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Synthesis and Swelling Behavior of Acrylate-Based Hydrogels

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The purpose of this investigation was to report the synthesis of a novel pH-sensitive acrylate-based hydrogel by polymerizing the comonomers 2-hydroxyethyl methacrylate, HEMA, acrylic acid, AA, and sodium acrylate, NaAc. The NaAc component was obtained by neutralization of AA with sodium hydroxide. Hydrogels were obtained by free radical copolymerization in aqueous solution in the presence of redox initiators, $Na_2S_2O_8/Na_2S_2O_5$, and ethylene glycol dimethacrylate, EGDMA, crosslinker. The copolymers were synthesized by varying neutralization percent of AA in the range of 10–100. The swelling behavior of the copolymeric gels were investigated as a function of pH, temperature, ionic strength, and AA neutralization percent. The polymer mesh size, ξ, molecular weight between crosslinks, M_c, and crosslinking density, q, were determined by using the Flory-Rehner equation in the pH range of 2–8 as 8.78–48.8 Å, 209–2667 g/mol, and 0.046–0.59, respectively. The diffusional exponent value, n, of the synthesized hydrogel was found to be 0.59, indicating a non-Fickian diffusion mechanism. It can be concluded that the hydrogel demonstrated a sharp change in its water absorbency, mesh size and molecular weight between crosslinks of the network with a change in pH of the swelling media. The latter properties suggest strong consideration of these hydrogels for use as oral drug delivery systems and ion-exchangers for removal of metal ions from aqueous media, owing to the carboxylate groups within the polymeric network.

Keywords: hydrogel; pH-sensitive hydrogels; acrylic acid; 2-hydroxyethyl methacrylate; molecular weigth between crosslinks; mesh size

1 Introduction

Hydrogels are three-dimensional, hydrophilic polymeric networks capable of imbibing large amounts of water or biological fluids. The networks are composed of homopolymers or copolymers, and are insoluble due to the presence of chemical or physical crosslinks (1).

Poly(2-hydroxyethyl methacrylate), PHEMA, is a synthetic hydrogel, which possesses high mechanical strength and resistance to significant chemical and microbial degradation (2). Much attention has been paid to improving the chemical and physical properties of PHEMA. Incorporation of a hydrophilic comonomer such as acrylic acid and sodium acrylate into PHEMA hydrogels significantly changes the swelling properties and they gain pH-sensitivity. Polymer networks containing ionic moities show a sudden or gradual change in their dynamic and equilibrium properties in response to the pH and ionic strength and due to the charge repulsion in the ionic hydrogels, they can absorb large amounts of water (3).

Ende and Peppas reported the transport of ionizable drugs and proteins in crosslinked poly(acrylic acid-co-hydroxyethyl methacrylate) hydrogels (4). Poly(sodium acrylate-co-hydroxyethyl methacrylate) hydrogel was also synthesized by inverse suspension polymerization as a superabsorbent polymeric material (5). A series of 2-hydroxyethyl methacrylate-co-acrylic acid-co-sodium acrylate copolymeric gels were prepared using N,N′-methylene bisacrylamide (NMBA) as the crosslinking agent for the purpose of drug release (6). Hydrogels of HEMA were also prepared by copolymerizing it with acrylamide, a hydrophilic monomer, in the presence of a hydrophilic polymer, polyethylene glycol (PEG) (7).

In order to be used as a drug delivery device, pH-thermoreversible hydrogels were also synthesized from N-isopropylacrylamide (NIPAAm), acrylic acid neutralized 50 mol% by sodium hydroxide, and N,N′-methylene bisacrylamide (NMBA) (8).

In this study, in order to improve the water sorption characteristics and physical properties the HEMA-based hydrogels, acrylate-based acidic (acrylic acid, AA) and its sodium salt comonomers of 2-hydroxyethyl methacrylate (HEMA) were used to synthesize poly(HEMA-co-AA-co-NaAc) hydrogel by crosslinking copolymerization process in the presence of ethylene glycol dimethacrylate as a crosslinker, EGDMA. Thus, incorporation of hydrophylic comonomers AA and NaAc into poly(HEMA) hydrogel significantly changed swelling behavior of poly(HEMA) hydrogel in aqueous media.

Temperature, pH and ionic strength-dependent swelling behavior of newly synthesized poly(HEMA-co-AA-co-NaAc)

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hydrogels have been studied and water uptake data have been analyzed with the help of a kinetic model. In addition, various network parameters including molecular weight between crosslinks, M_c, mesh size, ξ, and crosslinking density, q, have also been evaluated.

