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ORIGINAL PAPER

Polyacrylamide-gelatin polymeric networks: effect of pH and gelatin concentration on the swelling kinetics and mechanical properties

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Abstract This work presents the synthesis of polyacrylamide-gelatin (PAM-G) semi-interpenetrating hydrogels, as well as the study of the swelling capacity of this material at different pH's, and we report its Young modulus. The hydrogels were crosslinked with *N*,*N*′-methylenbisacrylamide and synthesized at different acrylamide/gelatin weight relationship. It was observed that the swelling capacity of the hydrogels increases when the gelatin concentration is increased; while the Young modulus (at the swelling equilibrium) decreases lightly. Therefore, the gelatin has a small effect in the Young modulus, unlike its influence in the swelling ability. The swelling experiments reveal that the PAM-G hydrogels increase its swelling capacity in alkaline mediums because the presence of the hydrophobic functional groups (mainly COO^-) in the gelatin structure.

Keywords Gelatin · Polyacrylamide · Semi-interpenetrating hydrogels · Swelling kinetics · Young modulus

Introduction

When two or more polymers are blended, the result is a multicomponent polymer. Those polymers can be formed in different ways; for example: simple polymer blends, graft polymers, block copolymers or interpenetrating networks. Interpenetrating polymer networks (IPN) are defined as a mix of two or more polymers forming a network which is synthesized in juxtaposition. However, most IPN's do

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not interpenetrate on a molecular scale. In semi-interpenetrating polymer networks (semi-IPN's) one o more polymers are cross-linked, and one or more polymers are linear or branched [1]. Semi-IPN hydrogels have been studied on their reversible volume changes in response to pH and ionic concentration [2, 3].

Gelatin is a polypeptide made by hydrolytic degradation of collagen. The conformation of the collagen molecule is a triple helix formed by three individual molecular strands held together by interchain hydrogen bonding. Gelatin is denatured collagen, and dissolves in water at temperatures above the melting temperature, existing as flexible individual coils in solution. Gelatin gels are well-known for their ability to form physical gels at room temperature and for their numerous uses in the food, pharmaceutical, and photographic industries. Several works reported the formation of gelatin hydrogels; these syntheses can be done using a crosslinking agent (like glutaraldehyde) or taking advantage of its triple helix in order to form a thermoreversible hydrogel [4–8].

Polymers and copolymers of acrylamide are the most commonly used hydrogels. Polyacrylamide gels are obtained by free-radical crosslinking copolymerization of acrylamide and *N*,*N*′-methylenebisacrylamide monomers. The applications and uses of hydrogels, in particular of polyacrylamide hydrogels, are diverse; they are used in abundance in the medical and agricultural industries [9–11]. They are also used in molecular biology laboratories as matrices for the separation of nucleic acid components during DNA sequence analysis and protein identification [12]. In the drug control delivery, there are several studies that show how the crosslinking density has an influence over delivery rates [13]. Polyacrylamide hydrogels can absorb high amounts of water and its swelling capacity is not very sensitive to pH. However, because water does not contribute to mechanical strength, these hydrogels present poor mechanical properties, in addition to its poor biodegradable properties. To increase the range of applications of polyacrylamide hydrogels, an option is the formation of a crosslinked polymer using a hydrophobic polymer with complementary properties [12].

In previous works has been reported the formation of interpenetrating networks of polyacrylamide/gelatin, and its biodegradation, and the influence of the concentration and pH of the medium over its swelling properties was studied [14–16]. In this work the synthesis of a polyacrylamide-gelatin hydrogel that forms a semi-interpenetrating network is presented. We prepared hydrogels with different gelatin concentrations, and polymerized in aqueous solution using *N*,*N*′-methylenebisacrylamide as crosslinking agent. The swelling kinetics and Young modulus were studied and compared with the properties of a conventional polyacrylamide hydrogel.

Experimental

Materials

Acrylamide (AM) with a hydrolytic degree of 99% from Scientific Polymer Products, and gelatin (G) 99% pure from Merck. *N*,*N*′-methylenebisacrylamide

(NMBA) as crosslinking agent (recrystallized with methanol) from Scientific Polymer Products, and 2′2-azobis(2-amidinopropane) dihydrochloride (V-50) as initiator, from Wako were used.

