PECs and to analyze their swelling kinetics and mechanism.

EXPERIMENTAL

Materials

Chitosan, with an average molecular weight of 2.0×10^5 g/mol and a 76% degree of deacetylation, was obtained from Jakwang Co., Korea. The HA, sodium form, with an average molecular weight of 1.7×10^6 g/mol, was obtained from Pacific Chemical Co., Ltd. (Seoul, Korea). The formic acid was purchased from Kanto Chemical Co., Inc., and the sodium hydroxide (NaOH) was from Duksan Pure Chemical. Co. Ltd., Japan. The water used in the experiments was distilled and deionized with a Milli-Q System (Millipore, Bedford, MA).

Preparation of polyelectrolyte complexes

Mixtures of HA and chitosan were prepared by dissolving the two components, at various ratios, in 50 wt % aqueous formic acid solution. The concentration of chitosan and HA in the solution was 1 wt %. A chitosan and HA solution mixture was obtained by mechanical stirring for 24 h. The compositions, chitosan and HA, in the PEC samples were 1:1 (CSHA11), 3:1 (CSHA31), and 5:1 (CSHA51). The solution mixtures were filtered using a glass filter. The mixed solutions were poured into petri dishes and dried in an oven for 48 h at 50°C. The petri dishes were then dipped in 0.1 *M* aqueous NaOH solution to remove any unreacted formic acid. The products obtained were further washed with distilled water to remove any unreacted chitosan and HA. The PEC films were dried in a vacuum oven for 1 week at 40°C.

Swelling experiment

The swelling ratios were obtained by weighing the initial and swollen samples at various time intervals and temperatures. To measure the swelling ratio, pre-weighed dry samples were immersed in deionized water. After the excess surface water was removed with filter paper, the swollen samples were weighed at various temperatures and time intervals. The swelling ratio at a given time was determined according to the equation

$$\text{Swelling ratio } (W_t) = \frac{W_s - W_d}{W_d}, \quad (1)$$

where W_s represents the weight at the a sample and absorbed water at a given time and W_d is the weight of the dry state sample. The equilibrium swelling ratio (W_∞) is the swelling ratio when no further change in weight is observed as a function of time.

RESULTS AND DISCUSSION

Figure 1 shows the swelling kinetics of the PEC films at 25°C, and their equilibrium swelling ratios various temperatures are shown in Table I. The samples swelled in water rapidly, reaching equilibrium within 30 min. The swelling percentage of the PEC films ranged from 243 to 322% at 25°C and changed with the chitosan content of the network. The swelling ratios also increased with increasing temperature. All PEC films swelled and reached equilibrium quickly as the temperature increased. The swelling ratio of the CSHA51 was higher than that of the CSHA11 and CSHA31 films. An increase in the chitosan fraction of the films was observed to lead to an increase in the equilibrium swelling ratio. This is attributed to the hydrophilic character of the chitosan. This behavior may be due not only to the degree of chitosan and HA network complexation, but also to the chitosan content having a large number of water-binding sites.²³

When a solid polymer is brought into contact with a penetrating liquid or vapor, the penetrant diffuses into the polymer, causing it to swell. Both concentration-gradient-controlled diffusion and relaxation-controlled swelling contribute to the rate and extent of penetrant sorption into the polymer. To analyze the sorption mechanism in this work, the diffusional phenomena were analyzed using the equation²⁴

$$M_t/M_\infty = kt^n, \quad (2)$$

where M_t and M_∞ represent the amount of water uptake at times t and ∞ , respectively; k is a characteristic constant of the hydrogel, and n is a characteristic exponent of the mode of transport of the penetrant.²⁵ This equation has been proposed as a simple method

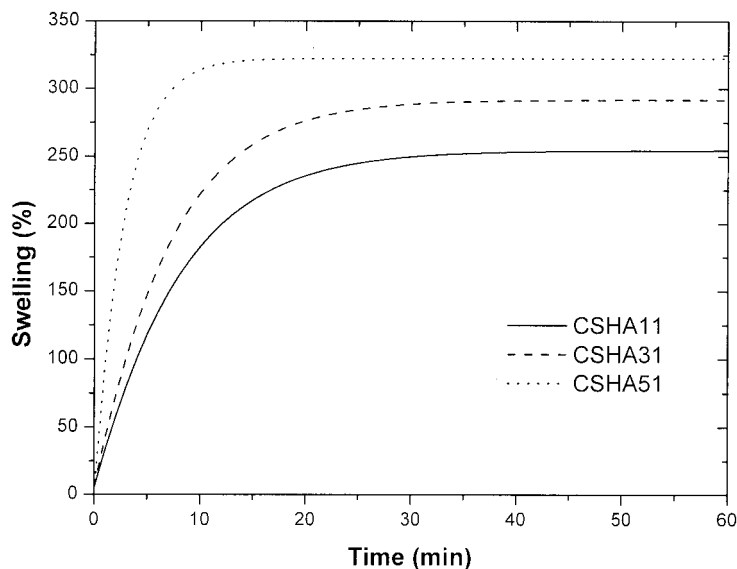


Figure 1 Liquid water uptake of CSHA11, -31, and -51 at 25°C.