These novel pH-sensitive acrylate-based hydrogels can be effectively used in oral drug delivery systems and metal ion removal from the aqueous media via ion-exchange mechanism.

2 Experimental

2.1 Materials

Acrylic acid, AA, and 2-hydroxyethyl methacrylate, HEMA monomers were obtained from Sigma-Aldrich (Steinheim, Germany). Sodium metabisulfite, $Na_2S_2O_5$, and sodium persulfate, $Na_2S_2O_8$, (Sigma-Aldrich, Steinheim, Germany) were used as redox initiators. Crosslinking was performed using ethylene glycol dimethacrylate, EGDMA, (Sigma-Aldrich, Steinheim, Germany). Sodium acrylate, NaAc, was synthesized by neutralizing acrylic acid with sodium hydroxide. n-heptane, H_3PO_4, KH_2PO_4, K_2HPO_4, HCl, and NaOH were purchased from Merck.

2.2 Synthesis of Hydrogels

Cylindrical hydrogels were prepared by performing free radical crosslinking copolymerization of HEMA, AA, and NaAc, using EGDMA as a crosslinking agent, $Na_2S_2O_5$ and $Na_2S_2O_8$ as the redox initiator system, which initiates the polymerization by forming radicals at room temperature. Poly(HEMA-co-AA-co-NaAc) hydrogel samples were synthesized by changing the preparation procedure and degree of AA neutralization. In the preparation of hydrogels denoted as Sample 1A, 1B, 1C, 1D, and 1E, amounts of HEMA, AA, and EGDMA in the feed mixture were held constant while degree of neutralized AA monomer was varied, in the range of 10–100%. For example, 1.03×10^{-2} mol HEMA, 3.65×10^{-3} mol AA, and 2.64×10^{-4} mol EGDMA were placed into a pyrex test tube and mixed in a vortex mixer for the preparation of Sample 1D. After dissolving 4.21×10^{-5} mol $Na_2S_2O_5$ and 3.36×10^{-5} mol $Na_2S_2O_8$ in 1.6 ml of 1.94 M NaOH solution, this mixture was combined with the monomer mixture. By doing so, AA monomer was neutralized to 85 mol% using 1.94 M NaOH solution and polymerization reaction was initiated, simultaneously. Finally, the resultant mixture in the pyrex test tube was immediately mixed in a Vortex mixer. The same procedure was followed for the preparation of Samples 1A, 1B, 1C, and 1E except the amount of NaOH used for the neutralization of AA.

In the synthesis of Sample 2, the polymer preparation procedure was changed in that 1.03×10^{-2} mol HEMA, 3.65×10^{-3} mol AA and 2.64×10^{-4} mol EGDMA were put into the pyrex test tube. The same amount of NaOH, 0.8 ml of 3.87 M, as in Sample 1D, was added into the monomer mixture in order to neutralize AA to 85 mol%, with the system mixed throughly in a vortex mixer. Then, 4.21×10^{-5} mol $Na_2S_2O_5$ and 3.36×10^{-5} mol $Na_2S_2O_8$ were dissolved in 0.8 ml distilled water and immediately added into the final mixture.

The polymerization reactions were run at room temperature for 1 day in the peyrex test tubes. After polymerization was completed, the cylidrical gels were cut into discs of 0.3 mm in thickness and 11 mm in diameter. They were then immersed into distilled water for 2 days to remove the residual unreacted monomers, crosslinking agent, and initiator before drying in an oven for one day at 37°C.

2.3 Swelling Studies

Swelling properties of the hydrogel samples, in the form of a disc, were explored by placing the dried samples into 50.0 ml phosphate buffer solution, pH 7.4, with ionic strengths of 0.05 and 0.15 M at 37°C, respectively. Ionic strengths of the swelling media were maintained at the desired values with the addition of NaCl. Swelling studies were also conducted at 10, 20, 37, and 50°C, respectively, until swelling equilibrium was attained. All the swelling studies were carried out in an incubator operating in the temperature range of -10 to 80°C (Nüve ES 110, Ankara, Turkey). In addition, the effect of pH cycling on the swelling behavior of synthesized hydrogels was investigated by changing pH from 8.0 to 4.0 and same cycle was repeated several times at 37°C. pH measurements were performed using an Orion Model 720A with a combined electrode (Beverly, MA 01915, USA). Furthermore, swelling studies for the Sample 2 were also carried out for the determination of molecular weight between crosslinks, mesh size and crosslink density at pH values of 2.0, 3.0, 5.0, 7.0, and 8.0 (I = 0.1 M) at 37°C, respectively.

