Preparation and Characterization of Novel pH-Sensitive Binary Grafted Polymeric Blends of Gelatin and Poly(vinyl alcohol): Water Sorption and Blood Compatibility Study

A. K. Bajpai, Manish Sharma

Bose Memorial Research Laboratory, Department of Chemistry, Government Autonomous Science College, Jabalpur (MP), 482 001, India

Received 24 November 2004; accepted 14 August 2005
DOI 10.1002/app.23370
Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: In this study, we attempted the synthesis and characterization of novel biocompatible hydrogels of binary polymeric blends of crosslinked poly(acrylic acid) grafted onto poly(vinyl alcohol) and gelatin by a redox polymerization technique. The end polymer was characterized by IR spectral analysis, differential scanning calorimetry measurements, and scanning electron microscopy. The prepared smart, environment-responsive hydrogels, containing polyelectrolyte domains, were assessed for their water sorption potential under various experimental conditions and were further used to evaluate important network parameters such as the crosslink density, number of elastically effective chains, and molecular mass between crosslinks. The diffusion mechanism of the solvent–polymer interaction was also analyzed to predict the behavior of continuously relaxing chains containing several carboxylate ions. The blood compatibility of premeditated hydrogels was also judged by *in vitro* methods such as protein adsorption, blood clot formation, and hemolysis percentage assay measurement. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 100: 599–617, 2006

Key words: biocompatibility; blends; hydrogels; radical polymerization; swelling

INTRODUCTION

Hydrogels are well known as networks of hydrophilic polymers that can absorb a significant amount of water (>20% of their dry mass) without dissolving or losing their structural integrity.[1,2] The water-containing macromolecular matrices possess many important biophysical properties, such as softness and rubbery texture, resemblance to living tissues, stability toward biofluids, compatibility with human organs, and permeability to various biomolecules, and, therefore, obviously deserve study as biomaterials in medical sciences.[3] The high water intake of hydrogels allows easier extraction of undesirable reaction byproducts before implantation and easy penetration of small molecules such as water, electrolytes, and metabolites into them *in vivo*. Some typical biomedical applications of hydrogels include the manufacturing of contact lenses, wound dressings,[4] controlled drug release systems,[5] artificial implants,[6] biosensors,[7] and surgical prostheses.[8]

Hydrogels are normally prepared by thermally induced,[9] redox-induced, or radiation-induced[10] polymerizations of vinyl monomers in the presence of a suitable crosslinking agent. It is customary to polymerize a hydrophilic monomer to obtain a highly swollen polymer; however, the introduction of an ionizable monomer into a polymeric system is a unique attempt to enhance the water uptake of the hydrogels. Among recently developed superabsorbents, acrylic acid (AAc) based superabsorbents have been extensively studied because of their ease of availability, low cost, hydrophilicity, and frequent polymerizability to high-molecular-weight polymers.[11] The hydrogels, into which ionizable groups such as carboxylic are incorporated when they are ionized, produce fixed ions that repel one another, and this repulsion leads to greatly enhanced swelling of the network. The limit to which the ionized hydrogel swells at equilibrium increases with an increase in the incorporation of functional ionizable groups of the network.[12] The equilibrium swelling ratio of hydrogels is another function of various properties[13] of the swelling medium, including the pH, temperature, and ionic strength. An increase in the concentration of the ions (ionic strength) in the swelling medium has been found to reduce the equilibrium swelling ratios of ionizable hydrogels. These crosslinked polyacrylates are unique materials because of their valuable applications, such as diapers, incontinence products, feminine hygiene products, hospital products, thickening agents, and condensation prevention agents.[14] In this study, the selection of poly(vinyl alcohol) (PVA) as one of the components of

Correspondence to: A. K. Bajpai (akbmrl@yahoo.co.in).

the hydrogel was due to its popularity in the biomedical community,[15–17] nontoxicity, noncarcinogenicity, biocompatibility, and desirable physical properties, such as its elastic nature, high degree of swelling in aqueous media, and good film-forming properties. All these qualities of hydrogels enable them for a variety of biomedical applications, such as contact lenses, artificial meniscus, and reconstruction of vocal cards. In addition, the hydrogels of PVA are known for avoiding protein adsorption and cell adhesion.[18–20]

However, the weak mechanical strength of these hydrogels restricts their applications when the material has to withstand prolonged stress. Thus, the introduction of another polymeric component into the hydrogel matrix might improve its mechanical properties.

The other polymer chosen in this work for the hydrogel preparation is gelatin, which is a biopolymer well known for its biodegradability, noncarcinogenicity, and hydrophilicity.[21] Moreover, the incorporation of this biopolymer into the PVA matrix could further improve its properties because of the presence of multifunctional groups in the gelatin molecules.

The blood compatibility of materials is an important factor in the development of various medical devices. Some fundamental research and practical technologies for clarifying and improving blood compatibility have been carried out,[22] and as a result of these efforts, many polymer surfaces with good blood compatibilities have been developed, such as a surface composed of a nonionic hydrophilic polymer,[23] biomembrane-like polymers,[24] and microphase-separated domains.[25] When a foreign material comes into contact with flowing blood, the water absorption is the foremost event before protein adsorption. Therefore, most of the physical and physiological properties of these materials are intimately related to the organization of water molecules within or on the surface of the materials,[26] and the water molecules have an important role in the reactions of cells such as adhesion and morphological changes. In this study, therefore, water-equilibrated samples of hydrogels were introduced into fresh blood samples to examine their hemolysis percentage assay, blood clot formation tendency, and protein adsorption on hydrogel surfaces. Albumin is the major constituent of blood plasma (ca. 60% of the total plasma proteins) and is one of the smallest proteins in the plasma (molecular weight = 66,000–69,000). The shape of this protein is a prolate ellipsoid with a size of about $15 \times 3.8 \times 3.8$ nm^3. It contains a comparatively large number of polar and charged residues and thus is highly soluble in water and negatively charged at pH 7.4 (isoelectric point = 4.7–5.5). It also has big hydrophobic patches on its surface. Since the first attempt in the 1950s to develop blood-compatible materials with a negatively charged surface for artificial vessels,[27] a number of mechanisms have been proposed to predict the exact blood-compatible characteristics of hydrogels, but the related factors and all the possible reasons are not yet fully understood.[28]

Thus, realizing the significance of hydrogels in biomedicine, we are reporting the results for the preparation and characterization of novel pH-sensitive binary poly(acrylic acid) (PAA)-grafted blends of gelatin and PVA and an assessment of the blood compatibility of the prepared hydrophilic matrix.

EXPERIMENTAL

Yellowish, granular, acid-processed gelatin (type A; isoelectric point = 7.6) was obtained from Merck (India) Ltd. (Mumbai, India) and was used as received. PVA (hot-processed; molecular weight = 14,000, degree of hydrolysis = 98.6%) was supplied by Loba Chemie (India) and was used without any pretreatment. AAc [Merck (India) Ltd., Mumbai, India] was purified and freed from the inhibitor by distillation under reduced pressure and the collection of the middle fractions only. The distilled monomer was stored in a dark bottle at 4°C. *N,N′*-Methylene bisacrylamide (MBA; Research Lab, Mumbai, India) and potassium persulfate (KPS; Loba Chemie), employed as the crosslinking agent and initiator, respectively, were used as received. Potassium metabisulfite (MBS; Loba Chemie, Mumbai, India) was used as an activator in the redox system. All the required chemicals were analytical-reagent-grade, and triple-distilled water was used throughout the study.

Methods

Preparation of the hydrogels

Hydrogels of various compositions were prepared by a redox polymerization technique.[29] Briefly, in a typical experiment, 1.0 g of gelatin and 1.5 g of PVA were dissolved in 20 mL of distilled water under hot conditions (>60°C) with continuous stirring, and into this transparent, homogeneous, and semiviscous liquid, 58.3 m*M* AAc was added, followed by the addition of 0.02 g of the crosslinker MBA and the redox initiator system, which consisted of 1.0 mL each of 0.001*M* MBS and 0.1*M* KPS.

The whole viscous mixture was transferred to a Petri dish (2-in. diameter Corning, Qualigen Fine Chemicals Division, Mumbai, India) after proper manual mixing and was then placed at 30°C for 5 days so that it changed into a thin, circular, semitransparent film. The hydrogel was purified by equilibration with water so that unreacted chemicals were leached out. The rectangular pieces of the dried hydrogels were stored in air-tight polythene bags to prevent the contact of moisture and fungus.

IR spectral analysis

The structural characterization of the prepared hydrogel was performed by the recording of Fourier transform infrared (FTIR) spectra of the gel of a definite composition on an FTIR spectrophotometer (Paragon 1000, PerkinElmer, Wellesley, MA).

Differential scanning calorimetry (DSC) measurements

The DSC measurements of the hydrogel were recorded on a DSC instrument (2100, Dupont) in the temperature range of 30–400°C under an N_2 atmosphere and at a heating rate of 10°C/min.

Scanning electron microscopy (SEM)

SEM (StereoScan, 430, Leica SEM, Bannockkurn, IL) was used to investigate the morphological features of the prepared hydrogel blend.

Dynamics of the water sorption process

Hydrogels containing various functional groups may interact with the external environment (e.g., temperature, ionic strength, and pH of the swelling agent). Their response to the environmental conditions may lead to an increase or decrease in the available mesh size of the hydrogels.[30–32] The equilibrium swelling ratio is an important parameter because it describes the amount of water within the hydrogel at equilibrium; it is also a function of various features of the hydrogel, such as the network structure, crosslinking density, hydrophilicity, and degree of ionization of the functional groups. Apart from this, there have been many efforts to make use of the processes of water penetration and subsequent solute release in polymer materials for designing controlled drug delivery systems.

To investigate the response of the hydrogel under different environmental conditions, a gravimetric method described elsewhere was adopted.[33] The dynamics of the swelling process can be followed by the determination of the amount of water imbibed at different time intervals and the calculation of the swelling ratio:

$$\text{Swelling ratio} = \frac{W_s}{W_d} \tag{1}$$

where W_s and W_d are the weights of swollen and dried gel samples at a particular time t, respectively.

The operative mechanism of water intake can be explained by this phenomenological rate law equation:

$$\frac{W_t}{W_\infty} = kt^n \tag{2}$$

where n is the swelling exponent; k is the swelling rate front factor; and W_t and W_∞ are the water intakes by the swollen hydrogel at time t and the equilibrium time, respectively, against different environments. A double-log plot of the swelling ratio versus the time provides the value of n, which determines the nature of the solvent diffusion process, that is, Fickian or non-Fickian diffusion kinetics.[34]

The kinetic data of the swelling process were further used to evaluate the diffusion coefficient of the solvent molecules in the hydrogel. The short-term approximation of the Fickian equation for a diffusing agent in a slab with boundary conditions is given by eq. (3):

$$\frac{W_t}{W_\infty} = 4\left[\frac{Dt}{\pi 1^2}\right]^{1/2} \tag{3}$$

where D is the diffusion constant of water (cm^2/s) and ℓ is the thickness of the dry hydrogel.[35] The slope of the straight line obtained from a plot between W_t/W_∞ and $\sqrt{t}$ gives the value of D.

