

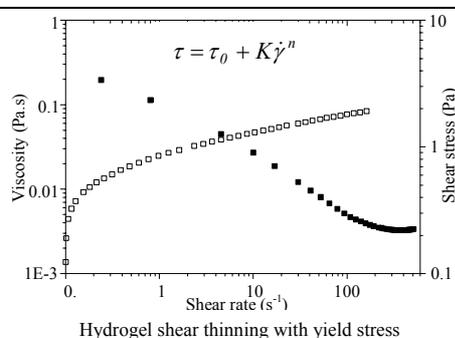
SWELLING KINETICS AND STEADY SHEAR RHEOLOGY OF PH SENSITIVE POLY(ACRYLAMIDE-CO-ITACONIC ACID) HYDROGELS

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Dynamic and equilibrium swelling properties poly(acrylamide-co-itaconic acid) hydrogels with high amount of diprotic acid were studied as a function of pH and buffer composition. In all compositions, maximum extents of swelling were reached at pH 9.18. The swelling of the hydrogels follows a second-order kinetic equation. Diffusion exponents indicate that the mechanisms of buffer uptake are governed by non-Fickian diffusion, but at $\text{pH} < \text{pK}_{a\text{gel}}$ the mechanism remained Fickian. The rheological properties were described by the Herschel-Bulkley and power-law models to explore their non-Newtonian behavior. The results showed that higher itaconic acid content raised the polymer viscosity and degree of shear-thinning.



INTRODUCTION

Hydrogels are water-swollen polymeric networks of chemically or physically crosslinked chains.¹⁻³ Ionic hydrogels are polymer networks containing pendant groups, such as carboxylic or sulfonic acid, which show gradual changes in their swelling behavior, as a result of varying the external pH. In aqueous media of appropriate pH, the pendant groups ionize and develop fixed charges on the polymer network, generating electrostatic repulsive forces responsible for pH-dependent swelling or de-swelling of the hydrogel.⁴ Hydrogels of poly(acrylamide) (PAAm) have found broad applications in drug delivery systems;⁵ to increase their swelling capacity, an ionic comonomer can be included into the reaction mixture. The obtained pH-sensitive hydrogels extend and shrink at pH value above and below the pK_a of the acidic comonomer. As an example, hydrogels of acrylamide and acidic comonomers

can be prepared by co-polymerizing acrylamide with a pH-sensitive comonomer, such as acrylic (AAc) or diprotic acids from maleic (MAc) or itaconic (IAc) acid.⁶⁻⁸ The biocompatibility and non-toxicity of itaconic acid have promoted its use for the preparation of pH-sensitive copolymers with acrylamide. The advantage of itaconic acid is the great hydrophilicity; it has two ionisable groups with different pK_a , showing a more pronounced pH-sensitivity of the system. For application as drug delivery devices, rheological and swelling changes in the gels need to be controlled in order to initiate solute transport in suitable conditions. In order to optimize hydrogel system for this specific application, swelling kinetic, diffusion and transport properties of water and solute through the pH-sensitive hydrogels must be studied. In a previous work, preparation, swelling properties and rheological behavior of Poly(acrylamide-co-acrylic acid) hydrogels were studied.⁹ In this work, we focus on the swelling

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kinetics and transport mechanisms in pH-sensitive poly(acrylamide-co-itaconic acid) hydrogels. For this, copolymers based on AAm and IAc at higher ratios of diprotic acid, were prepared by free radical crosslinking copolymerization. Swelling behavior of poly(AAm-co-IAc) hydrogels as a response to pH of the surrounding media was investigated. All hydrogels synthesized were characterized through infrared spectroscopy; the rheological behavior of the swollen-in-water hydrogel suspensions was evaluated.

EXPERIMENTAL

1. Materials

Acrylamide and itaconic acid monomers used in this study were obtained from Aldrich Chemicals and used as received; the crosslinker *N,N'*-methylene bisacrylamide (MBAAm), the activator *N,N,N',N'*-tetramethyl ethylene diamine (TEMED) and the initiator potassium persulphate (KPS) were all analytical grade and purchased from Panreac Monplet & Esteban, S.A. (Spain). Deionized water was used throughout the experiments in the preparation of hydrogels, of buffer solutions and in the swelling experiments.

