

Synthesis of *N*-Hydroxymethyl Acrylamide with β -Methyl Hydrogen Itaconate and Itaconic Acid Hydrogels: Effects of the pH, Composition, and Ionic Strength on the Swelling Behavior

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ABSTRACT: Copolymer gels were prepared by the radical copolymerization of *N*-hydroxymethyl acrylamide with itaconic acid and *N*-hydroxymethyl acrylamide with β -methyl hydrogen itaconate. The ratios of both monomers were varied from 25 to 75 mol %, and the effects of external stimuli such as the pH and ionic strength of the swelling media were investigated. The gels were pH-responsive, and an increase in the ionic strength of the solutions caused a

decrease in the equilibrium degree of swelling of the copolymer gels. The monomer reactivity ratios were determined with the Kelen–Tüdös method. Moreover, the copolymer composition had a significant effect on the equilibrium swelling behavior of the two copolymers investigated. © 2006 Wiley Periodicals, Inc. *J Appl Polym Sci* 100: 1735–1741, 2006

Key words: copolymerization; hydrogels; swelling

INTRODUCTION

Hydrogels are three-dimensional, crosslinked polymeric structures that are able to swell in an aqueous environment.^{1,2} The hydration power of water absorption is one of the most important factors and is determined by the functionality and quality of the hydrogel; moreover, this one directly influences the majority of the properties.

This capacity to imbibe a solvent depends on the pH and ionic composition of the solution containing the hydrogel.^{3–16} These materials are of great interest because of their promising applications as sensors, separation membranes, adsorbents, and materials in medicine and pharmacy as drug-delivery systems.^{4–13}

During the last decade, considerable research has been done on the characterization and swelling behavior of hydrogels prepared by simultaneous free-radical copolymerization and crosslinking in the presence of an initiator and crosslinking agent.^{17–19} Sen et al.²⁰ synthesized pH-sensitive hydrogels based on poly(1-vinyl 2-pyrrolidone-*co*-itaconic acid). They investigated the effect of external stimuli on the equilibrium swelling of the hydrogels. Recently, Katime and Rodríguez²¹ synthesized hydrogels from copolymers of acrylic acid and itaconic acid (IA) and showed that the hydrogels were potential absorbents of metal ions.

The swelling properties of hydrogels will affect their usability as biomaterials in medicine, pharmacy, and veterinary practice. A wide variety of biomaterials are used in contact with biological fluids. Many different biomaterials are used clinically, as components of implants or devices for diagnosis or therapy. Because the biological environment is composed mainly of water, water absorption is one of the important properties of biomaterials. In particular, low or high water sorption properties of hydrogels may be important for the use of sorbents in many immobilization techniques for biomolecules and cells and in many applications of biomaterials in biotechnology.²²

The aim of this study was to investigate the swelling properties of *N*-hydroxymethyl acrylamide (HMAM) based hydrogels as a function of the pH and ionic strength with two comonomers with different hydrophilicity grades, IA and β -methyl hydrogen itaconate (β MHI). The swelling properties of acrylamide-based hydrogels have been reported in many studies.^{23–26} However, the swelling behavior of HMAM with different hydrophilic comonomers has not been reported so far.

EXPERIMENTAL

Reagents

The two monomers HMAM and IA were obtained from Merck (Germany), and β MHI was prepared according to a published method.²⁷ Benzoyl peroxide was used as the initiator, and the NaCl used for solu-

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TABLE I
Experimental Data of the Radical Copolymerization of IA with HMAM at 70°C for 2 h in Dioxane

Copolymer	<i>f</i>	IA (mmol)	HMAM (mmol)	Solvent (mL)	Yield (%)	Molar ratio in the feed	Copolymer composition ^a
1	0.75	34.5	11.5	12	14.7	3.0:1.0	81.8/18.2
2	0.67	30.6	15.4	12	12.7	2.0:1.0	76.2/23.8
3	0.50	23.0	23.0	12	11.3	1.0:1.0	61.5/38.5
4	0.33	15.4	30.6	12	12.7	1.0:2.0	50.0/50.0
5	0.25	11.5	34.5	12	14.0	1.0:3.0	35.7/64.3

^a Determined from elemental analyses as molar percentages. *f*, the monomer feed ratio.

tion preparation was analytical-grade (both from Merck). All chemicals were used as received without further purification. *N,N*-Methylene bisacrylamide was used as a crosslinking agent.