Formation of PAM-G hydrogels

The polyacrylamide-gelatin (PAM-G) hydrogels were synthesized in different acrylamide-gelatin weight relationships (w_{AM}/w_G: 100/0, 95/5, 90/10, 85/15, and 80/20) in a solution polymerization at 45 °C. The gelatin was dissolved in water at 35 °C, this solution was mixed with an aqueous solution formed with AM, NMBA and V-50. Both solutions are mixed perfectly and placed in 20 ml vials. The vials are placed in an oven at 45 °C for 24 h. Then, the vial is opened and the hydrogel is washed in distilled water for 24 h. The hydrogels, obtained in the shape of rods, were cut to yield disks, and these disks were dried at room temperature for 48 h and later on at 40 °C until constant weight was achieved. Each dry disk was sanded until the thickness was close to 1 mm. The size of the disk was measured with a micrometer.

Swelling properties of PAM-G hydrogels

The discs were immersed in three different swelling solutions: water as neutral medium, pH 4.0 buffer solutions, and pH 10.0 buffer solution. Previously weighed dry samples were placed in the swelling solution and the weight of the swollen samples was measured against time, once equilibrium was reached the excess surface water was removed using filter paper. The swelling (H) for each disk sample at any given time (t) was calculated by the following expression:

$$H = \left(\frac{w_t - w_0}{w_0}\right)100 \tag{1}$$

Here w_t and w_0 represent the weights of the hydrogel at time t and of the xerogel, respectively.

Mechanical properties of PAM-G hydrogels

Compression test were done on hydrogel disks swollen to equilibrium conditions at 20 °C in a thermo-mechanical analyzer (TMA-7 Perkin-Elmer, Guadalajara, Mexico). The hydrogels swollen to equilibrium conditions were cut to yield rectangles and properly measured. The Young modulus was obtained from the slope of the initial linear zone (strain less than 5%) of the stress–strain curve according to Ferry [17].

$$\tau = -E(\lambda - 1) \tag{2}$$

where τ is the applied stress and λ is the deformation given by the ratio of the deformed (h) to the initial thickness (h_0) of the hydrogel disks.

Results and discussion

Swelling properties of PAM-G hydrogels

The polyacrylamide-gelatin semi-interpenetrating network was prepared by solution polymerization of the acrylamide using NMBA as crosslinking agent, in presence of a gelatin solution. The polyacrylamide hydrogels are transparent, have a soft consistency, and is difficult to see when immersed in water, due to because the refraction index of the swelled hydrogel is similar to the aqueous medium index [18]. In contrast, the swollen hydrogels with gelatin are yellowish and translucent, and can also be observed when immersed in an aqueous medium, since gelatin disperses light.

Figure 1 is an example of the results obtained in a swelling experiment. This figure shows the swelling in aqueous neutral-pH medium as function of the time for polyacrylamide-gelatin hydrogels with different gelatin concentrations. For all the samples the highest swelling is reached in about 100 h and this value correspond to the equilibrium swelling. Similar behaviors were observed for hydrogels that swelled in neutral and acid pH mediums. The increase in the swelling capacity in these hydrogels when the gelatin concentration increases, may be due to the significant hydrophilic character of the NH_2 and COO^- groups that are linked to the primary polymeric chain of the gelatin; therefore, a change in the gelatin concentration in the polyacrylamide-gelatin network modifies the hydrophilic character of the hydrogel, producing a change in its affinity for water or other aqueous solvents. Figure 2 shows the equilibrium swelling for hydrogels in neutral pH-medium as a function of gelatin concentration. We can observe how the equilibrium swelling increases linearly when the gelatin concentration also increases. This is probably due to the presence of an important quantity of ionizable groups in the gelatin; when the polymeric chains have ionizable groups there are hydrostatic repulsion between the groups, increasing the volume between polymeric chains, and also the swelling capacity of the hydrogel.

Figure 3 shows the swelling behavior for pure polyacrylamide hydrogels in three swelling pH-mediums. We can see that the polyacrylamide hydrogel is not easily affected by changes in pH of the swelling medium, most probably because this hydrogel does not have ionizable chemical groups that can influence the swelling process. The small differences observed between the lines in Fig. 3, can be attributed to the dimensional differences between samples, and the fact that the swelling rates are highly influenced by the chain dimensions of the hydrogel [19]. Figure 4 depicts the effect of the pH swelling medium on the swelling of the polyacrylamide-gelatin hydrogels. Korsmeyer and Peppas have reported that the swelling properties in a polyionic hydrogel are influenced by the composition and concentration of the buffer swelling solution and the acid ionization coefficient (pK_a, pH which an acidic functional group begins to ionizing) of the functional group linked to the polymer chain [19]; then, the changes in the swelling capacity are due to the presence of chemical species that behave in function of the pH of the swelling medium. A polyacrylamide-gelatin hydrogel contains a polyacrylamide crosslinked network and gelatin polymeric chains entangled; the gelatin structure is