Blood compatibility tests

Protein [bovine serum albumin (BSA)] adsorption. To judge the blood compatibility of the prepared hydrogels, blood protein–hydrogel interactions were investigated by the adsorption of BSA onto the hydrogel surfaces with the batch-contact method.[36] In a typical experiment, a 20-mL BSA solution (0.2% w/v), prepared in phosphate-buffered saline (pH 7.4) containing preweighed and preswollen hydrogel pieces, was mildly shaken for 30 min to prevent foam formation at the solution–air interface. After being shaken, the supernatant solution was analyzed for the residual BSA concentration by the recording of its absorbance at 277 nm (Systronics Model 2201 ultraviolet–visible double-beam spectrophotometer, Ahmedabad, India). The amount of BSA remaining in the solution was calculated by the construction of a calibration plot, and the amount of adsorbed BSA (mg/g) was calculated with the following equation

$$\text{Adsorbed BSA (mg/g)} = \frac{(C_o - C_a)}{w} \times V \tag{4}$$

where C_0 and C_a are the BSA concentrations (mg/mL) before and after adsorption, respectively; w is the weight of the swollen gel (g); and V is the volume of the protein solution.

Blood clot formation test. The antithrombogenic property of the hydrogel surface was evaluated by the recording of the weights of the clots formed as a result

of the surface–blood interaction, as described elsewhere.[37] In brief, the hydrogels under investigation were hydrated in 0.9% saline water at 30°C in a constant-temperature bath. To these swollen gels, 0.2 mL of acid citrate dextrose (ACD) blood was added, followed by an addition of 0.02 mL of a 4*M* $CaCl_2$ solution to start the thrombus formation. The thrombus formed was dried at 35°C for 48 h and weighed.

Hemolysis assay. Hemolysis is defined as the release of hemoglobin into plasma due to damage to the erythrocyte membrane.[38] The hydrogels were well equilibrated in normal saline water (0.9% w/v) for 48 h at 30°C, and human ACD blood (0.20 mL) was added to the surface of the hydrogels. After 20 min, 2.0 mL of a 0.9% NaCl solution was added to each sample to stop the hemolysis, and the samples were incubated for 60 min at 37°C. Positive and negative controls were obtained by the addition of 0.2 mL of human ACD blood and 0.9% NaCl, respectively, to 2.0 mL of triple-distilled water. Incubated samples were centrifuged for 45 min, the supernatant was taken, and its absorbance was recorded on a spectrophotometer at 545 nm. The hemolysis percentage was calculated with the following relationship:

$$\text{Hemolysis (\%)} = \frac{\text{A test sample} - \text{A (}-\text{)-control}}{\text{A (+)-control} - \text{A (}-\text{)-control}} \quad (5)$$

RESULTS AND DISCUSSION

Scheme of the polymerization

The preparation of a polymeric blend of poly(acrylic acid-*g*-gelatin) and poly[acrylic acid-*g*-poly(vinyl alcohol)] may be modeled via the redox-initiated free-radical polymerization technique shown in Scheme 1.

(i) Redox → $R^{\bullet}$

(ii) $R^{\bullet}$ + nAA + mMBA → $R-(AA)_{n-i}^{\bullet}-(MBA)_m-(AA)_i-$ (I)

(iii) $R^{\bullet}$ + PVA → $PVA^{\bullet}$ + RH

(iv) $R^{\bullet}$ + Gel (gelatin) → $Gel^{\bullet}$ + RH

(v) $PVA^{\bullet}$ + I → PVA–I

(vi) $Gel^{\bullet}$ + I → Gel–I

(vii) PVA–I + Gel–I → (Blend Hydrogel)

Scheme 1

IR spectral studies

The IR spectra of pure PVA, pure gelatin, and a prepared hydrogel blend of a definite composition are depicted in Figure 1(a–c), respectively, which clearly reveals that the IR spectra of the blend hydrogel presents combined spectral features of various functional groups of PVA, gelatin, and PAA. Moreover, Figure 1(c) appears quite distinct from the other spectra in Figure 1.

Figure 1(c) of the grafted blend clearly marks the presence of PVA and gelatin in the hydrogel, as confirmed by the peaks observed at 3425 (O—H stretching of the hydroxyl group and N—H stretching of the primary amide), 2374 (NH_3 stretching of gelatin), and 2927 cm^{-1} (asymmetric stretching of CH_2 of polymeric vinyl alcohol).

Figure 1(c) also confirms the presence of carboxylate groups of AAc in the blend, as evidenced by a strong band of carboxylate ions at 1597 (asymmetrical stretching of C═O), 2855 (asymmetric stretching of C—H of CH_2 of acid), and 2855 cm^{-1} (symmetric stretching of C—H of carboxylic acid). The evidence of the crosslinker in the prepared hydrogel blend is confirmed by the peak at 674 cm^{-1} (secondary amide) due to MBA. The FTIR spectrum of the hydrogel blend is much sharper and more intense than those of its components, gelatin and PVA. This could be due to the fact that because of the grafting of crosslinked PAA chains onto both gelatin and PVA, the macromolecular chains form a loose matrix in which the grafted chains favorably pack up themselves to construct a three-dimensional crystalline structure that exhibits well-defined sharp peaks.

DSC analysis

The thermal characterization of the prepared hydrogel was performed by the recording of DSC thermograms of pure gelatin, pure PVA, and the blend hydrogel, as depicted in Figure 2(a–c), respectively. As far as DSC of gelatin is concerned, two glass-transition temperatures (T_g's), located around 80–100 and 180–200°C, are clearly visible and have been assigned to the glass transitions of α-amino acid blocks in the peptide chain and the block copolymer model of gelatin, respectively. In the case of PVA, a sharp T_g at 123°C and a melting endotherm at 229°C have been obtained, as shown In Figure 2(b). In the DSC thermogram of the blend hydrogel, a minor endotherm appears at 68°C, which may be assigned to T_g of the gel, which is well below the T_g's of both gelatin and PVA. Thus, the

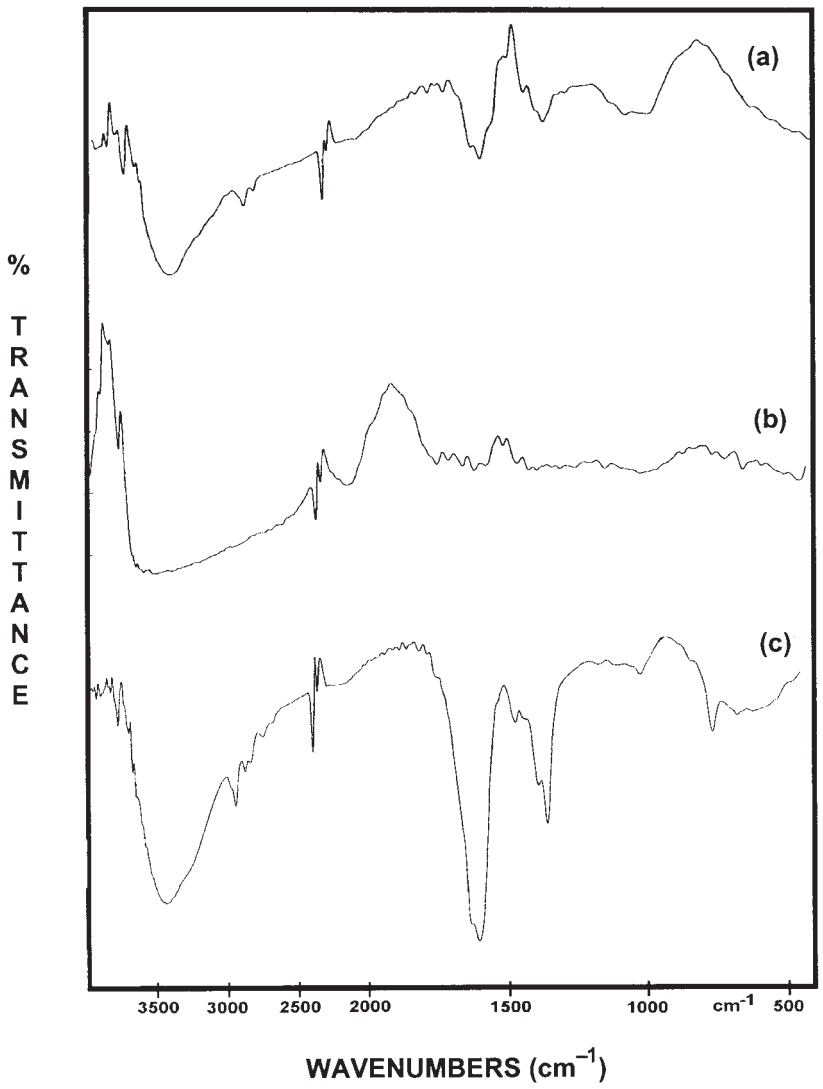


Figure 1 IR spectra of (a) pure PVA, (b) pure gelatin, and (c) a hydrogel blend.

decreased T_g values of both gelatin and PVA can be attributed to the grafting of crosslinked PAA chains onto the gelatin and PVA chains, which imparts flexibility to the polymeric chains of gelatin and PVA and thus lowers T_g.

The thermogram of the blend hydrogel also displays a broad endotherm from 80 to 220°C, thus clearly suggesting a loss of crystallinity of both gelatin and PVA due to the grafting of PAA chains. This may possibly be due to the fact that because of the grafting of PAA chains onto the gelatin and PVA, there occurs a loss of intermolecular hydrogen bonding in the two polymers, which obviously destroys crystallinity in the polymers.

Thus, it may conclusively be said that because of the grafting of vinyl polymeric chains onto the gelatin and PVA molecules, the overall crystallinity falls.

SEM analysis

Morphological features of the prepared hydrogel blend have been investigated by the recording of SEM micrographs of pure gelatin, pure PVA, and the hydrogel blend, as shown in Figure 3(a–c), respectively. Figure 3(a) shows that the surface of gelatin is heterogeneous, showing aggregated molecules scattered unevenly on the surface. On the other hand, the surface of PVA is quite homogeneous and has a glassy nature, as evident from Figure 3(b). However, the surface morphology of the blend, shown in Figure 3(c), appears to exhibit joint morphological features of both gelatin and PVA, with a porous surface having pore sizes in the range of 3–12 μm. The porous nature of the blend is further justified by the fact that, because of the grafting of crosslinked PAA chains onto the gelatin and PVA molecules, a loose macromolecular matrix is formed with voids of several micrometers.

