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ENHANCED WATER SORPTION OF A SEMI-INTERPENETRATING POLYMER NETWORK (IPN) OF POLY(2-HYDROXYETHYL METHACRYLATE) (PHEMA) AND POLY(ETHYLENE GLYCOL) (PEG)

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ABSTRACT

An attempt was made to enhance the water-sorption capacity of polymers of 2-hydroxyethyl methacrylate (HEMA) by preparing its semi-interpenetrating polymer network (IPN) with a hydrophilic polymer such as poly(ethylene glycol) (PEG). The effects of various factors, such as history of the polymer sample, chemical architecture of the IPN, presence of salt ions in the swelling medium, and temperature of the swelling medium, were investigated on the water sorption kinetics of the IPNs. The IPN was characterized by IR spectral analysis and various structural parameters, such as molecular weight between crosslinks (M_c), crosslink density (q) and number of elastically effective chains (V_e), were evaluated. The IPNs were also assessed for their antithrombogenic potential.

Key Words: Swelling; HEMA; PEG; Hydrogel

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INTRODUCTION

Three dimensional polymeric materials capable of imbibing large amounts (>20%) of water into their internal network structure and exhibiting no symptoms of dissolution in aqueous environments are termed as 'hydrogels' or 'hungry networks'.[1] This water containing macromolecular matrices possesses many important biophysical properties such as soft and rubbery texture, living tissue like resemblance, stability towards biofluids, compatibility to the human blood, permeability to biomolecules, etc., and, therefore, deserves to be employed as biomaterials in medical science.[2] Some typical biomedical applications of hydrogels are soft contact lenses,[3] wound dressings,[4] controlled drug release systems,[5] artificial implants,[6] dialysis membranes,[7] surgical prostheses,[8] etc.

One of the most significant hydrogel systems finding an ever greater number of biomedical uses is derived from the polymers of a hydrophilic monomer, 2-hydroxyethyl methacrylate (HEMA). Hydrophilic polymers based on HEMA have been widely studied due to their high water content, non-toxicity and favorable tissue compatibility, which leads to many applications such as bio-compatible materials. These applications include soft contact lenses,[9] kidney dialysis systems,[10] drug-delivery systems[11] and artificial lever support systems.[12] The presence of a hydroxyl group and a carbonyl group on each repeat unit makes this polymer compatible with water, and the hydrophobic α-methyl group and backbone impart hydrolytic stability to the polymer and support the mechanical strength of the polymer matrix.[13] Although polymers of HEMA, hereafter abbreviated as PHEMA, and their physical properties, such as diffusion, mechanical and viscoelastic behavior, thermal and dielectric properties, have been well investigated,[14] yet the wide acceptance of PHEMA is restricted due to their poormechanical strength, insufficient permeable character, and limited water intake.[15] It is, therefore, necessary to modify PHEMA gels to increase their water sorption capacity and this has been largely achieved by adopting different techniques as discussed below.

Vazquez et al.[16] prepared highly flexible hydrogels of HEMA by using the hydrophobic comonomer 2-ethylhexyl acrylate. The comonomer was also found to impart film forming characteristics to the copolymer. Some workers[17] employed hydrophilic monomers such as vinyl pyrrolidone and potassium sulfopropylmethacrylate and studied the water sorption characteristics of the copolymeric hydrogels.

Another effective route to modify the physicochemical properties of HEMA based hydrogels has been the preparation of interpenetrating networks (IPNs) which are defined as intimate combination of two polymers, at least one of which is synthesized or crosslinked in the immediate presence of other.[18] For instance, Jeyanthi and Rao[19] polymerized HEMA in the presence of collagen, a natural protein, and studied the water sorption and

anticancer drug delivery properties of the resulting hydrogel. Similarly, Ramraj and Radhakrishnan[20] synthesized an IPN of PHEMA and polyvinyl alcohol, investigated the water swelling capacity of the hydrogel and also studied morphological features of the films.

Among various synthetic polymers being used in designing hydrophilic macromolecular matrices, the polyethylene glycols (PEG) have been a prime choice of chemists for biotechnical and biomedical uses.[21,22] Primarily this is because of its biocompatibility, non-toxicity, non-immunogenicity and water solubility.[23] Another important property of PEG is its unusual effectiveness in excluding other polymers from its presence when in an aqueous environment. This property translates into protein rejection, formation of two-phase systems with other polymers and non-antigenicity. Moreover, the capacity of PEG to form hydrogen bonded polymer complexes with acrylic polymers has been exploited in developing responsive hydrogels.[24]

The fundamental property to which all such biomedical applications are credited lies in the swelling of the hydrogels when they come in contact with an aqueous environment.[25] A study of the dynamics of water sorption by the hydrogels, therefore, is of much importance as it not only monitors the progress of the swelling process, but also gives an insight into the mechanism of water transport which reflects the network structure of the hydrogel framework.[26] In the present investigation, therefore, we are reporting results on the water sorption kinetics of a semi-IPN composed of polyethylene glycol (PEG) and poly(2-hydroxyethyl methacrylate) (PHEMA).

EXPERIMENTAL

2-Hydroxyethyl methacrylate (HEMA) was obtained from Sigma Aldrich Co., and the monomer was freed from the inhibitor following a method discussed in the next section. Polyethylene glycol (PEG) (Wilson Laboratory, Bombay, India) was of low molecular weight (600) and used as received. The crosslinker used in polymerization of HEMA was ethylene glycol dimethacrylate (EGDMA) obtained from Merck, Germany, and used as received. Potassium persulphate and potassium metabisulphite were of Loba Chemie, India, and used as received. Ethylene glycol (Loba Chemie, India) was used as a cosolvent. Bidistilled water was always used wherever required in the study.

Physiological Fluids

For studying the swelling behavior of IPNs in biological media, the following fluids were simulated:

Saline Water	0.9% (w/v) NaCl solution
Synthetic Urine	2.0 g NaCl (0.8% w/v), 0.25 g $MgSO_4$ (0.10% w/v), 5.0 g urea (2% w/v), and 0.15 g $CaCl_2$ (0.06% w/v)

Purification of Monomer

Because of poor stability of HEMA, the high purity of the monomer is essentially required in hydrogels synthesis as the presence of impurities may greatly affect the swelling characteristics of the end polymer. Degradation of the monomer during transportation and storage at ambient temperatures may result in increased levels of methacrylic acid (MAA) and the naturally occurring crosslinker EGDMA. As illustrated in Fig. 1, the HEMA monomer readily undergoes three common reactions:

(1) HEMA may hydrolyze at the ester linkage to form MAA and ethylene glycol; (2) two molecules of HEMA may transesterify to form the crosslinker and ethylene glycol, (3) monomer may polymerize at the double bond resulting in oligomer or polymer. Although an inhibitor such as hydroquinone (300 ppm) has been added to minimize the later reactions, however, an ultra purity is desirable for producing reliable data.

