

# Swelling–Deswelling Behavior of Poly(acrylamide-*co*-maleic acid) Hydrogels

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Received 14 February 2000; accepted 24 July 2000

**ABSTRACT:** In this study the poly(acrylamide-*co*-maleic acid) hydrogels containing small amounts of maleic acid have been synthesized, and the effect of pH, ionic strength, and nature of counterions on the equilibrium water uptake has been investigated. The incorporation of small amount of maleic acid results in the transition of swelling mechanism from Fickian to non-Fickian. The equilibrium mass swelling has been found to increase with pH of the swelling medium while increase in ionic strength causes a decrease in the swelling. The amount of maleic acid present in the hydrogel affects the swelling behavior in rather an unusual way. With lower acid contents, the equilibrium mass swelling increases while higher concentrations of maleic acid cause a decrease in the degree of swelling. The hydrogels have been found to undergo a number of swelling–deswelling cycles when pH of the swelling medium changes from 8.0 to 2.0. Hydrogels require more time to deswell compared to the time required for swelling, which has been explained on the basis of the fact that gels follow different mechanisms for the two processes. Various swelling parameters such as equilibrium mass swelling, diffusion coefficient, intrinsic diffusion coefficient, swelling exponent, etc., have been evaluated. © 2001 John Wiley & Sons, Inc. *J Appl Polym Sci* 80: 2782–2789, 2001

**Key words:** Swelling–deswelling behavior; poly(acrylamide-*co*-maleic acid) hydrogels

## INTRODUCTION

As early as 1950, attempts were made for the development and use of environmental sensitive materials in biomedical and biotechnological applications. These attempts ultimately resulted in the discovery of a new class of polymer substances commonly known as hydrogels. The hydrogels are three-dimensional networks that can take up enormous amounts of water.<sup>1</sup> In the swollen state they are soft and rubbery, thus resembling a living tissue, and some of them also possess excellent biocompatibility.<sup>2</sup> Ongoing investigations on

natural and synthetic hydrogels have established their potential for use in several biomedical applications such as drug delivery systems,<sup>3</sup> soft contact lenses,<sup>4</sup> and implants. Other practical applications include the extraction solvents,<sup>5</sup> release of essential oils,<sup>6</sup> release of agrochemicals,<sup>7</sup> etc.

In the recent past, much work has been carried out on environment sensitive hydrogels that undergo controllable volume change in response to small variations in solution conditions such as pH,<sup>8</sup> ionic strength,<sup>9</sup> solvent composition,<sup>10</sup> temperature,<sup>11</sup> etc. Temperature and pH have been the most commonly used solution variables in the typical physiological, biological, and chemical systems.<sup>12</sup> In fact, pH-sensitive hydrogels have a variety of novel applications including site-spe-

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*Journal of Applied Polymer Science*, Vol. 80, 2782–2789 (2001)  
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cific drug delivery systems<sup>13</sup> and immobilized enzyme systems.<sup>14</sup>

The biocompatibility and nontoxicity of diprotic acids like maleic and itaconic acid have promoted their use in the synthesis of pH-responsive hydrogels through copolymerization with monomers such as acrylamide and N-vinyl-2-pyrrolidone, by using  $\gamma$ -radiations.<sup>15-17</sup> However, these methods suffer from the drawback that they require a costly instrumentation setup and also the concentration of monomers used is as high as 1 g of monomer in 1 mL of water.<sup>18</sup> On the other hand, the methods involving use of some chemical as a crosslinking agent are better in the sense that they require a relatively lower concentration of monomers, and are quite safe and economic. Therefore, the present work describes the synthesis of chemically crosslinked cylindrical hydrogels of poly(acrylamide-co-maleic acid) and study of their pH-dependent swelling behavior.