At certain time intervals, discs were taken out of the solutions, and the swollen weight of each disc at time t (W_s) was determined after removing the surface water by blotting with filter paper before weighing. Swelling percent, S%, was calculated using the following expression:

$$\text{Swelling percent (S\%)} = \frac{W_s - W_d}{W_d} \times 100 \qquad (1)$$

Where W_d is the dry weight of disc.

3 Results and Discussion

3.1 Network Parameters of Hydrogel

3.1.1 Determination of Molecular Weight between Crosslinks, M_c

A crosslinked polymer, when placed in a good solvent, rather than dissolving completely will absorb a portion of the

solvent and subsequently swell (9). Swelling is a simple and low-cost technique to characterize polymer networks (9). One of the important parameters characterizing a crosslinked hydrogel is the molecular weight between crosslinks, M_c. The molecular weight between crosslinks determines how far the network chains can expand to accommodate solvent molecules. A polymer network with a large value of M_c is able to swell to a higher degree than that of a network having a lower value of M_c. The following well-known Flory-Rehner equation can be used to calculate the M_c value:

$$M_c = -d_p V_s (\upsilon_{2,s}^{1/3} - \upsilon_{2,s}/2)\,[\ln(1-\upsilon_{2,s}) + \upsilon_{2,s} + \chi\upsilon_{2,s}^2]^{-1} \quad (2)$$

The volume fraction, $\upsilon_{2,s}$, of the swollen polymer is calculated using the following equation:

$$\upsilon_{2,s} = \left[1 + \frac{d_p}{d_s}\left(\frac{M_a}{M_b} - 1\right)\right]^{-1} \quad (3)$$

In Equations (2) and (3), d_p and d_s (1.0 g/ml) are the densities of the polymer and solvent, respectively. The density of the polymers were determined by a pycnometer using n-heptane as a non- solvent. M_b and M_a are the masses of the polymer before and after swelling; V_s is the molar volume of the solvent (18.0 ml/mol) and χ is the Flory-Huggins polymer-solvent interaction parameter. The values of χ for the HEMA and AA were taken from the literature (10, 11) and weighted average of these values were used in the calculation of M_c. Equilibrium swelling results of poly(HEMA-co-AA-co-NaAc) hydrogel, named as Sample 2, was used to determine M_c values at various pH media (pH 2.0–8.0 and I = 0.1 M) at 37°C. Experimental M_c values calculated using Equation (2), developed by Flory and Rehner, are listed in Table 1.

As seen in Table 1, the values of M_c increased with decreasing volume fraction of the swollen hydrogel at a fixed crosslinker ratio. In addition, the effect of the external medium pH on the M_c values of hydrogel was also investigated and it was seen that as the external medium pH was raised, M_c values increased significantly. For example, M_c value of the Sample 2 reached 2667 g/mol from 209 g/mol when the pH of the external medium was changed from 2.0 to 8.0. This change can be attributed to the fact that as the pH of the swelling medium changes from 2.0 to 8.0, the -COONa and COOH groups attached to the polymer chains ionize completely to give charged carboxylate, $-COO^-$, groups and Na^+ counter ions within the hydrogel. Because free counter ions remain inside the hydrogel to neutralize the fixed charges on the polymer chain, this high ion concentration inside the hydrogel results in high osmotic pressure and in turn high swelling percent and high M_c. Furthermore, carboxylate groups repel each other due to electrostatic repulsive forces, which causes the relaxation of the polymer network.

3.1.2 Determination of Crosslinking Density, q, and Mesh Size, ξ

Another significant parameter characterizing crosslinked polymers is the crosslinking density, q, which can be found using the following equation:

$$q = \frac{M_c}{M_r} \quad (4)$$

where M_r is the molar mass of the repeat unit and is defined as:

$$M_r = \frac{m_{HEMA}M_{HEMA} + m_{AA}M_{AA} + m_{NaAc}M_{NaAc}}{m_{HEMA} + m_{AA} + m_{NaAc}} \quad (5)$$

Here, m_{HEMA}, m_{AA}, and m_{NaAc} are the masses of the monomers HEMA, AA and NaAc, respectively. In addition, M_{HEMA}, M_{AA}, and M_{NaAc} are the molar masses of HEMA, AA, and NaAc, respectively.

The mesh size, ξ, which is a term that describes the avilable space for solute transport within the polymer network, is also an important paramater in analyzing crosslinked polymers and calculated according to equation (6), which is described in more detail by Canal and Peppas (12):

$$\xi = \upsilon_{2,s}^{-1/3}\left(\frac{2M_c}{M_r}\right)^{1/2} C_n^{1/2}\ell \quad (6)$$

Here, M_r is the molecular weight of the repeating unit; ℓ, the C-C bond length of 1.54 Å; and C_n, the characteristic ratio, is the weighted average of the C_n values of HEMA, 6.9 (4), and AA, 6.7 (11).