The impurity of methacrylic acid MAA in HEMA monomer was removed by stirring the monomer with 15% by weight of anhydrous sodium

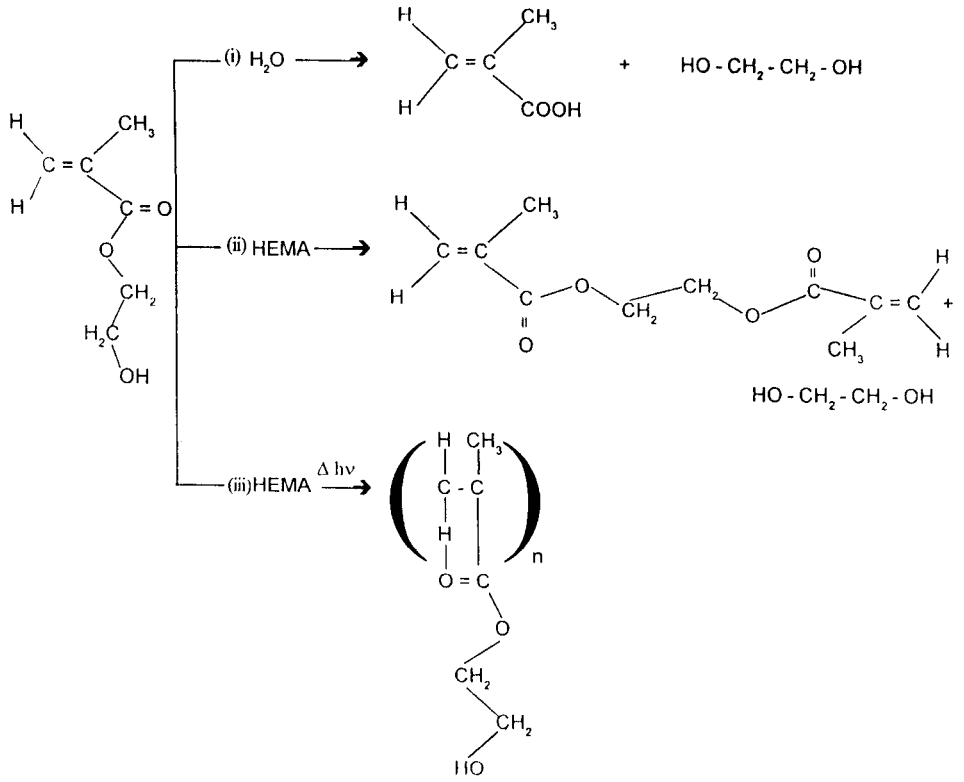

Figure 1. Synthesis of monomer 2-hydroxylethyl methacrylate (HEMA).

carbonate for 3 hr at 24°C, then vacuum filtering through Whatman filters papers. The yield on an initial volume of 100 mL of HEMA was 92%.

The impurity of EGDMA was then removed by first dissolving the above treated monomer in three times its volume of distilled water. Four extractions were performed with 50 mL of a 1:1 (volume) mixture of carbontetrachloride and cyclohexane, allowing the layers to separate for 30 min between extractions. The organic layer containing EGDMA was discarded after each extraction. The aqueous phase was placed under vacuum to remove any remaining organic solvent. The HEMA was then salted out with 100 g of NaCl, dried with anhydrous sodium sulphate, and filtered.

The partially purified HEMA monomer was vacuum distilled in the presence of 1 g of hydroquinone (added to prevent polymerization) at 60 mm Hg. The monomer was collected at 45°C with the distillation flask being heated in a water bath at 55°C. The collection flask was collected in an ice/acetone bath. The first and last fractions of the distillation product were discarded. After distillation, the pure HEMA was transferred to an opaque glass bottle and stored at 0°C until use.

Purity of HEMA

The purity of distilled HEMA was determined by high pressure liquid chromatography (HPLC). A Backmen system (Cold 127) equipped with an ultraviolet detector, a 25 cm × 46 mm id separation column ODS (C_{18}), 5 μm particle size were used. The uv detector was set at 217 nm. The mobile phase was methanol-water (60:40 v/v) and the flow-rate was kept at 1 mL/min. All samples were diluted with pure methanol to 1/1600. 10 μL samples were injected for each analysis. Samples of known concentrations of MAA and EGDMA were injected into the HPLC and the resultant chromatographs used to construct a standard curve of known concentration vs. area under the curve. The chromatograph showed three distinct peaks. The first peak, 3.614 min was identified as methacrylic acid (MAA). The next peak, 5.503 min, was the major peak due to HEMA monomer. The final peak, 15.3 min, was due to the crosslinker, EGDMA. The amounts of impurities of MAA and EGDMA in the monomer samples were found to be less than 0.01 mol% MAA and 0.001 mol% EGDMA.

Preparation of Semi-IPN

The IPN was prepared by a redox polymerization method as reported extensively in the literature.[27] In a typical experiment, into a petri dish (diam. 4", Corning) were added HEMA 32.9 mM PEG 0.33 g, ethylene glycol 71.6 mM as a cosolvent, EGDMA 0.53 mM potassium persulphate 0.04 mM

potassium metabisulphite 10.3 mM and water 0.20 mM. The mixture was degassed by purging dry N_2 for 30 min. The petri dish was then kept at 60°C for 72 hr so that the entire reaction mixture was polymerized and changed into a soft white circular disc. The IPN formed was purified by allowing it to swell in bidistilled water for one week so that the unreacted monomers and other chemicals were washed out. The swollen IPN was then cut into equal sized buttons (diam. 0.5 cm) and dried at room temperature for two weeks. Upon drying the IPNs became almost transparent. The IPNs were stored in airtight containers.

IR Analysis

The IPNs were characterized by IR analysis on a FTIR spectrophotometer (Perkin Elmer, Paragon 1000).

Penetration Velocity Measurements

The penetration velocity for each IPN composition was determined by the weight gain method as described by Peppas and Franson.[28] The penetration velocity was calculated from the slope of the initial portion of the penetrant uptake curve from the equation:

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

where v denotes the penetration velocity, dW_g/dt denotes the slope of weight gain vs. time curve, and ρ denotes the density of water. A denotes the area of one face of the disc and the factor 2 accounts for the fact that penetration takes place through both the faces. The penetration velocities calculated for different IPN compositions are displayed in Table 4.

Swelling Experiment

Swelling experiments and kinetics of water sorption were performed gravimetrically at 27°C as described in our earlier communication.[29] In brief, dried preweighed buttons of hydrogel (0.1 g) were placed a definite volume of bidistilled water as swelling medium, taken out at desired time intervals, soaked in between two filter papers by gently pressing and finally weighed. This process was continued until an almost constant weight of the swollen button was noticed. The dry buttons were almost fully transparent in unswollen state and became opaque white after water sorption. The equilibrium water content was calculated by the following equation:

$$\text{Equilibrium water content (EWC)} = \frac{W_s - W_d}{W_d} \times 100 \quad (2)$$

where W_s and W_d are the swollen and dry weights of the IPN buttons, respectively.