2. Preparation of hydrogels

Crosslinking copolymerization was carried out under N_2 atmosphere at 25 °C for 24 hours in the glass test tubes. The weight ratios of AAm/IAc monomer in the initial mixture were: 100:0, 90:10, 80:20 and 70:30 (samples IA00; IA10; IA20 and IA30 respectively). The amount of crosslinking agent MBAAm is the same for all compositions (5.0 wt%). After reaction, crosslinked polymers were removed from tubes, cut, dried and then subjected to extraction with water. Finally extracted gels were dried in a vacuum oven at 30 °C to constant mass.

3. Characterization

The spectroscopic characterization of hydrogels was performed by Infrared Spectroscopy (FT-IR) in KBr phase. Dried samples were analyzed in Shimadzu M850 Model, FT-IR Spectrophotometer with 40 scans in the range of 4000-400 cm^{-1} , with a 2 cm^{-1} resolution.

Swelling measurements

Swelling behavior of the gels was investigated in deionized water and saline solution (0.9 % NaCl) at room temperature; the effect of pH on the hydrogels swelling was examined in buffer media of varying pHs, ranging from 2.2 to 11.83. For the procedure, dried pre-weighed hydrogels were immersed in vials (250 ml) filled with deionized water (or buffer solution) and the swollen gels were taken out at regular time-intervals, wiped superficially with filter paper to remove surface-bound water, weighed and then re-immersed in the same bath. In order to reach the equilibrium mass swelling, the gels were immersed in liquid until their equilibrium swelling ($S_{w\infty}$) was attained (3 days). The mass swelling at time t was calculated from the following equation:^{10,11}

$$S_w(t) = \frac{m_t - m_0}{m_0} \quad (g/g) \quad (1)$$

where m_0 is the mass of the initial dry gel and m_t the mass of the swollen gel at time t .

The flow behavior of aqueous hydrogel suspensions under steady shear was studied at 20 °C in controlled stress AR-2000 Advanced Rheometer (T.A. Instruments), with Couette geometry, using a pair of coaxial cylinders with 15 mm of external diameter and gap of 1 mm. The aqueous suspension concentration of gel particles was of 0.1 wt%. Size of the dry particles was about 0.1-0.2 mm; the shear rate range was 0-400 s^{-1} .

RESULTS AND DISCUSSION

1. Hydrogels preparation and structure

Free radical crosslinking copolymerization of AAm and IAc in water leads to the formation of copolymers by intermolecular hydrogen bonding between the carboxylic groups and amide groups. Fig. 1 shows the Infrared spectra of pure PAAm and copolymers with IAc. From the spectra it is clear that the characteristic absorption peaks of poly(acrylamide) and its copolymers with itaconic acid are present: between 3420-3475 cm^{-1} (large) showing the N-H stretching of $-CONH_2$ and 1650-1700 cm^{-1} (strong) indicating the C=O stretching of $-CONH_2$; between 1686-1740 cm^{-1} (strong) indicating the C=O stretching of $-COOH$ and 1400-1567 cm^{-1} (weak) indicating the C-O stretching of $-COO^-$. Appearance of band at 2500-2800 cm^{-1} for copolymers suggests the formation of hydrogen bonding between the hydroxyl groups and amide groups.