Syntheses of the copolymers

The copolymers were prepared by the radical copolymerization of HMAM with IA and HMAM with β MHI with 0.1% crosslinking agent.

The copolymerization of the IA/HMAM and β MHI/HMAM copolymers was carried out with several feed compositions of both monomers (25–75 mol %). The general procedure was as follows: 12 mL of dioxane was transferred to septum-capped, nitrogen-purged flasks containing 23 mmol of HMAM, 0.5 mmol % benzoyl peroxide, and 23 mmol of IA. The ampule was degassed with freeze cycles and sealed in vacuo (10^{-3} mmHg). The copolymerization was carried out at 70°C for 2 h. The copolymer material was filtered off, washed with ether, collected, and dried in vacuo up to a constant weight.

Compositions of the copolymers

The copolymers, obtained in the form of long cylinders, were cut into pieces (3–4 mm long) and dried in a vacuum oven for 48 h to a constant weight. The copolymer composition was determined from elemental analysis data.

Swelling studies

The studies were carried out at 25°C in buffered solutions; either a 0.01M citrate buffer (pH < 7) or a phosphate buffer (pH > 7) was used, with the ionic strength adjusted to the specified value by the addition of NaCl.

Dried samples of the copolymers were placed in a solution of a defined pH (2–9) and ionic strength (0.0–0.1M) at 25°C. Every hour, each sample was removed from its solution. The swelling values (S_w 's) were calculated with the following equation:

$$S_w = (W_s - W_d) / W_d$$

where W_s is the weight of the swollen hydrogel at an equilibrium state and W_d is the weight of the dried hydrogel.

RESULTS AND DISCUSSION

Synthesis and characterization of the copolymers

The radical copolymerizations of IA with HMAM and β MHI with HMAM were conducted in dioxane with several monomer feed compositions. The resulting copolymers were insoluble in solvents such as water, chloroform, ethanol, methanol, pyridine, acetone, tetrahydrofuran, and dimethyl sulfoxide. The weight ratios of IA and HMAM and β MHI and HMAM in the copolymers were calculated from the C/N weight percentage ratios determined by elemental analysis (shown later in Tables III and IV).

The results, summarized in Tables I and II, show that for the system IA/HMAM, the copolymer contained 50.0 mol % IA when an initial monomer feed ratio of 1:2 was used (see Table I). For the system β MHI/HMAM, the copolymer contained 53.4 mol % β MHI when an initial monomer feed ratio of 1:3 was used (see Table II).

The yield of the copolymers, in both systems, decreased when the monomer feed ratio (IA/HMAM and β MHI/HMAM) decreased (Tables I and II). These results correlated well with the low values of the reactivity ratio (r_2) obtained for HMAM.

FTIR spectroscopy studies

The FTIR spectra of both copolymers are presented in Figures 1 and 2. The absence of the absorption band at 1640 cm^{-1} , characteristic of the carbon–carbon double bond, in the two investigated systems clearly indicates that a true copolymer was formed in both cases. In Figure 1, the absorption bands at 1703.3 and 1629.1 cm^{-1} illustrate the carbonyl group and the N–H stretching vibration of the IA/HMAM copolymer. In

TABLE II
Experimental Data of the Radical Copolymerization of β MHI with HMAM at 70°C for 2 h in Dioxane

Copolymer	f	β MHI (mmol)	HMAM (mmol)	Solvent (mL)	Yield (%)	Molar ratio in the feed	Copolymer composition ^a
1	0.75	34.5	11.5	6	47.41	3.0:1.0	86.3/13.7
2	0.67	30.6	15.4	6	46.65	2.0:1.0	82.8/17.2
3	0.50	23.0	23.0	6	45.97	1.0:1.0	69.7/30.3
4	0.33	15.4	30.6	6	28.72	1.0:2.0	59.0/41.0
5	0.25	11.5	34.5	6	23.29	1.0:3.0	53.4/46.6

^a Determined from elemental analyses as molar percentages. f , the monomer feed ratio.