to analyze sorption mechanisms. From this equation, the value of n can be used to determine the mechanism of sorption. For $n = 0.5$, Fickian diffusion will dominate; for $n > 0.5$, the solute transport will be non-Fickian; and when $n = 1$, the system mechanism will be relaxation controlled. Calculation of the exponent n was achieved by plotting the data in log-log plots, according to Eq. (3), using linear regression to determine the slope:

$$\log (M_t/M_\infty) = \log k + n \log t. \quad (3)$$

Figure 2 shows the results obtained by plotting the water uptake data of the PEC films at 25°C, according to Eq. (3). The n values of CSHA51, CSHA31, and CSHA11 were 0.93, 0.88, and 0.81, respectively. The transport of all PEC samples was non-Fickian, and they had diffusion- and relaxation-controlled systems. The slope of CSHA51 was higher than the others. CSHA51 had a higher swelling ratio than CSHA31 and CSHA11.

All samples obeyed a diffusion-controlled mechanism, even if only partial, so the swelling kinetics was analyzed by their diffusion coefficient. The diffusion coefficients of the thin films were calculated utilizing

the diffusion equations first developed by Crank and Park.²⁶ The thin film was suspended in the sorption apparatus, with the kinetics of sorption for a single step under humid conditions recorded in the usual manner. For a single step in controlled humidity, a double-sided thin film of thickness d , the initial kinetics of water uptake into the bulk may be described by the equation

$$\frac{M_t}{M_\infty} = \frac{4}{d} \sqrt{\frac{Dt}{\pi}}, \quad (4)$$

where M_t is the amount of water absorbed at time t ; M_∞ is the amount absorbed at thermodynamic equilibrium, and D is the diffusion coefficient. Equation (4) is typically valid for values of $M_t/M_\infty < 0.4$, where a plot of M_t/M_∞ against \sqrt{t} should be linear. The diffusion coefficients of the PEC samples can then be calculated from the plot, as shown in Figure 3. The water diffusion coefficients (cm^2/s) of all PEC samples were calculated from the gradients of the linear plots which were below $M_t/M_\infty < 0.4$. The diffusion coefficients of the PECs are listed in Table I. The diffusion coefficients of the PEC films ranged from 2.22×10^{-6} to

TABLE I
Various Parameters in Liquid Water (Swelling Ratio, Diffusion Coefficient, and Activation Energy)

	Swelling ratio (%)			Diffusion coefficient ($\times 10^6 \text{ cm}^2/\text{s}$)			Activation energy (kJ/mol)
	25°C	35°C	45°C	25°C	35°C	45°C	
CSHA11	243.7	282.1	296.2	2.22	4.36	8.89	54.58
CSHA31	283.6	295.8	307.7	2.56	5.35	9.68	52.42
CSHA51	322.3	333.7	347.0	4.15	6.75	10.05	37.14

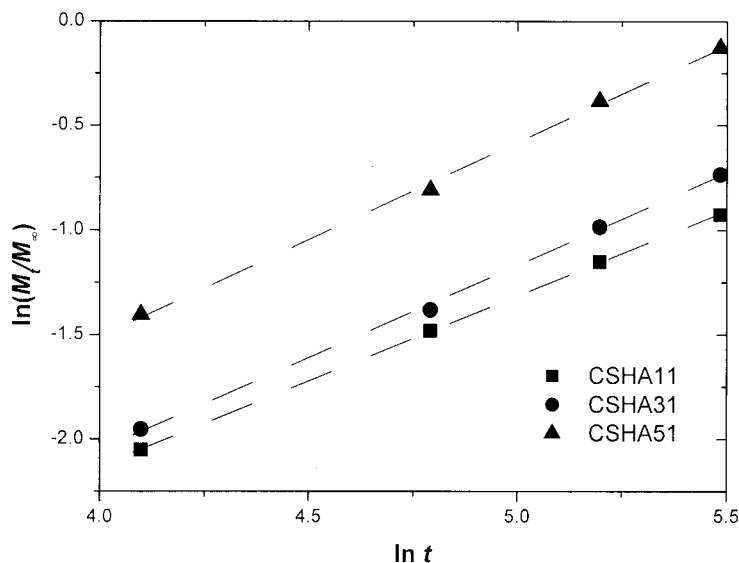


Figure 2 Plots of $\ln(M_t/M_\infty)$ against $\ln t$ for the CSHA films in liquid water.