2. Swelling kinetics

2.1. Swelling in deionized water and saline solution (0.9 % NaCl)

Diffusion involves migration of liquid into pre-existing or dynamically formed spaces between hydrogel chains; the swelling mechanism is then characterized by diffusion and relaxation time of the polymer network.¹² Based on experimental results, several authors have proposed a second-order model to describe the swelling kinetics of ionic hydrogels.¹³⁻¹⁵ Considering second-order kinetics, the swelling rate at any time may be expressed as:

$$\frac{dS_w}{dt} = K(S_{w\infty} - S_w)^2 \quad (2)$$

Sw_{∞} was estimated by fitting the swelling versus time data to the second order kinetic equation of the form:

$$\frac{t}{Sw(t)} = \frac{1}{Sw_{\infty}}t + \frac{1}{K_{S_w} Sw_{\infty}^2} \quad (3)$$

where $Sw(t)$ is the swelling at time t (min) and K_{S_w} ((g.gel/g.water).min⁻¹) is a second order swelling rate constant. The predictions of the second order kinetic equation (Eq. 3) follow quite well the experimental data for all compositions ($R^2 = 0.997-0.999$) demonstrating that the swelling of these hydrogels indeed obeys a second order swelling kinetic equation. From the slope and intercept of plots of Eq.3, values of swelling rate constant (K_{S_w}) and theoretical equilibrium swelling (Sw_{∞}) were calculated. For pure PAAm (IA00) Sw_{∞} was about 21.4 g H₂O/g gel. Increasing the mole ratio of hydrophilic comonomer (IAc) in feed composition from 10 to 20 and 30 %, increases the Sw_{∞} values from 65.4 to 101.3 and 132.8 g H₂O/g gel, respectively. These 1.5 and 2.0 times greater capacities are expected results, because it is well known that increasing the hydrophilic character of the network increases the ionization degree of the hydrogel and this, yields higher water absorption capacity.¹⁶

2.2. pH dependent swelling

It is well known that while PAAm does not respond to changes in pH buffer solutions, $Sw_{\infty}=8.9-10.6$ g H₂O/g gel for pH ranging from 2.2 to 11.8. On the other hand, copolymers of Poly(AAm-co-IAc) are typical pH-sensitive hydrogels that can deprotonate their carboxyl moieties in alkaline solution and protonate them in acidic solution. With increase in pH values, the equilibrium mass swelling of the copolymers increases up to a maximum value of 63.5 g H₂O/g gel at pH=9.18 and then it decreases at pH=11.83. It is known that ionization of the acid groups occurs once the pH of external medium is above the characteristic pK_a of these groups. For IAc the two values of characteristic pK_a are $pK_{a1}=3.85$ and $pK_{a2}=5.45$. At low pH (<5.45), carboxylic acid groups are protonated and exhibit hydrophobic character, leading in less liquid uptake into the polymer. As pH increases (>5.45), carboxylic groups ionize and concentration of anionic groups in hydrogel increases. This anionic character makes an additional pressure and electrostatic

repulsion within hydrogel and the swelling degree increases too. This behavior has been explained by a buffer action of the carboxylate group with an acid or base, as previously reported by Lee and Wu.¹⁷

2.3. Diffusion

It has been established that the above model (Eq. 3) cannot provide any information about mechanisms of diffusion; rather, it provides a simple approach to correlate experimental data.¹⁸ Based on power law model, liquid transport into polymer networks, *i.e.* swelling-time curves, may be described by the following equation:¹⁹⁻²¹

$$F = \frac{M_t}{M_{\infty}} = Kt^n \quad (4)$$

where F represents the swelling power of the gel network, M_t and M_{∞} are the mass of liquid absorbed at time t and mass of liquid absorbed at equilibrium, respectively, K is a constant related to gel structure and the penetrant fluid, t is the time and n is the diffusional exponent, which value is indicative of the transport mechanism. The swelling kinetics of hydrogels can be classified as diffusion-controlled (Fickian, $n=0.5$), Case I, and relaxation-controlled (non-Fickian, $0.5 < n < 1$) swelling, Case II. When diffusion occurs much faster than the relaxation of the polymer chains, the swelling kinetics is diffusion-controlled. Diffusion parameters were determined for the swelling of the hydrogels in water and buffer solutions:

Case II transport was observed for high swelling in deionized water ($n \geq 1$), due to a large increase in osmotic pressure driving forces at the time when solvent fronts met.²²