Figure 2, the carbonyl group at 1733.3 cm^{-1} and the C—N stretching vibrating band at 1015.8 cm^{-1} indicate the presence of HMAM in the copolymer β MHI/HMAM. On the other hand, in Figures 1 and 2, the bands that appear at 3071.5 and 3383.1 cm^{-1} are assigned to OH stretching (bonding) of the carboxylic groups of IA and β MHI, respectively. The bands in the range of 2622.6 – 2957.2 cm^{-1} in both FTIR spectra indicate the aliphatic C—H stretching vibration.

Monomer reactivity ratios

The monomer reactivity ratios for the two copolymerizations were determined from the monomer feed ratios and copolymer compositions obtained at high conversions with the Kelen–Tüdös (K–T) method.²⁸

The K–T equation was symmetrically transformed into

$$G = r_1 F - r_2 \quad (1)$$

by the introduction of the new parameters ξ , η , and $\alpha = (F_{\min} \times F_{\max})^{0.5}$, where F_{\min} and F_{\max} correspond to the smallest and largest fractions in the copolymer that are calculated. F is the fraction in the copolymer.

The transformed variables are defined as follows:

$$\eta = G / (r_1 + r_2 / \alpha)$$

$$\xi = F / (\alpha + F)$$

The r_1 and r_2 values were also determined according to eq. (2):

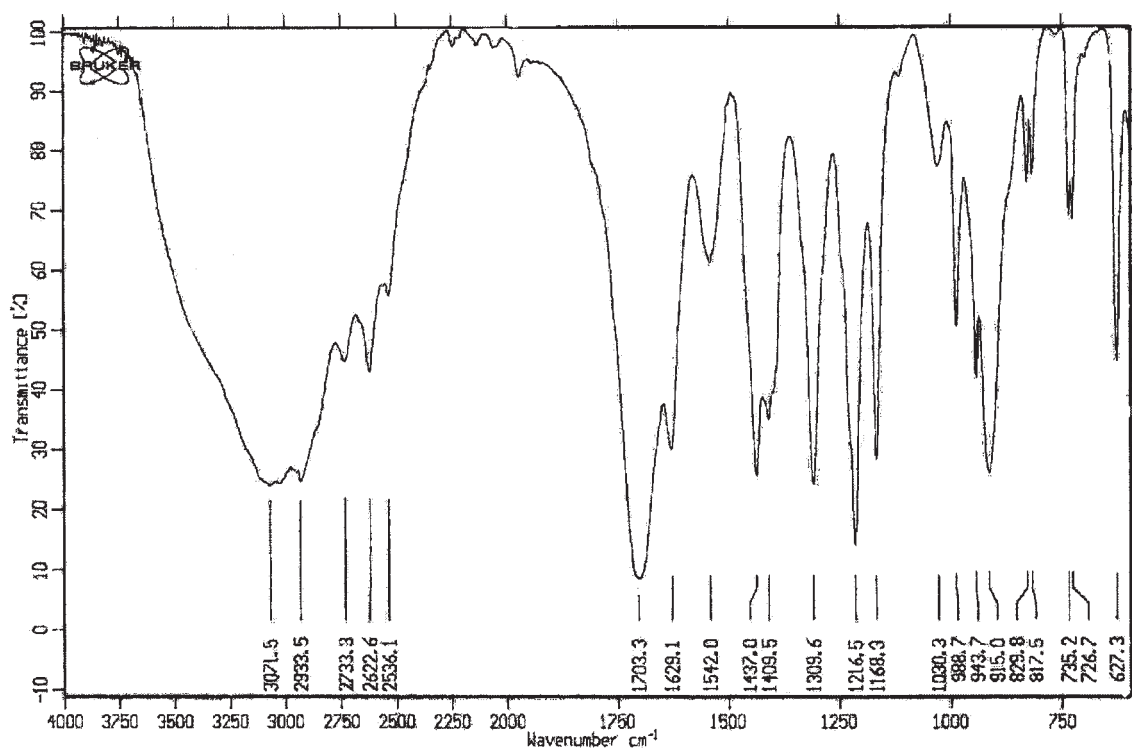


Figure 1 FTIR spectra of poly(IA-co-HMAM).

