

Ionizable Interpenetrating Polymer Networks of Carboxymethyl Cellulose and Polyacrylic Acid: Evaluation of Water Uptake

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ABSTRACT: A semi interpenetrating polymer network (IPN) of carboxymethyl cellulose (CMC) and crosslinked polyacrylic acid (PAA) has been prepared and its water-sorption capacity has been evaluated as a function of chemical architecture of the IPN, pH, and temperature of the swelling medium. The water uptake potential of the IPNs has also been investigated in inorganic salt containing aqueous solutions and simulated biological fluids. The IPN was

characterized by IR spectral analysis, and the network parameters such as average molecular weight between crosslinks (M_c), crosslink density (q), and number of elastically effective chains (V_c) have been evaluated by water-sorption measurements. © 2004 Wiley Periodicals, Inc. *J Appl Polym Sci* 93: 2054–2065, 2004

Key words: hydrogels; kinetics; diffusion; swelling

INTRODUCTION

Hydrogels are a novel class of hydrophilic materials that find exhaustive applications in biomedical fields.¹ A hydrogel is a network of hydrophilic polymers that can swell in water and hold a large amount of water while maintaining the structure. A three dimensional network is usually formed by crosslinking polymer chains by covalent bonds, hydrogen bonding, or physical entanglements.² Another approach to build up such hydrophilic networks could be by polymerizing a monomer in presence of a crosslinker and a preformed polymer that results in the formation of an interpenetrating polymer network (IPN).³ These hydrogels, which are also termed “hungry networks” or “intelligent polymers,” are among the best materials for a number of biomedical applications because of certain unique biophysical properties such as ease of fabrication to various geometrical forms, soft and rubbery texture, living tissue like resemblance, unusual stability to biofluids, minimum mechanical irritation to surrounding tissues, etc. Some of the prominent applications of hydrogels include artificial implants,⁴ dialysis membranes,⁵ and drug-delivery^{6,7}, as well as capacity to act as a carrier of a variety of bioactive agents like DNA,⁸ enzymes,⁹ agrochemicals,¹⁰ etc. Such loaded polymeric carriers swell and subsequently deliver a calculated amount of the entrapped

bioactive agents into the aqueous reservoirs. This process obviously forms the very foundation of drug-delivery technology and has been richly documented in the literature.^{11–13}

Stimuli-sensitive hydrogels have attracted considerable attention as intelligent materials in the biochemical and biomedical fields, since they can sense environmental changes and induce structural changes by themselves. In particular, pH-sensitive hydrogels that undergo swelling changes in response to pH of the surrounding medium have become increasingly important because of their potential applications in the development of targeted drug delivery systems.^{14,15} This not only improves therapeutic efficiency but also reduces or eliminates side effects of oral controlled drugs by reasonably delivering drugs to specific regions of the gastrointestinal (GI) tract. Among various methods of targeting the specific regions, the strategy utilizing pH changes within the GI tract¹⁶ is of current interest in controlled drug delivery systems.

Thus, realizing the significance of a pH-sensitive water swelling system, the present study aims at preparing semi interpenetrating polymer network (IPN) of carboxymethyl cellulose (CMC) and crosslinked polyacrylic acid (PAA) and investigating the water transport behavior of the synthesized IPN. CMC, a major commercial derivative of cellulose,¹⁷ is a highly water soluble anionic polysaccharide, which is widely used in pharmaceutical, cosmetic, and food applications.¹⁸ In the biomedical field, it is used to prevent postoperative adhesions¹⁹ and epidural scarring.²⁰ It also possesses the advantages of being biodegradable

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and economic. Moreover, its nontoxic, biocompatible, hydrophilic, chiral, and semirigid nature makes it a functional material of first choice. Selection of PAA as another component of IPN is well justified by its enormous use in the pharmaceutical industry.²¹

EXPERIMENTAL

Materials

Sodium salt of CMC (mol. wt. 90,000, viscosity of 4% solution at 25°C was 10.5 cps) was obtained from Sigma Aldrich Co. (St. Louis, MO) and used without any pretreatment. Acrylic acid (AA) was purchased from Research Lab, Mumbai (India) and was freed from inhibitor by vacuum distillation. N,N'-methylenebis acrylamide (MBA) (Central Drug House, Mumbai, India) was used as a crosslinking agent as received. Potassium persulphate (KPS) was obtained from Wilson Laboratories, Mumbai, India, and used as polymerization initiator. All other chemicals were of AR grade and triple distilled water was used throughout the experiments.

Preparation of IPN

1.5 g of CMC was dispersed into 20 mL of distilled water by constantly stirring for 2 h, and to this suspension were added 14.5 mM of AA, 0.129 mM of MBA, and 0.073 mM of KPS. The whole mixture was transferred into a Petri dish (diam. 7 cm, Corning glass Qualigens Fine Chemicals, Mumbai, India) and the Petri dish was kept at 50°C for 24 h. The whole mass solidified into a thin semitransparent film. The IPN so prepared was equilibrated with distilled water for 72 h so that the unreacted monomer and chemicals were leached out. The fully swollen IPN was cut into smaller circular discs (diam. 0.4 cm) and dried at room temperature for a week. The IPN buttons so formed were stored in airtight polyethylene bags.

IR spectra

The IR spectral analysis of dry IPN film was carried out on a Perkin-Elmer Spectrophotometer (Paragon 1000, FTIR Wellesley, MA).

Swelling measurements

The extent of swelling was determined by a conventional gravimetric procedure. In brief, a preweighed piece (0.1 g) of hydrogel was immersed into a thermostated triple distilled water bath and allowed to swell till the equilibrium swelling. The swollen piece was then taken out and pressed gently in between the two filter papers to remove excess water and finally weighed in a sensitive balance. The degree of swelling

was expressed in terms of the swelling ratio as given below:

$$\text{Swelling Ratio} = \frac{\text{Weight of the swollen gel}}{\text{Weight of the dry gel}} \quad (1)$$

All swelling experiments were performed in replicate number and a fair reproducibility was obtained.

Kinetics of swelling

Most often, the dynamics of water sorption process has been investigated either by monitoring the change in physical dimensions of the swelling hydrogel or by knowing the amounts of water imbibed by the hydrogel at various time periods. In the present work also, the latter procedure has been followed. For this purpose the swollen hydrogel was taken out at different time intervals and its weight was recorded. For the kinetic analysis of the results the following equation was applied²²:

$$M_t/M_\infty = kt^n \quad (2)$$

where k is the swelling rate front factor and n is the swelling exponent; and M_t and M_∞ are the water intakes at time t and equilibrium time, respectively. The value of n in the above equation provides an indication of the water transport mechanism. When $n = 0.5$, the swelling process is of Fickian nature and is diffusion controlled, while the value of n in between 0.5 and 1.0 suggests non-Fickian diffusion or more specifically, anomalous diffusion. When n becomes exactly equal to unity, then the diffusion is termed Case II diffusion. In some cases, the value of n has been found to exceed unity and it has been termed super Case II transport.

