

Mechanical Properties of Poly(*N*-isopropyl-acrylamide-co-itaconic acid) Hydrogels

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ABSTRACT: Hydrogels of *N*-isopropylacrylamide and itaconic acid were synthesized with different monomer ratios and with two crosslinking agent concentrations. The different xerogels were immersed in water and the swelling process was conducted up to equilibrium conditions at two temperatures (22 and 37°C). These temperatures are lower and higher than the transition temperature shown by PNIPA hydrogels. The mechanical properties of the different solvated hydrogels were examined by oscillatory shear measurements at 22 and 37°C. The copolymer volume fraction and the elastic storage modulus of the hydrogels decreased as the itaconic acid percentage in the copolymer increased. This behavior was attributed to the higher hydrophilic character of the itaconic acid comonomer. Effective crosslinking density, molar mass between crosslinks, and the polymer–solvent interaction parameter were determined from the experimental values of the elastic storage moduli and the copolymer volume fractions. © 2002 Wiley Periodicals, Inc. *J Appl Polym Sci* 85: 2540–2545, 2002

Key words: hydrogels; copolymerization; crosslinking; drug delivery systems; swelling

INTRODUCTION

Polymers and copolymers that exhibit the ability to absorb a considerable quantity of water without actual dissolution are termed *hydrogels*. Such materials are usually crosslinked and therefore can be considered as water-swollen polymer networks. Hydrogels have become of major interest because polymers are increasingly used in medi-

cal applications. Hydrogels are being used nowadays for membranes, catheters, contact lenses, and drug-delivery systems.^{1–4}

The equilibrium water content of the gel is a basic property, given that several useful applications require a suitable water content. Hydrogels with a higher water content are generally more advantageous because they show a higher permeability and biocompatibility. However, on increasing the water content the mechanical strength of the hydrogel decreases. To obtain a gel with a high water content and an acceptable mechanical strength, a composite molecular structure is necessary. This structure will consist of a hydrophilic component that absorbs large amounts of water and a hydrophobic component that improves the mechanical strength.⁵

In recent years different types of hydrogels sensitive to temperature or pH have been synthe-

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sized. Variations in these parameters raise interesting structural changes that could eventually be important for biomedical applications. Several hydrogels of N-substituted acrylamide derivatives, such as poly(*N*-isopropylacrylamide),^{6–8} poly(*N,N*-diethylacrylamide),⁹ poly(*N*-methylacrylamide),¹⁰ and practically hydrolyzed polyacrylamide¹¹ belong to the group of thermosensible hydrogels. Copolymerization is also an important aspect in this field because the transition temperature range can be modified by incorporating a more hydrophilic monomer to the hydrogel.^{12,13}

N-Isopropylacrylamide (NIPA) gels show a volume phase transition in water at about 34°C, going from a swollen to an unswollen state. This phenomenon could allow their use in intelligent systems for drug release,^{14–16} whose action would be triggered by the patient's temperature.

To improve our understanding of these systems, we have undertaken the study of hydrogels of NIPA copolymerized with itaconic acid as a possible drug-delivery system. In this investigation we have studied the mechanical properties of several poly(*N*-isopropylacrylamide-*co*-itaconic acid) gels synthesized with different compositions and crosslinking grades. Oscillatory shear measurements were carried out at two temperatures, 22 and 37°C.

EXPERIMENTAL

Materials and Synthesis

N-Isopropylacrylamide (NIPA, purity = 97%) and itaconic acid (purity > 99%) were used as monomers and purchased from Aldrich (Milwaukee, WI) and Merck (Darmstadt, Germany), respectively. *N,N'*-Methylenebisacrylamide (BIS) was employed as crosslinking agent and 2,2'-azobis(2-amidinopropane) dihydrochloride (V-50) as initiator and were purchased from Fluka Chemie (Buchs, Switzerland) and Wako Pure Chemical Industries Tokyo, Japan), respectively. All products were used without further purification, except BIS, which was purified by recrystallization in methanol.

Gels were prepared by radical crosslinking copolymerization at 40°C in a nitrogen atmosphere for 24 h. Monomers were dissolved in methanol at a total concentration of 25 wt %. The monomer weight ratio of NIPA/itaconic acid ranged from 100/0 to 80/20. The initiator concentration was 1.0% and the crosslinking agent concentrations

were 1.5 and 2.0 wt % with respect to the monomers. All solutions were degassed before polymerization. Once polymerization was over, gels were washed intensively with methanol and finally with water. By weighing the xerogels we found that the conversions to gel were practically total (~ 98%).

Xerogels were obtained by drying the gels at room temperature for 7 days and at 50°C for 2 days. Thin discs of the xerogels (diameter ~ 9 mm; thickness ~ 1 mm) were shaped by cutting.