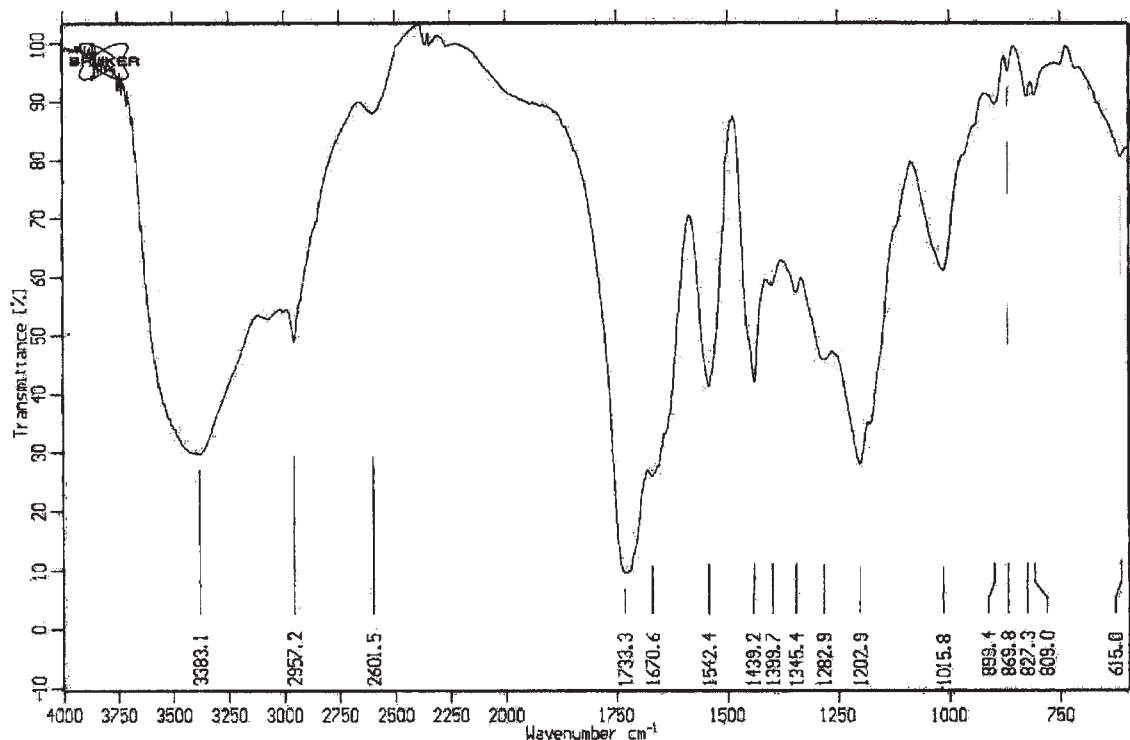


Figure 2 FTIR spectra of poly(β MHI-co-HMAm).

$$\eta = (r_1 + r_2 / \alpha)\xi \quad (2)$$

η and ξ are mathematical functions of the monomer molar ratios in the feed and in the copolymer, respectively, and α is an arbitrary denominator with any positive value that produces a more homogeneous distribution of data along η - ξ axes.

For the parameters ξ , η , and α , the following equations apply: $G = (m_1/m_2 - 1)/z$, $F = (m_1/m_2)/z^2$, $z = \log(1 - \delta_1)/\log(1 - \delta_2)$, $\delta_1 = \delta_2 y/X_0$, $\delta_2 = \text{wt \% } (\mu$

+ $X_0)/(\mu + y)/100$, $\mu = \mu_2/\mu_1$, $y = m_1/m_2$, and $X_0 = M_1/M_2$. wt % is the conversion; μ_1 and μ_2 are the molecular weights of monomers 1 and 2, respectively; M_1 and M_2 are the initial compositions of the monomers (mol); and m_1 and m_2 correspond to the monomer compositions in the copolymer for each monomer.

Figures 3 and 4 show η - ξ plots according to the K-T method, from which the monomer reactivity ratios were determined for both copolymer systems.

