Structural Parameters and Swelling Behavior of pH Sensitive Poly(acrylamide-*co*-acrylic acid) Hydrogels

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In the present work, hydrogels based on acrylamide (AAm) and acrylic acid (AAc), crosslinked with N,N'-methylenebisacrylamide (MBAAm) were prepared by free radical polymerization in solution. The effect of initial AAm/AAc mole ratio and nominal crosslinking ratio (moles of crosslinking agent/moles of polymer repeat unit) on the dynamic and equilibrium swelling behaviour of hydrogels was investigated. Hydrogels were characterized by the polymer volume fraction in the swollen state ($v_{2,s}$), the number average molecular mass between crosslinks ($\overline{M}_c$) and the mesh size (ξ). The swelling capacity of hydrogels was found to decrease with increasing nominal crosslinking ratio. The results show a significant influence of AAc monomer concentration on swelling behavior of poly(acrylamide-*co*-acrylic acid) hydrogels. Hydrogels containing higher acrylic acid content had a higher equilibrium mass swelling at pH 7.4 and in distilled water than at pH 3.0 where the acrylic acid is present in nonionized state. Further, swelling data was fitted to various models and model parameters were evaluated using regression technique. Model analysis indicated that the swelling transport followed non-Fickian mechanism. Scanning electron microscopy (SEM) revealed the macroporous surface morphology of the matrix with pore size varying between 2–64 microns depending on the amounts of AAc in the hydrogel.

Key words:
Acrylamide, acrylic acid, hydrogels, crosslinking, swelling, poly(acrylamide-*co*-acrylic acid)

Introduction

Hydrogels are three-dimensional crosslinked polymeric networks capable of absorbing and retaining large amounts of water and physiological fluids while remaining insoluble in aqueous solutions. Typically these hydrogels at equilibrium comprise 60–90 % fluid and only 10–30 % polymer.[1] Due to characteristic properties such as swellability in water, high water content and elastic nature similar to natural tissue, biocompatibility and lack of toxicity, hydrogels have been utilized in a wide range of biological, medical, pharmaceutical and environmental applications.[2–5]

Certain polymeric networks show a change in their dynamic and equilibrium swelling properties as the external conditions are changed. Depending on the nature of polymer, these hydrogels can undergo significant volume changes in response to slight changes in environment involving pH, temperature, ionic strength, buffer composition etc.[6–10] The dynamic swelling change can be used in the design of site specific drug delivery systems so that it is incapable of releasing the active agent until it is placed in an appropriate biological environment.[11–13] In case of anionic polymeric networks, ionization takes place as the pH of the external medium rises above the pKa of the ionizable moiety.[14] The polymeric network becomes more hydrophilic as the degree of ionization increases and the drug release is accomplished as the polymer swells. Because many of the potentially most useful pH-sensitive polymers swell at high pH values and collapse at low pH values, the delivery of active agent occurs upon an increase in the pH of the environment. Such materials are ideal for systems such as oral delivery, in which the drug is not released at low pH values in the stomach but rather at high pH values in the upper small intestine.[11,15–16]

In recent years, hydrogel-based drug-delivery devices have become a major area of research interest with synthetic hydrogels providing an effective and controlled way to administer drugs for treatment of a number of diseases. One of the important types of synthetic hydrogels are those of poly(acrylamide) (poly(AAm)) and poly(acrylic acid) (poly(AAc)), either based on crosslinked polymers, or combined with other comonomer units. Poly(AAm) hydrogels can absorb relatively high amounts of water; however their swelling capacity is not very sensitive to pH or electrolytes.[17] The development of a drug delivery system requires

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the control of the water content within the polymeric structure as it is one of the important factors influencing the solute transport. The permeation rate can be controlled either by changing the crosslinking densities or by preparing hydrogel with comonomer of controlled hydrophilicity. Poly(AAm-*co*-AAc) hydrogels, owing to the existence of hydrophilic –COOH and $–NH_2$ groups, have the capacity to absorb large amounts of water. Also, due to the presence of hydrophilic carboxylic acid side groups, the swelling behavior of these hydrogels is highly dependent on the pH of the surrounding medium.[18] Hence, poly(AAm-*co*-AAc) hydrogels have been investigated for use as adsorbents in water purification[19,20] and drug delivery systems etc.[21,22] In the present work, poly(AAm-*co*-AAc) hydrogels were prepared by using different initial AAm/AAc mole ratio and N,N'-methylenebisacrylamide (MBAAm) concentrations. The hydrogels prepared were characterized with respect to their swelling properties, network structures and diffusional behaviour. The effect of crosslinking ratio and composition of poly(AAm-*co*-AAc) hydrogels on the dynamic and equilibrium swelling behaviour of hydrogels in buffer solution of pH 7.4, pH 3.0 and double-distilled water at 37 °C was investigated in this study. The aforementioned hydrogels were characterized by means of the determination of the polymer volume fraction in the swollen state $v_{2,s}$, the number average molecular mass between crosslinks $\overline{M}_c$, and the mesh size ξ.

Table 1 – *Feed composition and sample designation in the preparation of poly(AAm-co-AAc) hydrogels with MBAAm = 0.2, 0.3 and 0.4 g/20 g monomer*

Sample Code No.	Mass of AAm/g	Mass of AAc/g	AAm/AAc (mole ratio)
A	20.0000	0.0000	100/0
B	18.9866	1.0134	95/5
C	17.9747	2.0253	90/10
D	15.9550	4.0450	80/20
E	13.9412	6.0588	70/30
F	11.9328	8.0672	60/40
G	9.9301	10.0700	50/50

Experimental

Materials

Acrylic acid (AAc) was procured from CDH (synthesis grade) and purified by distillation under reduced pressure. Acrylamide (AAm) (CDH, electrophoresis grade) was used as received without further purification. N,N'-methylene-bisacrylamide (MBAAm), (Merck, electrophoresis grade) was used as the crosslinker for the synthesis of hydrogels without further purification. Ammonium persulfate (APS), the initiator, and tetraethylene methylenediamine (TEMED), the accelerator, were used as redox initiator pair for the synthesis of hydrogels and were supplied by Merck (analytical grade). Potassium dihydrogen phosphate, sodium hydroxide were of analytical grade and double-distilled deionised water was used for preparing the solutions in the study.

Synthesis of hydrogels

The hydrogels were synthesized using a procedure based on the simultaneous radical polymerization and crosslinking of AAm and AAc.[18] The polymerization mixture composed of monomers (AAm and AAc) at a concentration of 20 % (w/v) in distilled water was added crosslinker (MBAAm) and redox initiator (APS and TEMED). Each hydrogel sample was prepared using 0.2 mL of initiator solution i.e. APS (0.05 g mL^{-1} water) and 0.25 mL accelerator solution i.e. TEMED (0.01 g mL^{-1} water) for each 10 mL solution of reactants prepared in distilled water. The reaction mixture was purged with high purity nitrogen for 30 minutes to remove the excess of oxygen that may interfere with the free radical polymerization reaction. The reaction was carried out in 10 mL sealed test tubes at a constant temperature of 40 ± 0.1°C using a water circulating bath (Julabo, F20-VC/3) for 24 h leading to complete gelation. The sample was then cooled to room temperature and the resulting hydrogels were removed from the glass tubes and uniformly cut into samples of short cylindrical shape. The obtained hydrogels were soft and elastic in nature. These hydrogels were immersed in an excess of distilled water in order to remove the unreacted reactants. Water was changed several times during the first 24 h and then once in at least seven days. The samples were first dried at room temperature and finally under vacuum at 40 °C to constant mass, and stored in dessicators containing anhydrous calcium chloride (a desiccant agent, CDH) for further use. The crosslinking ratio X, defined as moles of crosslinking agent MBAAm/moles of polymer repeat unit, used in the present study are 0.0046, 0.0069 and 0.0091. The moles of polymer repeat unit for determining the crosslinking ratio X, was taken as the weighted average of molecular mass of the two monomers present in the given hydrogel. Change in the ratio of AAm/AAc changes the value of moles of polymer repeat unit. However, in the present case since the ratio of molecular mass of AAm/AAc is nearly equal to one, there is no appreciable change in the value of X.