The significance of the proposed study lies in the fact that these hydrogels may be used as oral site-specific drug delivery devices for the treatment of diseases in the colon, such as inflammatory bowel disorder, because these gels (containing carboxylic groups) maximally swell in neutral or slightly alkaline pH, which is almost the pH of the surrounding fluid in the colon. On the other hand, in acidic pH they minimally swell. Therefore if such drug loaded gels are taken orally, they will deliver the minimum amount of encapsulated drug in the stomach (where pH = 2.0), and most of the drug will be released in the colon (where pH = 7.4). Here, it is worth mentioning that the hydrogels containing polyacrylamide are not suitable to be used as drug delivery devices because of harmful effects created by biodegradation of polyacrylamide in the human body. However, in place of polyacrylamide, some other biocompatible and nontoxic polymer can be used along with maleic acid to give pH-sensitive drug delivery systems.

## EXPERIMENTAL

### Chemicals

Acrylamide (AAM) and maleic acid (MA) were supplied by Loba chemicals, Bombay. The crosslinker *N,N'*-methylene bisacrylamide (MB) and initiator potassium persulfate (KPS) were received from BDH. Monomer acrylamide was recrystallized in methanol before use. Water used in

all the studies was double distilled and deionized with a pH  $\approx$  7.0.

### Preparation of Hydrogels

To synthesize cylindrical hydrogels, 5 mL of aqueous solutions of monomer mixtures were prepared by dissolving 1.0 of monomer AAM and 0, 45, and 65 mg of maleic acid in water to give different feed compositions (i.e. % mol ratio, AAM/MA) of 100.0 : 0.0, 97.4 : 2.6 and 96.2 : 3.8, respectively. To this, 25 mg of crosslinker MB was added, which was found to be sufficient to cause 100% gelation, as determined in preliminary studies by gravimetry.<sup>19</sup> After adding the initiator KPS, the homogeneous reaction mixture was poured into PVC straws and kept in an oven at 70°C for a period of 4 h. As the gelation was almost 100%, the percent mol ratio of monomers (i.e., AAM/MA) in the resulting hydrogels was equal to the initial feed compositions. Here it is worth mentioning that the considerations for selecting the feed compositions are first the solubility of monomers and the shape stability of swollen gels in the equilibrium state.

The resulting transparent cylindrical hydrogels were cut into pieces, each 2.54 cm long, and then washed with double distilled water, then dried in an oven at 40°C for 24 h. In all, three hydrogel samples were prepared in which the percent mol ratio of acrylamide to maleic acid was 100 : 0, 97.4 : 2.6, and 96.2 : 3.8, respectively. The samples will be denoted as P(AAM), P(AAM-MA)-I, and P(AAM-MA)-II, respectively.

### Swelling Studies

Completely dried hydrogel samples were left to swell in a solution of desired pH (1-9) at ionic strength  $\mu = 0.1M$  at a constant temperature 30°C. The swollen gels were taken out at regular time intervals, wiped superficially with filter paper, weighed, and placed in the same bath. The mass measurements were continued until the constant weight (equilibrium swelling) was attained for each sample. The percentage of mass swelling [%  $S_m$ ] and volume swelling [%  $S_v$ ] were obtained using following expressions<sup>19</sup>:

$$\%S_m = \frac{(m_t - m_o)}{m_o} \times 100$$

and

$$\%S_v = \frac{(m_t - m_o)}{m_o} \cdot \frac{d_p}{d_s} \times 100$$

where  $m_o$  and  $m_t$  are the initial mass and mass at different time intervals, respectively; and  $d_p$  and  $d_s$  are the solvent density and polymer density respectively.<sup>20</sup>