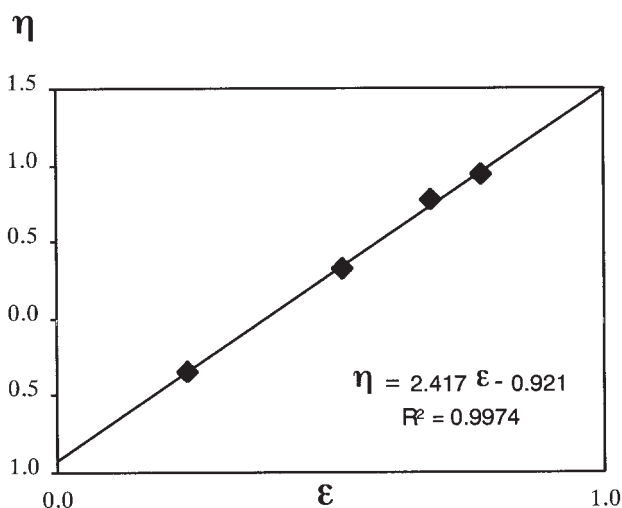


Figure 3 η - ξ representation of the copolymerization parameters for the K-T method for poly(IA-co-HMAm).

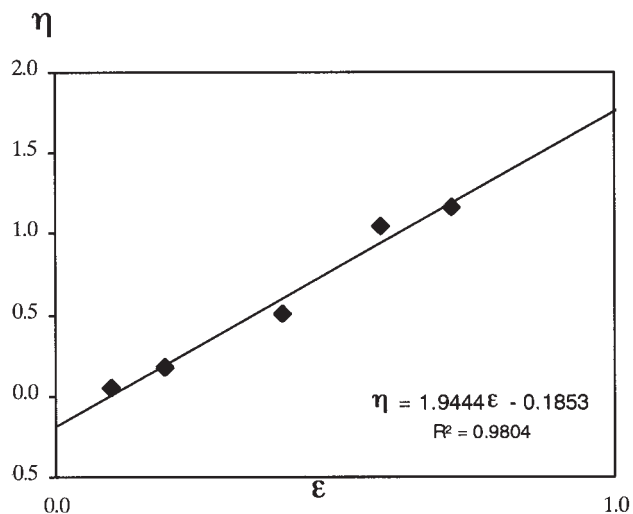


Figure 4 η - ξ representation of the copolymerization parameters for the K-T method for poly(β MHI-co-HMAm).

TABLE III
Data to Determine the Reactivity Ratios for Poly(IA-co-HMAm) with the K-T Method

Monomer feed (mol %)		Elemental analysis (%)			Copolymer composition (mol %)		Yield (%)	ξ	η
M_1 (IA)	M_2 (HMAm)	C	H	N	m_1	m_2			
75.0	25.0	46.35	5.42	4.42	81.8	18.2	14.7	0.770	0.925
66.7	33.3	46.42	5.57	6.18	76.2	23.8	12.7	0.677	0.767
50.0	50.0	46.59	5.84	8.09	61.5	38.5	11.3	0.512	0.316
33.3	66.7	46.77	4.96	2.71	50.0	50.0	12.7	0.286	OR
25.0	75.0	46.95	4.96	2.02	35.7	64.3	14.0	0.230	-0.334

η vs ξ , $\mu = 0.7769$ and $\alpha = 0.5633$. OR = outside the range.

The variable ξ can take any possible value in the 0–1 interval. A plot of η versus ξ gives a straight line, which upon extrapolation to $\xi = 0$ and $\xi = 1$ gives $-r_2/\alpha$ and r_1 , respectively. The data base, included in Tables III and IV, yielded reactivity ratios for poly(itaconic acid-co-N-hydroxymethyl acrylamide) [poly(IA-co-HMAm)] of $r_1 = 1.5$ (IA) and $r_2 = 0.50$ (HMAm) and for poly(β -methyl hydrogen itaconate-co-N-hydroxymethyl acrylamide) [poly(β MHI-co-HMAm)] of $r_1 = 1.8$ (β MHI) and $r_2 = 0.13$ (HMAm). The reactivity ratios indicated that the systems poly(IA-co-HMAm) and poly(β MHI-co-HMAm) could be considered a random incorporation of the homosegments of IA and β MHI, with a major tendency to alternate for β MHI-co-HMAm ($r_1 \times r_2 = 0.23$) in comparison with IA-co-HMAm ($r_1 \times r_2 = 0.75$).

Degree of swelling

The swelling behavior of poly(IA-co-HMAm) and poly(β MHI-co-HMAm) was investigated as a function of the pH at different ionic strengths (0.05–0.15M) and at room temperature (25°C). Figure 5 shows the swelling behavior of poly(IA-co-HMAm) and poly(β MHI-co-HMAm) after different times of swelling and with different copolymer compositions (76.2/23.8, 50.0/50.0, and 35.7/64.3 and 82.8/17.2, 59.0/41.0, and 53.4/46.6, respectively). The swelling of the hydrogels increased in the pH range of 7–9, at which the maximum swelling could be observed. This could be at-

tributed to the higher dissociation of acid groups in IA and β MHI in this pH range. Moreover, the swelling increased with time, but after some time, it leveled off. This value of swelling may be named the equilibrium swelling percentage.