Kinetics of Swelling

Mostly, the dynamics of water sorption process is 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 was followed. For this purpose, the swelling hydrogel was taken out at different time intervals and its weight was recorded. For the kinetic analysis of the results the following equation was applied.[30]

$$W_t/W_\infty = kt^n \quad (3)$$

where k is the swelling rate front factor and n is the swelling exponent; and W_t and W_∞ 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 between 0.5 and 1.0 suggests for non-Fickian diffusion or more specifically anomalous diffusion. When n becomes exactly equal to unity then the diffusion is termed as Case II diffusion. In some cases the value of n has been found to exceed unity and it has been termed as 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:

$$M_t/M_\infty = 1 - \sum_{n=0}^{\infty} \left\{8/(2n+1)^2\pi^2\right\} \exp\left\{-(2n+1)^2\pi^2(Dt/L^2)\right\} \quad (4)$$

where t is time and L is the initial thickness of the sheet. Although this equation is readily evaluated using a spreadsheet program, it is instructive to examine the short-time limiting expression as well,[31]

$$M_t/M_\infty = \left(4/\pi^{0.5}\right)\left(Dt/L^2\right)^{0.5} \quad (5)$$

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

Blood Compatibility Studies

In order to judge the blood compatible nature of the hydrogel surface a blood-clot formation method was adopted as described elsewhere.[32] In brief, the hydrogel samples were equilibrated with saline water (0.9% NaCl solution) for 24 hr in a constant temperature bath. To these water swollen and equilibrated samples were added 0.5 mL of acid citrate dextrose (ACD) blood followed by the addition of 0.03 mL of $CaCl_2$ solution (4 M) to start the thrombus formation. The reaction was stopped by adding 4.0 mL of deionized water and the thrombus formed was separated by soaking in water for 10 min at room temperature and then fixed in 36% formaldehyde solution (2.0 mL) for another 10 min. The fixed clot was placed in water for 10 min and after drying, its weight was recorded. The same procedure was repeated for the glass surface and IPNs of other compositions and respective weights of thrombus formed were recorded by a highly sensitive balance.

RESULTS AND DISCUSSION

Characterization of Network

IR Spectra

The IR spectra of the semi-IPN is shown in Fig. 2. The spectra clearly marks the presence of PEG in the IPN as evident from the observed absorption bands at 1249 cm^{-1} (C–O stretching vibration in alcohol), 1351 cm^{-1} (interaction between O–H bending and C–O stretching), and 1112 cm^{-1} (asymmetric C–O–C stretching). In addition, the presence of HEMA is confirmed by the observed bands at 1726 cm^{-1} (C=O stretching), 1154 cm^{-1} (O–C–C stretching), 3668 cm^{-1} (O–H stretching) and

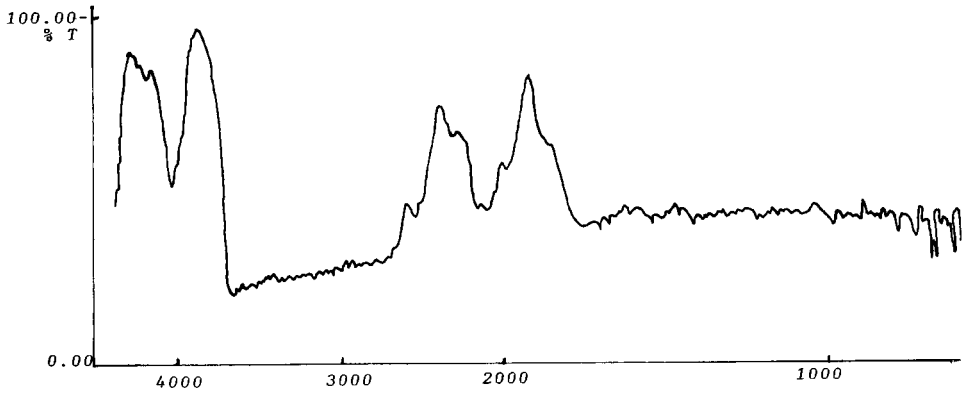

Figure 2. IR spectra of the semi-IPN.

1411 cm^{-1} (O–H bending) respectively. The spectra also indicate for the asymmetric stretch of methylene groups at 2901 cm^{-1}.

Network Parameters

One important structural parameter characterizing crosslinked polymer is M_c, the average molar mass between crosslinks, and 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 widely used to determine M_c. Early research by Flory and Rehner laid the foundation for analysis of equilibrium swelling. According to the theory of Flory and Rehner, for a network:

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

where V_1 is the molar volume of water (mL mol^{-1}), d_p is the polymer density (g mL^{-1}), and V_s is the volume fraction of polymer in the swollen IPN. χ is the Flory-Huggins interaction parameter between solvent and polymer.

The swelling ratio Q is equal to $1/V_s$. Here, the crosslink density, q, is defined as the mol fraction of crosslinked units:[33]

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

where M_o is the molar mass of the repeating unit.

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

$$v_e = d_p N_A/M_c \tag{8}$$

where N_A is Avogadro number.

The density of the IPN d_p was determined by pyknometry and found to be 1.15 g cm^{-3}. Other parameters such as V_1 and χ were noted from the literature.[34] Using Eqs. (6), (7) and (8), the values of M_c, q and v_e have been calculated for the IPNs containing different amounts of PEG, HEMA and crosslinker (EGDMA). The values calculated are summarized in Table 1.

Dynamic Model of Water Sorption

An IPN could be considered as an intimate mixture of crosslinked PHEMA and uncrosslinked PEG chains held to each other viz weak physical attractions, hydrogen bonding or through covalent attachments. In the

Table 1. Data Showing the Structural Parameters of the Semi-IPNs of Different Compositions

PEG (g)	HEMA (mM)	EGDMA (mM)	Average Mol. Wt. Between Crosslinks M_c	Crosslink Density $q \times 10^3$	No. of Elastically Effective Chains $v_e \times 10^{-20}$
0.33	32.9	0.53	2720	47.7	2.54
0.56	32.9	0.53	2130	61.0	3.24
0.89	32.9	0.53	1567	82.9	4.41
1.34	32.9	0.53	1380	94.2	5.01
0.33	41.1	0.53	1587	81.9	4.36
0.33	49.3	0.53	1090	119.2	6.34
0.33	57.5	0.53	707	183.8	9.18
0.33	32.9	1.16	1325	98.1	5.22
0.33	32.9	1.59	1700	118.1	6.29
0.33	32.9	2.12	688	188.9	10.0

present case the hydrogel consists of PEG and crosslinked PHEMA chains entangled with each other giving rise to a network arrangement of macromolecular chains as depicted in Fig. 3. When such a network comes in contact with a thermodynamically compatible solvent (such as water) the solvent molecules invade the network diffusing across the gel-liquid interface. Thus, a moving solvent front is observed in the hydrogel that clearly separates the unsolvated glassy polymer region ahead of the front from the swollen and rubbery gel phase behind it.[35] Just ahead of the front, the presence of the solvent plasticizes the polymer and causes it to undergo a glass to rubber transition.[36] Now the following possibilities arise:

(1) If the glass transition temperature of the polymer (Tg) is well below the experimental temperature, the polymer will be in the rubbery state and polymer chains will have a higher mobility that allows an easier penetration of the solvent.[37] 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} ($R_{diff} \ll R_{relax}$). The whole mechanism is modelled in Fig. 3(a).