ξ and q values of Sample 2 are presented in Table 1 as a function of pH. Results indicated that as the pH of the swelling medium increased from pH 2.0 to 8.0, ξ value for Sample 2 also increased from 8.78 to 48.80 Å. However, the crosslinking density decreased from 0.586 to 0.046. Thus, while the pH of the external medium increased, the hydrogel swelled to a greater extent and the space avilable between the crosslinks became larger. The data also indicated that the crosslinking density decreased with increasing external medium pH, indicating that there is more space between the crosslinks, ξ, and the hydrogel is less dense.

3.2 Dynamic and Equilibrium Swelling Studies

To investigate the influence of external conditions and effect of preparation procedure on the dynamic and equilibrium swelling properties of pH-sensitive poly(HEMA-co-AA-co-NaAc) hydrogel, swelling studies were performed and swelling percents were calculated using equation (1).

3.3 Effect of pH

Hydrogels, due to pH sensitivity, play a significant role in controlled oral drug delivery systems. These hydrogels can

Table 1. Network parameters determined from equilibrium swelling studies of Sample 2 at various pH media at 37°C (I = 0.1 M)

	Crosslinking ratio[a] × 10^2	Volume fraction of the swollen polymer, $\upsilon_{2,s}$	Molecular weight between crosslinks, M_c(g/mol)	Crosslink density, q	Mesh size, ξ (Å)
pH 2.0	1.90	0.607	209	0.586	8.78
pH 3.0	1.90	0.506	880	0.139	19.02
pH 5.0	1.90	0.209	1916	0.064	37.70
pH 7.0	1.90	0.164	2486	0.049	46.80
pH 8.0	1.90	0.160	2667	0.046	48.80

[a]Crosslinking ratio = number of moles of crosslinker/number of moles of monomers.

be prepared by the incorporation of weakly acidic monomers such as carboxylic acids. While those kinds of delivery systems show low swelling degree in acidic medium of the stomach, their swelling degree increases as they passes down the gastrointestinal truct due to an increase in the pH. Thus, a pH-sensitive drug delivery system protects the drug from the acidity of the stomach and releases the drug in the small intestine or colon depending upon the composition of the hydrogel. In this study, the effect of pH on the swelling behavior of the poly(HEMA-co-AA-co-NaAc) hydrogel was investigated by varying the pH of the swelling medium in the range of 2.0–8.0. Equilibrium swelling results were depicted in Figure 1, which reveals that equilibrium swelling percent increases as a function of pH for Sample 2. As can be seen from Figure 1, there was a slight increase in the equilibrium swelling value between pH 2.0 and 3.0. However, there existed a sharp increase in the equilibrium swelling value of Sample 2 when the pH of the swelling medium was increased from 3.0 to 5.0, which is above the pK_a value, 4.7, of the AA. This is because the ionization of the polymeric networks containing carboxylic acid groups takes place as the pH of the external medium increases (8). In addition, sodium carboxylate in the polymeric backbone dissociates at this pH value and electrostatic repulsion among the similarly charged -COO^- groups and osmotic pressure inside the hydrogel increase, resulting in the sharp increase in the swelling degree of the hydrogel.

The rapid increase in the equilibrium swelling continued until the pH of the swelling medium reached to 7.0. However, beyond this pH value, this effect was not significant since it reached an equilibrium state. These results proved the pH-sensitivity of the prepared hydrogel (Sample 2).

3.4 Effect of Ionic Strength

Swelling studies for Sample 2 were carried out in a phosphate buffer solution of pH 7.4 in order to investigate the effect of ionic strength on the swelling properties. The ionic strength of the swelling medium was changed from 0.05 to 0.15 M at a constant pemperature of 37°C. Figure 2 shows the swelling behavior of Sample 2 in a phosphate buffer solutions of pH 7.4 with ionic strengths of 0.05 and 0.15 M, respectively. It can be seen, as the ionic strength increased from 0.05 to 0.15 M, the swelling percent of the Sample 2 decreased because the difference in the concentration of mobile ions between the hydrogel and the solution was reduced. As a result, osmotic swelling pressure reduction resulted in lower swelling percent values. When the equilibrium was attained, swelling percent values of the Sample 2 were 328 and 259% for the ionic strengths of 0.05 M and 0.15 M, respectively. According to the Donnan osmotic pressure equilibrium, an increase in concentration of the movable counter ions of a solution leads to a decrease in the osmotic pressure within the hydrogel, causing the hydrogel to shrink (9). As far as swelling results are concerned, it can be concluded that the prepared hydrogel's swelling behavior is largely dependent upon the ionic strength of the swelling medium.