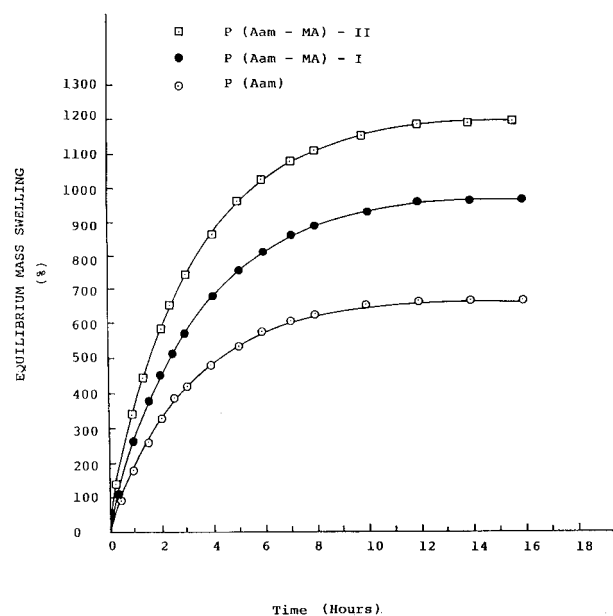
### Swelling–Deswelling Studies

For this, the initially dry hydrogel sample was placed in an alkaline solution of pH 8.0 and allowed to attain equilibrium swelling. Then the sample was withdrawn from the solution and placed in a solution of pH 2.0 until it deswelled to give a constant weight. The deswollen sample was again kept in alkaline solution at pH 8.0 to attain equilibrium swelling. This swelling–deswelling process was repeated a number of times.

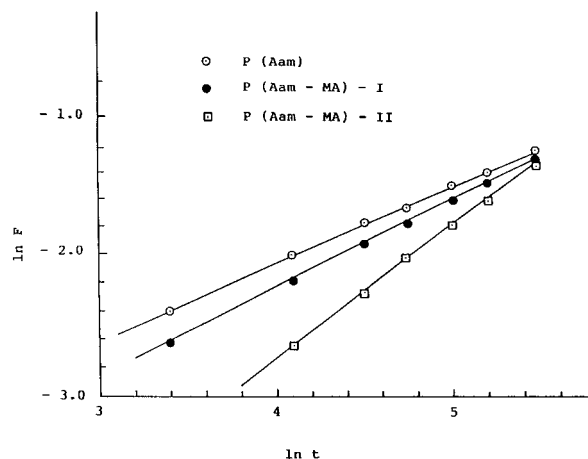
## RESULTS AND DISCUSSION

### Diffusion

When a glassy hydrogel is brought into contact with water, water diffuses into the polymer matrix, thus causing it to swell. Diffusion involves migration of water into preexisting or dynamically formed spaces between polymeric chains.



**Figure 1** The swelling curves of three hydrogel samples in distilled water at pH 7.0. Ionic strength = 0.1M; Temperature = 30°C.



**Figure 2** Plot of  $\ln t$  vs.  $\ln F$  for the three samples.

Swelling of hydrogel involves larger scale segmental motion, resulting ultimately into an increased distance of separation between hydrogel chains.<sup>21</sup>

The following equation was used to determine nature of the diffusion process:

$$F = \frac{M_t}{M_\infty} = kt^n \quad (1)$$

where  $M_t$  and  $M_\infty$  denote the amount of solvent that diffused into gel matrix at time  $t$ , and at infinite time (at equilibrium), respectively;  $k$  is a constant related with the structure of the network; and the exponent  $n$  describes the type of diffusion. For cylindrical shapes,  $n = 0.45$ – $0.50$  corresponds to Fickian diffusion, whereas  $0.50 < n < 1.0$  indicates the non-Fickian type diffusion. This equation is applied to the initial stages of swelling and plot of  $\ln F$  vs.  $\ln t$  yields straight lines up to almost a 60% increase in the mass of the hydrogel.

Figures 1 and 2 describe the dynamic uptake of water and the  $\ln F$  vs.  $\ln t$  plot for the three hydrogel samples, namely P(AAm), P(AAm-MA)-I and P(AAm-MA)-II in a salt solution of ionic strength 0.1M at pH 7.0 at 30°C. The values of  $n$  and  $k$ , as calculated from the slopes and intercepts of the straight lines, have been shown in Table I. It is clear that the swelling exponent  $n$  for the sample P(AAm) is 0.50, thus showing a Fickian type diffusion mechanism, whereas for the samples P(AAm-MA)-I and P(AAm-MA)-II, the values were found to be 0.59 and 0.68, respectively, which suggest the non-Fickian type swelling mechanism followed by two samples. This