(2) If the experimental temperature is below the Tg, the polymer chains are not sufficiently mobile to permit immediate penetration of the solvent in the polymer core. This gives rise to a non-Fickian diffusion process which includes Case II diffusion and anamalous 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 situations are depicted in Fig. 3(a) and 3(b), respectively.

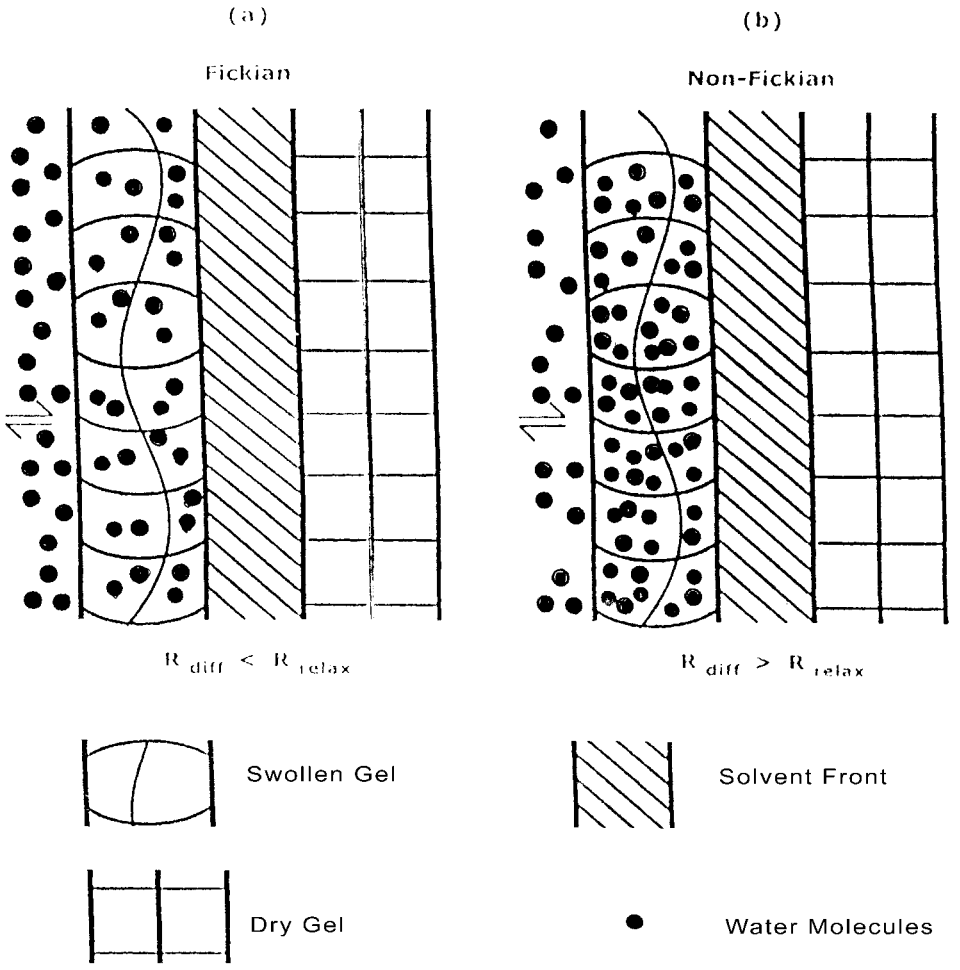

Figure 3. A model depicting the swelling mechanism of the IPN (a) Fickian transport, (b) non-Fickian transport (○) swollen gel, (▨) solvent front, (⊟) dry gel, (●) water molecules.

Effect of Sample History

During synthesis of the IPN there may be found unreacted monomer, initiator, crosslinker and performed polymer in the IPN, and the presence of these materials adds to the osmotic swelling pressure of the polymer until they diffuse out, thus altering the swelling kinetics observed. These impurities can be leached from the polymer sheets by swelling them in water. Thus, it is necessary to see if leaching cycles have an effect on subsequent swelling behavior. For this purpose IPN was removed from the petri dish, allowed to swell to equilibrium in water, dried in a vacuum oven, allowed to swell again, redried, and then allowed to swell for the third time. The observed water

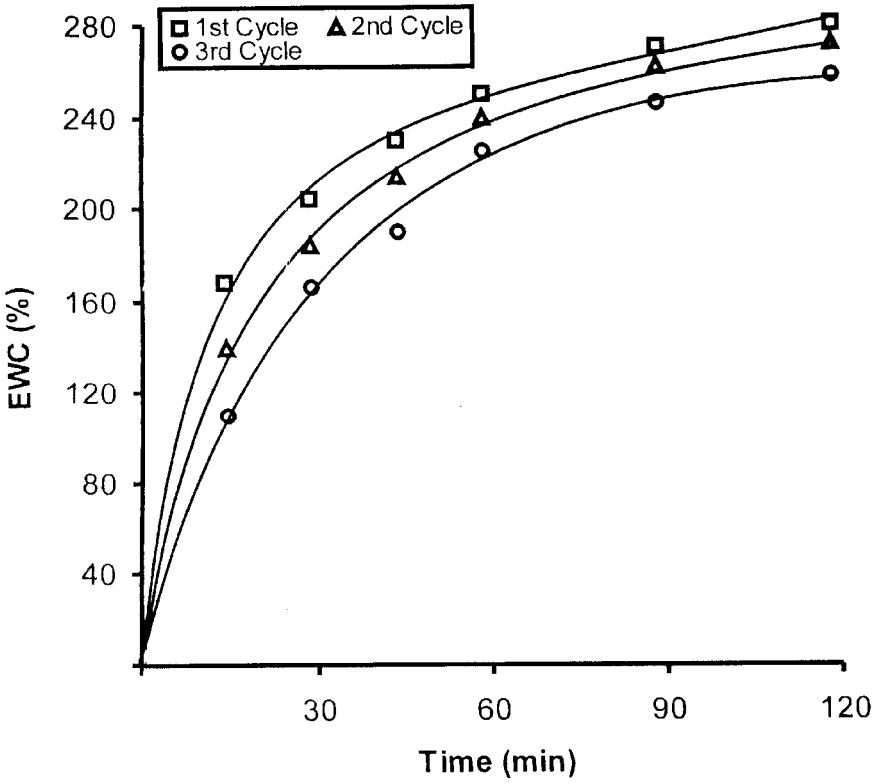

Figure 4. Effect of number of swelling/drying cycles on the sorption rate of IPN.

sorption results are shown in Fig. 4 which indicates that swelling kinetics do not change significantly over three swell/dry cycles. However, the equilibrium swelling substantially falls. This may be due to the slow loss of soluble materials from the IPN.