Network parameters

The average molar mass between crosslinks (M_c) and the crosslink density (q) are important structural pa-

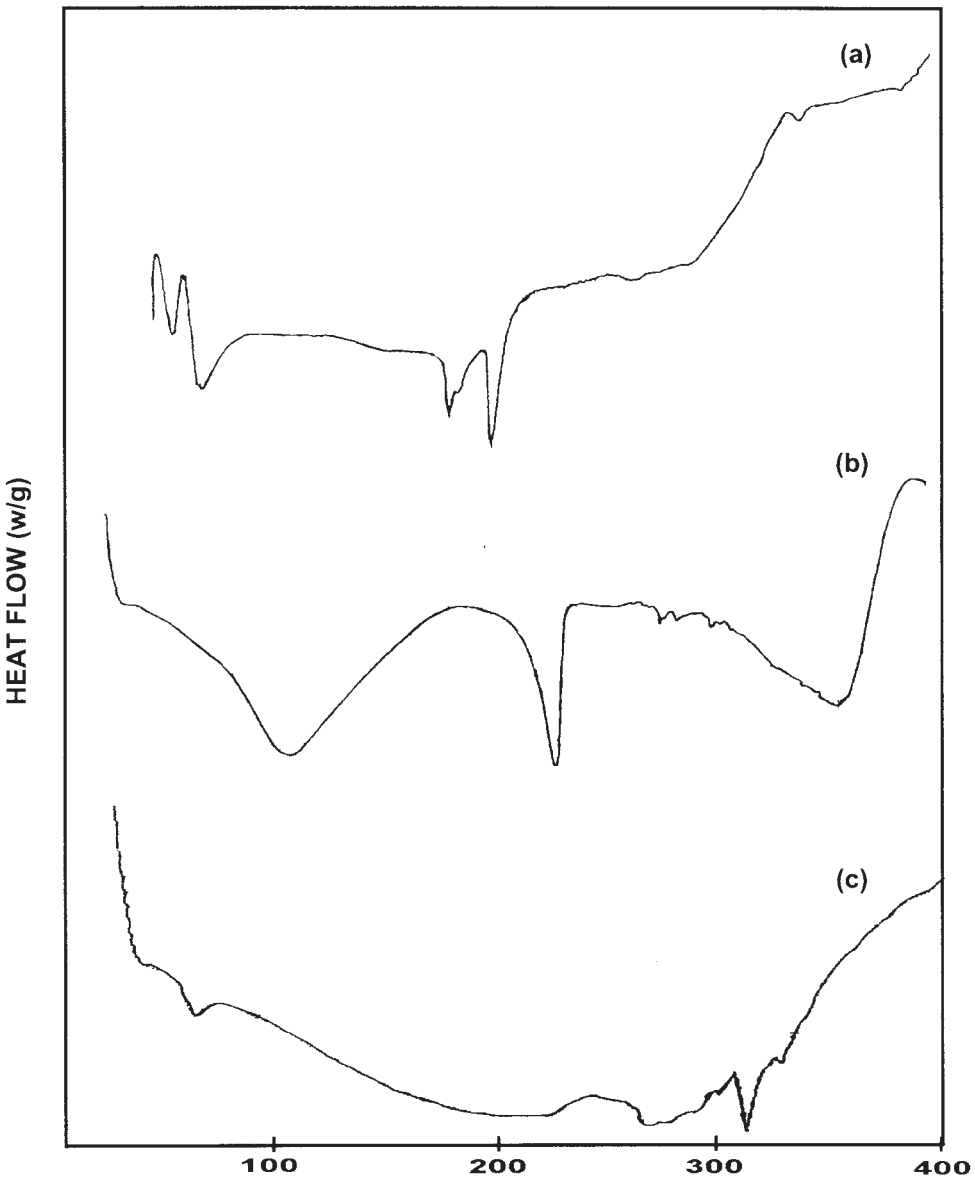


Figure 2 DSC thermogram of (a) pure gelatin, (b) pure PVA, and (c) a hydrogel blend.

rameters for crosslinked polymer matrices. The value of M_c has a great practical significance because this largely affects the physical and mechanical properties of the hydrogel blends.

According to the theory of Flory and Rehner, for a perfect polymeric network, the value of the number-average molar mass of the chains between crosslinks may be given as follows:

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

where V_1 is the molar volume of the solvent (mL/mol), d_p is the density of the polymer (g/mL), V_s is the volume fraction of the swollen gel, and χ is the Flory–Huggins interaction parameter between the solvent and polymer.[39] The equilibrium swelling ratio is approximately given by the inverse of the volume fraction of the polymer. q can be expressed in terms of the molar mass of repeating units (M_o) as follows:

$$q = \frac{M_o}{M_c} \tag{7}$$

The literature cites another crosslink density as the number of elastically effective chains (V_e) per unit of volume of a perfect polymeric network in terms of M_c as follows:

$$V_e = d_p \frac{N_A}{M_c} \tag{8}$$

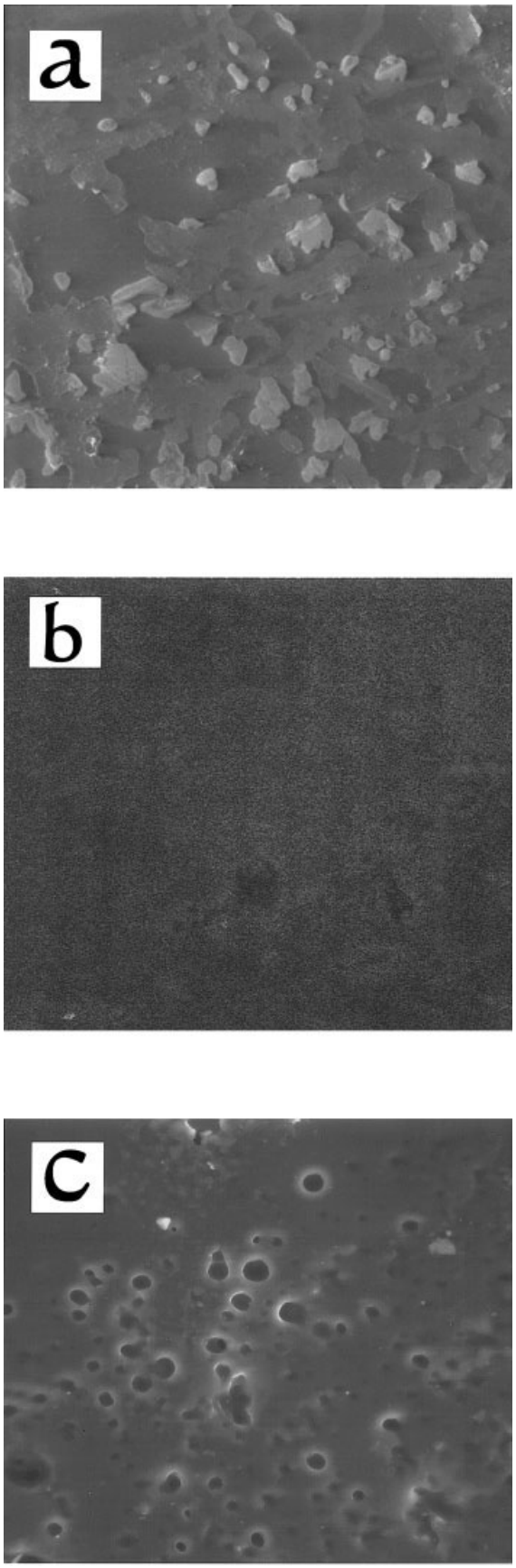


Figure 3 SEM micrographs of (a) pure gelatin, (b) pure PVA, and (c) a hydrogel blend.

where N_A is Avogadro's number. The density of the hydrogel was determined to be 0.37 g/cm^3. The values of M_c, q, and V_e of this network with various compositions of the hydrogels have been evaluated and are summarized in Table I.

Effect of the variation in the composition on the water-uptake potential

Effect of the monomer on the swelling

The swelling ratio (Q) of a hydrogel can be best described by Flory's swelling theory:

$$Q^{5/3} = \frac{[(i/2V_uS^{1/2}) + (1/2 - X_1)/V_1]^{1/2}}{(V_e/V_o)} \quad (9)$$

where i/V_u is the concentration of the fixed charge with respect to the unswollen network, S is the ionic concentration in the external solution, $(1/2 - X_1)/V_1$ is the affinity of the hydrogel to water, and V_e/V_o is the crosslink density of the hydrogel. Q is related to the ionic osmotic pressure, the crosslink density, and the affinity of the hydrogel to water. From this equation, it is very much clear that with an increase in the ionic content as well as the hydrophilicity of the composite material, the swelling ratio will increase.[40]

AAc is an ionic comonomer and has a major impact on all the swelling characteristics of this hydrogel. To investigate the effect of AAc variation in the hydrogel composition on the swelling ratio, AAc was added in the range of 14.7–58.3 mM. The results are shown in Figure 4 and clearly reveal that increasing the amount of the monomer increases the swelling ratio. The hydrogel with greater than 58.3 mM AAc could be prepared, but the much enhanced sorptivity of water made the gel much weaker for subsequent investigations.

The results can be explained by the fact that with an increasing concentration of the monomer in the gel, the number of charged carboxylic groups (—COO$^-$) increases, and because of the greater repulsion among these ionic groups, the polymeric chains are expanded; this results in increased swelling. Similar results have been reported elsewhere.[41]

Another remarkable feature visible in the curve of the swelling ratio versus the time is that after a definite time (4 h), the swelling ratio is sped up, as evident from the observed steep portion of the swelling curves. This enhanced swelling can be attributed to the fact that as the hydrogel starts imbibing water, the carboxylic groups (—COOH) present along the PAA chains in the interior part of the gel begin to dissociate to yield —COO$^-$ ions, which cause a sudden repulsion among the network chains. This obviously results in an enhanced swelling rate of the hydrogel.

TABLE I
Data Representing the Values of M_c, q, and V_e

Sample	Composition				$M_c \times 10^{-3}$	$q \times 10^3$	$V_e \times 10^{-20}$
	AAc (m*M*)	PVA (g)	Gelatin (g)	MBA (m*M*)			
1	14.7	2.0	1.0	0.12	1.58	44.93	141.01
2	29.1	2.0	1.0	0.12	1.81	39.2	123.09
3	43.7	2.0	1.0	0.12	2.76	25.7	80.72
4	58.3	2.0	1.0	0.12	11.6	6.18	19.20
5	58.3	1.5	1.0	0.12	2.50	28.4	89.12
6	58.3	1.5	1.0	0.19	827.5	0.08	0.27
7	58.3	1.5	1.0	0.25	368.6	0.19	0.60
8	58.3	1.5	1.0	0.32	193.6	0.36	1.15

Effect of the PVA variation

When the concentration of PVA varies in the range of 1.5–3.0 g, the swelling ratio also changes appreciably. Below 1.5 g of PVA, the hydrogel that formed showed very low mechanical strength, a smooth and rubbery nature, and much greater swelling in a shorter time span. The gel was quite unstable and was very difficult to handle for other important experimental observations and was, therefore, discarded. In this particular polymeric matrix, the gel with 1.5 g of PVA showed the maximum swelling ratio, and beyond this concentration, more PVA caused a depression in the swelling ratio, as depicted in Figure 5. The results can be explained by two facts. First, the amount of increased PVA shows less swelling despite the hydrophilic character of PVA, and this is due to the much greater chain density of the network. The increasing crosslink density with an increase in the PVA content