Hydrogel characterization

Swelling behavior

Hydrogels were characterized by determining polymer volume fraction in the swollen state ($v_{2,s}$), the number average molecular mass between crosslinks ($\overline{M}_c$) and the mesh size (ξ) using the observed swelling data. Hydrogel volume in dry state (V_d) and hydrogel volume when swollen to equilibrium (V_s) were determined using eqs. (1) and (2):[24–25]

$$V_s = \frac{m_{a,s} - m_{h,s}}{\rho_h} \tag{1}$$

$$V_d = \frac{m_a - m_h}{\rho_h} \tag{2}$$

where m_a is the mass of the initially dry polymer in air, m_h is the mass of the dry polymer in *n*-heptane, $m_{a,s}$ is the mass of the swollen hydrogel in air after reaching equilibrium swelling, $m_{h,s}$ is the mass of swollen hydrogel in *n*-heptane after equilibrium swelling and ρ_h is the density of *n*-heptane (0.688 g cm^{-3}). Mass of hydrogel in a nonsolvent (*n*-heptane) was obtained by placing the sample in a stainless steel mesh basket suspended in *n*-heptane before swelling measurements were made and after equilibrium swelling was achieved. The polymer volume fraction of the hydrogel in swollen state $v_{2,s}$ was evaluated from swelling data using the following relationship:[26]

$$v_{2,s} = \frac{V_d}{V_s} \tag{3}$$

where V_d is the volume of the dry polymer, and V_s is the volume of the hydrogel after equilibrium swelling. The determination of swollen hydrogel volume (V_s) required the placement of hydrogel sample in buffer and allowing it to attain equilibrium.

Swelling measurements

To study the effect of pH on swelling behavior of the hydrogels, weighed amounts of dry, thin, polymeric hydrogel disc samples were placed in buffer solution of pH 7.4, pH 3 and distilled water at 37 °C. The hydrogels were weighed on a top loading electronic balance (Sartorius) with an accuracy of ±0.0001 g. All the swelling studies were carried out in 100 mL of swelling medium. At intervals, the swollen gels were lifted, blotted on filter paper, and weighed. While weighing the gels, care was taken to remove the superficial buffer on the surface, so that only the weight of the buffer incorporated into the hydrogel was considered. The swelling studies were carried out until equilibrium in swelling was reached. The equilibrium swelling was attained in 2 – 3 days. Swelling S (mass swelling or degree of swelling) of samples at any time t was calculated using eq. (4):

$$S = \frac{m_t - m_0}{m_0} \tag{4}$$

The equilibrium degree of swelling S_{eq}, after hydrogels had swollen to equilibrium in the swelling media was calculated using eq. (5):

$$S_{eq} = \frac{m_{eq} - m_0}{m_0} \tag{5}$$

Here m_t is the mass of the swollen hydrogel sample at time t, and m_0 is the initial dry mass of the hydrogel sample, m_{eq} is the mass of the swollen hydrogel sample at equilibrium. For swelling studies, an average value of four replicates was taken.

Scanning electron microscopy

SEM analysis was carried out using JSM 6100 SEM. Prior to examination, samples were gold-sputter coated to render them electrically conductive.

Results and discussion

Hydrogel structural parameters

Based on equilibrium swelling data, the number average molecular mass between crosslinks, $\overline{M}_c$, was calculated using eq. (6):[2,18,25]

$$\frac{1}{\overline{M}_c} = -\frac{\frac{\bar{v}}{V_1}\left[\ln(1 - v_{2,s}) + v_{2,s} + \chi v_{2,s}^2\right]}{\left(v_{2,s}^{1/3} - \frac{1}{2} v_{2,s}\right)} \tag{6}$$

Here, V_1 is the molar volume of water, $v_{2,s}$ is the polymer volume fraction in the swollen state, $\bar{v}$ is the specific volume of the polymer (taken as 0.67), $\overline{M}_c$ is the number average molecular mass between the crosslinks, and χ is the Flory-Huggins polymer-water interaction parameter. The values of parameters V_1 and χ used in eq. (6) are presented in Table 2. The theoretical number average molecular mass between crosslinks, $\overline{M}_{c,t}$, was calculated using eq. (7):[26]

$$\overline{M}_{c,t} = \frac{M_r}{2X} \tag{7}$$

Here, M_r is the molecular mass of the polymer repeat unit determined as weighted average for given sample and X is the nominal crosslinking ratio. The values of $\overline{M}_c$ and $\overline{M}_{c,t}$ thus obtained are reported in Table 3 at pH 7.4, pH 3.0 and distilled

Table 2 – *Characteristic parameters used in eq. 6 and 8*

Component	Parameter		Value	Reference
poly(AAm)	χ	Flory-Huggins polymer-water interaction parameter	0.49	33
poly(AAc)	χ	Flory-Huggins polymer-water interaction parameter	0.5	32
poly(AAm)	$C_{n,}$	Flory characteristic ratio of the polymer	2.72	34
poly(AAc)	C_n	Flory characteristic ratio of the polymer	6.7	32
water	V_1	molar volume of water	18.1 $cm^3\ mol^{-1}$	32
poly(AAm), poly(AAc)	l	length of the C-C bond along the polymer backbone	0.154 nm	32

Table 3 – *Structural parameters of swollen poly(AAm-co-AAc) hydrogels at 37 °C at various crosslinking ratio, X/mol mol^{-1}*

Sample	X = 0.0046 $\overline{M_{c,t}}$ = 7786			X = 0.0069 $\overline{M_{c,t}}$ = 5216			X = 0.0091 $\overline{M_{c,t}}$ = 3931		
	$\overline{M_c}$/g mol^{-1}	ξ/μm	$v_{2,s}$	$\overline{M_c}$/g mol^{-1}	ξ/μm	$v_{2,s}$	$\overline{M_c}$/g mol^{-1}	ξ/μm	$v_{2,s}$
	eq. 6	eq. 8	eq. 3	eq. 6	eq. 8	eq. 3	eq. 6	eq. 8	eq. 3
Sample in pH 7.4									
A	155134	4.37	0.0561	101413	3.35	0.0656	82413	2.94	0.0706
B	355457	7.57	0.0416	221500	5.64	0.0494	169507	4.77	0.0545
C	926565	14.21	0.0293	510312	9.79	0.0364	442210	8.94	0.0385
D	2582934	28.55	0.0201	1661995	21.68	0.0236	1310458	18.66	0.0258
E	3482527	36.27	0.0180	2905657	32.38	0.0192	2383546	28.57	0.0207
F	5299543	49.44	0.0154	4430313	44.12	0.0165	3371267	37.20	0.0182
G	7225790	62.69	0.0137	5461171	52.57	0.0152	4096426	43.81	0.0170
Sample in pH 3.0									
A	191305	4.98	0.0521	94706	3.22	0.0669	71271	2.69	0.0742
B	121093	3.89	0.0612	83472	3.08	0.0700	63161	2.59	0.0775
C	106530	3.71	0.0642	71935	2.90	0.0739	55529	2.47	0.0811
D	79984	3.30	0.0712	51734	2.51	0.0832	49367	2.44	0.0846
E	69935	3.20	0.0746	43454	2.38	0.0885	29736	1.88	0.1013
F	54527	2.88	0.0817	28265	1.91	0.1033	21931	1.63	0.1128
G	29138	2.04	0.1020	17883	1.51	0.1210	13533	1.27	0.1334
Sample in DW									
A	181529	4.81	0.0529	97413	3.27	0.0662	62819	2.49	0.0774
B	365288	7.71	0.0411	138796	4.22	0.0584	72860	2.83	0.0736
C	842028	13.41	0.0303	180631	5.14	0.0530	84924	3.21	0.0696
D	1422494	19.70	0.0250	206528	5.93	0.0505	96485	3.70	0.0664
E	1818163	24.22	0.0228	244099	6.94	0.0475	112056	4.27	0.0631
F	1953935	26.57	0.0222	310928	8.46	0.0435	138445	5.11	0.0585
G	2463073	32.05	0.0204	427175	10.65	0.0400	166318	5.98	0.0547