3.5 Effect of Temperature

The effect of temperature on the equilibrium swelling percent of Sample 2 is shown in Figure 3. Equilibrium swelling studies were conducted as a function of temperature at pH 7.4 (phosphate buffer solution) with the ionic strength of 0.15 M. Sample 2 reached the maximum equilibrium swelling degree, 285%, at 10°C. However, there was a slight decrease in the swelling value at the temperatures of

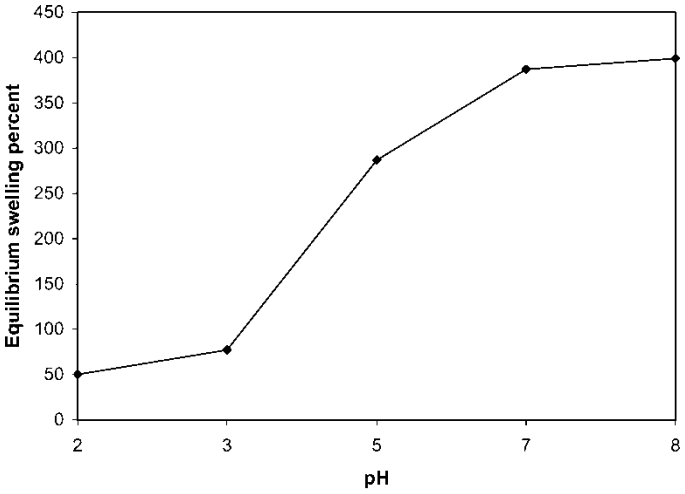

Fig. 1. Equilibrium swelling behavior of Sample 2 at various pH media of ionic strength of I = 0.1 M at 37°C.

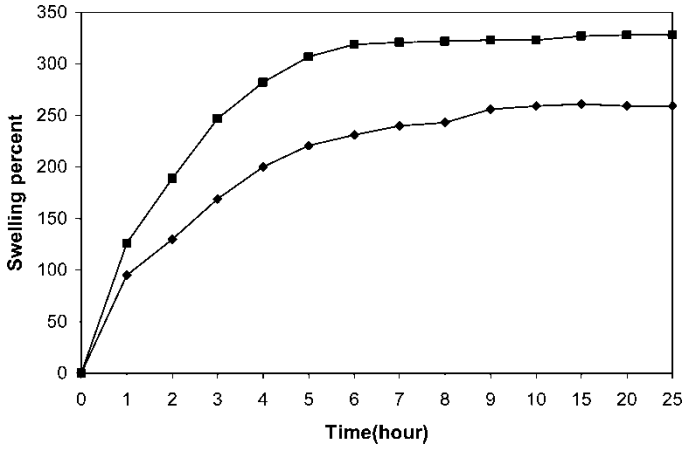

Fig. 2. Effect of ionic strength on the swelling behavior of Sample 2 at 37°C (pH 7.4; ◆ (I = 0.15) and ■ (I = 0.05 M)).

20, 277%, and 37°C, 257%, respectively. This behavior may be attributed to the hydrogen bond between the water molecules and the polymer chain, which is greater at low temperatures. When the temperature is increased to 50°C, the free water moves from the external medium into the hydrogel, causing the hydrogels to swell to a higher degree compared to that at 37°C. This swelling behavior in response to temperature change is quite different from the ones in the litereture. For example, Lee and Lin investigated the influence of temperature on the swelling properties of acrylate-based hydrogels containing HEMA and AA and they experienced a minimum swelling value at 55°C, compared to ones obtained at lower temperatures (6).

3.6 Reversibility Studies

Figure 4 presents the effect of cycling of pH on the swelling behavior of hydrogel Sample 2. The swelling medium pH was changed from 8.0 to 4.0, and the same cycle was repeated three times. The first swelling study was carried out at pH 8.0 buffer so that Sample 2 reached its equlibrium swelling value and then hydrogel was transferred into pH 4.0 medium for 8 h, followed by 8 h in pH 8.0 buffer solution. In pH 8.0 buffer solution, carboxylic acid groups, COOH, ionizes, resulting in the formation of carboxylate groups, COO^-. Since the carboxylate groups in the polymeric chain repel each other, swelling increases rapidly. On the contrary, when the hydrogel sample was transferred into pH 4.0 medium, the carboxylate groups are protonated and carboxylic acid groups, COOH, are obtained, resulting in a decrease in the electrostatic repulsive forces between carboxylate groups. As a result, swelling percent value of the hydrogel decreases.