**Table I** The Parameters of Swelling and Diffusion of Hydrogels in Distilled Water at pH 7.0

Gel Sample	% $S_m$	% $S_v$	$k \times 10^2$	$n$	$D \times 10^3 \text{ cm}^2 \text{ min}^{-1}$	$\bar{D} \times 10^3 \text{ cm}^2 \text{ min}^{-1}$
P(AAm)	660	780	3.2	0.51	4.12	5.08
P(AAm-MA)-I	982	1022	2.5	0.61	6.03	7.64
P(AAm-MA)-II	1214	1392	0.9	0.72	7.89	9.10

Temperature = 30°C; Ionic strength = 0.1M.

shows that water transport mechanism becomes non-Fickian as the small amount of maleic acid is incorporated into the polymer matrix. This transition of swelling mechanism from Fickian to non-Fickian due to incorporation of acid content may be explained as follows.

For the sample containing no maleic acid in the polymer matrix, the diffusion of water into the hydrogel is rate limiting, thus imparting almost normal or Fickian swelling behavior to the hydrogel, whereas in the case of samples with maleic acid content, the ionization of carboxylic groups (as the pH of swelling medium is 7.0) of maleic acid inside the polymer matrix imparts ionic character to the hydrogel. Therefore, not only the ion-osmotic swelling pressure  $\pi_{\text{ion}}$  increases, but the electrostatic repulsion between adjacent ionized carboxylate groups also leads to a greater chain expansion. Now the former factor encourages the diffusion of water into the gel phase in accordance with the Donnan membrane equilibrium, whereas the later one enhances the macromolecular chain relaxation process. These two factors are comparable, and hence, responsible for the anomalous or non-Fickian transport. Similar observations have also been reported by other workers.<sup>19</sup>

In hydrogel characterization, the diffusion coefficients were calculated from the following relationship:

$$D = 0.049/(t/4l^2)_{1/2} \quad (2)$$

where  $D$  is expressed in  $\text{cm}^2 \text{ min}^{-1}$ ;  $t$  is the time at which swelling is half the equilibrium value; and  $l$  is the radius of the cylindrical polymer sample. The intrinsic diffusion coefficient  $\bar{D}$  may be given as

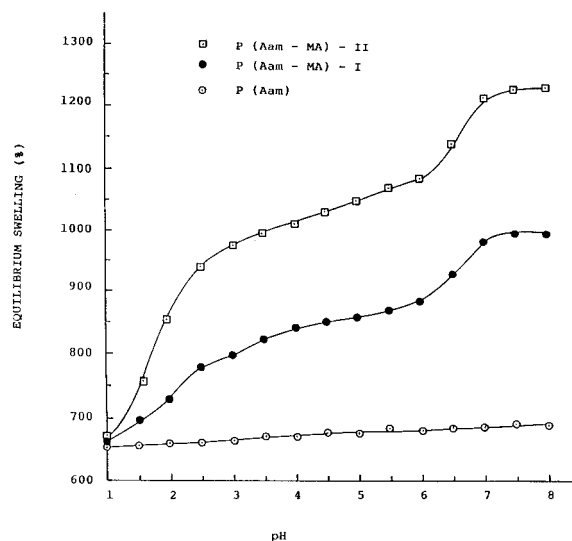
$$\bar{D} = D[1 - V]^{-3} \quad (3)$$

where  $V$  is the volume fraction of the solvent penetrating the polymer matrix by the time  $t$

defined above.<sup>20</sup> The values of %  $S_m$ , %  $S_v$ ,  $D$ , and  $\bar{D}$  have been shown in the Table I. It is clear from Table I that percentage equilibrium swelling increases as the amount of maleic acid in the hydrogel increases. This may be attributed to the fact that number of hydrophilic groups of the P(AAm-MA) copolymer are greater than those of the P(AAm) sample. Moreover, the ionization of maleic acid also increases the ion osmotic swelling pressure, thus resulting in greater swelling of these hydrogels.