Another interesting parameter to affect swelling of IPNs is the aspect ratio, i.e., the ratio of sample disc diameter to its thickness. The results are presented in Table 2 which clearly reveals that the EWC increases significantly as the aspect ratio of the IPN was reduced. The observed increase in swelling may be attributed to the reason that a lower aspect ratio implies for a greater surface area of the IPN which results in a rise in the EWC.

Effect of PEG on Swelling

The swelling ratio (Q) of a hydrogel can be best described by Flory's swelling theory as given below,

Table 2. Effect of Aspect Ratio of the IPNs on their Equilibrium Water Contents (EWCs)

PEG (g)	HEMA (mM)	EGDMA (mM)	Aspect Ratio	EWC (%)
0.33	32.9	0.53	7.5	384
0.33	32.9	0.53	6.2	410
0.33	32.9	0.53	5.4	492

$$Q^{5/3} = \left[\left(i/2VuS^{1/2}\right) + (1/2 - X_1)/V_1\right]^{1/2}/(V_e/V_o) \tag{9}$$

where i/Vu is the concentration of fixed charge referred to the unswollen network; 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. Q has a relation to the ionic osmotic pressure, crosslinked density, and affinity of the hydrogel with water from the above equation. As the monomer employed is nonionic, the total fixed charge will be zero. Thus, the swelling will be a direct function of the hydrophilicity of the gel.

PEG, being a hydrophilic polymer and one of the components of the hydrogel, influences the degree of swelling significantly. To investigate the effect of PEG on the degree of swelling of the hydrogel, the concentration of PEG in the feed mixture was varied in the range 0.33 to 1.34 g. The swelling results are depicted in Fig. 5 which reveals that the equilibrium water content (EWC) first increases when PEG is added, then it monotonously decreases from beyond 0.33 g. However, EWC does not go below the value for PHEMA (without PEG) even when 1.34 g PEG is added. The results can be explained as below.

When the concentration of PEG is increased up to 0.33 g in the gel, the hydrophilicity of the network significantly increases which eventually results in an enhanced swelling of the hydrogel. In a quantitative sense, factor $(1/2 - X_1)/V_1$ predominates and affects the extent of swelling directly. However, beyond 0.33 g of PEG the network density increases appreciably because of an increase in number of PEG chains in the network and this consequently results in a domination of factor (V_e/V_o) in the Flory's equation. Since factor (V_e/V_o) represents the crosslinked density of the hydrogel, obviously its large value in the network will result in a lesser number of penetrant water molecules to diffuse across the water-hydrogel interface. This clearly brings about a fall in the EWC of the hydrogel. Similar type of results have also been reported by other workers.[38]

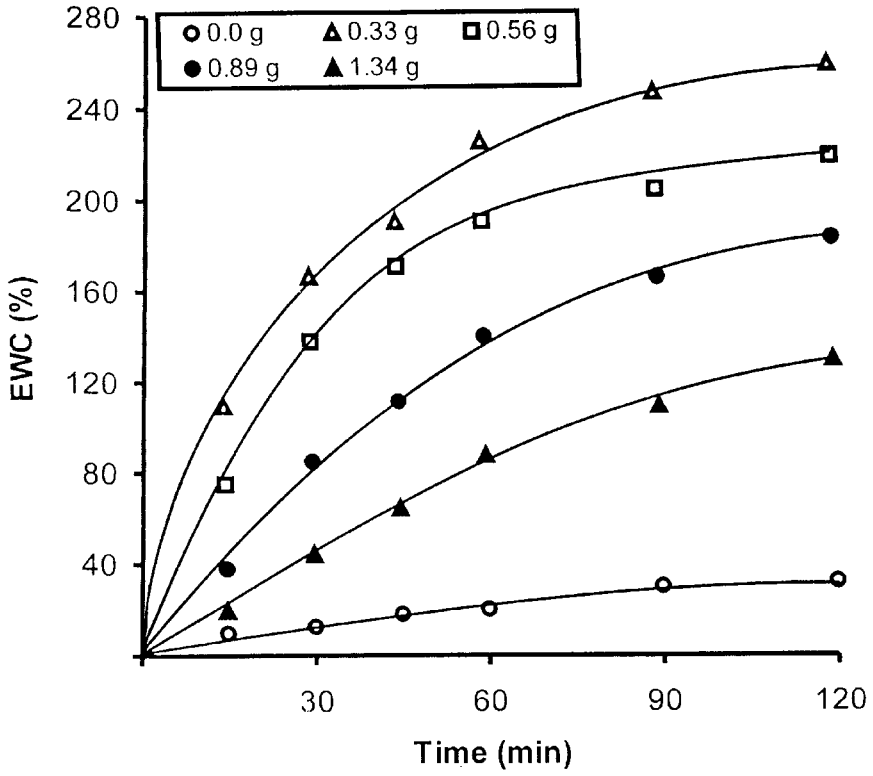

Figure 5. Effect of PEG content in the feed mixture of the IPN on its equilibrium water content.

Effect of HEMA on Swelling

In order to study the effect of monomer (HEMA) on the EWC of the hydrogel, the concentration of the HEMA was varied in the range 32.9 to 57.5 mM in the feed mixture. The results displayed in Fig. 6 indicate that the EWC decreases with increasing PHEMA concentration in the gel. The results are not unusual and have been previously reported.[39] The reason may be that increasing PHEMA content in the IPN results in a greater number of crosslinked PHEMA chains in the network which increases the crosslink density of the network. Thus, in an increased crosslinked gel the relaxation of macromolecular chains becomes restrained and, therefore, the swelling of the hydrogel will decrease.