water respectively. From Table 3, it is observed that the experimental values of molecular mass between the crossinks $\overline{M}_c$, are much larger than those predicted by theory $\overline{M}_{c,t}$. This can be attributed to the real network formed as against the ideal Gaussian networks.[25–27] High values of $\overline{M}_c$ imply loosely crosslinked hydrogels. In ionic polymers, $\overline{M}_c$ may be controlled by the monomer concentration (in this case AAc) in the polymerization reaction mixture.[14] The results in Table 3 show that the average molecular mass between the crosslinks $\overline{M}_c$ is affected not only by the AAc content of the hydrogels, but also by the nominal crosslinking ratio, *X*, and the pH of swelling medium. The increasing concentration of AAc in the reaction mixture leads to a marked increase in $\overline{M}_c$ for swelling studies conducted in pH 7.4 and distilled water (DW) as shown in Table 3. However, at pH 3, with increase in amount of acrylic acid in hydrogel, $\overline{M}_c$ decreases, which can be attributed to the fact that networks of acrylic acid are nonionised at a pH of 3, and are in compact conformation. Physical entanglements, chemical crosslinks, and hydrogen bonding between acid units (self-association) are important parameters[14] that affect the rate of chain diffusion, thus reducing the observed $\overline{M}_c$ at a pH of 3. With increase in pH, ionization of network disrupts the self-associations thus contributing to the electrostatic repulsion between adjacent ionized groups, leading to chain expansion and increase in the mesh size. This parameter reaches a limiting value as the polymer becomes completely ionized.

The molecular mass between the crosslinks, $\overline{M}_c$, was also found to decrease with an increasing nominal crosslinking ratio, *X*, as listed in Table 3 at pH 7.4, pH 3.0 and distilled water respectively.

Using the calculated values of number average molecular mass between crosslinks, $\overline{M}_c$ and the values of C_n for various monomer ratios, the mesh size, ξ, was determined using eq. (8).[28,29]

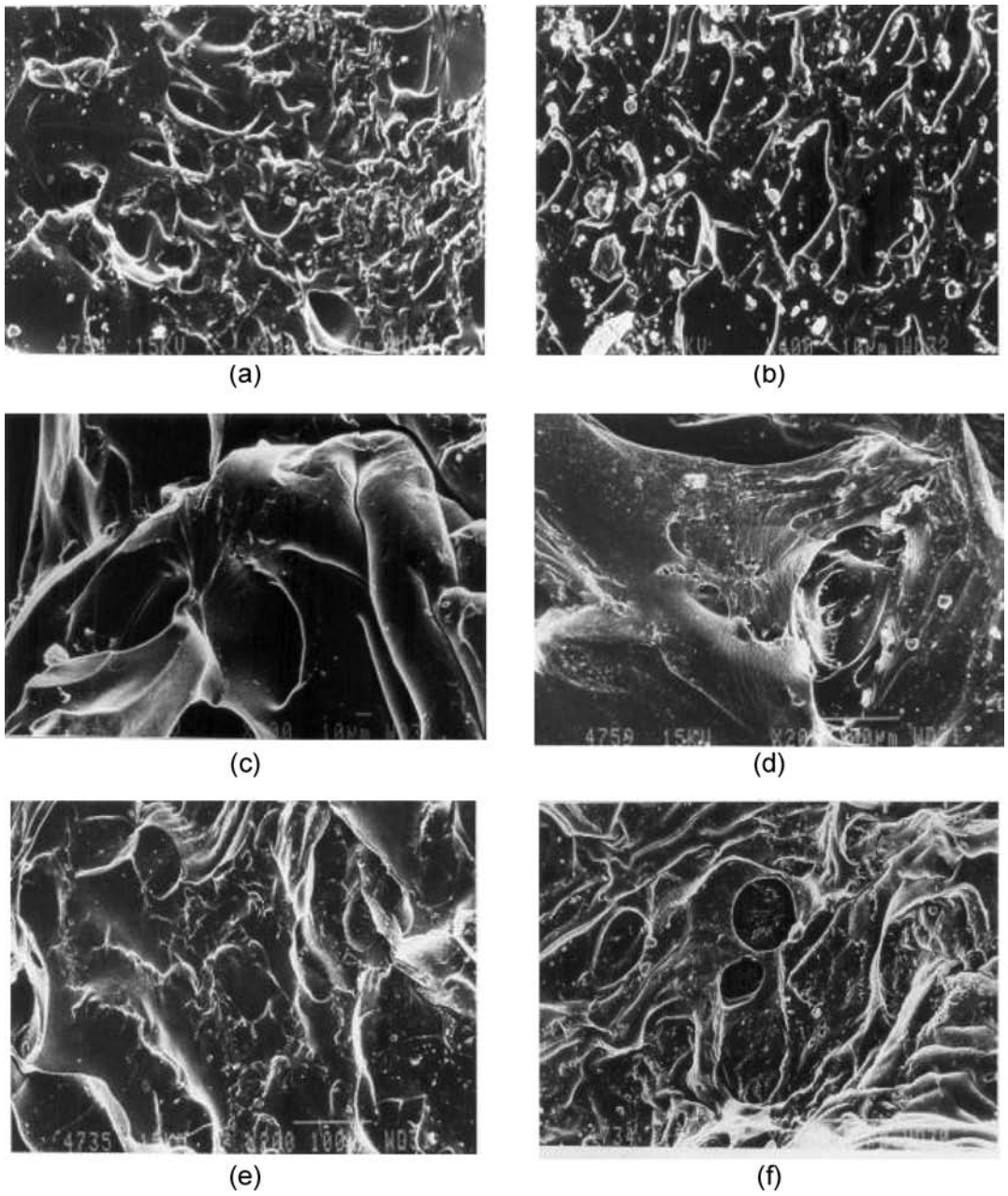
$$\xi = v_{2,s}^{-1/3} \sqrt{\frac{2C_n \overline{M}_c}{M_r}}\, l \qquad (8)$$