It was seen from the experimental results that Sample 2 did not indicate perfect pH-dependent reversible behavior. However, swelling percent values for Sample 2 were almost the same after each 8 h period for both of the swelling media of pH 4.0 and 8.0, indicating the pH-dependent reversible behavior. Moreover, Sample 2 did not lose its elasticity during pH cycling.

3.7 Effect of Neutralization Percent of AA on the Swelling Behavior

The increase in ionic monomer within the polymer matrix causes an enhancement in its swelling capacity due to increased chain relaxation as well as osmotic swelling pressure (13). In order to see the effect of neutralization percent of AA, an ionic monomer, on the swelling behavior of poly(HEMA-co-AA-co-NaAc) hydrogel, a number of hydrogels containing varying degree of neutralized percent of AA, in the range of 10–100%, were synthesized by keeping crosslinking ratio constant, 1.90×10^{-2}, for all the hydrogels. Swelling studies were carried out in pH 7.4 phosphate buffer solution with I = 0.15 M at 37°C. As depicted in

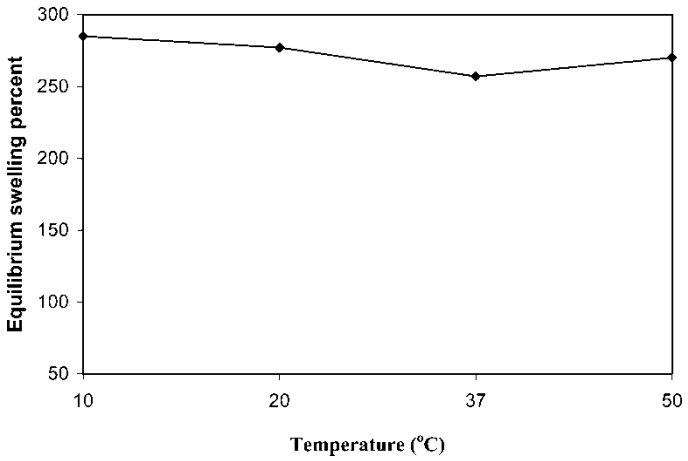

Fig. 3. Equilibrium swelling behavior of Sample 2 (pH 7.4, I = 0.15 M) as a function of temperature.

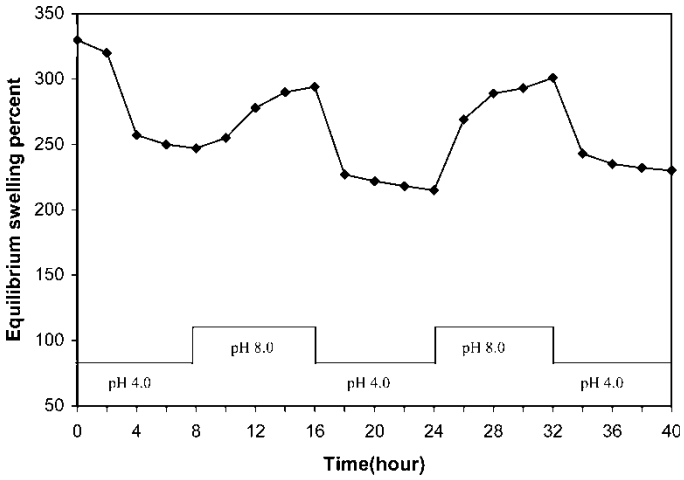

Fig. 4. Cyclic swelling behavior of Sample 2 in phosphate buffers (pH 4.0 and 8.0) with ionic strength of I = 0.15 M at 37°C.

Figure 5, equilibrium swelling decreases, especially beyond the 20% neutralization, as the neutralization degree of AA increases. For instance, while equilibrium swelling percent was 409% for the hydrogel containing 20% neutralized AA, it decreased to 323% for the one containing 50% neutralized AA. There may exist several reasons related with this unexpected swelling behavior. First, it may be that the polymerization rate is so fast that low molecular weight polymeric chains are obtained, due to an increased amount of carboxylate groups and this causes a decrease in the equilibrium swelling value. Second, the reason may be counterion condensation, causing a decrease in the repulsive forces among $-COO^-$ groups in the polymer chain by a shielding effect. As a result of this shielding effect, swelling might be decreasing as the degree of neutralization increases.