The sorption curves also imply that at lower HEMA concentration the equilibrium sorption arrives relatively earlier than that at higher HEMA content. The observed results can be explained by the fact that at lower monomer concentration both the diffusion of water molecules and chain

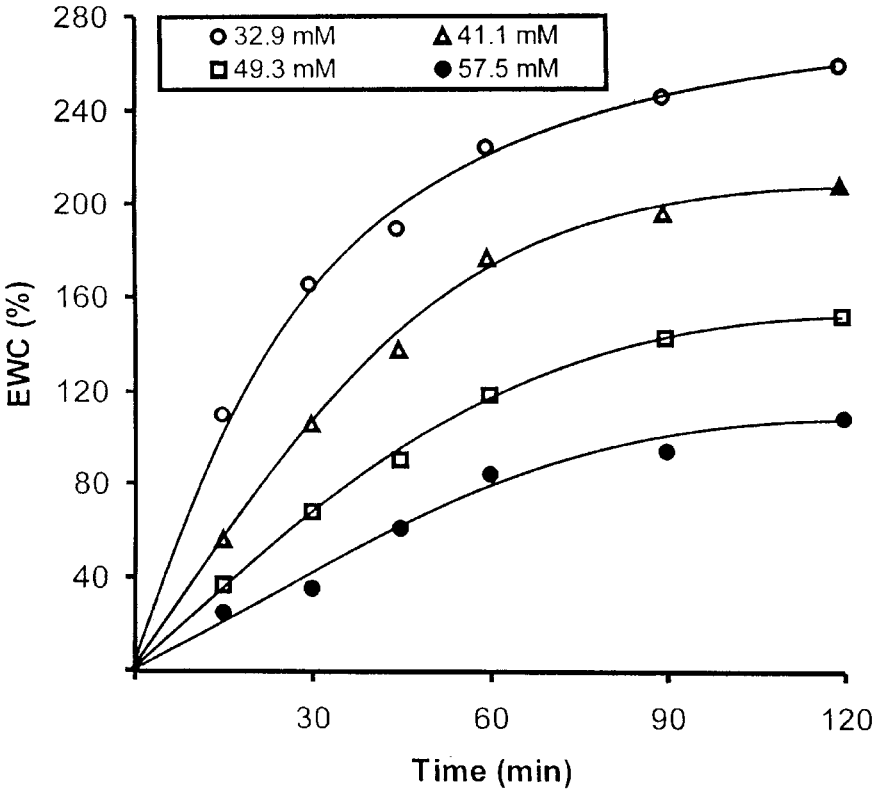

Figure 6. Variation in equilibrium content of the IPN with varying content of the HEMA in the feed mixture.

relaxation occur comparatively faster and this leads to an early arrival of sorption equilibrium. On the other hand, at higher HEMA concentration both the solvent diffusion and chain relaxation processes take place slowly and this allows penetrant water molecules to require more time to diffuse across the network. This obviously results in a late attainment of sorption equilibrium.

Effect of Crosslinker

One of the important factors controlling the swelling behavior of crosslinked HEMA is the balance of hydrophobic and hydrophilic interactions between polymer chains and water molecules. The balance of hydrophobic and hydrophilic forces in a polymer could be controlled by the addition of crosslinking agent and by varying the hydrophobic co-monomer composition. These processes could also be helpful in raising the selectivitiy of water content and mechanical strength of hydrogel for different applications.

In the present study, the hydrophobicity into the IPN has been incorporated by crosslinking HEMA polymer with a hydrophobic crosslinking agent such as EGDMA. It is known that the crosslinking agent when varied in the feed mixture of the IPN affects its swelling behavior in a complex way.[40] In the present investigation, the crosslinker ethylene glycol dimethacrylate (EGDMA) has been charged into the feed mixture in the concentration range 0.53 to 2.12 mM and the subsequent swelling results are shown in Fig. 7. It is clear from the results that the EWC is greatly reduced with increasing amounts of crosslinker in the hydrogel. One more remarkable feature of the swelling curves is that at higher concentration of EGDMA, the equilibrium swelling is attained faster. The observed results could be attributed to the fact that increasing crosslinker in the hydrogel results in a greater number of crosslink points in the network which obviously gives rise to a compact network structure in which both the diffusion of water molecules

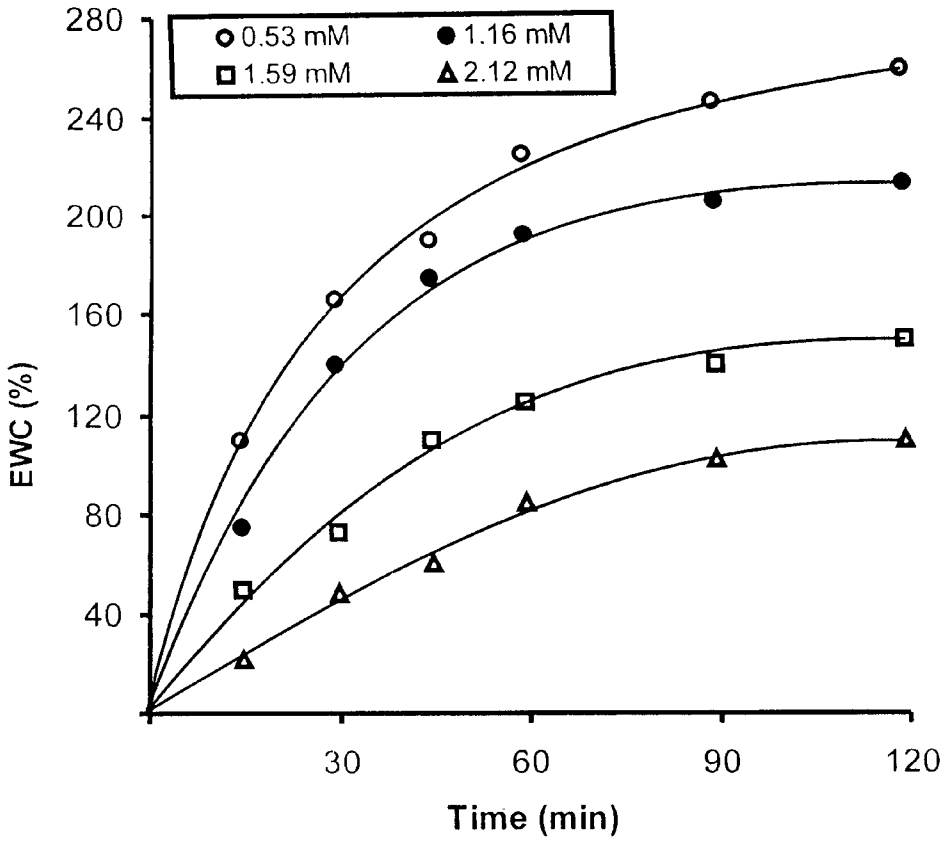

Figure 7. Effect of crosslinker on the equilibrium water content of the IPN.

and relaxation of macromolecular chains become difficult and, therefore, the degree of swelling decreases.

Another explanation for the reduced EWC may be that due to increase in crosslink points in the gel the average molecular weight[41] between the two crosslinks decreases (Table 1) which results in a reduced size of the free volumes between the macromolecular chains which could have been made available to water molecules for sorption. This phenomenon will lead to a decrease in the swelling of the hydrogel. Some authors[16] have reported an increase in the glass transition temperature (T_g) of the polymer which then results in a decrease in the overall swelling of the network.