For ordinary diffusion, Fick's law is the appropriate constitutive equation for the mass transfer flux, and a mutual diffusion coefficient can be defined relative to the polymer-fixed frame of reference. For a plane sheet, the diffusion coefficient D can be calculated from the following equation:

$$M_t/M_\infty = 1 - \sum_{n=0}^{\infty} \{8/(2n+1)^2\pi^2\} \times \exp\{-(2n+1)^2\pi^2(Dt/L^2)\} \quad (3)$$

where t is time and L is the initial thickness of the dry IPN disc. Although the equation is readily evaluated using a spreadsheet program, it is instructive to examine the short-time limiting expression as well:

$$\frac{M_t}{M_\infty} = (4/\pi^{0.5})(Dt/L^2)^{0.5} \quad (4)$$

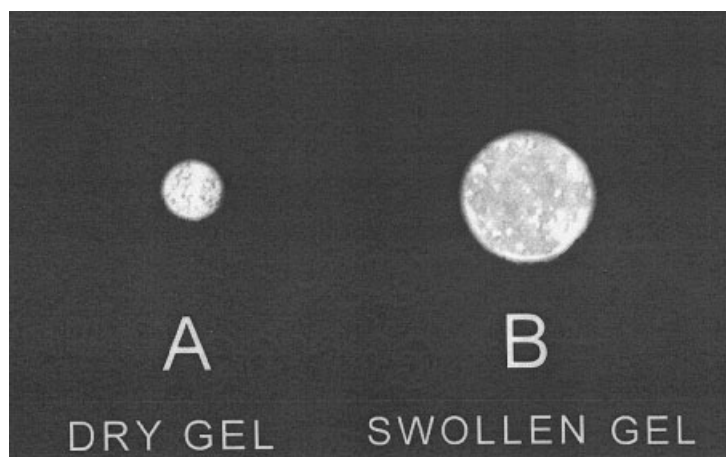


Figure 1 A photograph depicting (A) dry gel, and (B) swollen gel.

The above equation clearly implies that a plot between M_t/M_∞ and \sqrt{t} will yield a straight line and, from the slope of the graph, the value of diffusion constant D can be calculated.

Penetration velocity measurements

The penetration velocity for each IPN composition was determined by the weight gain method as described by Peppas and Franson.²³ The penetration velocity was calculated from the slope of the initial portion of the penetration uptake curve from the equation:

$$v = \left(\frac{dM_g}{dt} \right) \cdot \left(\frac{1}{\rho} \right) \left(\frac{1}{2A} \right) \quad (5)$$

where v denotes the penetration velocity, dM_g/dt denotes the slope of weight gain versus time curve, and ρ denotes the density of the IPN. A denotes the area of one face of the IPN disc and the factor 2 accounts for the fact that penetration takes place through both the faces.

Swelling in physiological fluids

For studying the water transport behavior of IPNs in biological media, the following fluids (100 mL) were simulated:

- Saline Water : 0.9 g NaCl
- Synthetic Urine : 0.8 g NaCl, 0.10 g $MgSO_4$, 2.0 g urea, and 0.06 g $CaCl_2$
- KI: 15 g
- Urea: 5 g
- D-glucose: 5 g

RESULTS AND DISCUSSION

Appearance of the IPN

A photograph of dry and swollen IPN is depicted in Figure 1.

Characterization of IPNs

IR spectra

The IR spectra of the semi IPN composed of CMC and crosslinked PAA chains is depicted in Figure 2.

The spectra clearly show a broad band around 3500 cm^{-1} , which is typical of hydrogen bonded (bridged) O-H stretch from alcoholic OH of CMC and PAA and bound water in the IPN. The observed band also implies for N-H stretching due to MBA (crosslinker). In the spectra shown, two prominent peaks at 1653 and 1391 cm^{-1} were observed for the asymmetrical and symmetrical stretching of COO^- groups due to CMC. The methylene groups (CH_2) of PAA are quite evident at 2928 cm^{-1} due to asymmetrical stretching mode of C-H bond. As can be seen in the spectra, a sharp band occurs at 2366 cm^{-1} , which could be assigned to the sodium salt of CMC, which gives an additional band at 2366 cm^{-1} in addition to the two characteristic carbonyl absorption bands. The spectra also indicate the presence of MBA at 1032 cm^{-1} (C-N stretching).

Network studies

One of the most important structural parameters characterizing crosslinked polymer is the average molecular mass between crosslinks, which is directly related to the crosslink density. The magnitude of M_c significantly affects the physical and mechanical properties of crosslinked polymers and its determination has great practical significance. Equilibrium swelling is

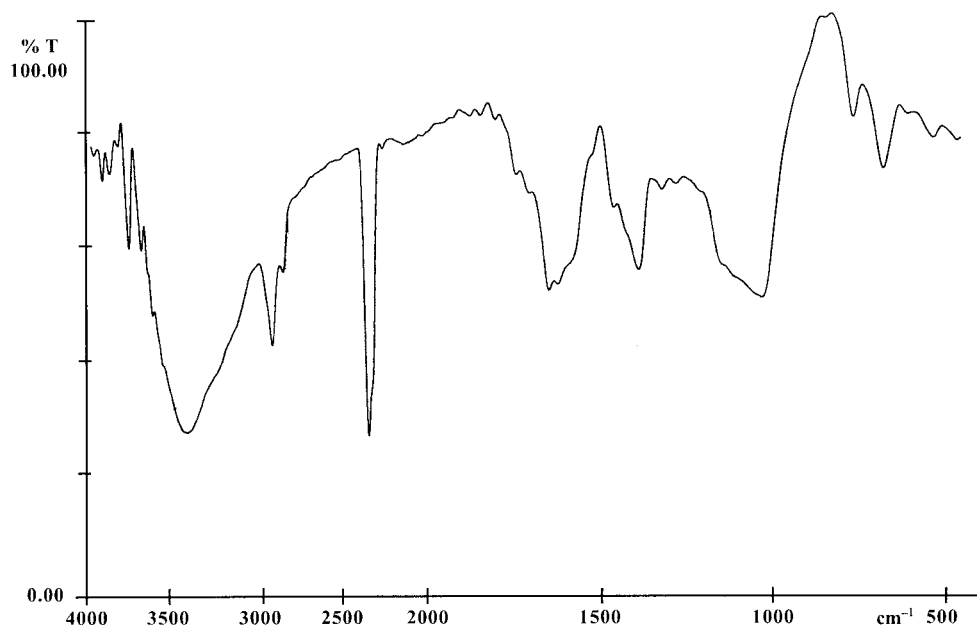


Figure 2 IR spectra of the IPN.