Controlling the concentration of crosslinking agent is not the only way to modify the crosslink density and not all double bonds on a particular crosslinking agent will form elastically active crosslinks (14). Primary cyclization occurs when a pendant double bond of a multi-functional monomer reacts intramolecularly with the propagating radical on the same chain. Although an equivalent amount of crosslinking agent may be present and incorporated into the network, when cyclization is occurring, the polymer produced is less crosslinked and does not exhibit the expected mechanical properties, equilibrium swelling, and diffusional properties (14). Because of the above mentioned facts, a third reason may be the intramolecular cyclization, which is very common in free radical crosslinking copolymerization reactions. The reason why the equilibrium swelling reduces beyond 20% neutralization may be attributed to the fact that the extent of cyclization decreases because negatively charged carboxylate groups, $-COO^-$, along the macromolecular chain repel each other, causing the propagating radical to be further away from the pendant double bonds of crosslinker molecules. This effect causes reduction in primary cyclization and equilibrium swelling. The sharp decrease in equilibrium swelling,when the neutralization degree of AA was increased from 20 to 50%, confirms this explanation. However, when the degree of neutralization was raised from 50 to 85%, an increase in equilibrium swelling was obtained, reaching 364% from 323. This may be due to the fact that addition of more NaOH caused ionic strength of the reaction mixture to increase, resulting in less repulsion between negative carboxylate groups. As a result of reduced repulsion, a pendant double bond and a propagating radical come closer to each other and more primary cyclization and high swelling occurred. Above 85% neutralization degree, the remaining COOH groups were neutralized and due to increased repulsion between negatively charged carboxylate groups, pendant double bonds and propagating radicals go further apart, resulting in less cyclization and less swelling, 297%.

3.8 Effect of Changing Preparation Procedure on the Swelling Behavior

The network formation of crosslinked polymer hydrogels synthesized by a free radical mechanism is significantly influenced by the polymerization conditions. In the preparation of Sample 2, initiator redox couple, $Na_2S_2O_5/Na_2S_2O_8$, was added into the monomer mixture after the neutralization of AA with NaOH. On the other hand, Sample 1D was prepared in a such way that initiator redox couple was first dissolved in NaOH solution and then added into the monomer mixture. Apart from the preparation of Sample 2, neutralization of AA and initiation of the polymerization were carried out at the same time in order to see whether there would be a difference in the swelling behavior or not. Results of the swelling studies were depicted in Figure 6 for Samples 1D and 2. Results indicated that equilibrium swelling values of both Samples were quite different from each other. For instance, swelling percent of Samples 1D

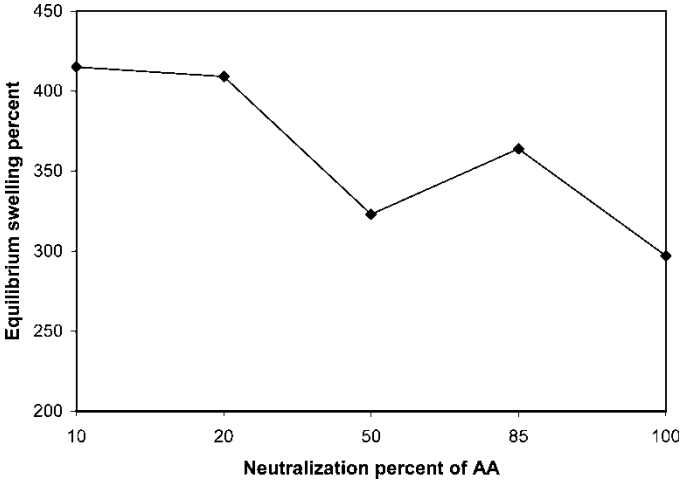

Fig. 5. Effect of neutralization degree of the acrylic acid on the equilibrium swelling behavior of hydrogels at pH 7.4 and 37°C (I = 0.15 M).

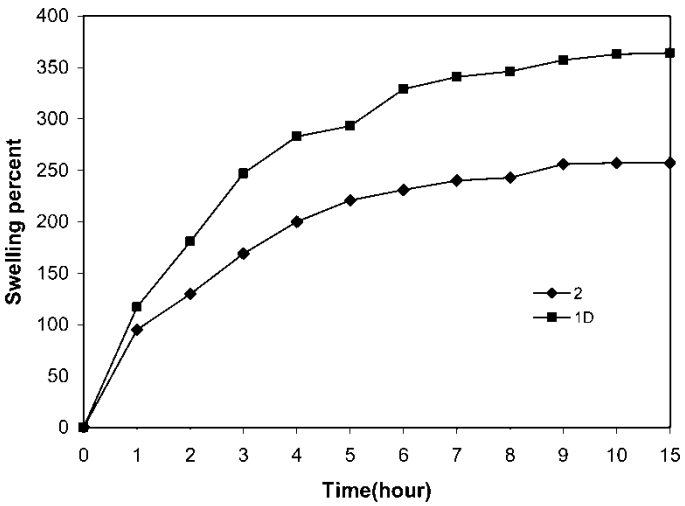

Fig. 6. Swelling kinetics of Samples 1D and 2 as a function of time at pH 7.4 (I = 0.15 M) and 37°C.