In buffer solutions, no significant change in the diffusional exponent value was observed for pure PAAm with increasing pH; in all the swelling media diffusion and transport mechanism remain non-Fickian ($n=0.6-0.7$): this result confirms that the PAAm is pH-insensitive. For the copolymers poly(AAm-co-IAc), the first protonation of acid groups occurs at pH=4.01 and was completed at pH=2.2 (Fickian diffusion was overall observed with $n=0.48-0.51$), at pH=7 and above these groups ionize and the hydrogels swell (the diffusion mechanism becomes non-Fickian with $n=0.7-0.9$). A slight increase in n values with increased pH was observed for all copolymer compositions, the swelling become controlled by polymer chains relaxation.

3. Rheological behavior of copolymer samples

The flow properties with shear rate for the hydrogel suspensions are illustrated in Fig. 2. Typical shear stress-shear rate and viscosity-shear rate data for the aqueous polymer suspensions of different compositions are presented in the curves. The hydrogel suspensions exhibited non-Newtonian flow and shear-thinning behavior. The shear stress-shear rate data were analyzed by using conventional flow equations known as the model describing the flow behavior of the gel polymers very well. Herschel-Bulkley²³ (Eq. 5) model was more satisfactory to describe the flow behavior of the gels suspensions:

$$\tau = \tau_0 + K\dot{\gamma}^n \quad (5)$$

where τ is the shear stress (Pa), $\dot{\gamma}$ is the shear rate (s^{-1}), τ_0 is the yield stress (Pa), K is the consistency coefficient ($Pa \cdot s^n$) related to a high shear limiting viscosity, and n is the flow behavior index, a material parameter that determines their shear thinning nature. All polymer samples exhibit a good fit to Herschel-Bulkley, pseudo-plastic with yield stress, model ($R^2=0.992-0.996$); the values of K and τ_0 were directly proportional to the amount of IAc monomer, while the relationship between n and IAc content is opposite. All values of n are less than 1 (0.71; 0.72; 0.73 and 0.74 for IA30, IA20, IA10 and IA00 respectively), indicating that all samples belong to pseudoplastic fluids.

The presence of yield stress indicates that a three-dimensional network is formed at no shear conditions due to crosslink density and H-bonding in the hydrogels.²⁴ Under shear stress, the three-dimensional network is broken down. As seen from Fig. 2 the polymer viscosity drops at low shear rate, however in this very low-shear range, the zero-shear viscosity increases with increase in IAc content indicating that the hydrogel structure became as a quasi-solid. The higher is the IAc content in hydrogel, the harder are the particles and the smaller is the amount of water that can be used for lubricating. The very high-shear range shows that the infinite-shear viscosity has a limiting value of 3.3×10^{-3} Pa.s for PAAm and about 3.5×10^{-3} Pa.s for the Poly(AAm-co-IAc) copolymers: in this range the gels behavior become more predominant elastic gel.

CONCLUSIONS

The equilibrium degree of swelling and flow properties of hydrogels based on AAm and IAc can

be tuned by varying the amount of comonomer and pH of the surrounding swelling media. The PAAm is pH-insensitive, while its copolymers with IAc show significant increase in degree of swelling with pH. The swelling of the hydrogels follows a second-order kinetic equation. Water diffusion into these hydrogels is of non-Fickian type, due to maximum expansion of the polymer network. In buffered swelling media, the mechanism of diffusion was anomalous (non-Fickian). However, the diffusion remained Fickian at $pH < pK_{a_{gel}}$. The hydrogel suspensions exhibited non-Newtonian flow and shear-thinning behavior, apparent viscosity decreases as shear rate increases, and an initial yield stress is observed. Modeling analysis showed that the Herschel-Bulkley model fits well the behavior of the suspensions. The yield stress and consistency index values increase gradually with IAc content suggesting that more structured networks are obtained. On the other hand, the flow behavior index, n , gradually decreases with IAc content, indicating a slight gain in pseudo-plasticity for hydrogels. From the swelling kinetics and rheological behavior, these pH-responsive P(AAm/IAc) hydrogels have potential applications in controlled drug release.

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