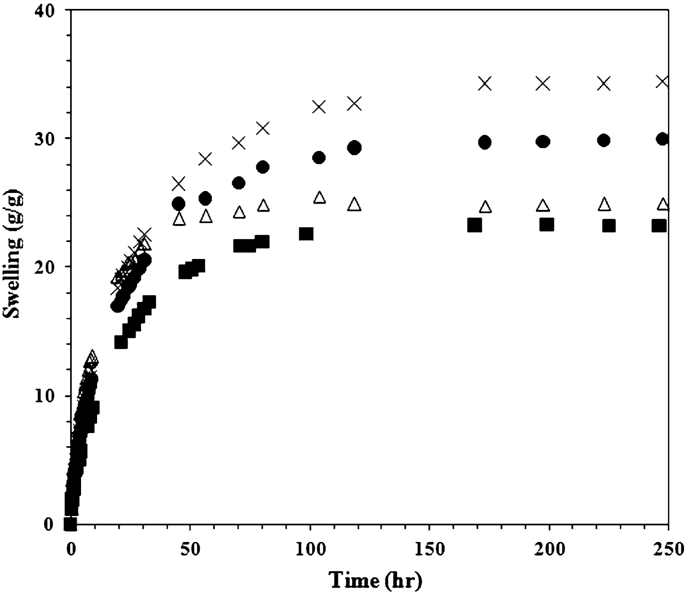

Fig. 1 Swelling at different times for the polyacrylamide-gelatin hydrogels that swell in a neutral-pH medium and with 0 wt% (*filled square*), 5 wt% (*open triangle*), 10 wt% (*filled circle*), and 20 wt% (*multi symbol*) in gelatin

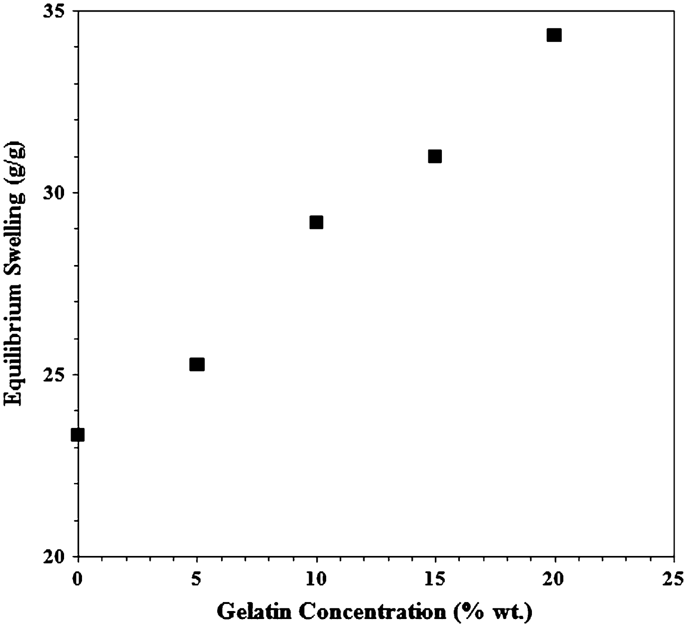

Fig. 2 Equilibrium swelling at different gelatin concentrations

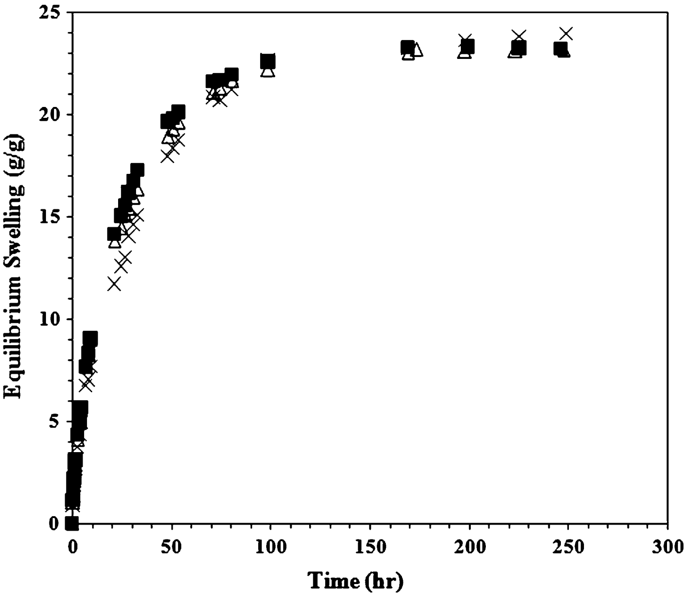

Fig. 3 Equilibrium swelling at different times for polyacrylamide hydrogels that swell in three different pH mediums: acid (*open triangle*), neutral (*filled square*), and basic (*multi symbol*)