Gel Swelling

Xerogel discs were immersed in an excess of deionized water to achieve the equilibrium swelling at 22 and 37°C and at a constant pH of 5.9. Once the gels reached the equilibrium swelling they were cut to get final discs with a diameter of 20 mm.

Dynamic Mechanical Properties

Oscillatory shear measurements were performed in a Polymer Laboratories (Shropshire, UK) dynamical mechanical thermal analysis system. The mechanical mode used was the torsion one with two torsion plates with a diameter of 20 mm. The elastic storage G' and loss moduli G'' were measured as a function of frequency between 0.1 and 5.0 Hz at a maximum strain amplitude of 6.25 mrad. The measurement temperatures were 22 and 37°C and were controlled with a precision of 1°C.

RESULTS AND DISCUSSION

The volume fraction of copolymer ϕ_2 in the hydrogels was obtained from measurements conducted in thin discs having measured diameters of dry (D_0) and swollen (D) polymer. On the basis of isotropic volumetric swelling, the volume fraction was calculated from

$$\phi_2 = \left(\frac{D_0}{D}\right)^3$$

The volume fraction is plotted as a function of the copolymer composition for two crosslinking agent concentrations and at two temperatures (22 and 37°C) in Figure 1. In all cases the volume fraction of copolymer decreases with the itaconic acid percentage in the copolymer. The more hy-

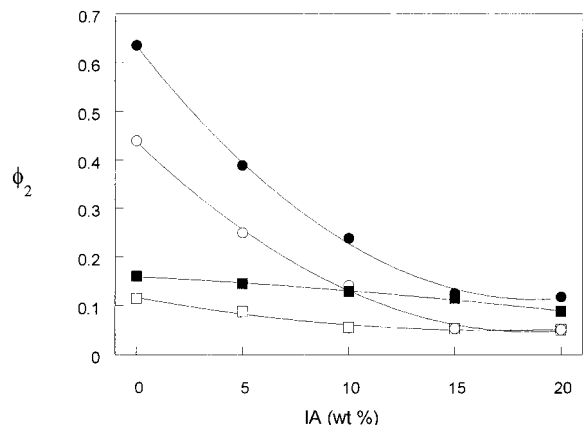


Figure 1 Volume fraction of copolymer ϕ_2 against itaconic acid percentage for two *N,N'*-methylenebisacrylamide concentrations, 1.5 (unfilled symbols) and 2.0% (filled symbols), and at two temperatures, 22 (□) and 37°C (○).

drophilic character of the itaconic acid favors the migration of water molecules into the hydrogel. For any itaconic acid percentage and temperature the increment in the crosslinking agent concentration increases to that of an increment in the volume fraction of copolymer. A higher concentration of BIS causes an increment in the number of joints in the polymer network, which reduces the possible expansion of the network and therefore the number of water molecules capable of passing into the hydrogel.

On raising the temperature above the transition temperature ($\sim 34^\circ\text{C}$) a sharp increment of ϕ_2 is observed for the PNIPA hydrogels. It is known that PNIPA gels undergo a volume phase transition in water at the transition temperature, from a swollen state to a shrunken state, by increasing temperature.^{17,18} This is attributed to dissociation of the hydrophobic interactions between NIPA segments and water. Shibayama et al.^{19,20} have suggested that there are two types of water molecules in the hydrogels, that is, one associated with the phase transition $n-n_0$, and the other with the lower limit for the hydrophobic hydration n_0 . However, as the itaconic acid percentage in the hydrogel increases, the effect of the volume phase transition decreases, to lower than the ϕ_2 differences between both experimental temperatures (22 and 37°C). For an itaconic acid percentage of 20 wt %, no experimental difference was detected for both crosslinking agent concentrations. This fact suggests that the presence of the hydrophilic comonomer, itaconic acid, reduces

the magnitude of the volume phase transition, reaching an itaconic acid percentage at which no transition is detected.

Measurements of the real and imaginary parts, G' and G'' , of the complex shear modulus were also made as a function of the frequency by applying to the hydrogel a small deformation oscillatory shear strain of frequency ω . Hydrogels with different copolymer compositions and two crosslinking agent concentrations were analyzed at two temperatures (22 and 37°C). Figure 2 shows the plots of $\log G'$ against $\log \omega$ for four hydrogels with two copolymer compositions (NIPA/IA: 100/0, 85/15), two crosslinking agent concentrations (BIS: 1.5, 2.0%), and at 22°C. According to the results presented in this figure, the storage moduli were independent of frequency over the experimental range for the different hydrogels studied. Another feature observed in all the examined gels was that G' exceeded G'' over the entire range of frequency used by 1 or 2 orders of magnitude. This behavior is consistent with the dynamic mechanical behavior expected for a crosslinked network. For a rubbery gel (i.e., above its glass transition), G' and G'' are parallel and largely frequency insensitive.