and 2 were 364 and 257 at 15 h, respectively. Thus, by changing the preparation procedure, two different poly(HEMA-co-AA-co-NaAc) hydrogels were obtained although both of them contained the same amount of neutralized AA, 85%, HEMA and EGDMA. In spite of the fact that the initiation mechanism of the redox couple is not clear, it is considered that the sulfate radicals, produced by the reaction of persulfate ions with the metabisulfite ions, initiate the polymerization (15).

This reaction can be written as follows:

$$S_2O_8^{2-} + S_2O_5^{2-} \longrightarrow SO_4^{-\bullet} + SO_4^{2-} + S_2O_5^{-\bullet} \qquad (7)$$

Bokias et. al (15) synthesized poly(N-isopropylacrylamide) and poly(acrylic acid) by aqueous radical polymerization initiated by the redox couple ammonium persulfate/sodium metabisulfite and they concluded that concentration of ammonium persulfate did not practically affect the M_w of the products for both polymers. In contrast, they reported that metabisulfite radicals had a molar mass control ability, inversely proportional to the concentration of reducing agent.

In the preparation of Sample 1D, the redox couple was dissolved in NaOH solution at pH 13.0. However, in the preparation of Sample 2, the redox couple was added into the monomer mixture after the neutralization of AA and pH of the medium was 6.0. For this reason, activity of the metabisulfite might have been reduced at pH 6.0 and this might have resulted in low molecular weight polymeric chains and in turn less swelling. This conclusion is consistent with the result obtained by Bokias et al.(15).

3.9 Analysis of Kinetic Data

When a glassy polymer is placed into a solvent, the solvent penetrates into the polymer and this results in swelling by entering spaces between macromolecular chains of the polymer. In order to analyze solvent transport mechanism of the polymeric samples, the first 60% of the fractional water uptake, M_t/M_∞, is analyzed using the following equation (16):

$$\frac{M_t}{M_\infty} = kt^n \qquad (8)$$

Where M_t is the mass of water absorbed at time t, M_∞ is amount of water absorbed at equilibrium, k is hydrogel characteristic constant and n is the swelling exponent describing the type of solvent transport mechanism. The constants n and k are calculated from the slope and intercept of the plots of $\ln(M_t/M_\infty)$ values vs. ln t values obtained from the swelling studies.

For a cylindrical sample, the value of $n = 0.45$ shows a Fickian water transport mechanism, while $n = 0.89$ indicates a Case II transport mechanism and for $0.45 < n < 0.89$, the water transport mechanism is non-Fickian, indicating that the both diffusion and polymer relaxation processes are responsible from the water uptake of the polymer (16). The values of k, n, and coefficient of regression equation, r were 0.34, 0.59, 0.9924, respectively. The value of n shows that the type of solvent transport mechanism is non-Fickian type. Thus, it can be concluded that solvent transport mechanism for the Sample 2 is both diffusion and chain relaxation controlled. Effect of chain relaxation on the solvent transport into the polymer can be attributed to the electrostatic repulsion between adjacent ionized carboxylate groups.

4 Conclusions

It was proven that the swelling behavior of novel poly(HEMA-co-AA-NaAc) hydrogel was dependent on pH of the external medium and ionic strength. In addition, pH-reversibility and effect of temperature on the swelling properties of the hydrogel samples were also investigated and it was determined that Sample 2 showed a moderate pH-reversible behavior in response to pH-cycling from 4.0 to 8.0. The mechanism of water diffusion into these hydrogels was non-Fickian type since the value of swelling exponent was 0.59. Furthermore, hydrogel mesh size is of special importance in the drug release studies because of the screening effect of the hydrogel. For this reason, hydrogel mesh size should be large enough for the drug molecules to pass through the hydrogel mesh. The experimental values of the mesh sizes of the hydrogels were in the range of 8.78–48.8 Å at the pH values of 2.0–8.0. This mesh size range is large enough for most drugs, including peptide and protein drugs. It should be emphasized that the pH-sensitive behavior of the prepared hydrogel is of importance in oral drug delivery. Finally, the synthesized sodium acrylate-based hydrogels may be good canditates for the removal of toxic metal ions via complexation and ion-exchange mechanism via -COONa and -COOH groups attached to the macromolecular chains.

5 References

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