ionizable because the basic ionization coefficient (pK_b, pH which a basic functional group begins to ionizing) of the NH_3^+ is about 6.5 and the pK_a of the COOH is about 4.7 in gelatin [20]. Then in acid medium the present chemical species of the gelatin are NH_3^+ and COOH; in basic medium the species are NH_2 and COO^-; and in pH's between 4.0 and 7.0 the present species are anyone of the above-mentioned chemical groups (NH_3^+, COO^-, NH_2 or COOH). In an acidic environment, the swelling is controlled mainly by the NH_3^+, in basic medium by COO^-, and between pH 4.0 and 7.0 by NH_3^+ and COO^-. In Fig. 4, we can observe that in basic medium the swelling is higher; this behavior is due to the presence of the hydrophobic functional groups (mainly COO^-) in the gelatin structure. The polyacrylamide-gelatin hydrogels begin hydrolysis in a pH close to 10.0, giving up carboxy groups. The swelling in these hydrogels increase in a significant way with the addition of gelatin; therefore, the ionization of all carboxylic groups in gelatin increases the swelling of the hydrogels.

Swelling kinetics for the PAM-G hydrogels

In most of the pharmaceutical applications is important to know the order of the swelling kinetics, because this phenomena affects all the drug delivery process that involve this kind of hydrogel. There are a few rigorous theories about the swelling process in hydrogels. Schott has proposed that the swelling process can be described with a second order kinetic equation [21]; in this case, the swelling rates are expressed as:

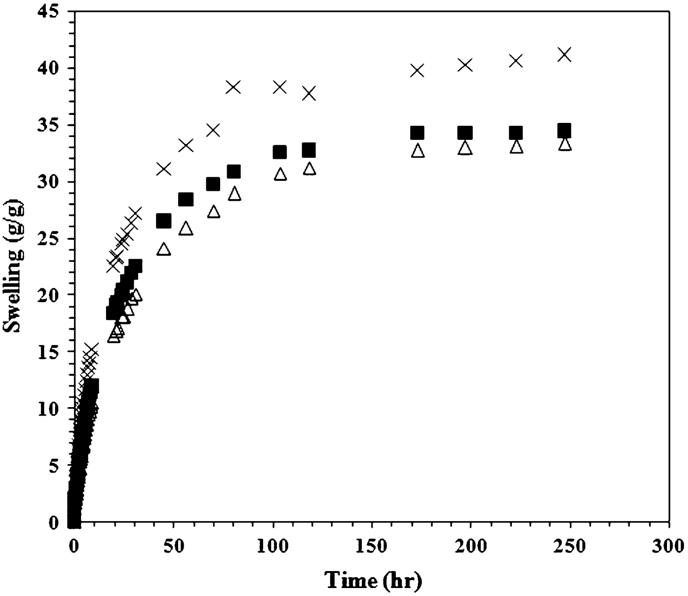

Fig. 4 Swelling at different times for a polyacrylamide-gelatin hydrogel with a 20 wt% in gelatin that swell in three different pH mediums: acid (*open triangle*), neutral (*filled square*), and basic (*multi symbol*)

$$\frac{\mathrm{d}H}{\mathrm{d}t} = k\left(H_{\mathrm{eq}} - H\right)^2 \tag{3}$$

where H is the water uptake of the hydrogel at time t (the swelling), H_{eq} is the water uptake at equilibrium (equilibrium swelling), and k is a rate constant. Integrating Eq. 3 for the interval $t = 0$ (xerogel) to $t \to \infty$ (completely swollen hydrogel) we have a linear relationship from which k is determined:

$$\frac{t}{H} = A + Bt \tag{4}$$

where A is $1/k(H_{\mathrm{eq}})^2$ and B is $1/H_{\mathrm{eq}}$. The rate constants obtained are presented in Table 1. We can consider that the swelling process is carried out by specific interactions between the molecules in the aqueous swelling solution and the chemical groups present in the polymeric network (amines, amides, carboxy, etc.); this fact implies that there are many kinds of polymer-solution interactions. Then, we can infer that the swelling rates are not highly influenced by the gelatin or by the swelling medium, since the range of values can be considered almost constant in accordance with the thermodynamic criteria.