The variation of the elastic storage modulus as a function of the copolymer composition for both crosslinking agent concentrations and at 22 and 37°C is plotted in Figure 3. For each case, the elastic storage modulus decreases as the itaconic acid percentage in the copolymer increases. This behavior suggests a decrease in the joint density of the hydrogels as the itaconic acid content in-

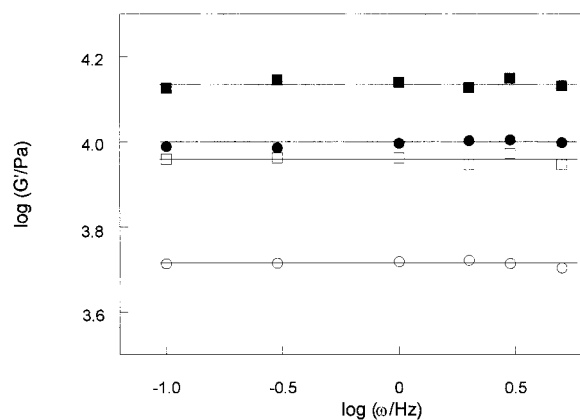


Figure 2 Dynamic mechanical spectrum of the elastic storage modulus G' for hydrogels with two NIPA/IA compositions, 100/0 (□) and 85/15 (○) and two crosslinking agent concentrations, 1.5 (unfilled symbols) and 2.0% (filled symbols), and at 22°C.

creases as a consequence of the swollen grade. As seen previously, an increment in the itaconic acid increases to a decrease in the volume fraction of copolymer because of the higher hydrophilic character of the itaconic acid comonomer. With a behavior similar to that of the copolymer volume fraction, the effect of the volume phase transition on the elastic storage modulus decreases with the itaconic acid percentage in the copolymer. As expected, an increment in the crosslinking agent concentration causes an increment in the elastic storage modulus. However, for hydrogels with a high content of NIPA this effect is more significant for temperatures lower than the transition temperature than for higher temperatures. According to the behavior shown by G' and ϕ_2 , when the temperature goes above the transition temperature T_c , the abrupt change in the mechanical properties could be ascribed to the volume transition at T_c .^{21,22}

The effective crosslinking density ν_e was determined according to the following expression:

$$\nu_e = \frac{G\phi_2^{1/3}}{RT}$$

The variation of ν_e as a function of the copolymer composition for both crosslinking agent concentrations and at 22 and 37°C is plotted in Figure 4.

In all cases, the effective crosslinking density decreases with the itaconic acid percentage of the copolymer. This decrease is caused by an increment of the solvating water as the itaconic acid content increases. This comonomer is more hydro-

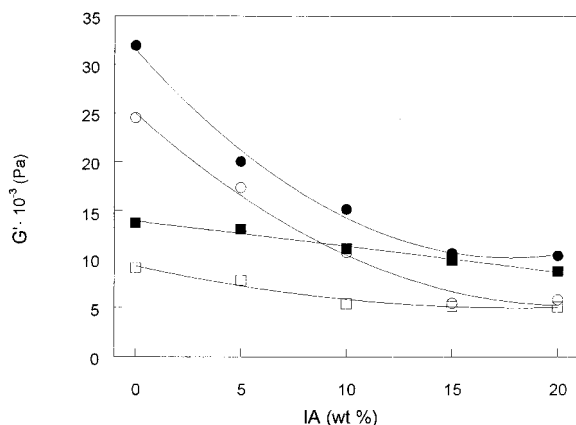


Figure 3 Elastic storage modulus as a function of itaconic acid percentage for two crosslinking agent concentrations, 1.5 (unfilled symbols) and 2.0% (filled symbols), and at two temperatures, 22 (□) and 37°C (○).

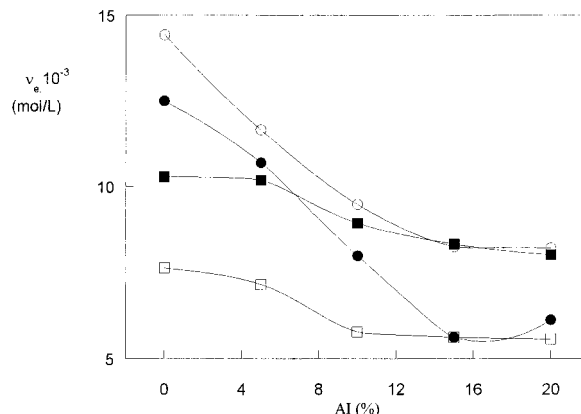


Figure 4 Effective crosslinking density as a function of itaconic acid percentage for two crosslinking agent concentrations, 1.5 (unfilled symbols) and 2.0% (filled symbols), and at two temperatures, 22 (□) and 37°C (○).

philic than NIPA and therefore the solvation capability of the hydrogel increases as the itaconic acid percentage increases. As expected, for a given itaconic acid percentage, ν_e increases with the crosslinking agent concentration. An increment in the effective crosslinking density is also observed when the temperature goes from 22 to 37°C. This increment is a consequence of the volume reduction of the hydrogel that occurs during the volume phase transition of the PNIPA gels.