Here, M_r is the molecular mass of the repeat unit, C_n is the Flory characteristic ratio of the polymer and l is the length of the C–C bond along the polymer backbone. In eq. (8), the characteristic ratio, C_n, of the poly(AAm-*co*-AAc) hydrogels was taken as the weighted average of C_n values of poly(AAm) and poly(AAc) chain according to their molar ratio in the hydrogel of a given composition. The different parameters necessary to perform all the calculations are presented in Table 2. The values of mesh size ξ, observed in different swelling mediums are reported in Table 3. Mesh size is the space available for transport of solute in a network. It is clear that the mesh size in a given composition of hydrogel decreases with increasing polymer volume fraction. Also, the mesh size of the networks increased with increase in acrylic acid content of the hydrogel, when swollen in buffer of pH 7.4 and DW. The increase in the mesh size results in increased water contents in the hydrogel. Since acrylamide is non-ionic and acrylic acid has a pKa value of 4.7, it is expected that the network should collapse when swollen in acidic buffer of pH 3.0, and accordingly their mesh size will be lowered. It was observed that the mesh size of poly(AAm-*co*-AAc) hydrogels decreased when swelling studies were conducted in acidic buffer of pH 3.0. The mesh sizes of the networks varied between 2 and 62 microns, implying that permeation of molecules with a wide range of sizes would be possible. Poly(AAm-*co*-AAc) hydrogels possessed higher particle pore size (63–44 μm) in buffer of pH 7.4, when compared to poly(AAm) hydrogels (4–2 μm) in the same medium for varying crosslinking ratios *X*. Scanning electron micrographs of hydrogel samples swollen in buffer of pH 7.4 after freeze drying, are shown in Fig. 1, for different AAm/AAc mole ratios. The cross-sectional views of the hydrogels present an irregular surface pattern with macro/micro pores within the hydrogel. Hydrogels formed with higher acrylic acid content have a more open and porous channel structure in buffer of pH 7.4, which is in agreement with the observations from swelling studies. Fig. 1 also shows the SEM of 70/30 AAm/AAc hydrogel formed with different MBAAm concentrations. The pore size is found to decrease with increase in MBAAm concentration.

The equilibrium polymer volume fractions of hydrogels swollen to equilibrium, $v_{2,s}$, are presented in Table 3 for varying crosslinking ratios *X*. It is observed that increasing crosslinking ratio leads to denser networks and adjusting the amount of crosslinking agent in the synthesis process can be an effective means of controlling the crosslinked structure of hydrogels.

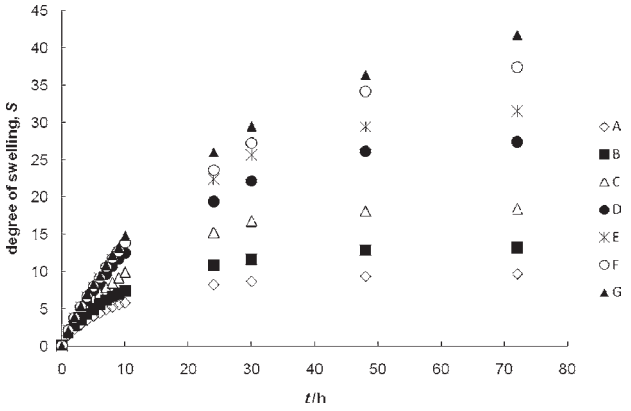
Swelling analysis

For characterization of the response of the hydrogels to external conditions, samples were allowed to swell to equilibrium in aqueous buffers of pH 3.0 and 7.4 to simulate the pH of the gastric and enteric cavities respectively, and also in distilled water at a temperature of 37 °C. The pH values were selected to allow comparison of swelling behaviour of hydrogels in both the ionized (pH > 4.7) and nonionized states (pH < 4.7), as AAc has a pK_a value of 4.7 and AAm is nonionic.

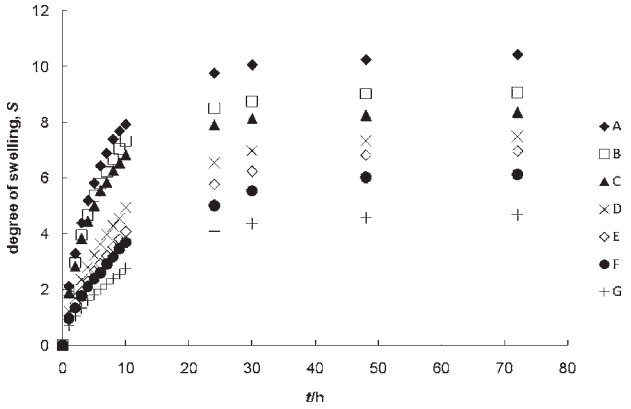


F i g . 1 – *Scanning electron micrographs of cross-sections of freeze-dried hydrogels swollen in buffer of pH 7.4 for different AAm/AAc mole ratio in hydrogels: (a) 100/0 (b) 90:10 (c) 80:20 (d) 50:50 (e) 70:30 at nominal crosslinking ratio X = 0.0091 mol mol^{-1} and (f) 70:30 at nominal crosslinking ratio X = 0.0046 mol mol^{-1}*

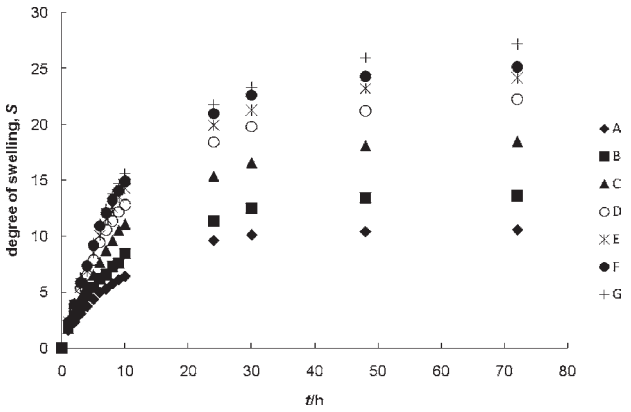
The water intake of initially dry gels was monitored for a long time and the measurements were continued until a constant mass was reached for each hydrogel sample. The dynamic swelling behaviour of hydrogels is shown in Fig. 2(a–c) at a nominal crosslinking ratio, $X = 0.0046$ mol mol^{-1} in buffers of pH 7.4, 3.0 and distilled water respectively. Similar curves were obtained for other crosslinking ratios. As can be seen from these figures, swelling of hydrogel increases with time until a certain point when it becomes constant. This constant value is taken as the equilibrium swelling for a given hydrogel sample. The results in Table 4 elucidate the effect of pH of buffer solution as well as the effect of acrylic acid content in the hydrogel on the equilibrium mass swelling (or degree of swelling) of hydrogel samples (S_{eq}). Equilibrium mass swelling of poly(AAm) hydrogel (sample A) does not seem to be affected by the pH of the solution as almost the same equilibrium mass swelling was obtained at pH 7.4, in distilled water and at pH 3. This could be due to the inherent non-ionic character of poly(AAm). However, equilibrium mass swelling of poly(AAm-*co*-AAc) hydrogels in buffer solution of pH 7.4 and distilled water is found to be significantly more in comparison to their equilibrium



F i g . 2 a – *Dynamic swelling behaviour of poly(AAm-co-AAc) hydrogels in buffer of pH 7.4 at nominal crosslinking ratio, X = 0.0046 mol mol^{-1}*



F i g . 2 b – *Dynamic swelling behaviour of poly(AAm-co-AAc) hydrogels in buffer of pH 3 at nominal crosslinking ratio, X = 0.0046 mol mol^{-1}*



F i g . 2 c – *Dynamic swelling behaviour of poly(AAm-co-AAc) hydrogels in distilled water at nominal crosslinking ratio, X = 0.0046 mol mol^{-1}*

mass swelling in buffer solution of pH 3.0. It is well known that the swelling of hydrogel is induced by the electrostatic repulsion of the ionic charges of its network. Acrylic acid contains carboxyl groups (–COOH) and the ionization of these groups above its pKa causes the swelling to increase. With increase in the content of AAc in poly(AAm-*co*-AAc) hydrogels, the equilibrium mass swelling ratio increases at pH 7.4 and DW, and as can be seen, the swelling curves are similar in shape for all the hydrogels investigated. It can be noticed that the equilibrium mass swelling values of poly(AAm-*co*-AAc) hydrogels are influenced greatly by the content of AAc in the hydrogel and hence it can serve as an effective means to control their swelling behaviour. The increase in crosslinking ratio lowers the equilibrium mass swelling ratio of poly(AAm-*co*-AAc) hydrogels that could be due to increased rate of formation of crosslinks, resulting in higher crosslink density. Tables (4–6) show that values of equilibrium mass swelling of poly(AAm-*co*-AAc) hydrogels range from 1009–4175 % at pH 7.4, 905–323 % at pH 3.0, 716–2717 % in distilled water at different initial AAm/AAc mole ratio in comparison to the values of equilibrium mass swelling of poly(AAm) hydrogels which range from 973–754 % at pH 7.4, 1044–716 % at pH 3.0, 1062–680 % in distilled water at increasing crosslinking ratios. The equilibrium mass swelling capacities of poly(AAm-*co*-AAc) hydrogels is greater than those of poly(AAm) hydrogels at pH 7.4 and DW due to the presence of hydrophilic groups in acrylic acid molecules. And with increasing number of hydrophilic groups in poly(AAm-*co*-AAc) hydrogels, swelling capacity also increases. Whereas the equilibrium mass swelling capacity of poly(AAm-*co*-AAc) hydrogels decreases with increase in hydrophilic groups at pH 3.0 due to non-ionization of these hydrophilic groups.