Effect of Medium on Swelling

It has been both theoretically and experimentally established that the equilibrium swelling behavior of a polymer network in a solvent is the result of a balance between osmotic and the restoring elastic pressure. The presence of solution in the surrounding aqueous medium is capable of tilting this balance,[42] which may result in either an increase or decrease in swelling. The influence of solutes on the swelling behavior of IPNs has been examined by performing swelling experiments in presence of solutes such as potassium iodide (KI), urea and D-glucose (all 5% w/v), and in physiological fluids such as saline water (0.9% NaCl) and artificial urine. The equilibrium water sorption values presented in Table 3 reveal the following interesting results:

(1) It is reported that solvents such as potassium iodide and urea show an increase in EWC which may be attributed to the fact that whereas KI has a lyotropic property, the urea, on the other hand, is capable of breaking hydrogen bonds of the bound water and permeating into the interface region that is considered to exist in the hydrophilic polymer system.[43] However, in the present case the observed decrease in swelling with urea could possibly be due

Table 3. Effect of Medium on the Swelling Behavior of the IPN[a]

MEDIUM	EWC (%)
Water	310
KI (15%)	425
Urea (5%)	368
D-glucose (5%)	280
Saline water	166
Synthetic urine	210

[a]PEG 0.33 g, HEMA 32.9 mM, and EGDMA 0.53 mM.

to increase in osmotic pressure of the external solution which obviously results in a fall in the EWC.

(2) It is also implied by the results that a remarkable fall in the EWC is observed when swelling is performed in D-glucose, saline water and artificial urine. The observed decrease in EWC may again be due to an increase in osmotic pressure of the external solution.

Effect of Salts

The influence of the presence of salts in the swelling medium of a hydrogel is of importance in agriculture and biomedical applications, viz. water reservoirs in agriculture and hydrogels as implants for drug release applications.[44] In principle, changes in the swelling behavior due to the presence of salts 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.[45]

In the present study the components of IPNs are hydrophilic but in undissociable polymers in water 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 microsolutes (salts can be structure makers or structure breakers) association of the hyrophobic sites of the macromolecule, and formation of complexes between polymer and ions contribute to the overall effect.[46]

Apart from the above-mentioned possible consequences of salt ions, another significant effect the salt ion concentration may have the osmotic pressure of the swelling system that normally results from a net difference in concentration of mobile ions between the interior of gel and exterior of solution. Although several different types of models such as thermodynamic, mechanochemical, and scaling theories have been developed to explain the possible effect of salt ions on the swelling of the hydrogels, however, Donnan equilibrium theory can well interpret the results. According to this theory, the osmotic pressure is mainly contributed by π_{ion} as given below,[47]

$$\pi_{ion} = RT \sum_i (C_i^g - C_i^s) \tag{10}$$

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 implies that the greater the difference between the concentrations of mobile ions inside and outside the gel, the greater would be the osmotic pressure and larger would be the swelling of the gel.

In the present investigation, the effect of electrolytes on the swelling ratio of the hydrogel has been studied by adding halides of potassium to the swelling medium in the concentration range 0.01 to 0.4 M. The reason for selecting different anions rests upon the fact that the decisive role in swelling

of poly HEMA hydrogels is played by the anions as concluded by Dusek et al.[46] The results displayed in Fig. 8 reveal that the swelling ratio constantly decreases with increasing concentration of salts and the order of effectiveness in bringing about the depression in swelling follows the given sequence:

$$Cl^- > Br^- > I^-$$

The observed results are quite expected and are in accordance with Eq. 10. Obviously, as the concentration of ions increases in the outer solution, the osmotic pressure accordingly decreases and this, consequently, results in a lower degree of swelling of the IPN. The order of effectiveness of the added anions appears justified on the basis of their relative salting out property.

Just the opposite trend (increase in swelling) has been obtained while performing water-sorption experiments in the presence of thiocyanate ions (CNS^-) in the concentration range of 0.01 M to 0.40 M. A possible explanation for the observed increase in swelling may be that the thiocyanate anions are adsorbed onto the polymer molecules, charging them negatively. Repulsions between like-like charges produce chain expansion and an

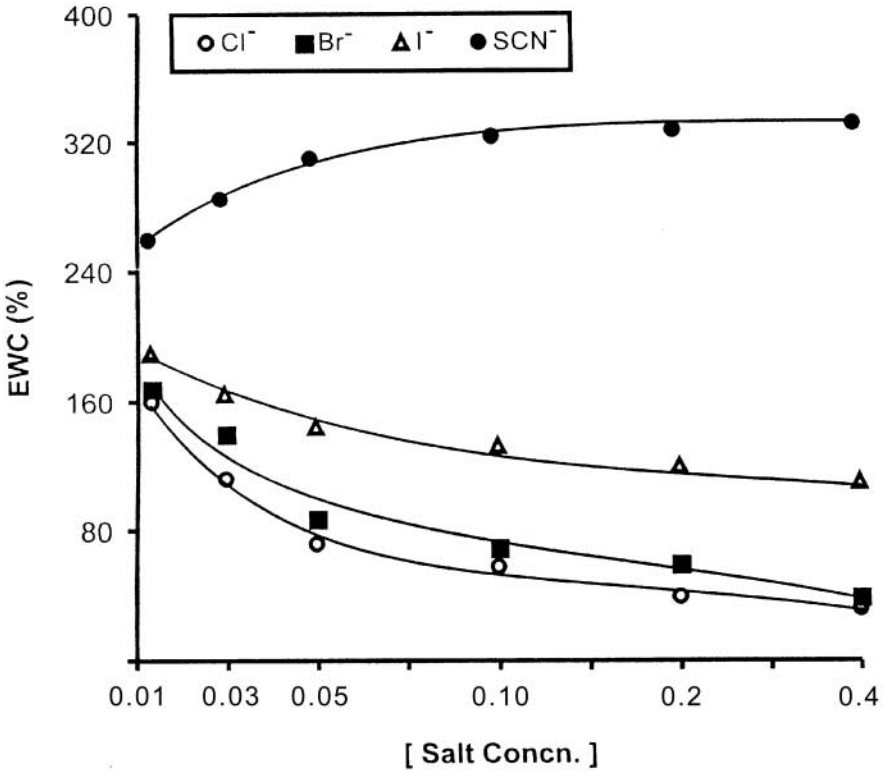

Figure 8. Effect of addition of salt ions on the water sorption capacity of the IPNs.

increase in water uptake is noticed. Further effects of this partial negative charge of the polymer are: (1) reduction of the hydrophobic character of the polymer chain, (2) reduction of the association of hydrophobic group, and (3) electrostatic attraction of cations and their hydration layer. The overall effect is, therefore, an increase in water content.

Analysis of Kinetic Data

As discussed previously, the swelling of a hydrogel is mainly contributed by the two dynamic processes, first, the diffusion of the penetrant water molecules and second, the relaxation of the macromolecular chains of both PEG and crosslinked PHEMA. These two processes are quantified by Eqs. (2) and (4).