The molar mass between crosslinks M_c was easily estimated with the following equation:

$$M_c = \frac{\rho_2}{\nu_e}$$

where ρ_2 is the copolymer density.

The variation of the molar mass between crosslinks as a function of the copolymer composition for both crosslink agent concentrations and at 22 and 37°C is plotted in Figure 5. The molar mass between crosslinks increases with the itaconic acid percentage of the copolymer and decreases with the crosslinking agent concentration. This magnitude shows an increase in behavior over that shown by the effective crosslinking density, given that both magnitudes are inversely proportional, $M_c \propto 1/\nu_e$.

Finally, values of the polymer–solvent interaction parameter χ were calculated from the following expression, valid at swelling equilibrium²³:

$$\ln(1-\phi_2) + \phi_2 + \chi\phi_2^2 + \nu_e V_1(\phi_2^{1/3} - 2\phi_2 f^{-1}) = 0$$

where f is the functionality of the crosslinking agent and V_1 (mol dm^{-3}) is the molar volume of water at a temperature T (K), which was obtained by the expression²⁴

$$V_1 = 10^{-3}\{18.05 + [3.6 \times 10^{-3}(T - 298)]\}$$

The calculated χ values are shown in Figure 6, where the polymer–solvent interaction parameter is plotted as a function of the copolymer composition for both crosslinking agent concentrations and at 22 and 37°C. A decrease of the polymer–solvent interaction parameter is shown as the itaconic acid percentage increases, confirming the water goodness with respect to the itaconic acid. The slight increment in χ with increasing crosslinker concentration could be explained by the lower hydrophilic character of BIS. Similar behaviors have been found for other hydrogel systems.^{25–27}

By applying the Flory–Rehner theory, Erbil et al.²⁶ determined values of χ , ν_e , and M_c at 22°C for NIPA/IA hydrogels prepared under different experimental conditions. These investigators found χ values of 0.53 and 0.51 for the NIPA homopolymer and the copolymer, respectively. These values are very similar to those that we have found from mechanical measurements, 0.54 and 0.52. However, the values of ν_e and M_c determined by Erbil et al.²⁶ are quite different from those found in this study.

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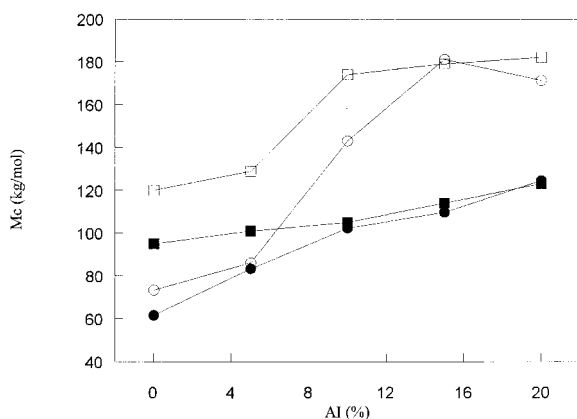


Figure 5 Molar mass between crosslinks against itaconic acid percentage for two crosslinking agent concentrations, 1.5 (unfilled symbols) and 2.0% (filled symbols), and at two temperatures, 22 (□) and 37°C (○).

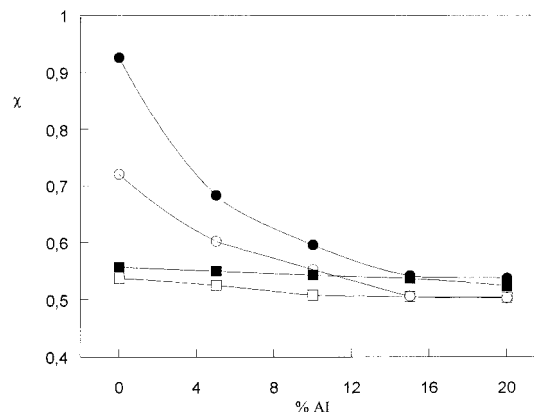


Figure 6 Polymer–solvent interaction parameter as a function of itaconic acid percentage for two crosslinking agent concentrations, 1.5 (unfilled symbols) and 2.0% (filled symbols), and at two temperatures, 22 (□) and 37°C (○).

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