In order to study the effect of pH and composition of hydrogels on the kinetics of water uptake of hydrogels, water uptake data was fitted using the following models. Model I was fitted to the first 60 % of the water uptake data whereas Model II and III were fitted to the entire data.

Model I[31]

$$\frac{S}{S_{eq}} = kt^n \tag{9}$$

Model II[25,31]

$$\frac{t}{S} = A + Bt \tag{10}$$

Model III[32]

$$S = S_{eq}(1 - e^{-t/\tau}) \tag{11}$$

In Model I, S is the degree of swelling (or mass of solvent imbibed) at any time t, S_{eq} is the degree of swelling when equilibrium is reached (or amount of solvent imbibed at equilibrium), k is the swelling

Table 4 – *Effect of acrylic acid content on swelling kinetic parameters of poly(AAm-co-AAc) hydrogels at X = 0.0046 mol mol^{-1}, using Models I and II*

Sample	n eq. 9	k eq. 9	MRQE (Model I) eq. 12	S_{max} eq. 10*	S_{eq} eq. 5	MRQE (Model II) eq. 12	A eq. 10	D 10^6/cm^2 s^{-1} eq. 14
Sample in pH 7.4								
A	0.605	0.012	0.0666	10.9890	9.7334	0.0581	0.748	2.1520
B	0.622	0.01	0.0666	15.1515	13.1852	0.0656	0.641	2.2111
C	0.689	0.006	0.0940	22.2222	18.4929	0.0548	0.531	2.7035
D	0.787	0.003	0.0127	35.7143	27.4058	0.0388	0.511	2.8128
E	0.811	0.002	0.1757	41.6667	31.5485	0.0310	0.494	2.8272
F	0.821	0.002	0.0217	52.6316	37.4096	0.0386	0.517	2.6567
G	0.848	0.001	0.3612	58.8235	41.7523	0.0281	0.508	2.5460
Sample in pH 3.0								
A	0.628	0.015	0.0449	11.2360	10.4381	0.0330	0.382	3.4283
B	0.626	0.016	0.0364	9.7087	9.0520	0.0468	0.395	3.5944
C	0.615	0.019	0.0226	8.8496	8.3482	0.0468	0.399	3.3861
D	0.603	0.013	0.0571	8.4034	7.4926	0.0575	0.865	1.7605
E	0.600	0.012	0.0350	8.0000	6.9648	0.0774	1.169	1.2437
F	0.595	0.013	0.0235	6.9444	6.1180	0.0778	1.270	1.1684
G	0.586	0.013	0.0439	5.3476	4.6740	0.0805	1.670	1.0017
Sample in DW								
A	0.630	0.011	0.0227	12.1951	10.6218	0.0627	0.677	1.8527
B	0.671	0.008	0.0640	15.6250	13.5777	0.0403	0.568	3.3284
C	0.732	0.005	0.1057	21.7391	18.4312	0.0557	0.475	4.4175
D	0.777	0.004	0.0520	26.3158	22.2948	0.0432	0.412	4.8293
E	0.818	0.003	0.0859	28.5714	24.1734	0.0631	0.389	5.7286
F	0.834	0.003	0.0411	30.3030	25.1615	0.0705	0.366	6.8012
G	0.842	0.002	0.2756	32.2581	27.1704	0.0624	0.369	6.6234

*S_{max} = 1/B

constant characteristic of polymer network and n is the diffusional exponent characterizing the mechanism of diffusion of solvent into the network. For cylindrical geometry, the value of diffusional exponent n as 0.45 signifies a Fickian diffusion mechanism, while $n \geq 0.89$ indicates a Case II diffusion mechanism, while the value of n in the range $0.45 < n < 0.89$, indicates that the diffusion mechanism is anomalous or non-Fickian, where both diffusion and polymer relaxation control the overall rate of water uptake.[31] The representative curves of swelling kinetics of hydrogels are given in Figs. 3(a–c). The plots between S/S_{eq} versus t on log-log scale yielded a straight line up to nearly a 60 % increase in the mass of the hydrogel. The values of diffusional exponent n and diffusion constant k determined from the slope and intercept of the lines are reported in Tables 4, 5 and 6 for swelling studies conducted at 37 ± 0.1 °C in buffer solutions of pH 7.4 and 3.0 and distilled water, at various nominal crosslinking ratios X. It can be seen from the tables that the value of n increased with the increase in the acrylic acid content of the hydrogels, as well as, when the pH of the external swelling medium was increased from 3.0 to 7.4. This indicates that the solvent transport mechanism becomes non-Fickian as gel ionization becomes prominent. The dynamic swelling behavior of crosslinked polymers is dependent upon the relative magnitude of the solvent diffusion and polymer relaxation

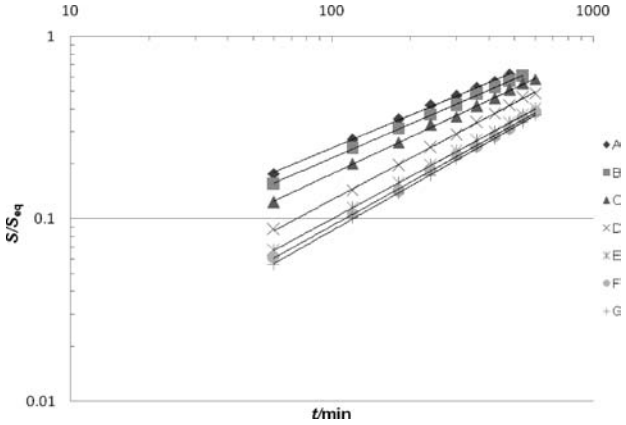


Fig. 3a – *Plot of S/S_{eq} vs time for poly(AAm-co-AAc) hydrogels in buffer of pH 7.4 at nominal crosslinking ratio, X = 0.0069 mol mol^{-1}*

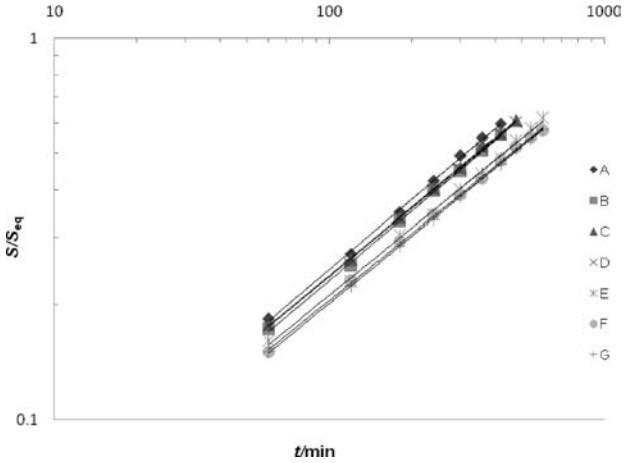


Fig. 3b – *Plot of S/S_{eq} vs time for poly(AAm-co-AAc) hydrogels in buffer of pH 3.0 at nominal crosslinking ratio, X = 0.0069 mol mol^{-1}*