### pH Effect

The effect of pH of the swelling media on the swelling behavior of three hydrogel samples, studied at the ionic strength 0.1M at 30°C, has been depicted in Figure 3. It is clear from Figure 3 that the sample P(AAm) does not show any change in the equilibrium mass swelling with the pH of the external medium, while for the samples

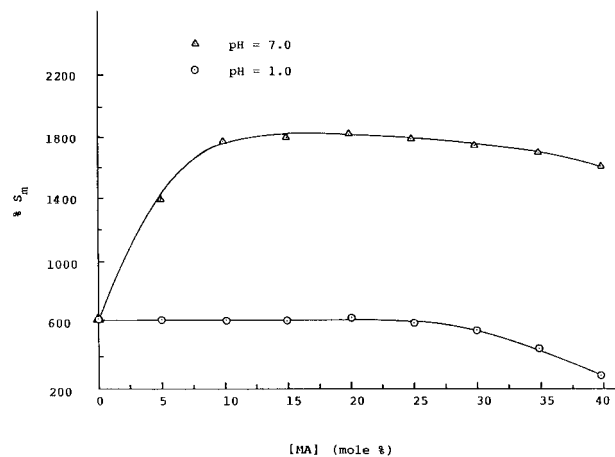


**Figure 3** The effect of pH of the swelling medium on the mass equilibrium swelling of hydrogels. Ionic strength = 0.1M; Temperature = 30°C.

containing maleic acid, the equilibrium mass swelling increases with pH of the swelling solution. The pH-independent swelling behavior of hydrogel sample P(AAm) may be attributed to the fact that the polymer matrix is purely nonionic in nature, and does not contain any ionizable groups. Therefore, variation in pH of the swelling media does not produce any change in swelling capacity. However, the situation is quite different with the sample containing maleic acid. A close look at the figure reveals that the increase in the equilibrium mass swelling is rather much more pronounced near the pH 2.0 and 7.0, which may be due to the complete dissociation of acidic groups of maleic acid around these pH values, because first and second  $pK_a$  for maleic acid are 1.85 and 6.06, respectively.<sup>22</sup> Therefore, when pH of the external solution increases beyond 2.0, the ionization of carboxylic groups in the gel matrix causes a sudden increase in the swelling due to increased ion osmotic swelling pressure as well as chain relaxation resulting from the electrostatic repulsion among carboxylate groups inside the polymer matrix. Similarly, when the pH of the swelling medium passes through 7.0, again a sudden rise in equilibrium swelling is observed, which may be attributed to further ionization of carboxylic groups. The two  $pK_a$  values as determined from Figure 3 were found to be 2.0 and 6.5, respectively, which are slightly greater than the actual values 1.85 and 6.06. This may be due to some hinderance offered in the ionization of carboxylic groups in the polymer matrix due to the crosslinked structure of the hydrogel. To sum up, the observed increase in equilibrium swelling capacity with the rise in pH of the external solution arises from the ionization of carboxylic groups of maleic acid, which ultimately causes an increase not only in the ion osmotic swelling pressure but also in the extent of chain relaxation process.

#### Effect of Maleic Acid Content

Figure 4 depicts the equilibrium mass swelling of P(AAm-MA) hydrogel samples as a function of mol % of maleic acid in the polymer matrix, studied at pH 1.0 and 7.0 at 30°C. The results, shown in the figure, are quite interesting. At pH 1.0, the equilibrium swelling of P(AAm-MA) sample remains almost constant and then decreases slowly as the acid content in the hydrogel increases. However, results are different when the same effect is studied at pH 7.0 of the swelling media. Here, the equilibrium swelling first increases,



**Figure 4** Effect of maleic acid content on the mass equilibrium swelling of hydrogel at pH 1.0 and 7.0. Temperature = 30°C; Ionic strength = 0.1M.