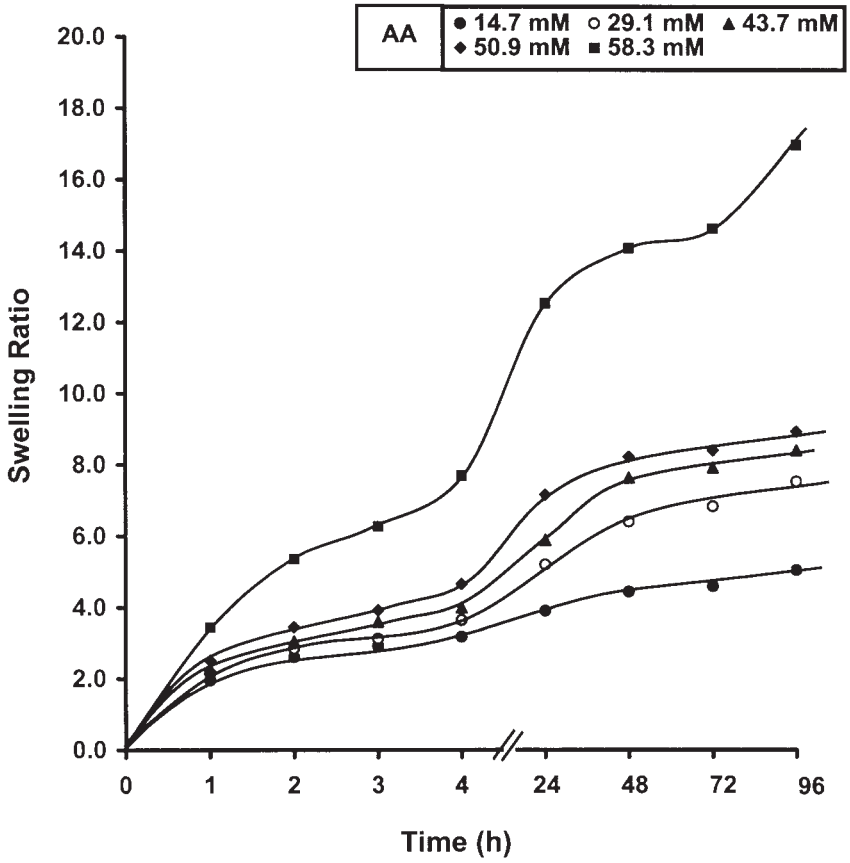


Figure 4 Effect of various concentrations of the monomer (AAc) in the blend hydrogel on the swelling ratio of the hydrogel at a fixed composition ([gelatin] = 1.0 g, [PVA] = 2.0 g, [MBA] = 0.12 m*M*, [KPS] = 0.36 m*M*, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C).

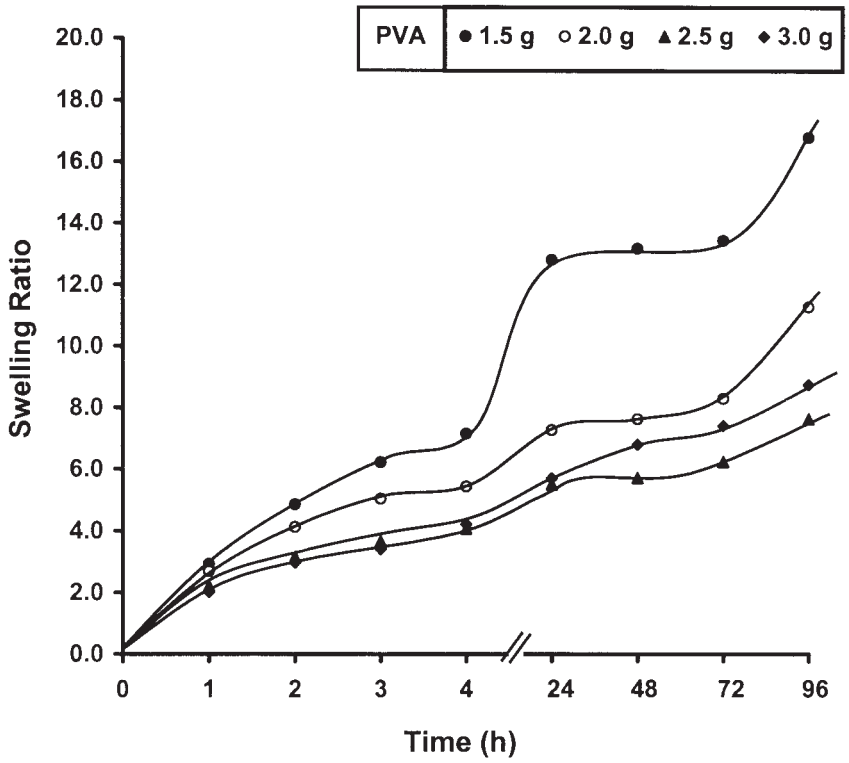


Figure 5 Effect of various concentrations of PVA on the swelling ratio of the hydrogel at a fixed composition ([AAc] = 58.3 m*M*, [gelatin] = 1.0 g, [MBA] = 0.12 m*M*, [KPS] = 0.36 m*M*, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C).

in the blend inhibits the diffusion of penetrant water into the matrices. Similar results have also been reported elsewhere, in which the observed decrease in the swelling ratio was attributed to the fact that the addition of PVA decreased the mesh size of the network available for the accommodation of the water molecules and, as a result, the swelling ratio was suppressed.[42]

Second, the observed drop in the swelling ratio at a higher PVA content in the hydrogel blend can also be attributed to the fact that at higher PVA contents, the volume fraction of PVA increases and, therefore, the water molecule will have to travel a longer path while diffusing into the hydrogel matrix. This clearly brings about a fall in the swelling ratio.

Effect of gelatin

Gelatin is a well-known biodegradable and hydrophilic polymer containing a large number of functional groups, such as —COOH and —NH_2, to which the water molecules are known to attach.

In this study, the influence of gelatin has been examined on the swelling behavior of the gel by the addition of gelatin into the feed mixture in the range of 0.5–2.0 g. The results shown in Figure 6 clearly indicate that the swelling ratio of the polymeric blend is maximum at 0.5 g of gelatin, and as the amount of gelatin increases, the swelling ratio decreases, despite the hydrophilicity of gelatin. The polymeric blend with the lowest amount of gelatin, that is, 0.5 g, was very weak in its mechanical strength and was even very difficult to handle because of its smooth and thin rubbery nature. To increase the mechanical strength, more gelatin was added as gelatin is known for its mechanical strength also. The decrease in the swelling can be attributed to the fact that an increased volume fraction of the biopolymer matrix results in a reduction in the free volume available within the hydrogel network accessible to the invading water molecules. Moreover, because of an increase in the volume fraction of the polymer, the water molecules have to travel a longer path to enter the network, and this obviously results in a decrease in the swelling ratio.

A close examination of the swelling profile curves clearly indicates that although in the curve of the swelling ratio versus the time at the lowest gelatin content no steep rise in the swelling ratio appears after 4 h, for higher gelatin contents, the hydrogels exhibit a steep rise in the swelling ratio after a definite time interval (4 h). A possible reason for the observed findings may be that because gelatin is itself amphipathic in nature, that is, both —NH_2 (basic) and —COOH (acid) are in the biopolymer, its swelling results in the dissociation of —COOH groups, which, because of similar negative charges, produce repulsion among

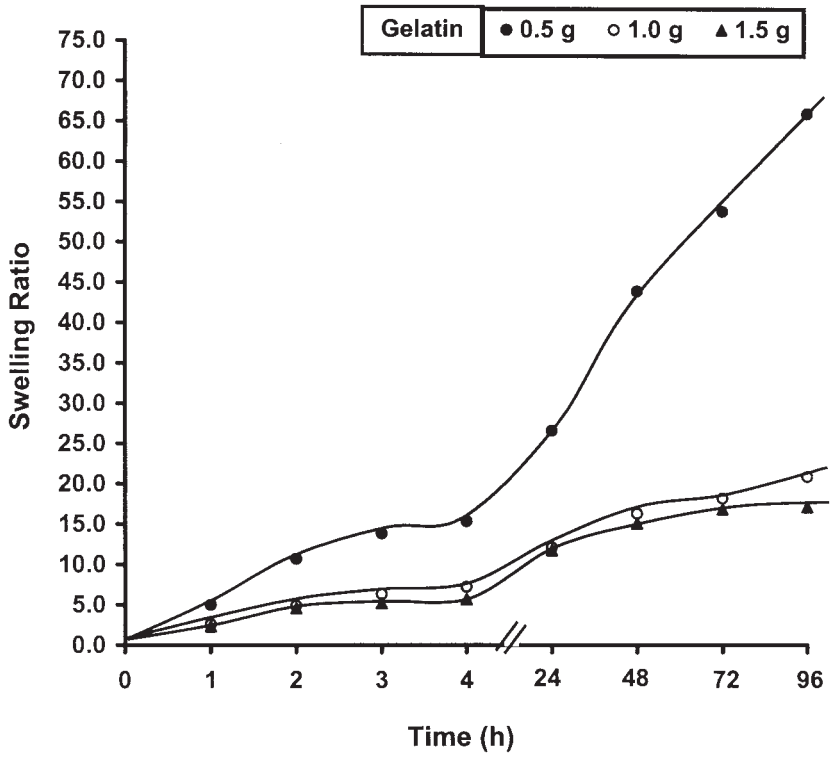


Figure 6 Effect of various amounts of gelatin in the hydrogels on their swelling ratio at a fixed composition ([AAc] = 58.3 m*M*, [PVA] = 1.5 g, [MBA] = 0.12 m*M*, [KPS] = 0.36 m*M*, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C).

the network chains, thus enhancing the swelling rate. However, this effect is prominently seen only at higher gelatin contents in the hydrogel as at lower gelatin contents in the hydrogel, the functional groups of the gelatin molecule may be shielded because of their localization in the interior part of the gel.

Effect of the crosslink density

MBA, employed as a crosslinker in this study, showed a greater impact on the swelling pattern of the polymeric matrices. To investigate the effect of the crosslinker on the swelling behavior of the hydrogel, various amounts of the crosslinker, ranging from 0.06 to 0.34 m*M*, were added to the feed mixture when different samples of the hydrogel were prepared. The results are depicted in Figure 7, which clearly shows that up to a definite concentration of MBA (i.e., 0.19 m*M*), the hydrogel blend exhibits an increased swelling ratio, whereas beyond this concentration of the crosslinker, swelling decreases considerably.