widely used to determine M_c . Early research by Flory and Rehner laid the foundation for the analysis of equilibrium swelling. According to the theory of Flory and Rehner, for a perfect network,

$$M_c = -V_1 d_p \frac{(V_s^{1/3} - V_{s/2})}{\ln(1 - V_s) + V_s + \chi V_s^2} \quad (6)$$

where M_c is the number average molar mass of the chain between crosslinks; V_1 is the molar volume (ml mol^{-1}); d_p is the polymer density (g ml^{-1}); V_s is the volume fraction of polymer in the swollen IPN; and χ is the Flory-Huggins interaction parameter between solvent and polymer.²⁷

The swelling ratio is equal to $1/V_s$. Here, the crosslink density q is defined as the mole fraction of crosslinked units.

$$q = M_0/M_c \quad (7)$$

where M_0 is the molar mass of the repeating unit.

Other authors defined a crosslink density, V_e , as the number of elastically effective chains totally included in a perfect network; per unit volume is simply related to q since

$$V_e = d_p N_A / M_c \quad (8)$$

where N_A is the Avogadro number. Then

$$V_e = d_p N_A q / M_0 \quad (9)$$

The values of V and χ were taken from related literature.^{28,29} The density d_p of the IPN was determined to be 0.33 g cm^{-3} .

The values of M_c , q , and V_e of the networks have been calculated and summarized in Table I for varying IPN compositions.

Mechanism of water transport

The IPN in the present case could be regarded as a network of CMC and crosslinked PAA chains bonded

TABLE I
Data Showing the Network Parameters of the IPNs
of Varying Compositions

CMC (gm)	AA (mM)	MBA (mM)	KPS (mM)	M_c	$q \times 10^3$	$v_e \times 10^{-19}$
1.0	14.5	0.129	0.073	1592.60	45.2	12.47
1.5	14.5	0.129	0.073	28434.52	2.5	0.69
2.0	14.5	0.129	0.073	9301.50	7.7	2.19
2.5	14.5	0.129	0.073	8813.95	8.1	2.25
1.5	7.3	0.129	0.073	3320.00	21.7	5.98
1.5	14.5	0.129	0.073	28434.52	2.5	0.69
1.5	21.8	0.129	0.073	1592.60	45.2	12.47
1.5	36.4	0.129	0.073	903.10	79.7	22.00
1.5	14.5	0.064	0.073	9895.74	7.2	2.00
1.5	14.5	0.129	0.073	28434.52	2.5	0.69
1.5	14.5	0.194	0.073	3151.80	22.8	6.30
1.5	14.5	0.259	0.073	1929.87	37.3	1.02
1.5	14.5	0.129	0.073	28434.52	2.5	0.69
1.5	14.5	0.129	0.110	6231.52	11.5	3.18
1.5	14.5	0.129	0.147	6229.36	11.5	3.19
1.5	14.5	0.129	0.184	2222.96	32.4	8.94

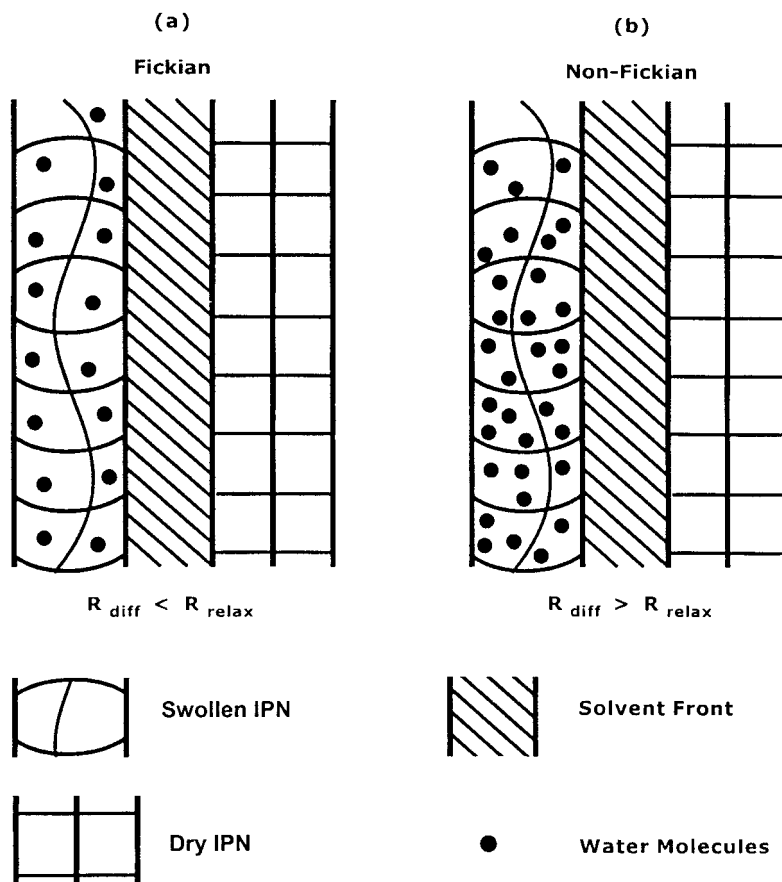


Figure 3 A hypothetical model describing swelling of the IPN (a) Fickian, (b) non-Fickian.

to each other via physical type of forces and, thus, creating free volumes of varying meshes for accommodating penetrant water molecules. The dynamic nature of the water sorption process could be realized by considering the situation when the IPN contacts a thermodynamically compatible solvent, such as water. As the penetrant solvent invades the IPN surface, a moving front is observed that clearly separates the unsolvated glassy polymer region ahead of the front from the swollen and rubbery gel phase behind it.²⁴ Just ahead of the front, the presence of solvent plasticizes the polymer and causes it to undergo a glass to rubber transition.²⁵ Now, the following possibilities could arise:

- (i) If the glass transition temperature (T_g) of the polymer is well below the experimental temperature, the polymer will be in the rubbery state and the IPN chains will have a greater mobility that allows an easier penetration of water molecules.²⁶ This clearly results in a Fickian diffusion (Case I), which is characterized by a solvent diffusion rate R_{diff} slower than the polymer relaxation rate, R_{relax} ($R_{diff} \ll R_{relax}$).
- (ii) If the experimental temperature is below T_g , the IPN chains may not be sufficiently mobile to

permit immediate penetration of the solvent in the polymer core. This gives rise to a non-Fickian diffusion process that includes Case II diffusion and anomalous diffusion depending on the relative rates of diffusion and chain relaxation (for Case II, $R_{diff} \gg R_{relax}$ and for anomalous, $R_{diff} \sim R_{relax}$).