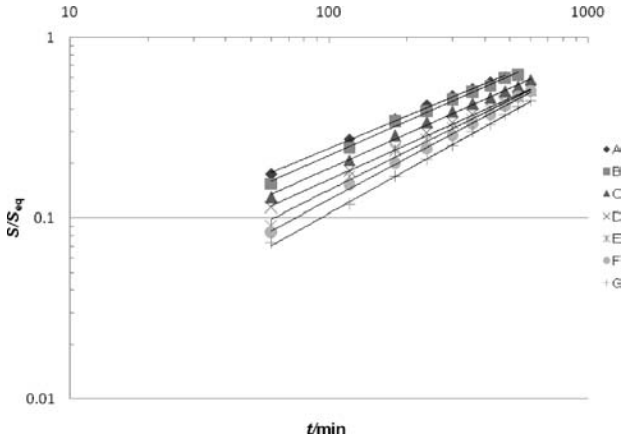


Fig. 3c – *Plot of S/S_{eq} vs time for poly(AAm-co-AAc) hydrogels in distilled water at nominal crosslinking ratio, X = 0.0069 mol mol^{-1}*

times. Fickian transport is observed when solvent diffusion controls the process. In ionic networks, ionization may control the solvent diffusion process, thus affecting the relative magnitude of diffusion and relaxation times. Macromolecular relaxations become more prominent in alkaline solutions. Thus, non-Fickian (anomalous) transport is observed as the pH of the surrounding fluid increases above pK_a. In general, increase in the degree of ionization contributes to the electrostatic repulsion between adjacent ionized carboxylate groups leading to chain expansion, which in turn affects macromolecular chain relaxation. The results obtained are in conformation with these observations.

Model II represents second order kinetics that can be used to explain the extensive swelling of hydrogels.[25,31] Here, S is the degree of swelling at time t, $A = 1/(dS/dt)_0$, is the reciprocal of the initial swelling rate of the hydrogel, $B = 1/S_{max}$ is the inverse of maximum (or equilibrium) swelling of hydrogel. Figs. 4, 5 show the linear regression of the representative swelling curves fitted to Model II (eq. (10)) for hydrogels at a nominal crosslinking ratio, $X = 0.0091$ in buffers of pH 7.4 and 3.0. Similar swelling curves were obtained for hydrogels at other nominal crosslinking ratios. The initial swelling rate and the values of maximum swelling of

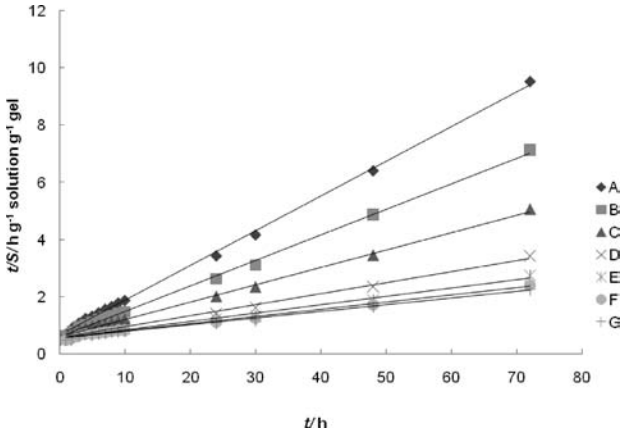


Fig. 4 – *t/S vs t curves for poly(AAm-co-AAc) hydrogels in buffer of pH 7.4 at nominal crosslinking ratio, X = 0.0091 mol mol^{-1}*

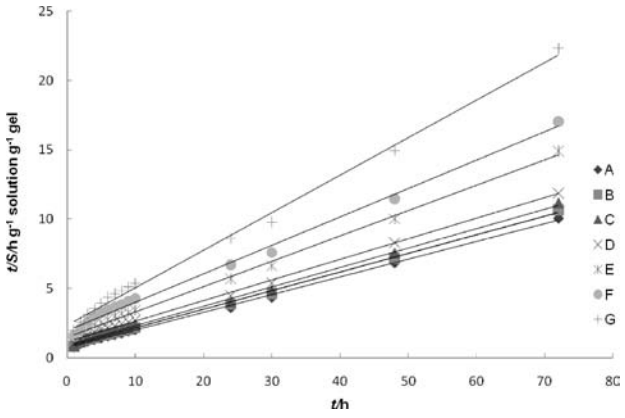


Fig. 5 – *t/S vs t curves of poly(AAm-co-AAc) hydrogels in buffer of pH 3.0 at nominal crosslinking ratio, X = 0.0091 mol mol^{-1}*

Table 5 – *Effect of acrylic acid content on the swelling kinetics parameters of poly(AAm-co-AAc) hydrogels at X = 0.0069 mol mol^{-1}, using Models I and II*

Sample	n eq. 9	k eq. 9	MRQE (Model I) eq. 12	S_{max} eq. 10*	S_{eq} eq. 5	MRQE (Model II) eq. 12	A eq. 10	D 10^6/cm^2 s^{-1} eq. 14
Sample in pH 7.4								
A	0.599	0.015	0.0290	9.0090	8.1115	0.0503	0.666	2.2710
B	0.620	0.012	0.0330	12.5000	11.1077	0.0542	0.590	2.4826
C	0.673	0.007	0.1206	17.8571	15.2816	0.0514	0.553	2.6288
D	0.760	0.003	0.2167	29.4118	23.2964	0.0464	0.528	2.6011
E	0.774	0.002	0.2945	38.4615	28.7989	0.0571	0.534	2.2111
F	0.793	0.002	0.1583	47.6190	33.4139	0.0562	0.549	2.0730
G	0.816	0.002	0.0103	52.6316	36.3272	0.0463	0.532	2.1520
Sample in pH 3.0								
A	0.611	0.014	0.0617	8.9286	8.1839	0.0526	0.622	2.5735
B	0.606	0.013	0.0276	8.4746	7.6567	0.0571	0.760	2.1394
C	0.596	0.015	0.0228	8.0000	7.2150	0.0548	0.810	2.0117
D	0.593	0.015	0.0293	6.8493	6.1913	0.0555	0.945	1.7681
E	0.584	0.014	0.0361	6.4516	5.7046	0.0824	1.279	1.2533
F	0.581	0.014	0.0158	5.4645	4.7912	0.0816	1.630	1.0017
G	0.585	0.013	0.0482	4.4843	3.8935	0.0860	2.036	0.9314
Sample in DW								
A	0.597	0.015	0.0382	9.1743	8.3371	0.0454	0.710	2.0036
B	0.633	0.011	0.0790	10.5263	9.5655	0.0343	0.666	2.2281
C	0.638	0.009	0.0952	12.0482	10.5453	0.0519	0.779	1.8919
D	0.644	0.008	0.0461	13.1579	11.1071	0.0717	0.916	1.5616
E	0.717	0.005	0.0588	14.2857	11.9105	0.0479	0.931	2.0771
F	0.765	0.003	0.1939	16.3934	13.0239	0.0480	0.940	2.1772
G	0.796	0.002	0.2661	18.8679	14.6817	0.0473	0.962	1.9155

*S_{max} = 1/B

hydrogels were calculated from the intersection and slope of the lines, the values are presented in Tables 4, 5 and 6. From these Tables a reasonable agreement between the experimental values of maximum equilibrium swelling ratio S_{eq} and the values predicted by Model II within the accuracy of the experimental data is observed at pH 3 and in distilled water.