The results can be explained by the fact that MBA itself is a bifunctional and hydrophilic monomer, and its incorporation into this particular hydrogel results in an increased hydrophilicity, which, in turn, leads to an enhanced swelling ratio. The results are further justified by the network parameter data (Table I), which clearly show that after a definite concentration of the crosslinker, the value of M_c decreases; this obviously reduces the mesh size of the free volume accessible to the water molecules, and, therefore, the swelling ratio decreases. In other words, the observed decrease in the swelling ratio is quite expected as an increase in the amount of the crosslinker makes the hydrogel more and more compact, and as a result, the water penetration becomes increasingly difficult.[43] Some workers have reported an increase in T_g of the polymer with increasing crosslink density, and thus the glassy nature of the matrix does not permit loosening of the macromolecular chains, which results in lower water sorption.[44]

Effect of pH

pH-responsive macromolecular devices have been frequently used to develop controlled release formulations for oral administration, which remain the most clinically acceptable way of drug delivery.[45] The oral administration of macromolecular drugs remains a significant challenge because peptides and proteins are susceptible to hydrolysis and digestion by the acid and enzymes in the gastrointestinal tract; also, the bioavailability of orally delivered peptides and proteins is very low because of poor membrane permeability.[46] The pH-responsive swelling behavior is basically due to ionization of the functional groups in the

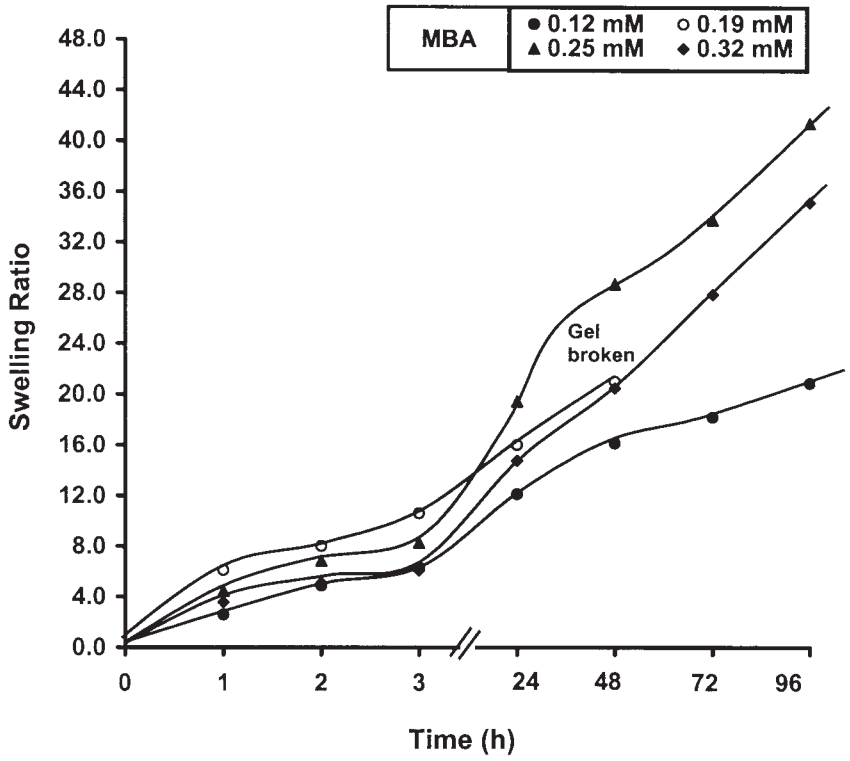
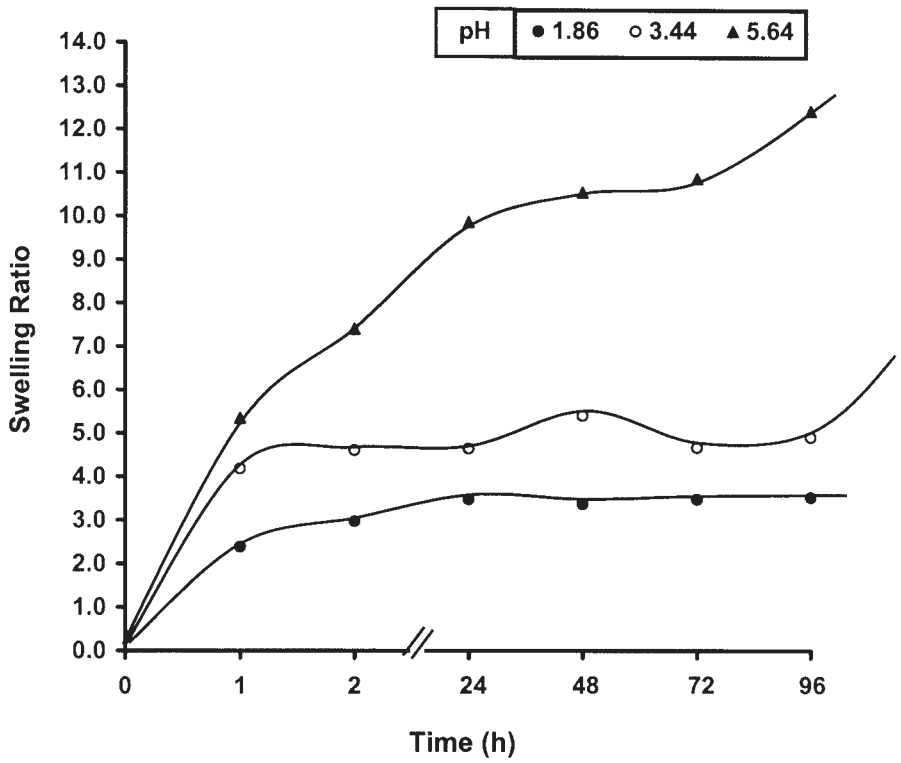


Figure 7 Effect of various concentrations of the crosslinker (MBA) on the swelling ratio of the hydrogel blend at a fixed composition ([AAc] = 58.3 m*M*, [PVA] = 1.5 g, [gelatin] = 1.0 g, [KPS] = 0.36 m*M*, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C).

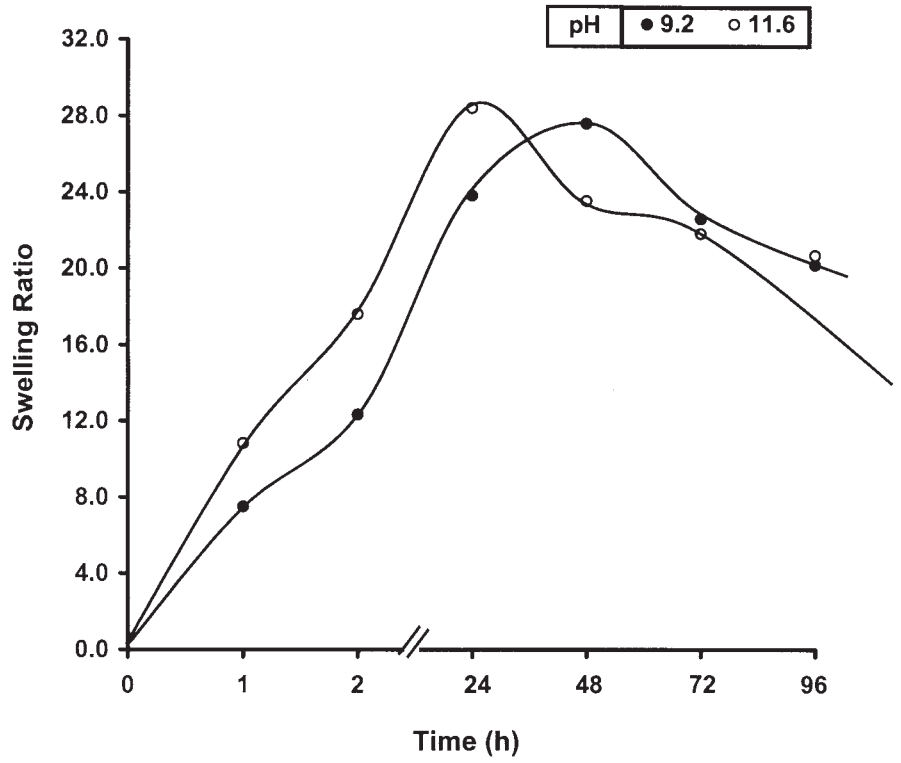
gel, which depends on the pH of the surrounding medium. In an anionic hydrogel, an increase in the degree of ionization contributes to electrostatic repulsion between the charged groups along the chains and, therefore, swells the gels to a higher degree. These highly swollen hydrogels contain large amounts of unbonded water, which allows greater solute release. In this study, the influence of the pH on the swelling ratio of the hydrogel has been investigated through changes in the pH of the external medium from 1.86 to 11.60. The results are depicted in Figure 8(a,b), respectively. Figure 8(a), showing the response of the hydrogel in an acidic medium, clearly reveal that the swelling ratio increases with an increase in the pH of the medium. The results can be explained by the fact that with increasing pH of the swelling medium, the carboxylic groups of PAA are ionized and generate carboxylate ions along the macromolecular chains, which, because of mutual repulsion, facilitate chain relaxation and cause greater swelling.

At pH 5.64, the amount of water absorbed into the polymeric network is much larger than that at pH 1.86 at a given swelling time. This is due to the fact that the pH of the swelling medium is well above pK_a of crosslinked PAA in the hydrogel, which is about 4.2.[47] In this case, the carboxylic acid group of PAA in the gel is 100% dissociated, thus producing an optimum repulsion in the network, which, in turn, results in much greater desorption of water.

The swelling profile curves also imply that the rate of swelling increases with increasing pH of the medium. The observed increasing rate of swelling may be attributed to the fact that at relatively lower pHs, the network chains are firmly bonded to one another via hydrogen bonding because of an excess of —COOH groups. Thus, because of their restricted mobility, the swelling rate rises slowly. On the other hand, at a higher pH, such as 5.04, the dissociation of —COOH groups to carboxylate ions results in a reduction of hydrogen bonds along the network chains and thus imparts to them faster mobility. This obviously results in an enhanced swelling rate and swelling ratio as well. The influence of an alkaline pH on the swelling profiles of the hydrogel is depicted in Figure 8(b), which clearly reveals that the swelling ratio is significantly enhanced with an increasing pH of the medium. Moreover, the swelling ratio starts decreasing after a definite time (48 h). The observed steep increase in the water sorption is quite obvious as in an alkaline medium, the —COOH groups present in both the grafted PAA chains and gelatin molecules also undergo dissociation to yield carboxylate anions, which, because of greater relaxation in the network chains, cause



(a)



(b)

Figure 8 (a) Effect of the pH of the swelling medium in an acidic mode on the swelling ratio of the hydrogel blend at a definite composition ([AAc] = 58.3 m*M*, [PVA] = 1.5 g, [gelatin] = 1.0 g, [MBA] = 0.25 m*M*, [KPS] = 0.36 m*M*, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C) and (b) effect of the pH of the swelling medium in a basic mode on the swelling ratio of the hydrogel blend at a definite composition ([AAc] = 58.3 m*M*, [PVA] = 2.0 g, [gelatin] = 1.0 g, [MBA] = 0.25 m*M*, [KPS] = 0.36 m*M*, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C).