Both the possibilities of diffusion and relaxation controlled water-transport process are modeled in Figure 3.

Effect of CMC on swelling

Inclusion of a hydrophilic polymer into a gel network is normally expected to enhance the water-sorption capacity of the hydrogel. In the present investigation, too, the influence of increasing CMC content in the feed mixture of the IPN has been studied on the swelling characteristics of the IPN by varying the amount of CMC in the range 1.0 to 2.5 g. The results are displayed in Figure 4, which indicate that when CMC content is increased up to 1.5 g, the swelling ratio increases; while beyond 1.5 g of CMC content, the water sorption capacity of network decreases.

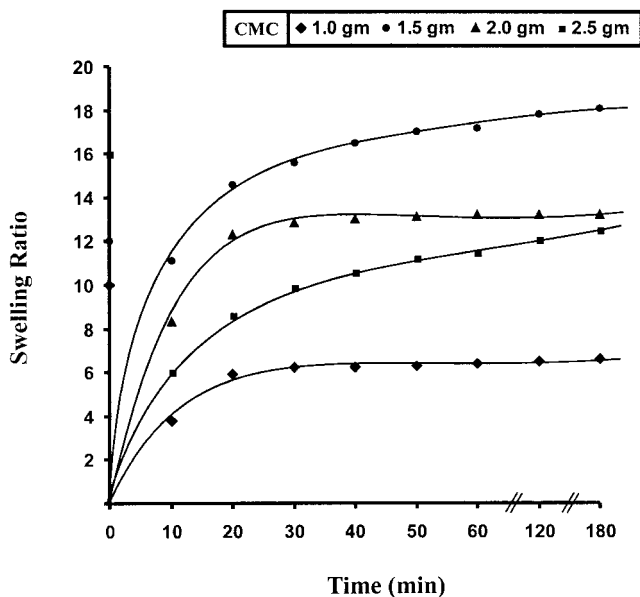


Figure 4 Effect of CMC content of the IPNs on their swelling ratio for a definite IPN composition. [Acrylic acid] = 14.5 mM, [MBA] = 0.129 mM, [KPS] = 0.073 mM, Temp. = 23 ± 0.2°C.

The observed results may be attributed to the fact that with initial increase in concentration of CMC, the hydrophilicity of the IPN also increases, which obviously results in an enhanced water sorption. However, beyond 1.5 g of CMC content in the IPN, the density of macromolecular chains becomes so high that penetration of water molecules into the IPN becomes rather difficult, and this clearly results in a decreasing swell-

ing ratio of the IPN. The swelling results are further supported by both the network parameters and numerical values of diffusion constants (D) and penetration velocities of water molecules as summarized in Tables I and II, respectively. It is clear from the tables that all the above-mentioned parameters increase when CMC increases from 1.0 to 1.5 g, while a decrease in above parameters is obtained beyond 1.5 g of CMC content in the IPN.

Effect of AA

The swelling ratio (Q) of a hydrogel can be best quantified by the following Flory’s equation,

$$Q^{5/3} = [(i/2V_u S^{1/2}) + (1/2 - X_1)/v_1]^{1/2} / (v_e/v_o) \quad (10)$$

where i/V_u is the concentration of fixed charge referred to the unswollen IPN; S, the ionic concentration in the external solution; $(1/2 - X_1)/v_1$, the affinity of the hydrogel with water; and v_e/v_o , the crosslinked density of the hydrogel. Thus, Q is a function of the ionic osmotic pressure, crosslinked density, and affinity of the hydrogel with water. In the present study, the effect of ionic monomer, AA, has been investigated on the degree of water sorption by varying its concentration in the range 7.3 to 36.4 mM in the feed mixture of the IPN. The results are displayed in Figure 5, which reveals that the swelling ratio increases from 7.3 to 14.5 mM of AA, while beyond 14.5 mM there is observed a constant fall in the extent of swelling. The results could be attributed to the reason that with increasing AA concentration in the IPN, the concen-

TABLE II
Various Kinetic Parameters of the Water Sorption Process for Different Compositions of the IPNs

CMC (gm)	AA (mM)	MBA (mM)	KPS (mM)	Temp. (°C)	n	D × 10 ⁶ cm ² s ⁻¹	v × 10 ⁻³ cm s ⁻¹	Mechanism
1.0	14.5	0.129	0.073	23	0.70	12.0	10.2	Anomalous
1.5	14.5	0.129	0.073	23	0.83	27.0	21.7	Anomalous
2.0	14.5	0.129	0.073	23	0.74	11.3	15.2	Anomalous
2.5	14.5	0.129	0.073	23	0.70	5.9	10.0	Anomalous
1.5	7.31	0.129	0.073	23	0.59	17.0	9.7	Anomalous
1.5	14.5	0.129	0.073	23	0.83	27.0	21.7	Anomalous
1.5	21.8	0.129	0.073	23	0.82	10.6	7.1	Anomalous
1.5	36.4	0.129	0.073	23	0.82	11.7	4.1	Anomalous
1.5	14.5	0.064	0.073	23	0.80	14.8	11.8	Anomalous
1.5	14.5	0.129	0.073	23	0.83	27.0	21.7	Anomalous
1.5	14.5	0.194	0.073	23	0.87	14.6	8.9	Anomalous
1.5	14.5	0.259	0.073	23	0.83	12.6	6.8	Anomalous
1.5	14.5	0.129	0.013	23	0.83	27.0	21.7	Anomalous
1.5	14.5	0.129	0.110	23	0.77	8.6	15.2	Anomalous
1.5	14.5	0.129	0.147	23	0.90	4.7	16.9	Anomalous
1.5	14.5	0.129	0.184	23	0.98	4.8	15.7	Case II
1.5	14.5	0.129	0.073	5	0.96	12.1	6.6	Case II
1.5	14.5	0.129	0.073	10	0.90	20.0	12.0	Anomalous
1.5	14.5	0.129	0.073	23	0.83	27.0	21.7	Anomalous
1.5	14.5	0.129	0.073	35	0.96	12.6	10.8	Case II