Kinetics of swelling was also studied by fitting the swelling data to Voight-based equation Model III (eq. (11)), where τ is the rate parameter which is a measure of solvent penetration. With the observed data, model parameters were evaluated using standard non-linear regression technique and the results summarized in Tables 7, 8 and 9. In order to compare the relative performance of these models, mean relative quadratic error (MRQE) was calculated using eq. (12) for all the three models listed in Tables 4–9. From these tables it is observed that Model II fits the data better than Model III as its MRQE values are lower.

$$MRQE = \sqrt{\frac{\sum\left(\frac{S_{cal} - S_{exp}}{S_{exp}}\right)^2}{N-1}} \qquad (12)$$

For hydrogel characterization, short time approximation method was used for the calculation of diffusion coefficient D for poly(AAm-*co*-AAc) hydrogels. The short time approximation method is

Table 6 – *Effect of acrylic acid content on the swelling kinetics parameters of poly(AAm-co-AAc) hydrogels at X = 0.0091 mol mol^{-1}, using Models I and II*

Sample	n eq. 9	k eq. 9	MRQE (Model I) eq. 12	S_{max} eq. 10*	S_{eq} eq. 5	MRQE (Model II) eq. 12	A eq. 10	D 10^6/cm^2 s^{-1} eq. 14
Sample in pH 7.4								
A	0.585	0.017	0.0293	8.2645	7.5449	0.0466	0.664	2.1436
B	0.620	0.013	0.0104	11.2360	10.0938	0.0528	0.586	2.5460
C	0.666	0.008	0.0368	16.6667	14.2589	0.0572	0.594	2.3844
D	0.735	0.004	0.1127	26.3158	21.0516	0.0721	0.565	2.7035
E	0.754	0.003	0.1479	34.4828	26.2782	0.0656	0.553	2.2796
F	0.759	0.003	0.0520	40.0000	29.9413	0.0628	0.542	2.0443
G	0.781	0.002	0.2593	43.4783	31.8673	0.0549	0.537	2.1269
Sample in pH 3.0								
A	0.608	0.014	0.0582	7.8740	7.1572	0.0440	0.740	2.1436
B	0.594	0.015	0.0454	7.4627	6.7465	0.0574	0.823	2.0117
C	0.591	0.015	0.0326	7.1942	6.4480	0.0621	0.916	1.7681
D	0.577	0.015	0.0183	6.7568	6.0431	0.0761	1.177	1.2437
E	0.576	0.015	0.0162	5.4945	4.8208	0.0786	1.508	1.1622
F	0.567	0.014	0.0455	4.9020	4.2162	0.0984	1.995	0.9903
G	0.563	0.015	0.0489	3.7037	3.2257	0.0891	2.387	1.0017
Sample in DW								
A	0.596	0.015	0.0561	7.4627	6.7962	0.0510	0.909	1.7605
B	0.612	0.012	0.0462	7.9365	7.1640	0.0469	0.847	2.1269
C	0.629	0.012	0.0333	8.4746	7.7119	0.0354	0.797	2.2538
D	0.640	0.011	0.0425	9.0909	8.2435	0.0321	0.772	2.3844
E	0.660	0.01	0.0446	9.5238	8.7065	0.0228	0.735	2.6895
F	0.658	0.009	0.0918	10.7527	9.4233	0.0516	0.888	2.1520
G	0.678	0.007	0.0335	11.9048	10.1961	0.0660	1.014	2.0443

*S_{max} = 1/B

valid for the first 60 % of swelling of crosslinked polymers in a chosen solvent. Eq. (13)[31] as applicable to cylindrical shape was used to calculate the diffusion coefficient D:

$$F = 4\left[\frac{Dt}{\pi L^2}\right]^{1/2} - \pi\left[\frac{Dt}{\pi L^2}\right] - \frac{\pi}{3}\left[\frac{Dt}{\pi L^2}\right]^{3/2} + \ldots \quad (13)$$

where D is the diffusion coefficient in cm^2 s^{-1}, t in seconds, L is the radius of cylindrical polymer sample in cm, and $F\left(\frac{S}{S_{eq}}\right)$ denotes the fraction of solvent diffusing into the hydrogel at time t. Neglecting higher order terms, Eq. 13 reduces to:

$$F = 4\left[\frac{Dt}{\pi L^2}\right]^{1/2} \quad (14)$$

For all hydrogels, F vs $t^{1/2}$ plots were obtained at different crosslinking ratios and coefficient of diffusion was estimated from the slope of the curves $\left(D = \frac{\pi L^2 (slope)^2}{16}\right)$. Some representative plots are shown in Figs. 6 and 7 for studies conducted in buffer of pH 7.4 and pH 3, using a nominal crosslinking ratio of 0.0091. The values of the diffusion coefficient D obtained from eq. (14) are listed in Tables 4–6. It is difficult to draw any correlation between the diffusion coefficient with nom-

Table 7 – *Effect of acrylic acid content on the swelling kinetics parameters of poly(AAm-co-AAc) hydrogels using Model III at X = 0.0046 mol mol^{-1}*

Sample	S_{eq} eq. 11	τ/h eq. 11	S_{eq} eq. 5	MRQE (Model III) eq. 12
Sample in pH 7.4				
A	9.3328	9.3594	9.7334	0.1184
B	12.7187	10.7000	13.1852	0.1232
C	18.4067	12.4005	18.4929	0.0989
D	27.1907	16.4842	27.4058	0.0796
E	31.7067	18.0700	31.5485	0.0629
F	38.5926	23.0285	37.4096	0.0831
G	43.2005	24.8145	41.7523	0.0700
Sample in pH 3.0				
A	10.1070	5.8438	10.4381	0.0780
B	8.8013	5.4030	9.0520	0.0725
C	8.1128	5.1499	8.3482	0.0729
D	7.2572	8.5973	7.4926	0.1107
E	6.7525	10.4699	6.9648	0.1305
F	5.9081	9.9989	6.1180	0.1308
G	4.6041	10.3956	4.6740	0.1323
Sample in DW				
A	10.5537	9.7140	10.6218	0.1070
B	13.2249	9.8561	13.5777	0.0929
C	18.0072	10.6851	18.4312	0.0729
D	21.5504	10.8437	22.2948	0.0474
E	23.3884	10.8286	24.1734	0.0417
F	24.4926	10.6726	25.1615	0.0358
G	26.1045	11.2717	27.1704	0.0401

Table 8 – *Effect of acrylic acid content on the swelling kinetics parameters of poly(AAm-co-AAc) hydrogels using Model III at X = 0.0069 mol mol^{-1}*

Sample	S_{eq} eq. 11	τ/h eq. 11	S_{eq} eq. 5	MRQE (Model III) eq. 12
Sample in pH 7.4				
A	7.9940	7.69	8.1115	0.1025
B	10.982	8.965	11.1077	0.1066
C	14.981	10.727	15.2816	0.0958
D	23.072	14.601	23.2964	0.0775
E	29.665	18.209	28.7989	0.0745
F	34.777	21.588	33.4139	0.0761
G	38.245	22.663	36.3272	0.0638
Sample in pH 3.0				
A	7.9873	7.0755	8.1839	0.0925
B	7.5201	7.9628	7.6567	0.1028
C	7.0355	7.9739	7.2150	0.1141
D	6.0448	8.0139	6.1913	0.1144
E	5.8172	9.6527	5.7046	0.1308
F	4.7415	10.4342	4.7912	0.1418
G	3.8884	10.6601	3.8935	0.1397
Sample in DW				
A	7.9506	7.7430	8.3371	0.1060
B	8.9333	7.8851	9.5655	0.0979
C	10.0773	10.2599	10.5453	0.1142
D	10.8922	12.7983	11.1071	0.1249
E	11.5700	13.3310	11.9105	0.0982
F	13.0644	14.6591	13.0239	0.0721
G	14.7296	16.3895	14.6817	0.0630