$10.05 \times 10^{-6} \text{ cm}^2/\text{s}$. These values changed with the chitosan content. The diffusion coefficient of CSHA51 was higher than that of the CSHA11 and CSHA31 films, which was caused by the complex structure of PEC. The intermolecular ionic connections in the PECs increased with increasing HA content. With increases in temperature, the values of the diffusion coefficients were found to increase due to the greater water penetration into the PECs. This result is general, because the diffusion coefficient is a function of the temperature and increases with increasing temperature.

The temperature dependence of the calculated diffusion coefficients was analyzed using an Arrhenius-type equation:

$$D = D_0 \exp(-E_D/RT), \quad (5)$$

where E_D is the apparent activation energy for the diffusion process. As shown in Figure 4, the experimental values from the plots of the logarithm of D versus $1/T$ were linear; allowing the activation energy to be calculated from the gradient of the straight line. The calculated values of PECs are reported in Table I. The activation energy was observed to increase with increasing the HA content. CSHA11 had the lowest diffusion coefficient among all hydrogels prepared, so the water molecules diffuse most slowly into CSHA11. The activation energy of the PECs ranged from 37.14

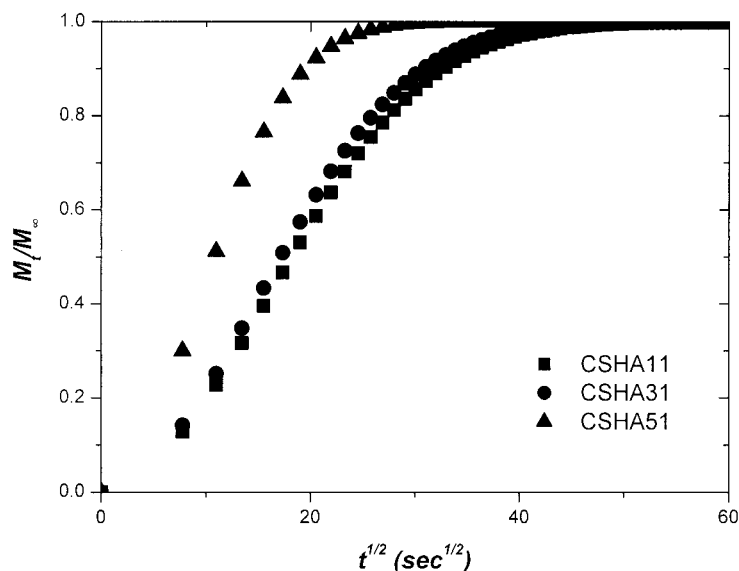


Figure 3 Plots of water uptake against $t^{1/2}$ for the CSHA films in liquid water.

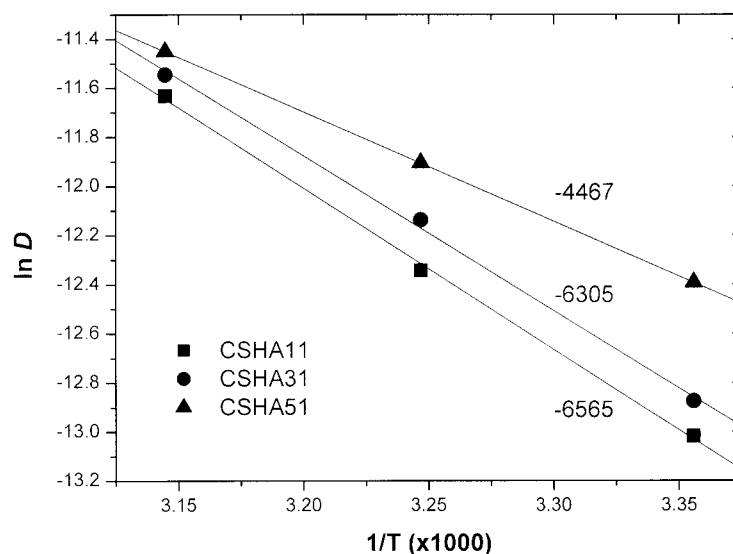


Figure 4 Plots of $\ln D$ against $1/T$ for the CSHA films in liquid water.

to 54.58 kJ/mol, and the PECs were proven to be hydrophilic.

CONCLUSION

The equilibrium swelling ratios of the chitosan/HA PEC films increased with increasing chitosan content. All chitosan/HA PEC films were non-Fickian systems, obeying diffusion- and relaxation-controlled mechanisms. CSHA51 had the highest diffusion coefficient of all PEC films prepared. All PEC films were hydrophilic.

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