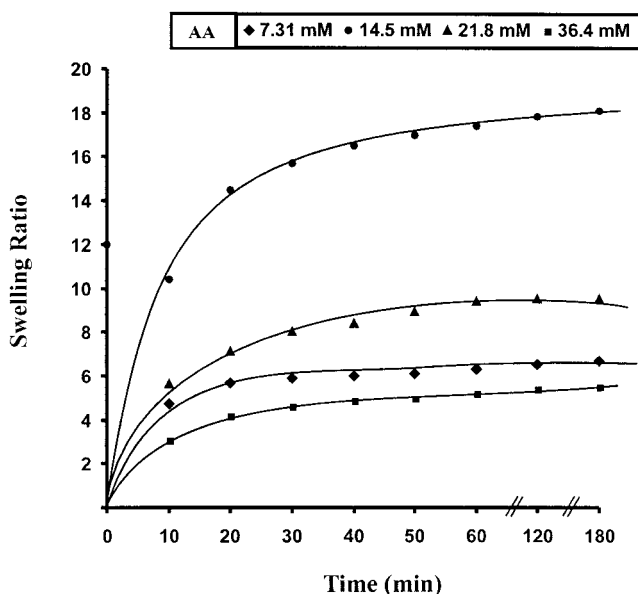


Figure 5 Effect of AA content of the IPNs on their swelling ratio for a definite IPN composition [CMC] = 1.5 g, [MBA] = 0.129 mM, [KPS] = 0.073 mM, Temp. = $23 \pm 0.2^\circ\text{C}$.

tration of fixed charges, that is, i/V_u increases within the gel and as predicted from the above equation, the swelling ratio increases. Another plausible explanation may be that with increasing number of carboxylate ions (COO^-) along the crosslinked PAA chains, the electrostatic repulsion among the COO^- groups become operative and results in a loosening of the network chains causing an enhanced sorption.

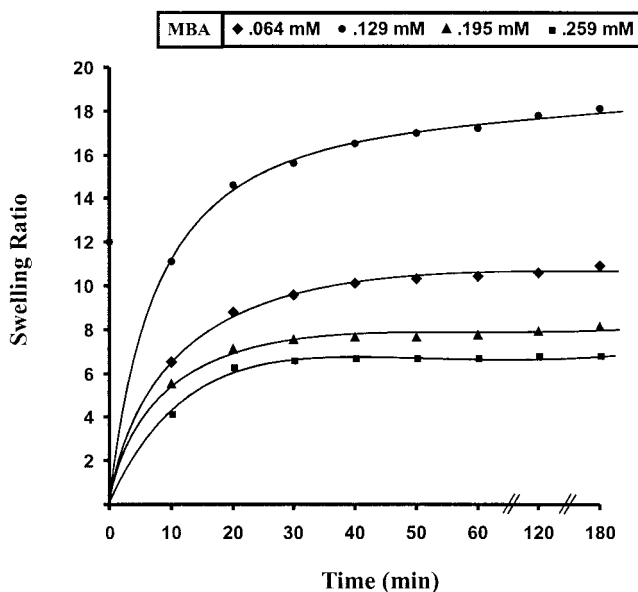


Figure 6 Variation in the swelling ratio with varying MBA content of the IPN for a definite IPN composition [CMC] = 1.5 g, [Acrylic acid] = 14.5 mM, [KPS] = 0.073 mM, Temp. = $23 \pm 0.2^\circ\text{C}$.

However, beyond 13.8 mM concentration of AA, the number of PAA chains becomes so great that the IPN becomes densely packed, resulting in a reduction in mesh sizes of the network. This obviously lowers the diffusion of solvent molecules into the IPN and results in a decreasing penetration velocity of the solvent front. Both of these parameters lead to a decreased swelling ratio at higher AA concentration. The structural parameters of the IPN and the kinetic parameters of swelling support the observed findings.

Effect of crosslinker

A change in crosslinked density of a hydrogel normally results in an appreciable change in water sorption property of the hydrogel. *N,N'*-methylene bis acrylamide (MBA), which is a hydrophilic monomer, also has been employed as a crosslinker in the present study. The effect of MBA on the water sorption capacity of IPN has been investigated by varying its concentration in the range 0.064 to 0.259 mM and the results are shown in Figure 6. The results clearly reveal that the swelling ratio of IPN increases with increasing concentration of MBA from 0.064 to 0.128 mM, while beyond 0.128 mM a significant fall in water sorption is noticed.

The observed results may be explained by the fact that with increasing MBA, the hydrophilicity of the network slightly increases, which, in turn, enhances water sorption. The observed fall in swelling ratio beyond 0.128 mM of MBA may be explained on the basis of the fact that with increasing MBA content in

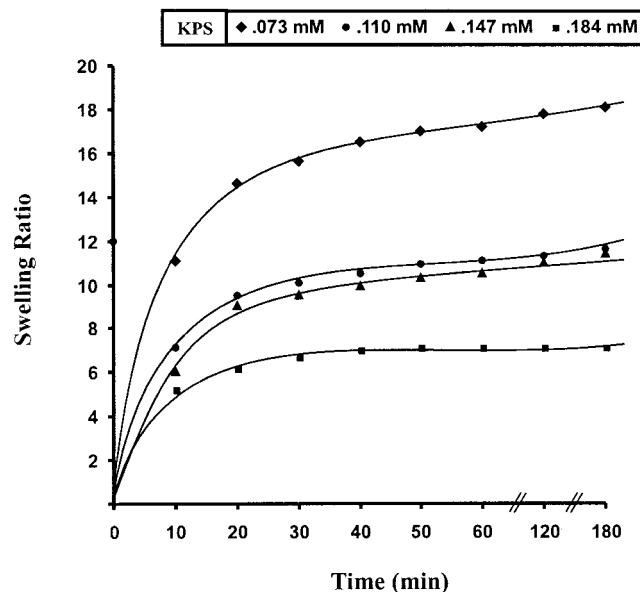


Figure 7 Effect of initiator (KPS) content of the IPNs on their swelling ratio for a definite IPN composition. [CMC] = 1.5 g, [Acrylic acid] = 14.5 mM, [MBA] = 0.129 mM, Temp. = $23 \pm 0.2^\circ\text{C}$.

the IPN, the crosslinked density of the IPN increases, which results in narrow mesh sizes of the network, which slows down the penetration of water molecules into the IPN and, therefore, decreases the swelling ratio. Alternatively, it has also been reported³⁰ that introduction of crosslinker results in an increased glass transition of the polymer, which obviously lowers the swelling ratio. The observed results are in excellent agreement with the quantitative parameters summarized in Tables I and II.