Figures 6 shows the results for the AI/HMAm and β MHI/HMAm gels with different comonomer ratios at various pHs. The gels were swollen in buffered media with $I = 0.05M$. From these data, it was observed that the swelling increased as the content of IA and β MHI increased. These observations were explained by the increased hydrophilicity imparted to the copolymers by the IA and β MHI comonomers.

Moreover, the swelling of the hydrogels increased with the pH. In all compositions, the maximum swelling occurred in the pH range of 7–9 because of the higher dissociation of acid groups of IA and β MHI in this pH range. The first and second dissociation constants of IA were $pK_{a1} = 3.85$ and $pK_{a2} = 5.44$,²⁹ and pK_a of β MHI was 6.02.

The poly(IA-co-HMAm) gel swelled 200% more at pH 9 than the poly(β MHI-co-HMAm) gel at pH 9. A plausible explanation for this difference in swelling may be found if we consider the chemical nature of the two weakly ionizable comonomers used in both copolymers. IA has twice as many carboxyl groups per chain length as β MHI. Therefore, the observed swelling behavior was a result of the higher number of ionizable groups on the copolymer, which enhanced

TABLE IV
Data to Determine the Reactivity Ratios for Poly(β MHI-co-HMAm) with the K-T Method

Monomer feed (mol %)		Elemental analysis (%)			Copolymer composition (mol %)		Yield (%)	ξ	η
M_1 (β MHI)	M_2 (HMAm)	C	H	N	m_1	m_2			
75.0	25.0	49.75	5.69	1.39	86.3	13.7	47.41	0.708	1.165
66.7	33.3	49.69	5.73	1.76	82.8	17.2	46.65	0.583	1.042
50.0	50.0	49.38	5.90	3.47	69.7	30.3	46.97	0.404	0.511
33.3	66.7	49.19	6.01	4.54	59.0	41.0	28.72	0.195	0.176
25.0	75.0	49.06	6.08	5.26	53.4	46.6	23.29	0.100	0.050

η vs ξ , $\mu = 0.7014$ and $\alpha = 0.6789$.

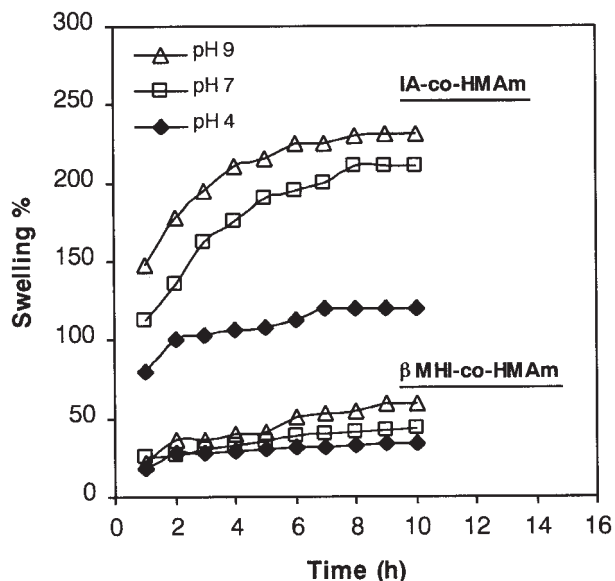


Figure 5 Swelling isotherms of IA/HMAm and β MHI/HMAm with different copolymer compositions [(Δ) 76.2/23.8, (\square) 50.0/50.0, and (\blacklozenge) 35.7/64.3 and (Δ) 82.8/17.2, (\square) 59.0/41.0, and (\blacklozenge) 53.4/46.6, respectively] as a function of time, in buffered solutions at pHs 4, 7, and 9, at $I = 0.05M$ (NaCl) at 25°C.

repulsive forces of the charged groups with neighboring chains. This electrostatic repulsion was responsible for the network swelling with the expected reduction of hydrostatic pressure inside the network.