then remains almost the same, and then finally decreases slowly with further increase in maleic acid content. These results are rather unexpected and contrary to the expected behavior, according to which the increase in acid content should have been accompanied by the increase in equilibrium swelling. However, an attempt may be made to explain the observed findings. When the pH of the swelling medium is 1.0 (which is below the  $pK_a$  values of maleic acid), the maleic acid present in the polymer matrix remains in almost unionized form, and hence, hydrogels behave like a nonionic polymer matrix, and therefore, initially for the range of lower maleic acid contents the hydrogels show almost the same equilibrium swelling. However, when the maleic acid content is further increased, the unionized maleic acid provides greater hydrophobicity to the system, thus discouraging the solvent entrance to the gel matrix. Moreover, it has been reported that maleic acid also actively participates in the crosslinking of the gel matrix,<sup>23</sup> and therefore, the effect of crosslinking is much more pronounced when relatively higher concentration of maleic acid is present in the hydrogel. Hence, due to increased crosslinking, the free space per-unit crosslinks, available for the accommodation of water in the polymer matrix decreases, which finally results in lower swelling capacity of the hydrogels. This accounts for the observed decrease in the equilibrium swelling when maleic acid is present in higher concentrations in the polymer network.

When the same effect is studied at the pH 7.0, the swelling behavior of hydrogels is observed to

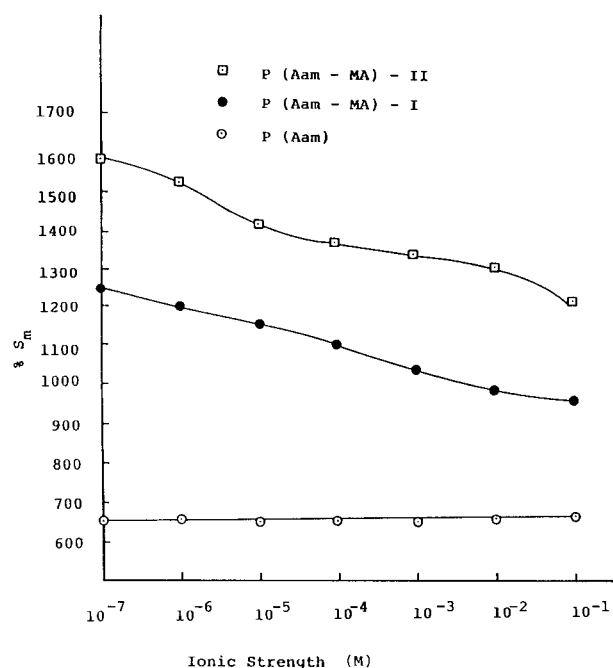


be different. The equilibrium swelling capacity first increases with maleic acid contents, then it becomes almost constant for a definite range of concentration, and then it decreases very slowly with further rise in concentration of maleic acid in the hydrogels. For the lower concentrations of maleic acid in the hydrogels, the equilibrium swelling capacity increases with acid content due to ionization of carboxylic groups (at pH 7.0) in the polymer matrix which, in turn, increases the ion osmotic swelling pressure as well as the extent of chain relaxation process. Now, when acid content is further increased, the increase in equilibrium swelling (due to ion osmotic swelling pressure and chain relaxation) is almost counterbalanced by the hydrophobic character imparted by the unionized maleic acid as well as crosslinking provided by maleic acid. This results in almost no change in the degree of swelling. Finally, when the content of maleic acid in the hydrogels becomes sufficiently high, the equilibrium swelling decreases slightly due to predominant role of hydrophobic character of unionized maleic acid and the crosslinking effect.

#### Ionic Strength Effect

The effect of ionic strength of the external media on the equilibrium mass swelling of the three hydrogel samples has been studied at pH 2.0 and 7.0, as depicted in Figure 5. It is clear from the figure that P(AAm) hydrogel does not show any response to the variation in the ionic strength of the swelling media, whereas for the samples containing maleic acid, the equilibrium swelling decreases with the increase in the ionic strength. As the sample P(AAm) does not contain any ionizable groups in the polymer matrix, it behaves like a nonionic gel, thus showing almost the same equilibrium swelling capacity for the whole range of ionic strength studied.