Effect of initiator on swelling

Initiator has a direct impact on the physical properties of a polymer as a change in its concentration does result in a change in the molecular weight of the end polymer. In the present case, potassium persulphate has been used as a polymerization initiator and its concentration has been varied in the range 0.073 to 0.180 mM in the feed mixture of the IPN. The results are displayed in Figure 7, which clearly indicates that the swelling ratio constantly decreases with increasing concentration of initiator (KPS). The results are quite expected and may be explained by the fact that increased initiator concentration results in a lower molecular weight of the polymer, which, in turn, produces network of small mesh sizes. In other words, this also implies for a greater crosslinked IPN, which is evident from the network parameters summarized in Table I.

Effect of pH on swelling

pH responsive hydrogels constitute an important class of biomaterials that play a significant role in designing targeted drug delivery.³¹ The underlying principle for targeted drug delivery is the pH controlled swelling of hydrogel, which normally results from the change in relaxation rate of network chains with changing pH of the medium. In the present study, the influence of pH on the water sorption capacity of IPN has been investigated by varying the pH of the swelling medium in the range 1.5 to 11.0. The results are displayed in Figure 8, which indicates that the swelling ratio increases with increasing pH of the medium in the range 1.5 to 6.5, while beyond 6.5, a fall in the water sorption is noticed. The results may be explained as below:

- (i) When pH of the medium is low, the carboxylic groups of CMC and PAA are almost in undissociated state and, therefore, the two macromolecular chains are tightly held-up via H-bonding forces. When pH of the swelling medium rises, the carboxylic groups dissociate into negatively charged carboxylate ions (COO^-) and, thus, as a result, H-bonds are broken, thereby relaxing the network chains. This obviously

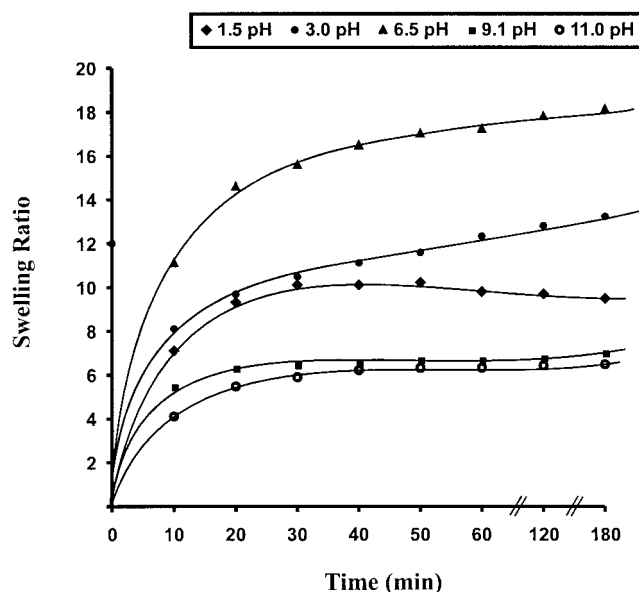


Figure 8 Variation in swelling ratio of the IPN with pH of the swelling medium for a definite IPN composition. [CMC] = 1.5 g, [Acrylic acid] = 14.5 mM, [MBA] = 0.129 mM, [KPS] = 0.073 mM, Temp. = $23 \pm 0.2^\circ\text{C}$.

leads to a faster diffusion of water molecules into the network and the swelling ratio increases. It is also likely that because of the repulsion operating between the carboxylate anionic groups, the network chains get relaxed and the swelling ratio increases.

- (ii) When the pH exceeds 6.5 and enters alkaline range, the number of carboxylate anions reaches at maximum and produce greater repulsion within the IPN matrix. This obviously results in much greater relaxation of macromolecular chains of the IPN, which causes expulsion of water molecules from within the IPN into the swelling medium due to the weakening of hydrogen bonds established between water molecules and IPN chains. This obviously results in a decrease in swelling ratio of the IPN. The expulsion of bound water molecules at large relaxation of macromolecular chains has also been observed by Lee and Chen³² while studying the effect of increasing temperature on the swelling of the copolymeric hydrogels.

Effect of salts on swelling

The presence of salts in the swelling medium is an important event in the biomedical field. In principle, changes in the swelling behavior due to the presence of a salt can affect the mechanical properties of the material as well as the "tortuosity" of the matrix, which gives rise to different diffusion coefficients of drug release.³³

The interaction between polymer and solvents is greatly altered by salts. For instance, the presence of salt ions may enhance polymer/water mixing conditions (salting-in) or may impair them (salting out). Partial effects such as electrostatic ones, water structuring due to microsolute (salts can be structure makers or structure breakers), association of the hydrophobic sites of the macromolecule, and formation of complexes between polymer and ions contribute to the overall effect.³⁴

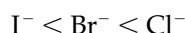
Apart from the above-mentioned possible consequences of salt ions, they also affect osmotic pressure of the swelling system resulting from the difference between the ionic concentration of interior of the IPN and external solution. According to Donnan equilibrium theory, the osmotic pressure is mainly contributed by π_{ion} as given below,³⁵

$$\pi_{\text{ion}} = RT \sum_i (C_i^g - C_i^s) \quad (11)$$

where C_i is the mobile ion concentration of species i and superscripts "g" and "s" represent gel and solution phases, respectively. The above equation clearly reveals that the larger the difference between the ionic concentrations, the greater would be the osmotic pressure and consequently the extent of swelling also.

Effect of anions

In the present study, halides of potassium have been added into the swelling medium and their effect on swelling ratio has been noticed. The results are shown in Figure 9, which clearly indicates that the swelling ratio of the IPN decreases with increasing ionic concentration, and the added anions obey the following order of increasing effectiveness in suppressing the swelling ratio,



The observed results are quite obvious as with increasing concentration of salt ions, the numerical value of the term $(C_i^g - C_i^s)$ gives a decreasing value, which results in a lower degree of swelling.