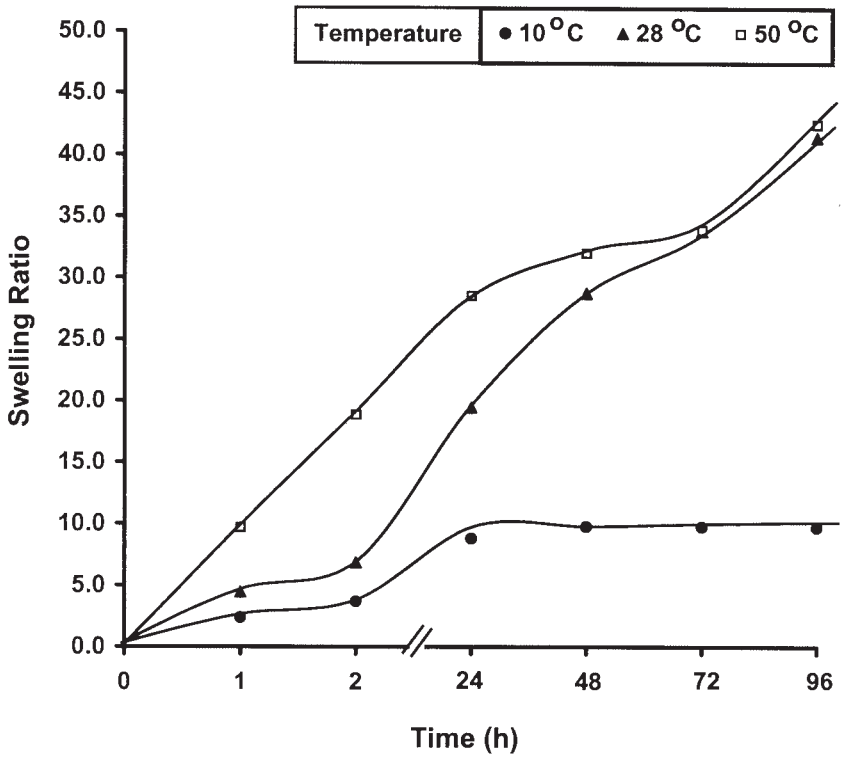


Figure 9 Effect of the temperature of the swelling medium on the swelling ratio of the hydrogel for a definite composition ([AAc] = 58.3 m*M*, [PVA] = 1.5 g, [gelatin] = 1.0 g, [MBA] = 0.25 m*M*, [KPS] = 0.36 mM, [MBS] = 4.04 m*M*).

much greater swelling of the hydrogel. The decrease observed in the swelling ratio after optimum swelling could be attributed to the gradual collapse of the swollen hydrogel.

Effect of the temperature

To investigate the effect of the temperature of the swelling medium on the water-uptake potential of the prepared hydrogel, experiments were performed at different temperatures ranging from 10 to 50°C. The results are shown in Figure 9, which clearly shows that the swelling ratio increases with the increasing temperature of the swelling bath.

The explanations of the observed results are based on the fact that with increasing temperature, the segmental mobilities of the hydrogel chains increase effectively, and consequently, the water sorption capacity of the hydrogel increases. Some authors, however, have noted a decrease in swelling at higher temperatures, which has been attributed to the cleavage of hydrogen bonds between the water molecules and network chains. However, no such results have been noticed in this case.

According to the Claussius–Clapyeron equation

$$\frac{d[\ln(W_\infty)]}{d(1/T)} = -\Delta H_m/R \tag{10}$$

where ΔH_m is the enthalpy of mixing between a dry polymer and an infinite amount of water and R is the gas constant. The value of ΔH_m has been calculated from a graph plotted between W_∞ and the reciprocal of swelling temperature ($1/T$) and found to be 5.40 J/deg/mol.

Effect of ionic interactions

Theoretical and experimental considerations[48,49] have established that there is a balance between the osmotic pressure and the polymer elasticity that sets the physical dimensions of the hydrogels. The osmotic pressure results from a net difference in the concentration of mobile ions between the interior of the gel and the exterior solution.

According to the theory of Donan membrane equilibrium, when a gel is placed in contact with a liquid, the chemical potential of the solvent (μ) in both the gel and the solution phase must be the same at equilibrium:

$$\Delta\mu_1^g = \Delta\mu_1^s \tag{11}$$

where the superscripts g and s represent the gel and solution phases, respectively.

In terms of the osmotic pressure (π), the equation can be rewritten as follows:

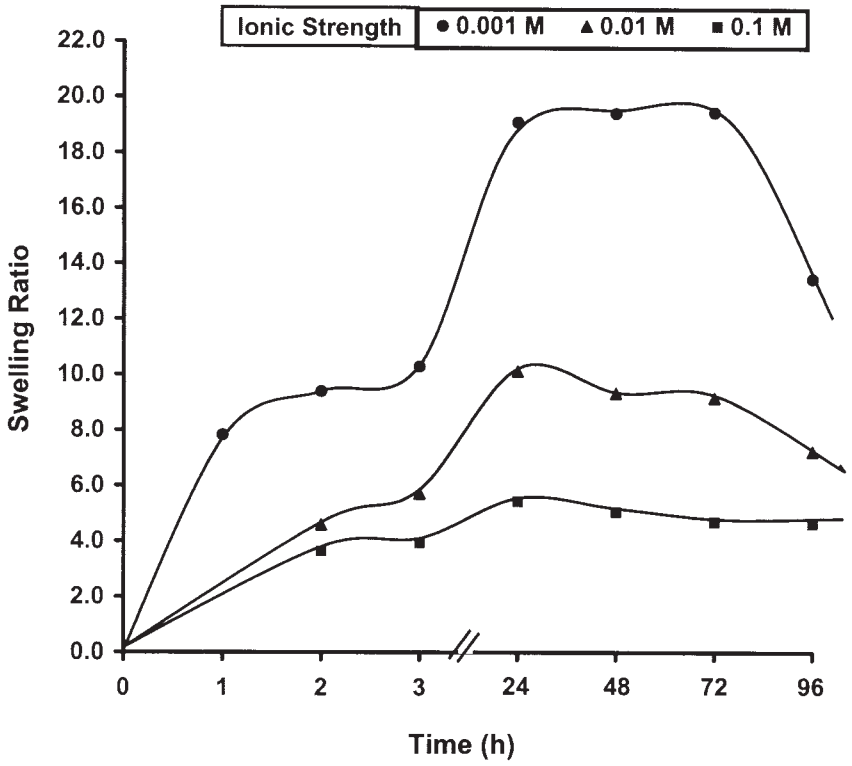


Figure 10 Effect of increasing the ionic strength of the swelling medium on the swelling ratio at a fixed composition of the hydrogel blend ([AAc] = 58.3 m*M*, [PVA] = 1.5 g, [gelatin] = 1.0 g, [MBA] = 0.25 m*M*, [KPS] = 0.36 mM, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C).

$$\pi = \frac{-(\mu_1^g - \Delta\mu_1^s)}{V_1} = 0 \qquad (12)$$

In the case of an ionic system, the osmotic pressure is mainly contributed by π ions, which are due to the counterion difference between the gel and the outer solution. In a modified form, eq. (12) can be written as follows:

$$\pi_{\text{ion}} = RT\sum(C_i^g - C_i^s) \qquad (13)$$

where C_i is the mobile ion concentration of species i and superscripts g and s represent the gel and solution phases, respectively. From the equation, it is very clear that the greater the difference is between the concentrations of mobile ions inside and outside the gel, the greater the osmotic pressure is and the larger the swelling is of the hydrogel.

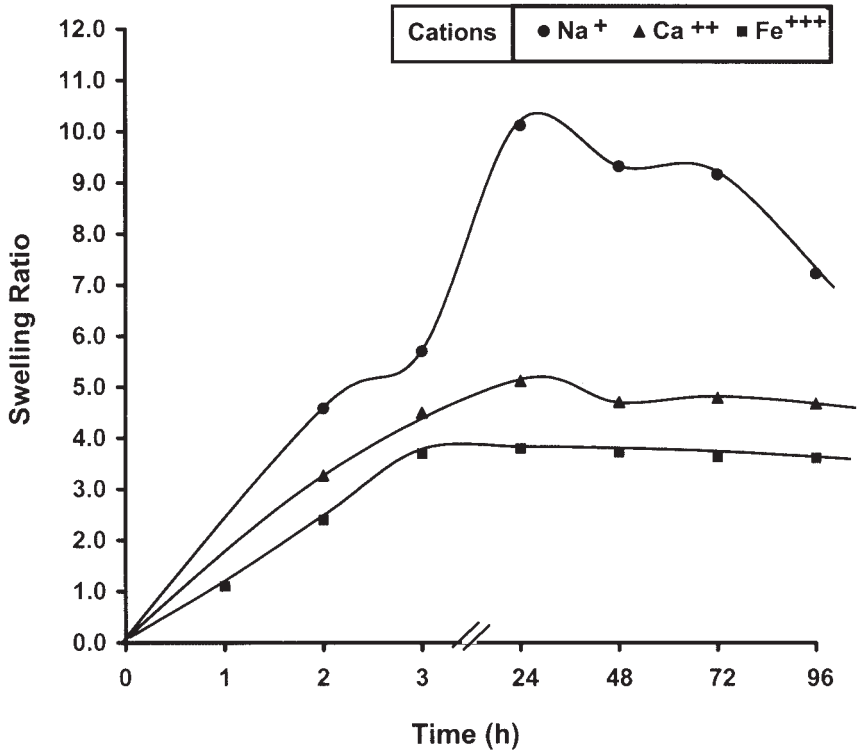
Ionic strength and swelling

With the variation of concentration of NaCl in the outer swelling bath, in the range of 0.001–0.1*M*, the swelling ratio is appreciably depressed with increasing salt concentration, as shown in Figure 10. The observed depression in the swelling ratio can be attributed to the fact that the addition of ions to the outer medium results in a decrease in the value of $\mu_i^g - \mu_i^s$ in eq. (12), which consequently lowers osmotic pressure π and thus bring about a fall in the swelling ratio.

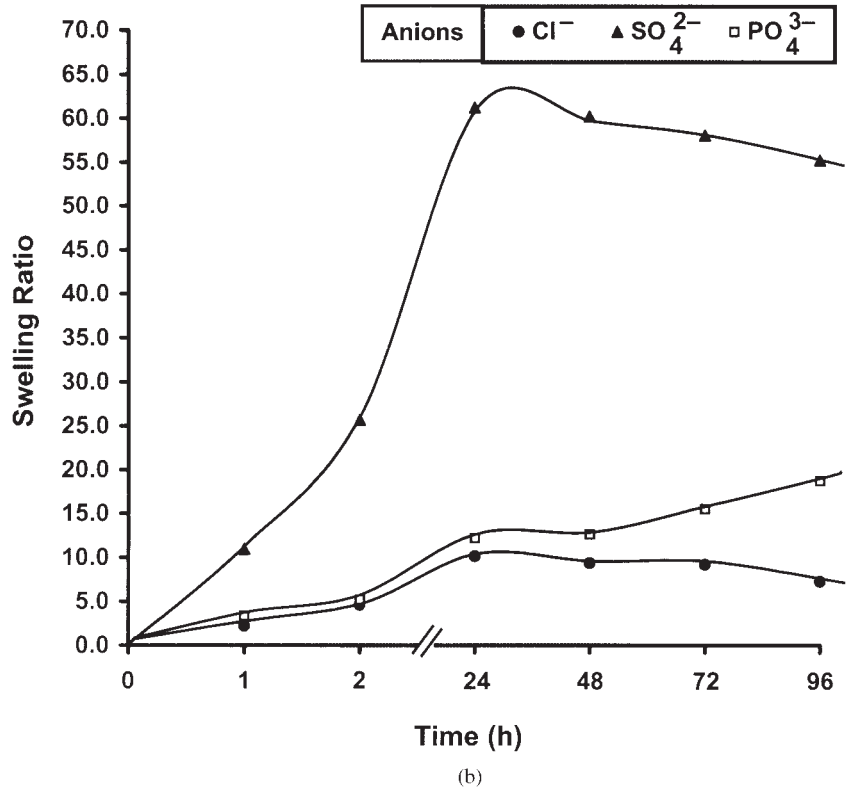
A remarkable feature visible in the swelling profiles of the hydrogel is the phenomenon of the shrinking of the gel after a definite swelling period (24 h). The observed fall in the swelling ratio may be attributed to the fact that once the hydrogel swells to an optimum value, the pores of the gel widen, thus allowing the cations from the swelling bath to diffuse into the bulk of the swollen gel. These cations bind to the negatively charged —COO^- ions present along the network chains and obviously result in a shrinking of the network chains, bringing about a fall in the amount of the imbibed water.