For the P(AAm-MA) hydrogels the dissociation of carboxylic groups present in the polymer matrix (at the experimental pH 7.0) imparts ionic character to the hydrogels, and therefore, ion osmotic swelling pressure  $\pi_{ion} = RT \sum(C_g - C_s)$ , where  $C_g$  and  $C_s$  are the concentrations of counter/mobile ions in the gel and solution phase, respectively, and become the governing factor in the overall swelling process. Obviously, with the increase in ionic strength of the swelling medium, the  $\pi_{ion}$  decreases, which ultimately reduces the equilibrium swelling capacity of the hydrogels. In another set of experiments the equilibrium swell-

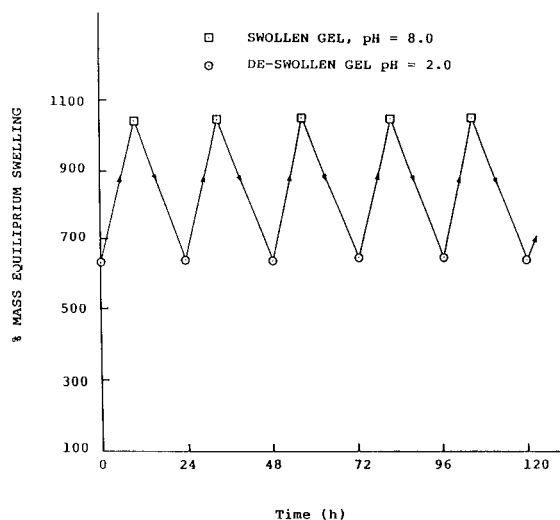


**Figure 5** Effect of ionic strength of the swelling medium on the equilibrium swelling of hydrogels. Temperature = 30°C; pH = 7.0.

ing of the samples P(AAm-MA) was studied as a function of ionic strength of the swelling medium at pH 2.0. It was observed that the ionic strength did not affect the equilibrium water uptake of the hydrogels. This may be attributed to the fact that at the experimental pH 2.0 (which is below the  $pK_a$  values of the gels) the polymer matrix remains almost in unionized form, thus showing no change in equilibrium water uptake with varying ionic strength of the swelling medium. Similar observations have also been reported in a large number of studies related with the swelling behavior of polyelectrolyte gels.<sup>24</sup>

#### Swelling-Deswelling of Gels

Figure 6 shows the successive swelling-deswelling cycles for the hydrogel P(AAm-MA)-I when the gel, after being equilibrated in an external medium of pH 8.0, is put in acidic medium at pH 2.0. The hydrogel is found to exhibit a number of cycles without undergoing any deformation in shape. It is also clear from the figure that the swelling of the hydrogel is relatively faster than the deswelling process, as the former requires almost 9 h to reach the equilibrium swelling, whereas deswelling takes place in about 15 h. The reason for this is that the two processes, namely



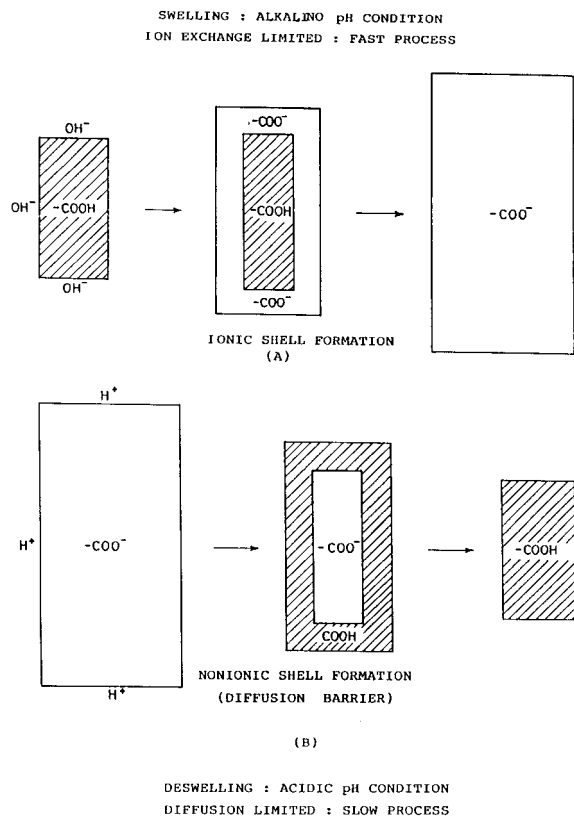
**Figure 6** Swelling-deswelling cycles for the hydrogel P(AAm-MA)-I. Temperature = 30°C; Ionic strength = 0.1M.

swelling and deswelling, follow different mechanisms, as has been schematically illustrated in Figure 7.