The maximum depression in swelling ratio is caused by Cl^- ions, whereas the minimum by I^- ions. The order of effectiveness may be explained by the reason that the Cl^- ions, being smallest in size among the three halide ions, may diffuse into the interior of the IPN and thus increase the ionic concentration (C_i^g) within the IPN. This obviously tends to swell the network. On the other hand, in the case of the largest sized I^- ions, their diffusion into the network results in a greater swelling of the network because of existing repulsion forces between the anionic network

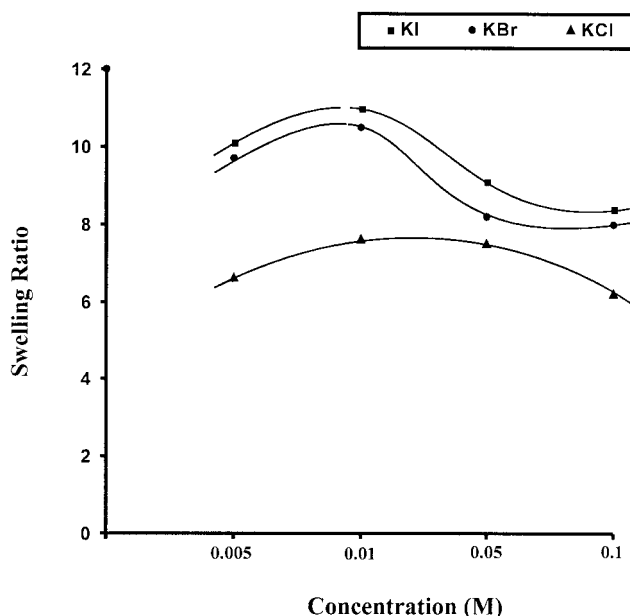


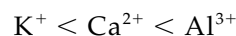
Figure 9 Effect of addition of anions of potassium on the swelling ratio of the IPN of definite composition. [CMC] = 1.5 g, [Acrylic acid] = 14.5 mM, [MBA] = 0.129 mM, [KPS] = 0.073 mM, Temp. = $23 \pm 0.2^\circ\text{C}$.

chains and I^- ions. This, as a result, produces a minimum decrease in swelling ratio.

It is worth mentioning here that in the case of addition of Cl^- ions, a slight increase in swelling ratio is observed in the initial concentration range of added salt (KCl). This is due to the reason that because of greater diffusion of Cl^- ions into the IPN, the ionic concentration (C_i^g) within the gel exceeds that in the outer solution (C_i^s). This clearly increases the swelling ratio to a marginal degree.

Effect of cations

For investigating the influence of cations on the water sorption behavior of the IPNs, chloride salts of K^+ , Ca^{2+} , and Al^{3+} were added in the concentration range 0.005M to 0.1M and the observed findings are shown in Figure 10. The results indicate that with K^+ and Ca^{2+} ions, the swelling ratio slightly increases in the lower concentration range of added salts (from 0.005 to 0.01M), while beyond 0.01M, the swelling ratio decreases. In the case of Al^{3+} ions, a constant decrease in swelling ratio is noticed. The order of increasing effectiveness at higher concentration (0.1M) is as follows:



The results may be explained by the fact that in the case of K^+ and Ca^{2+} ions in the lower concentration range, K^+ and Ca^{2+} ions diffuse into the interior of the

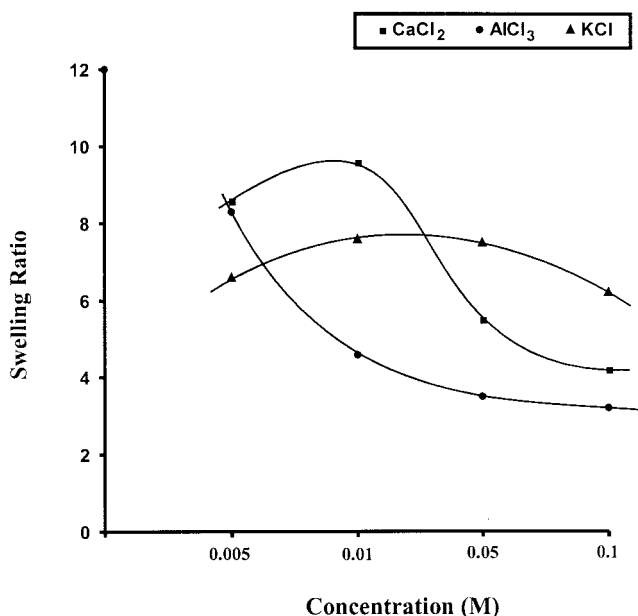


Figure 10 Effect of addition of cations of chlorides on the swelling ratio of the IPN of definite composition. [CMC] = 1.5 g, [Acrylic acid] = 14.5 mM, [MBA] = 0.129 mM, [KPS] = 0.073 mM, Temp. = $23 \pm 0.2^\circ\text{C}$.

IPN and may increase the ionic concentration (C_i^g), thus resulting in a marginal increase in the swelling ratio. However, at higher salt concentration the concentration term (C_i^g) increases significantly, thus decreasing the term ($C_i^g - C_i^s$), which brings about a fall in the swelling ratio. On the contrary, the behavior of Al^{3+} ions is altogether different as their addition results in a constant fall in the swelling ratio. The possible explanation may be that because of relatively larger size, they may not diffuse into the IPN and thus constantly lower the value of ($C_i^g - C_i^s$), causing a fall in the swelling ratio. Similar type of results has also been published elsewhere.³⁶

Effect of temperature on swelling

The temperature of the swelling medium influences water uptake by hydrogels in many ways. A rise in temperature enhances water diffusion and segmental mobility of macromolecular chains, which results in a greater degree of swelling. On the contrary, greater thermal energy may also detach bound water molecules and thus may suppress swelling. In the present study, the effect of temperature on swelling ratio of the IPN has been studied in the range 5 to 35°C . The results are displayed in Figure 11, which shows that the swelling ratio constantly increases up to 23°C while beyond it, a fall is observed. The results are quite obvious and may be interpreted on the basis of the explanation given above. The results obtained are further supported by the kinetic data as summarized

in Table II. Some workers have reported a constant fall in water uptake with increasing temperature³⁷; however, no such observation was noticed in the present case.

To quantify the temperature effect, the Gibbs–Helmholtz equation can be applied, according to which

$$\frac{d \ln(M_\infty)}{d(1/T)} = -\Delta H_m/R \quad (12)$$

where R is a gas constant and ΔH_m is the enthalpy of mixing between the dry polymer and an infinite amount of water. When M_∞ is plotted against the reciprocal of the swelling temperature ($1/T$), a straight line is obtained (not shown). The value of ΔH_m was calculated to be 2.04 KJ/mol.