Effect of cations

The influence of cations and their respective charges have been investigated on the swelling ratio of the hydrogel by the addition of 0.01*M* NaCl, $CaCl_2$, and $FeCl_3$ to the swelling medium. The results are displayed in Figure 11(a), which clearly reveals that there is an overall depression in the swelling ratio of the hydrogel in comparison with the swelling of the gel when no electrolyte is present. The observed decrease



(a)



(b)

Figure 11 (a) Effect of the size of various cations on the swelling ratio of the hydrogel blend at a fixed composition ([AAc] = 58.3 m*M*, [PVA] = 1.5 g, [gelatin] = 1.0 g, [MBA] = 0.25 m*M*, [KPS] = 0.36 m*M*, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C) and (b) effect of the size of various anions on the swelling ratio of the hydrogel blend at a fixed composition ([AAc] = 58.3 m*M*, [PVA] = 1.5 g, [gelatin] = 1.0 g, [MBA] = 0.25 m*M*, [KPS] = 0.36 m*M*, [MBS] = 4.04 m*M*, temperature = 28 ± 0.2°C).

TABLE II
Data Representing the Values of *n* and *D* at Various Compositions of the Hydrogels

Sample	Composition				n	$D \times 10^6$ (cm^2/v)	Mechanism
	AAc (m*M*)	PVA (g)	Gelatin (g)	MBA (m*M*)			
1	14.7	2.0	1.0	0.12	0.50	1.10	Fickian
2	29.1	2.0	1.0	0.12	0.66	0.54	Non-Fickian
3	43.7	2.0	1.0	0.12	0.50	0.50	Fickian
4	58.3	2.0	1.0	0.12	0.73	1.47	Non-Fickian
5	58.3	1.5	1.0	0.12	0.88	1.19	Non-Fickian
6	58.3	2.0	1.0	0.12	0.76	0.93	Non-Fickian
7	58.3	2.5	1.0	0.12	0.56	0.89	Non-Fickian
8	58.3	3.0	1.0	0.12	0.60	0.97	Non-Fickian
9	58.3	1.5	0.5	0.12	0.66	1.48	Non-Fickian
10	58.3	1.5	1.0	0.12	0.68	0.67	Non-Fickian
11	58.3	1.5	1.5	0.12	0.76	0.17	Non-Fickian
12	58.3	1.5	1.0	0.12	1.07	1.23	Case II
13	58.3	1.5	1.0	0.19	0.69	0.48	Non-Fickian
14	58.3	1.5	1.0	0.25	0.64	0.23	Non-Fickian
15	58.3	1.5	1.0	0.32	0.57	0.12	Non-Fickian

in the swelling ratio due to the addition of salt is quite expected and is explained in the previous paragraph.

A close examination of the swelling profiles imply that the added cations obey the following increasing order of effectiveness in suppressing the swelling ratio:

$$Fe^{3+} > Ca^{2+} > Na^{+} \quad (14)$$

The observed order of effectiveness may be explained by the fact that although $FeCl_3$ produces the largest number of ions upon dissociation, NaCl produces the least. As a result, the greatest depression in the osmotic pressure is caused by $FeCl_3$, whereas the smallest is caused by NaCl. These osmotic pressures consequently bring about respective decreases in the swelling ratio of the gel.

The swelling profiles also reveal that after a definite time (24 h), the swollen hydrogel starts shrinking. The following increasing order of effectiveness in bringing about the shrinking is obeyed:

$$Na^{+} > Ca^{2+} \quad (15)$$

Almost no shrinking effect is produced by Fe^{3+} ions, and this may be explained by the fact that, being the smallest ion with the greatest charge density, Fe^{3+} causes the maximum degree of hydration and, therefore, is hindered in entering the bulk of the swollen gel. This clearly results in almost no shrinkage in the hydrogel network. On the other hand, Na^{+} and Ca^{2+} ions, being greater in size than Fe^{3+} ions and possessing low charge density, undergo hydration to a much smaller extent and, as a result, transport into the bulk of the swollen gel, thus causing shrinking of the network.

Effect of anions

The influence of the addition of anions on the swelling of the hydrogel has been investigated by the addition of sodium salts of Cl^{-}, SO_4^{2-}, and PO_4^{3-} ions in equimolar amounts. The results are displayed in Figure 11(b), which clearly reveals that although in the case of chloride ions the swelling ratio constantly decreases beyond a definite time (24 h), an increase in the swelling ratio is seen in the case of sulfate and phosphate ions. The increase observed with sulfate ions is much greater than that with phosphate ions. The observed results may be attributed to the fact that sulfate and phosphate ions, when diffused into the bulk of the swelling gel, produce enhanced repulsion within the hydrogel network and, therefore, result in a significant swelling of the hydrogel. The relative order of effectiveness of sulfate and phosphate ions may be explained by the fact that the phosphate ion, being much greater in ionic size than the sulfate ion, is hindered in diffusing into the bulk of the swelling hydrogel and, therefore, brings about a less marked rise in the swelling ratio.

Analysis of the sorption data

The mechanism of water transport through the swelling gel is determined by several key factors, such as the equilibrium water content, chemical architecture of the gel, and relative rates of diffusion of water molecules and relaxation of macromolecular chains.[50] In this study, the influence of the chemical composition of the hydrogel has been investigated on the mechanism of water sorption, and the kinetic swelling data are summarized in Table II. As mentioned in an earlier part of this article, the value of n, calculated

TABLE III
Data Showing the Variation in the Diffusion Mechanism with Increasing pH of the Swelling Medium around the pK_a Value of PAA

Sample	pH	n	Diffusion mechanism
1	1.86	0.50	Fickian
2	3.44	0.54	Fickian
3	5.64	0.59	Non-Fickian
4	9.20	1.0	Case II

from eq. (2), provides information about whether the swelling process is Fickian (diffusion-controlled), non-Fickian (anomalous), or case II (relaxation-controlled).

It is clear from the data presented in Table II that except for the few cases in which the water sorption is Fickian in nature (n = 0.50), the value of n varies between 0.5 and 1.0, indicating an anomalous type of water-transport mechanism for most of the hydrogel compositions. The observed results could be attributed to the fact that because of the grafting of crosslinked PAA chains onto PVA and gelatin, the macromolecular matrix forms a loose three-dimensional structure with wide pores and adequate chain flexibility. Thus, the relative rates of water molecule diffusion and network chain relaxation become almost identical, and this results in an anomalous type of water-transport mechanism.

The effect of the pH of the swelling medium on the water sorption mechanism has been examined by the monitoring of the kinetics of the swelling process under various pH conditions. The results are presented in Table III, which reveals that upon the variation of the pH of the medium in the range of 1.86–9.20, the swelling process also varies from Fickian to case II, that is, from diffusion-controlled to relaxation-controlled. The observed results may be explained by the fact that with increasing pH of the medium, the carboxylic groups present in the network undergo dissociation, thus producing repulsion between the network chains in the hydrogel. The repulsion produced in the network widens the mesh sizes of the hydrogel, and this speeds up the rate of diffusion of water molecules into the network and simultaneously accelerates the relaxation of network chains. In this way, the rates of diffusion and chain relaxation becomes almost equal, and thus an anomalous transport mechanism is achieved.

Blood compatibility

One of the main problems of blood-contacting materials is thrombus formation on the artificial surface, where platelet adhesion and subsequent activation on foreign surfaces are crucial events preceding a possible embolism.[51] This has hampered the clinical success of blood-contacting devices and has made it necessary to use anticoagulants.[52] Because platelet adhesion/activation is mediated by adsorbed plasma proteins,[53] it is important to study all these processes before the application of the biomaterial and the development of better blood-compatible devices.

Most of the studies have been aimed at attempting to correlate the blood compatibility of foreign materials to the adsorption of proteins and cell adhesion, which are known to occur at the very first interaction of the material and the flowing blood.[54] The investigations have shown that the blood-compatible behavior of implants mainly depends on the various properties of surface materials, such as the surface charge, wettability, surface free energy, topography or roughness, and presence of specific groups on the surface.[55] In addition, it has recently been pointed out that the water structure on the surface of the material is one of the most important factors affecting blood compatibility.[56] The potential advantage of using hydrogels as blood-compatible materials is based on the low observed value of interfacial tension between the hydrogel surface and blood flow, which ultimately reduces the blood cell adhesion and protein adsorption on hydrogel surfaces.[57,58] In this study, therefore, the *in vitro* blood compatibility of the hydrogel has been determined in terms of the blood clot formation, percentage of hemolysis, and protein (BSA) adsorption tests.

The importance of protein adsorption on the hydrogel surface lies in the fact that it determines the mechanism and extent of intrinsic coagulation and adhesion of platelets. The adsorption of proteins onto a polymer surface is a complex process, and the extent of adsorption is determined by numerous factors, such as hydrophilicity, hydrophobicity, polar, nonpolar, charged, or uncharged parts of the polymer, and protein content.

The effect of the PVA content in the blend has been investigated on the blood compatibility parameters in the concentration range of 1.5–3.0 g. The results clearly show that with increasing PVA in the blends, the protein adsorption, weight of blood clots, and percentage of hemolysis decrease, and this indicates an enhanced blood compatibility of the gels. The observed enhanced blood compatibility may be attributed to the hydrophilic, inert, and flexible nature of PVA chains.