Mechanical properties of PAM-G hydrogels

In order to determine the Young modulus (E), compression tests were made in the acid, basic and neutral swelling mediums. The results obtained are presented in Fig. 5, which displays the Young's moduli measured at equilibrium water uptake

Table 1 Swelling kinetics rate constants (*k* in hydrogel g/water g h) for the polyacrylamide-gelatin hydrogels

Gelatin concentration (wt%)	*k*		
	pH 4	pH 7	pH 10
0	2.70×10^{-5}	2.81×10^{-5}	1.26×10^{-5}
5	2.65×10^{-5}	2.07×10^{-5}	2.08×10^{-5}
10	1.95×10^{-5}	2.07×10^{-5}	1.21×10^{-5}
15	2.17×10^{-5}	2.06×10^{-5}	1.68×10^{-5}
20	1.40×10^{-5}	1.58×10^{-5}	1.43×10^{-5}

versus the pH of the swelling solutions for different gelatin concentrations. The increase in gelatin concentration causes a decrease in the modulus, and this behavior is because the water has a little influence in the hydrogel modulus, and also because the polymeric network is mechanically strong. In general, the Young modulus decreases when the swelling is increased. Therefore, the gelatin has a small effect in the Young modulus, unlike its influence in the swelling ability. In Fig. 5, also can be observed that Young modulus in the hydrogel without gelatin is almost constant in the three swelling mediums. Therefore, for the polyacrylamide-gelatin hydrogels, the modulus is moderately smaller in basic medium, suggesting than the hydrogel has a higher swelling capacity in basic medium.

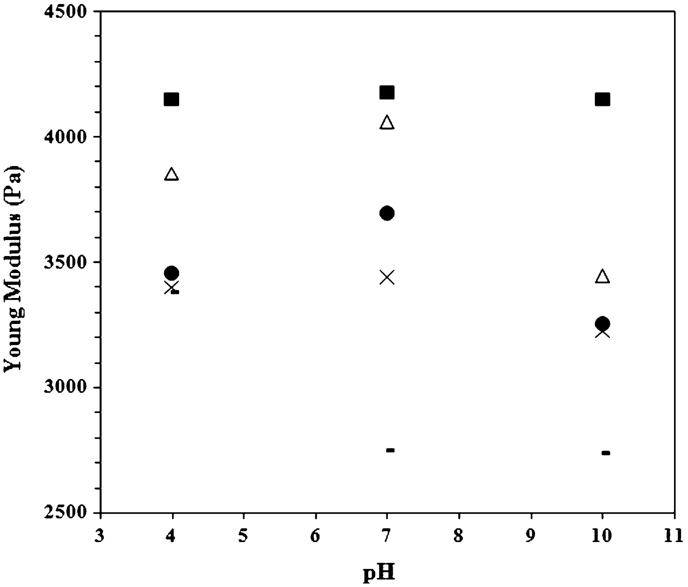

Fig. 5 Young modulus as function of the medium pH for the polyacrylamide-gelatin hydrogels that swell in three different pH mediums and with 0 wt% (*filled square*), 5 wt% (*open triangle*), 10 wt% (*filled square*), 15 wt% (*multi symbol*), and 20 wt% (*dash*) in gelatin

Conclusions

For the polyacrylamide-gelatin hydrogels studied, its swelling properties are highly influenced by the stoichiometric relationship between the acrylamide and gelatin, as well as the pH of the swelling medium. The swelling kinetics follows the second-order kinetics; we propose that the gelatin concentration and the nature of the swelling solvent determine the water uptake kinetics behavior. When the gelatin concentration in the polymeric network increases, the swelling capacity in the hydrogel increases; this swelling capacity is not observed in conventional hydrogels (hydrogel without gelatin), where the pH of the medium has no influence. This parameter only affects when the hydrogel contains gelatin, and the swelling ratios were higher in basic medium. The Young moduli of hydrogels with gelatin are similar to the ones without gelatin, even though the polyacrylamide-gelatin hydrogels absorb more liquid than conventional hydrogels. A plausible explanation is that the PAM-G hydrogels swell mainly due to the character of the hydrophilic groups, but in both kinds of hydrogels the particles act as reinforcement nodes yielding similar Young modulus. In summary, we have presented evidence that an increase in the gelatin concentration in the polyacrylamide-gelatin hydrogels leads to higher water uptake, but not necessarily, better mechanical properties, in the different pH swelling mediums.

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