When the completely swollen gel is placed in the external medium of pH 2.0, the deswelling process starts with the formation of the uncharged and nonionic shell layer on the surface, and it gradually moves towards the core region of the gel. This dehydrated and nonionic gel layer retards the further release of water as a diffusion barrier. This may be the most probable explanation for the slower deswelling kinetics. However, when the deswollen gel is placed in external medium of pH 8.0 (alkaline solution), a more hydrated and charged layer (due to ionization of —COOH groups) is first formed on the surface of the gel. Through this, the counterions can easily be imbedded into the collapsed core region. Therefore, the overall swelling kinetics may be governed by the ion-exchange rate.

#### Effect of Counterions

Table II depicts the effect of counterions on the equilibrium mass swelling of P(AAm), P(AAm-MA)-I, and II hydrogel samples studied at pH 7.0 at 30°C. It is clear that for the sample P(AAm), the equilibrium swelling does not change with nature of counterions which may be attributed to the fact that as the hydrogel sample does not contain any ionizable groups, in the polymer network, its swelling capacity remains almost unaf-



**Figure 7** (A) Swelling of a deswollen gel in alkaline medium. (a) Deswollen gel is put in alkaline solution of pH 8.0. (b) The formation of ionic shell takes place on the surface, which approaches towards core region. (c) Finally the whole gel swells. (B) Deswelling of a swollen gel in acidic medium. (a) The swollen gel is put in acidic solution of pH 2.0. (b) Nonionic dehydrated core forms on the surface, which acts as diffusion barrier. (c) Finally the whole gel is collapsed.

ected with the nature of counterions. However, the equilibrium water uptake decreases as the valency of the counterion changes from 1 to 2. The observed decrease in equilibrium swelling may be

**Table II** Equilibrium Mass Swelling (%  $S_m$ ) of Hydrogels in Aqueous Solutions of NaCl and CaCl<sub>2</sub> at Constant Ionic Strength 0.1M and Temperature 30°C

Salt Solution	Hydrogel Samples		
	P(AAm) % $S_m$	P(AAm-MA)-I % $S_m$	P(AAm-MA)-II % $S_m$
NaCl	660	982	1214
CaCl <sub>2</sub>	652	892	1107

attributed to the presence of ionizable groups in the hydrogel networks. Now, assuming the complete ionization of carboxylic groups at the experimental pH 7.0, the amount of sodium ions required to bind with carboxylate ions to maintain electroneutrality condition will be almost double the amount of calcium ions for the same degree of ionization inside the polymer network. This results in a decreased ion osmotic swelling pressure, and therefore, a decrease in equilibrium water uptake. As it is clear from Table II that a decrease in the equilibrium mass swelling values is not very large, it can be concluded that the degree of ionization of the fixed ionizable groups inside the polymer matrix is very small. In addition, aqueous electrolytic solutions do not have any buffering capacity, and this contributes to a lower degree of ionization.

## CONCLUSIONS

The introduction of small amount of maleic acid into the nonionic polyacrylamide hydrogels imparts ionic character to them, and the gels undergo transition from Fickian to non-Fickian swelling behavior in an aqueous media of pH 7.0, which may be attributed to the chain relaxation process that takes place inside the gel phase due to ionization of carboxylic groups. These gels have been found to show a good response to pH, ionic strength, and nature of counterions in the swelling media. The gels also exhibited a number of swelling-deswelling cycles when the pH of the external medium changed from 8.0 to 2.0, respectively. Thus, by adjusting the amount of maleic acid and the crosslinking ratio in the polymer matrix, these gels can be made to swell to a very small extent in acidic and to a maximum extent in neutral or slightly alkaline solutions, and hence, can be used as site-specific drug delivery systems along the gastrointestinal (GI) tract.

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