Effect of simulated biofluids on swelling

It is well established, both theoretically and experimentally, that the swelling is a net result of osmotic and the restoring elastic pressure. The presence of solute in the surrounding aqueous medium is capable of tilting this balance,³⁸ which may result in either a decrease or increase in swelling. In the present study, the IPN sample of a definite composition was swollen in different biofluids and the results are shown in Figure 12. The results clearly indicate that a substantial fall in the swelling ratio is noticed in all biofluids. The results obtained could be explained on the basis of the increased concentration of various ionic species in

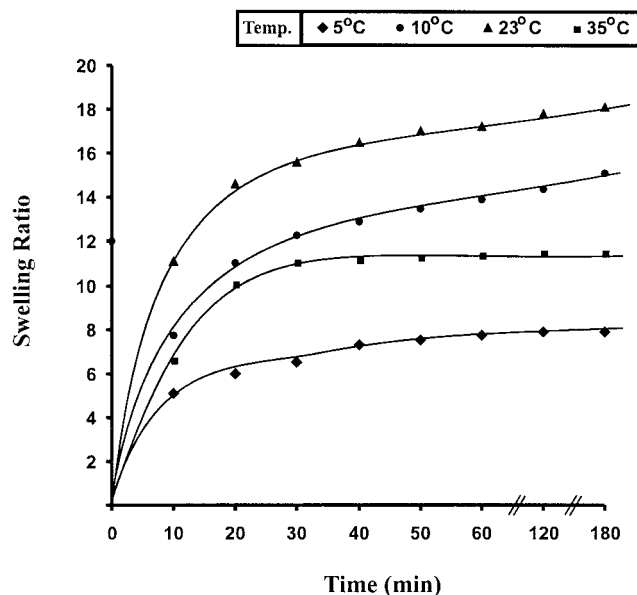


Figure 11 Effect of temperature on the swelling ratio of the IPN of definite composition. [CMC] = 1.5 g, [Acrylic acid] = 14.5 mM, [MBA] = 0.129 mM, [KPS] = 0.073 mM.

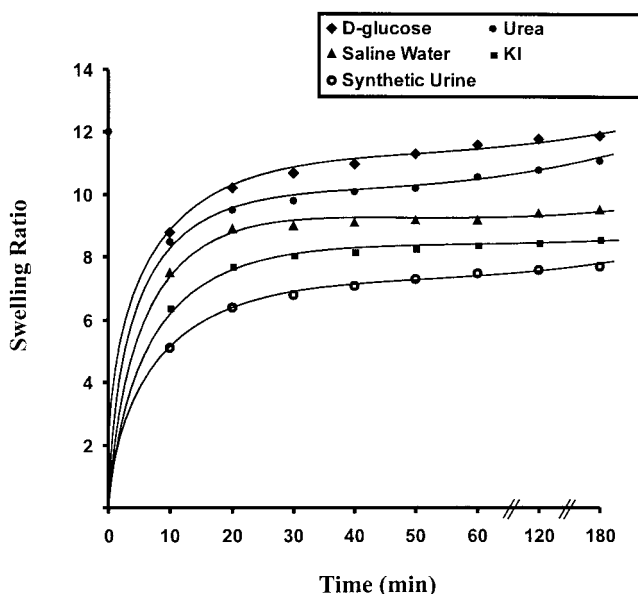


Figure 12 Swelling of the IPN in various simulated biological fluids. [CMC] = 1.5 g, [Acrylic acid] = 14.5 mM, [MBA] = 0.129 mM, [KPS] = 0.073 mM, Temp. = $23 \pm 0.2^\circ\text{C}$.

the external medium, which will obviously lower the swelling ratio.³⁵ In the case of urea, its capacity to break hydrogen bonds between water molecules and IPN chains may be responsible for the lower amount of water uptake.³⁹

Analysis of kinetic data

Dynamic water uptake measurements are important not only from kinetic considerations but also from the mechanistic point of view. As mentioned previously, the value of n , which is determined by Equation 2, indicates whether the water transport is Fickian or non-Fickian in nature. The value of n has been calculated for different IPN compositions and summarized in Table II. The following paragraph discusses the mechanistic insights of the water transport process under varying experimental protocols:

It is clear from the Table that for IPN compositions prepared at varying concentrations of CMC, AA, and MBA, the value of n fluctuates in between 0.5 and 1.0, thus suggesting an anomalous type of swelling process that is characterized by almost equal rates of solvent (water) diffusion and chain relaxation ($R_{\text{diff}} \sim R_{\text{relax}}$). However, for IPNs prepared at varying KPS concentrations, the value of n increases in the anomalous region; and at 0.18 mM of KPS, the value of n becomes almost unity, thus indicating a Case II transport process, the most desirable condition in pharmacokinetics. Similarly, when temperature of swelling medium is low (5°C), the process of water uptake is determined by relaxation of IPN chains and about unity value of n is obtained. However, upon further

increasing the temperature up to 23°C , the diffusion of water molecules becomes faster and the rates of chain relaxation and solvent diffusion become again almost equal, giving rise to an anomalous type of swelling process. But at still higher temperature (35°C), the value of n again acquires a unity value, implying a Case II transport process, that is, relaxation controlled swelling process. This appears quite justified also as at much higher temperature, diffusion of water molecules becomes faster than chain relaxation and thus a relaxation controlled swelling is obtained. It is worth mentioning here that at 35°C , a lower value of D and v is obtained, which may be attributed to the reason that at this temperature water molecules start detaching from IPN chains, and may cause frictional resistance to the invading water molecules.

CONCLUSION

Interpenetrating polymer network (IPN) of CMC and crosslinked PAA forms highly hydrophilic, ionizable, and pH sensitive hydrogel matrix, which shows enormous water uptake behavior. The water sorption capacity of the IPN is greatly dependent on the chemical architecture of the hydrogel matrix.

It is found that when the concentrations of CMC, AA, and N,N' -methylene bis acrylamide increase in the feed mixture, the swelling ratio of the IPN initially increases, while after definite conventions of the IPN components, a fall in water uptake is noticed. However, a constant decrease in degree of water sorption is observed with increasing concentration of potassium persulphate (initiator).

The IPNs also display a pH dependent water sorption property. An optimum swelling is obtained at pH 6.5, whereas the swelling ratio decreases on both sides of pH 6.5. The IPNs also exhibit an increasing swelling ratio with increasing temperature (5 to 23°C), while a fall in swelling is observed beyond 23°C .

The presence of inorganic salts such as KCl, KBr, and KI suppress the water sorption capacity of the IPNs when added in increasing concentrations (0.001M to 0.1M) into the swelling medium. The effectiveness of added anions decrease in the order $\text{Cl}^- > \text{Br}^- > \text{I}^-$. In the case of addition of cations, such as K^+ and Ca^{2+} , initially the swelling ratio increases marginally and then it decreases; while in the case of Al^{3+} ions, the swelling capacity of the IPN constantly decreases with increasing salt concentration.

The IPNs also show a reduced level of swelling in simulated biological fluids such as the KI solution, glucose solution, urea solution, saline water, and artificial urine.

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