In the cases of increasing concentrations of gelatin in the hydrogel blends, the biocompatible parameters decrease; this is quite expected because of the well-known biocompatible nature of gelatin. Another reason may be that the PAA chains are grafted onto the gelatin backbone via free amino groups, which are well known to form polyelectrolyte complexes with acidic groups of cellular elements of blood. Thus, the

TABLE IV
Data showing the Weights of Blood Clots formed, Percentages of Hemolysis, and Amounts of BSA Adsorbed by Gels of Different Compositions

Sample	Composition				Weight of blood clots formed (g)	Hemolysis (%)	BSA adsorbed (mg/g)
	AAc (m*M*)	PVA (g)	Gelatin (g)	MBA (m*M*)			
1	14.7	2.0	1.0	0.12	0.026	89.17	34.65
2	29.1	2.0	1.0	0.12	0.022	92.12	34.48
3	43.7	2.0	1.0	0.12	0.021	92.23	26.25
4	58.3	2.0	1.0	0.12	0.019	87.38	21.05
5	58.3	1.5	1.0	0.12	0.029	88.5	27.38
6	58.3	2.0	1.0	0.12	0.019	87.38	21.05
7	58.3	2.5	1.0	0.12	0.013	84.6	20.05
8	58.3	3.0	1.0	0.12	0.011	81.6	18.10
9	58.3	1.5	0.5	0.12	0.038	89.8	21.73
10	58.3	1.5	1.0	0.12	0.029	88.5	18.98
11	58.3	1.5	1.5	0.12	0.016	74.07	16.84
12	58.3	1.5	1.0	0.12	0.029	88.5	27.38
13	58.3	1.5	1.0	0.19	0.024	88.4	24.90
14	58.3	1.5	1.0	0.25	0.022	88.03	23.90
15	58.3	1.5	1.0	0.32	0.021	76.08	23.65
16	Glass				0.007	—	—
17	Poly bag				0.021	50.09	30.42

reduction in the number of amino groups of gelatin results in an increase in the blood compatibility.[59]

In an attempt to correlate the adsorption of proteins to the blood compatibility of the hydrogels, protein adsorption experiments were carried out, and the results are summarized in Table IV. It is clearly implied by the table that with increasing concentrations of PVA, PAA, gelatin, and MBA in the blend, the amount of adsorbed BSA constantly decreases, and the observed decrease is consistent with the blood clot formation results, which also exhibit a regular fall in the amount of blood clots. The observed decrease in the amounts of adsorbed protein may be attributed to the fact that as the components of the blend are hydrophilic in nature, their increased amount in the blend imparts greater hydrophilicity to the blend, which obviously makes the blend surface more protein-resistant. It is, however, notable from the summarized data that these hemolysis results are not very consistent with those of the blood clot and protein adsorption experiments.

In the case of an increasing concentration of the crosslinker (MBA) in the blend, the observed enhanced blood compatibility can be attributed to the fact that increasing the concentration of the crosslinker results in an increase in the crosslink density of the network, which ultimately enhances the stiffness and smoothness of the material; thus, the surface morphology may offer less interaction between the blend material and the blood component, which may lead to a lower amount of blood clots formed and other described factors, thus enhancing the blood compatibility of the polymeric material.

CONCLUSIONS

A novel blend of PVA and gelatin both grafted with crosslinked PAA has resulted in a high-water-imbibing macromolecular matrix with remarkable blood compatibility. The IR spectra of the blend present sharp bands and provide clear evidence of the presence of characteristic functional groups of PVA, gelatin, and PAA in the grafted blend. The thermal characterization of the end polymer also suggests an amorphous and loose network that may be attributed to the grafting of bulky PAA chains onto both PVA and gelatin. A morphological study by SEM has indicated the porous nature of the surface with pore sizes ranging between 3 and 12 μm.

The water sorption potential of the blend hydrogel is greatly dependent on the chemical architecture of the hydrogel. When the concentrations of AAc, PVA, gelatin, and the crosslinker are varied in the feed mixture of the blend, the swelling ratio increases up to a definite concentration of the components initially, but beyond it, a fall in the swelling ratio is noticed. The blend also shows lower mechanical strength with an increasing swelling ratio. The prepared hydrogel blends show an optimum swelling ratio at extreme acidic and alkaline pHs of the swelling media. The blends also show a response to the presence of various cations and anions. The swelling ratio increases constantly with an increasing temperature of the swelling bath. The water sorption mechanics is non-Fickian, that is, anomalous for most of the compositions of the blends.

The grafted blends of the prepared hydrogel display a fair degree of blood compatibility as judged from protein (BSA) adsorption, blood clot formation, and hemolysis percentage tests conducted *in vitro*. The values of these parameters decrease with moderately increasing concentrations of PVA, gelatin, PAA, and the crosslinker (MBA) in the feed mixture of the blends. Thus, a blend with highly crosslinked PAA chains grafted onto a large amount of PVA and gelatin displays optimum blood compatibility.

The authors acknowledge the Director of the Indian Institute of Technology (Mumbai, India) for carrying out Fourier transform infrared, scanning electron microscopy, and differential scanning calorimetry analysis.

References

1. Peppas, N. A.; Mikos, A. G. In Hydrogels in Medicine and Pharmacy; Peppas, N. A., Ed.; CRC: Boca Raton, FL, 1986; Vol. 1, p 1.
2. Park, K.; Shalaby, W. C. W.; Park, H. In Biodegradable Hydrogels for Drug Delivery; Park, K.; Shalaby, W. C. S.; Park, H., Eds.; Technomic: Lancaster, PA, 1993; p 1.
3. Charila, T. V.; Constable, I. J.; Crawford, G. J.; Vijayshekran, S.; Thomson, D. E.; Chen, Y. C.; Fletcher, W. A.; Griffin, B. J. Biomaterials 1993, 13, 26.
4. Rosaik, J. M.; Ulanski, P.; Pajewski, L. A.; Yoshiv, F.; Makkuchi, K. Radiat Phys Chem 1995, 46, 161.
5. Andrepoulos, A. G.; Playlaria, M. J Biomater Appl 1998, 12, 291.
6. Jayanthi, R.; Rao, K. P. Biomaterials 1990, 11, 238.
7. Ikada, Y. Polym J 1991, 23, 551.
8. Williams, D. E. Concise Encyclopedia of Medical and Dental Materials; Pergamon: Oxford, 1990.
9. Yoshida, R.; Ichijo, H.; Hukuta, T.; Yamaguchi, T. Makromol Rapid Commun 1995, 16, 305.
10. Chirila, T. V.; Chem, Y.-C.; Griffin, B. J.; Constable, I. J. Polym Int 1993, 32, 221.
11. Lim, D.-W.; Yoon, K.-J.; Ko, S.-W. J Appl Polym Sci 2000, 78, 2525.
12. Bajpai, A. K.; Shrivastava, M. J Sci Ind Rev 2001, 60, 131.
13. Guideman, L. F.; Peppas, N. A. J Appl Polym Sci 1995, 55, 919.
14. Buchholz, F. L. In Adsorbent Polymer Technology; Brannon-Peppas, L.; Harland, R. S., Eds.; Elsevier: New York, 1990; p 23.
15. Pinche, C.; Zaldivav, D.; Gallardo, A.; San Roman, J. J Appl Polym Sci 1994, 54, 959.
16. Kim, S. J.; Perk, J.; Kim, S. I. React Funct Polym 2002, 55, 53.
17. Ruiz, J.; Mantecon, A.; Cadiz, V. J Appl Polym Sci 2002, 85, 1644.
18. Schmedler, R. H.; Masters, K. S.; West, J. S. Biomater 2002, 23, 4325.
19. Smetana, J. K. Biomaterials 1993, 14, 1046.
20. Schmedien, R. H.; Masters, K. S.; West, J. L. Biomaterials 2002, 23, 4325.
21. Okino, H.; Nakayama, U.; Tanaka, M.; Matsuda, M. J Biomed Mater Res 2002, 59, 233.
22. Williams, D. E. Concise Encyclopedia of Medical and Dental Materials; Academic: London, 1996.
23. Bajpai, A. K.; Shrivastava, M. J Macromol Sci Pure Appl Chem 2001, 38, 1123.
24. Kulik, E.; Ikada, Y. J Biomed Mater Res 1996, 30, 295.
25. Iwasaki, Y.; Eika, Y.; Morimoto, N.; Nakabayashi, Y.; Ishihara, K. J Biomed Mater Res 2000, 52, 701.
26. Kitano, H.; Ichikawa, K.; Fukuda, M.; Mochizuki, A.; Tanaka, A. J Colloid Interface Sci 2001, 242, 133.
27. Sawyer, P. N.; Patel, J. W. Surgery 1953, 34, 491.
28. Gracia, C.; Anderson, J. M.; Bareusberg, S. A. Trans Am Sci Intern Organs 1980, 26, 294.
29. Bajpai, A. K.; Shrivastava, M. J Macromol Sci Pure Appl Chem 2000, 37, 1069.
30. Hariharan, D. L.; Peppas, N. A. J Membr Sci 1993, 18, 1.
31. Khare, A. R.; Peppas, N. A. Biomaterials 1995, 16, 559.
32. Chou, L. Y.; Blanch, H. W.; Prausnitz, J. M. J Appl Polym Sci 1992, 45, 1411.
33. Plathe, F. M. Macromolecules 1998, 31, 6721.
34. Bajpai, A. K.; Bajpai, J.; Shukla, S. J Macromol Sci Pure Appl Chem 2002, 39, 492.
35. Crank, J. The Mathematics of Diffusion; Clarendon: Oxford, 1978; p 239.
36. Bajpai, A. K.; Shrivastava, M. J Macromol Sci Pure Appl Chem 2001, 38, 1123.
37. Singh, D. K.; Ray, A. K. J Appl Polym Sci 1994, 53, 1115.
38. Sharp, M. K.; Mohammad, S. F. Ann Biomed Con 1998, 20, 788.
39. Ding, Z. Y.; Akinbis, J. J.; Saloger, R. J Polym Sci Part B: Polym Phys 1991, 20, 1035.
40. Flory, D. J. Principles of Polymer Chemistry; Cornell University Press: Ithaca, NY, 1953.
41. Rhim, J. W.; Sohn, M. Y.; Lee, K. H. J Appl Polym Sci 1994, 52, 1217.
42. Bajpai, J.; Bajpai, A. K.; Shukla, S. React Funct Polym 2001, 50, 16.
43. Shukla, S.; Bajpai, A. K.; Bajpai, J. Macromol Res 2003, 11, 273.
44. Ramaraj, A.; Radhakrishnan, G. Polymer 1994, 35, 2167.
45. Kim, B.; Flamme, K. L.; Peppas, N. A. J Appl Polym Sci 2003, 89, 160.
46. Lee, V. H. J Controlled Release 1990, 13, 213.
47. Ende, M. T. A.; Peppas, N. A. J Appl Polym Sci 1996, 59, 673.
48. Flory, P. J. Principles of Polymer Chemistry; Cornell University Press: Ithaca, NY, 1953.
49. Flory, P. J. Proc R Soc London Ser A 1996, 1, 391.
50. Ritzer, P. L.; Peppas, N. A. J Controlled Release 1987, 5, 953.
51. Mustard, J.; Groves, H.; Kinlough-Ralfbone, R.; Packham, M. Ann NY Acad Sci 1987, 12, 516.
52. Markwardt, F. Thromb Haemost 1996, 66, 144.
53. Tzoneva, R.; Heuchel, M.; Groth, T.; Altankou, G.; Sebrecht, W.; Paul, D. J Biomater Sci Polym Ed 2002, 13, 1033.
54. Tsai, W. B.; Grunkemeter, J. M.; Horbett, T. A.; Lew, K. R. J Biomed Mater Res 1999, 44, 130.
55. Tsuruta, T. Adv Polym Sci 1996, 126, 1.
56. Tanaka, M.; Mochizuki, A.; Shiroya, T.; Motomura, T.; Shimura, K.; Onishi, M.; Okahata, Y. Colloids Surf A 2002, 203, 195.
57. Kim, S. W.; Feijen, F. Crit Rev Biocompatibility 1987, 3, 229.
58. Andrade, J. D. J Assoc Adv Med Inst 1973, 7, 110.
59. Aita, S.; Minoura, N.; Tagula, K.; Fujiwara, Y. Biomaterials 1987, 8, 481.