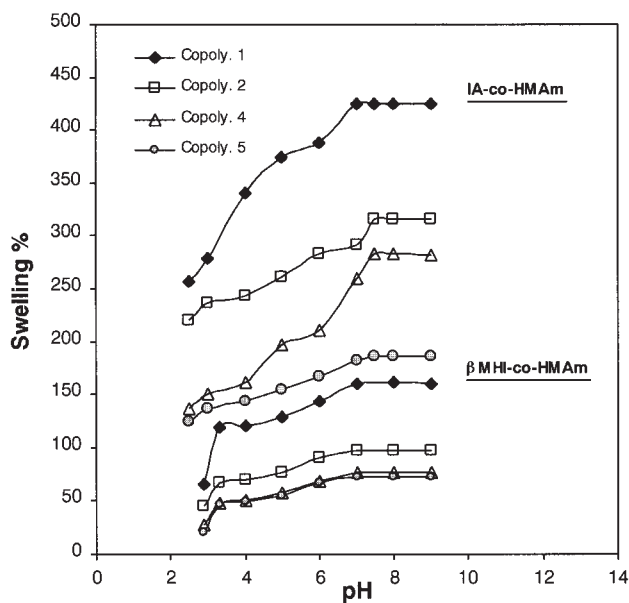


Figure 6 Swelling isotherms of IA/HMAm and β MHI/HMAm copolymers as a function of the pH, in buffered solutions at different pHs, at $I = 0.05M$ (NaCl) at 25°C, for a period of 10 h.

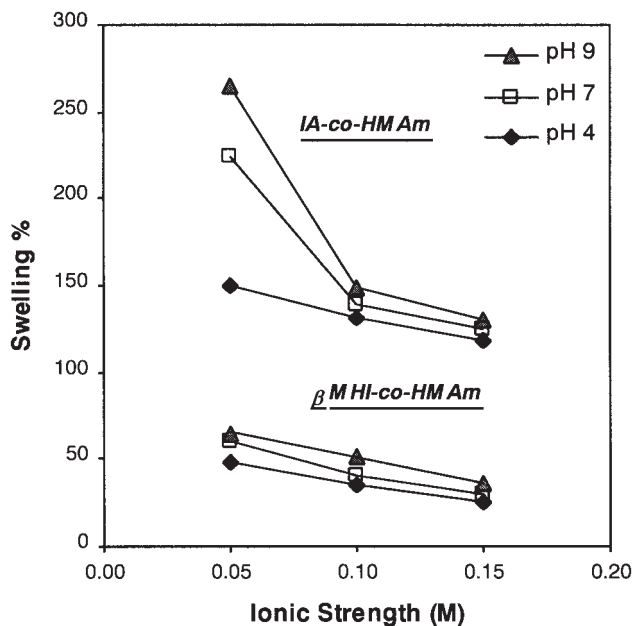


Figure 7 Effect of the total ionic strength on the equilibrium swelling of poly(IA-co-HMAm) and poly(β MHI-co-HMAm), at different pHs, for a period of 5 h.

Effect of the ionic strength on the equilibrium swelling degree

The effect of the ionic strength on the equilibrium swelling degree of the IA/HMAm and β MHI/HMAm copolymers was investigated at 25°C. The results are given in Figure 7. The pH of the solution was adjusted to 4, 7, and 9 to study the effect of the ionic strength on three swelling degrees. As shown in Figure 7, with increasing ionic strength of the solution, the equilibrium swelling degree values showed a continuous decrease in all cases.

CONCLUSIONS

Copolymer gels of poly(IA-co-HMAm) and poly(β MHI-co-HMAm) were prepared by radical copolymerization. All the obtained polymers were insoluble in water and in some common organic solvents.

The reactivity ratios indicated that the systems IA/HMAm and β MHI/HMAm could be considered a random incorporation.

The swelling characteristics of both copolymer gels showed an increase in the pH range of 7–9, at which the swelling maximum was observed.

The copolymer composition had a significant impact on the equilibrium degree of the swelling behavior of both copolymer gels.

A change in the ionic strength of the swelling solution from 0.05 to 0.15M caused a decrease in the equilibrium degree of swelling.

The ionic strength and the pH were the basic parameters affecting the equilibrium degree of swelling of the poly(IA-co-HMAm) and poly(β MHI-co-HMAm) gels.

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