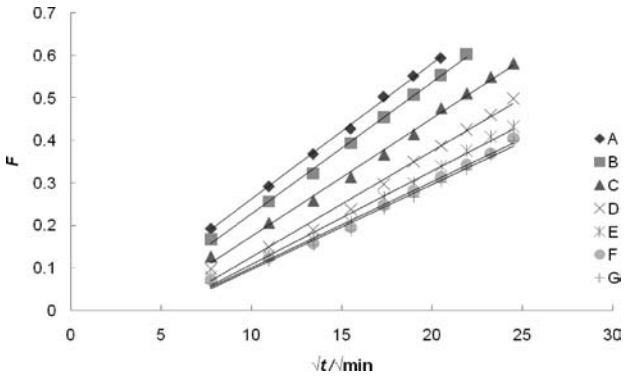


Fig. 6 – *F vs $\sqrt{t}$ curves for poly(AAm-co-AAc) hydrogels in buffer of pH 7.4 at nominal crosslinking ratio, X = 0.0091 mol mol^{-1}*

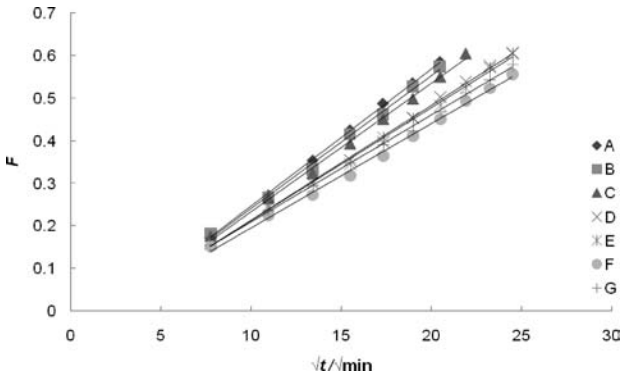


Fig. 7 – *F vs $\sqrt{t}$ curves for poly(AAm-co-AAc) hydrogels in buffer of pH 3.0 at nominal crosslinking ratio, X = 0.0091 mol mol^{-1}*

Table 9 – *Effect of acrylic acid content on the swelling kinetics parameters of poly(AAm-co-AAc) hydrogels using Model III at X = 0.0091 mol mol^{-1}*

Sample	S_{eq} eq. 11	τ/h eq. 11	S_{eq} eq. 5	MRQE (Model III) eq. 12
Sample in pH 7.4				
A	7.356	7.127	7.5449	0.1066
B	9.896	8.1370	10.0938	0.0986
C	13.938	10.719	14.2589	0.1013
D	21.202	14.390	21.0516	0.0878
E	26.917	17.400	26.2782	0.0859
F	30.567	19.191	29.9413	0.0880
G	32.446	20.043	31.8673	0.0823
Sample in pH 3.0				
A	6.993	7.458	7.1572	0.0999
B	6.629	7.811	6.7465	0.1073
C	6.332	8.2150	6.4480	0.1135
D	5.847	9.389	6.0431	0.1300
E	4.753	9.845	4.8208	0.1348
F	4.189	11.265	4.2162	0.1481
G	3.199	10.4701	3.2257	0.1454
Sample in DW				
A	6.455	8.009	6.7962	0.1111
B	6.873	8.012	7.1640	0.1062
C	7.306	7.842	7.7119	0.0969
D	7.7803	8.046	8.2435	0.0957
E	8.141	7.923	8.7065	0.0913
F	8.939	10.192	9.4233	0.1061
G	9.753	12.429	10.1961	0.1148

inal crosslink ratio and composition of hydrogel at pH 7.4 and DW, however, the diffusion coefficient for poly(AAm-*co*-AAc) hydrogels were lower than those for poly(AAm) hydrogels at pH 3.0.

Conclusions

In this study, swelling behavior of poly(AAm-*co*-AAc) hydrogels prepared by free radical polymerization in solution, has been investigated in buffer solutions of pH 7.4, pH 3.0 and distilled water. The crosslinked structure of hydrogel was found to have an important influence on the kinetics of swelling. The equilibrium swelling studies were used to determine important parameters of crosslinked structure of hydrogels, including the number average molecular mass between two consecutive crosslinks ($\overline{M}_c$). The results show that an increase in the nominal crosslinking ratio (X) in the reaction mixture leads to a decrease in the values of number average molecular mass between crosslinks ($\overline{M}_c$), and the distance between the macromolecular chains or pore size (ξ) decreases.

Hydrogels of poly(AAm-*co*-AAc) have shown a high degree of swelling in buffer of pH 7.4 and distilled water in comparison to poly(AAm) hydrogels due to the presence of hydrophilic groups which ionize in this media. Poly(AAm-*co*-AAc) hydrogel systems showed equilibrium degree of swelling in the range 10.09–41.75 at pH 7.4 and 7.16–27.17 in distilled water at different initial AAm/AAc mole ratio and crosslinking ratios. However, the values of equilibrium degree of swelling of poly(AAm) hydrogels were among 9.73–7.54 at pH 7.4 and 10.62–6.80 in distilled water at increasing crosslinking ratios. It was seen that swelling of poly(AAm-*co*-AAc) hydrogels decreased in buffer of pH 3.0 due to non-ionization of hydrophilic groups at this pH. The equilibrium degree of swelling of poly(AAm-*co*-AAc) varied between 9.05–3.22 in comparison to values of 10.43–7.15 for poly(AAm) hydrogels.

Equilibrium swelling data were used for the evaluation of swelling parameters like swelling exponent (n) and swelling coefficient (k). In all the experiments, swelling exponent n, (eq. (9)) was observed to be more than 0.5 indicating the presence of non-Fickian diffusion process in these gels.

ACKNOWLEDGEMENTS

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List of symbols

- A – reciprocal of the initial swelling rate
- B – inverse of equilibrium degree of swelling
- C_n – Flory characteristic ratio of the polymer
- D – diffusion coefficient, cm^2 s^{-1}
- F – fraction of solvent diffused into hydrogel at any time t
- l – length of C–C bond along the polymer backbone, nm
- L – radius of cylindrical polymer sample, cm
- $v_{2,s}$ – polymer volume fraction in the swollen state
- ξ – mesh size, μm
- m_t – mass of swollen hydrogel sample at time t, g
- m_0 – mass of dry hydrogel sample, g

m_{eq} – mass of swollen hydrogel sample at equilibrium, g
M_r – molecular mass of polymer repeat unit
MRQE – mean relative quadratic error
$\overline{M_c}$ – number average molecular mass between crosslinks, g mol^{-1}
$\overline{M_{c,t}}$ – theoretical number average molecular mass between crosslinks, g mol^{-1}
n – diffusional exponent
S – mass swelling or degree of swelling at any time t
S_{eq} – experimental value of equilibrium degree of swelling
S_{max} – calculated value of maximum (equilibrium degree of swelling) (eq. 10)
t – time, s
χ – Flory-Huggins polymer-water interaction parameter
$\bar{v}$ – specific volume of the polymer, cm^3 g^{-1}
V_d – volume of dry polymer, cm^3
V_s – volume of hydrogel after equilibrium swelling, cm^3
V_1 – molar volume of water, cm^3 mol^{-1}
m_a – mass of dry polymer in air, g
m_h – mass of dry polymer in *n*-heptane, g
$m_{a,s}$ – mass of swollen hydrogel in air after equilibrium swelling, g
X – nominal crosslinking ratio, mol mol^{-1}
k – swelling constant
ρ_h – density of *n*-heptane, g cm^{-3}
τ – rate parameter, h

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