Although the water uptake by the hydrogel is contributed by many other factors such as the elasticity of the network, solvent-polymer interaction, polymer-polymer interaction etc., however, the swelling exponent n given by Eq. (3) is a significant parameter in predicting the relative contributions of the diffusion and chain relaxation processes towards the swelling phenomenon. With the help of Eqs. (3) and (4), the values of n and D have been calculated and summarized in Table 4. Now, the following analysis could be made on the basis of n and D values.

With increasing the PEG content in the feed mixture of the hydrogel in the range 0.33 to 1.34 g, the value of n increases in the non-Fickian region as revealed by the data in Table 4. This clearly indicates that the water transport mechanism tends to become more and more Fickian in nature with increasing PEG in the hydrogel. This appears justified also as with increasing PEG chains in the hydrogel the network will become more compact and this results

Table 4. Data Showing the Kinetic Parameters of the Swelling of Semi-IPNs of Different Compositions

PEG (g)	HEMA (mM)	EGDMA (mM)	Swelling Exponent n	Diffusion Constant $D \times 10^8$ (cm^2/s)	Penetration Velocity $v \times 10^3$ (cm/s)	Mechanism
0.33	32.9	0.53	0.48	6.2	34.1	Fickian
0.33	32.9	0.53	0.50	5.9	24.8	Fickian
0.89	32.9	0.53	0.52	5.0	12.5	Fickian
1.34	32.9	0.53	0.56	4.2	6.2	Anomalous
0.33	41.1	0.53	0.48	4.6	16.1	Fickian
0.33	49.3	0.53	0.50	3.8	11.1	Fickian
0.33	32.9	1.16	0.54	8.8	26.0	Anomalous
0.33	32.9	1.59	0.56	5.4	14.8	Anomalous
0.33	32.9	2.12	0.64	4.8	7.4	Anomalous

in a restricted mobility of macromolecular chains. Thus, the water transport will become relaxation controlled, i.e., $R_{relax} \ll R_{diff}$.

On the other hand, increasing hydrophilic monomer (HEMA) tends to increase the value of n towards Fickian value in the Fickian range, i.e., the swelling process moves to acquire more diffusion controlled nature. This appears convincing also as increasing monomer results in a larger number of crosslinked PHEMA chains and this slows down the diffusion of water molecules across the hydrogel. Thus a slower rate of diffusion gives rise to a Fickian or diffusion controlled water sorption process.

A similar type of effect of increasing crosslinker concentration on n values has been noticed which indicates that with increasing EGDMA content in the hydrogel, the crosslinking density obviously increases and this naturally results in a slower relaxation of macromolecular chains. This clearly leads to a relaxation controlled swelling process and, therefore, the value of n increases in anomalous region as given by Table 4.

Effect of Temperature on Swelling

The influence of temperature on the swelling of a hydrogel is of much significance because it directly controls the diffusion of water molecules into the gel, segmental mobility of the network chains and water polymer interaction. In the present study the effect of temperature on the swelling characteristics of the hydrogel has been investigated by varying the temperature in the range 10° to 40°C. The results (Fig. 9) reveal that the EWC constantly decreases with increasing temperature of the swelling medium. The results can be explained by the fact that when the temperature is increased the hydrogen bonds between the water molecules and PHEMA chains get broken, thus converting bound water molecules into free water molecules. Similar types of results have also been reported by other workers.[48] In some studies, an increased degree of swelling has been observed with increasing temperature because of rapid segmental mobility of network chains, however, no such observations are present in our case.

To analyze the temperature effect, the Gibbs-Helmholtz equation can be applied according to which:[49]

$$\frac{d\ln(W_\infty)}{d(1/T)} = -\Delta H_m/R \tag{11}$$

where R is a gas constant and ΔH_m is the enthalpy of mixing between the dry polymer and infinite amount of water. When W_∞ is plotted against reciprocal of temperature (1/T), a straight line with positive slope is obtained (Fig. 10) which implies for an exothermic process. The value of ΔH_m was calculated to be 4.14 kcal/mol.

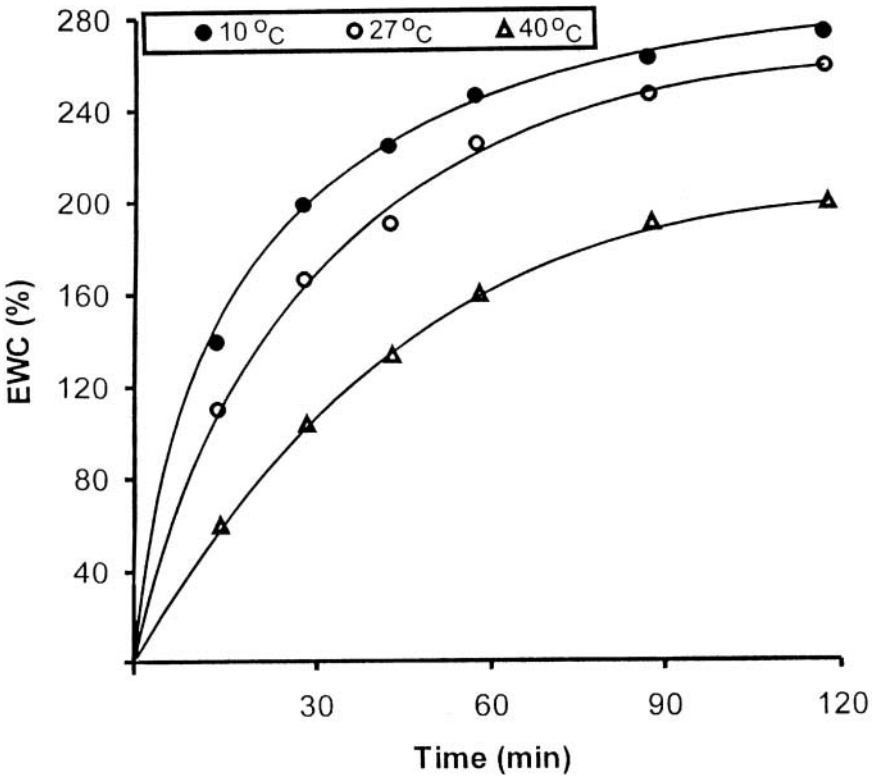

Figure 9. Effect of temperature on the EWC of the IPNs.

Antithrombiogenicity of IPN

In addition to having an adequate water content and a fair mechanical strength, the implantable materials must also show minimum tendency to initiate blood clot formation on their surface. Thus, the antithrombogenic potential of the IPNs was assayed by blood-clot test as described in the Experimental section. The results of clot formation tests shown in Table 5 indicate that whereas increasing HEMA and PEG content of the IPN results in less amount of blood clot formed, the increasing crosslinker content on the other hand, causes more blood-clot formation on the IPN surfaces. The observed results are quite obvious and support the logic that the greater the hydrophilic nature of the surface, the lesser the tendency of blood-clot formation. As the crosslinker EGDMA is hydrophobic in nature, its increasing content in the IPN will favor protein adsorption and as a consequence, also clot formation.

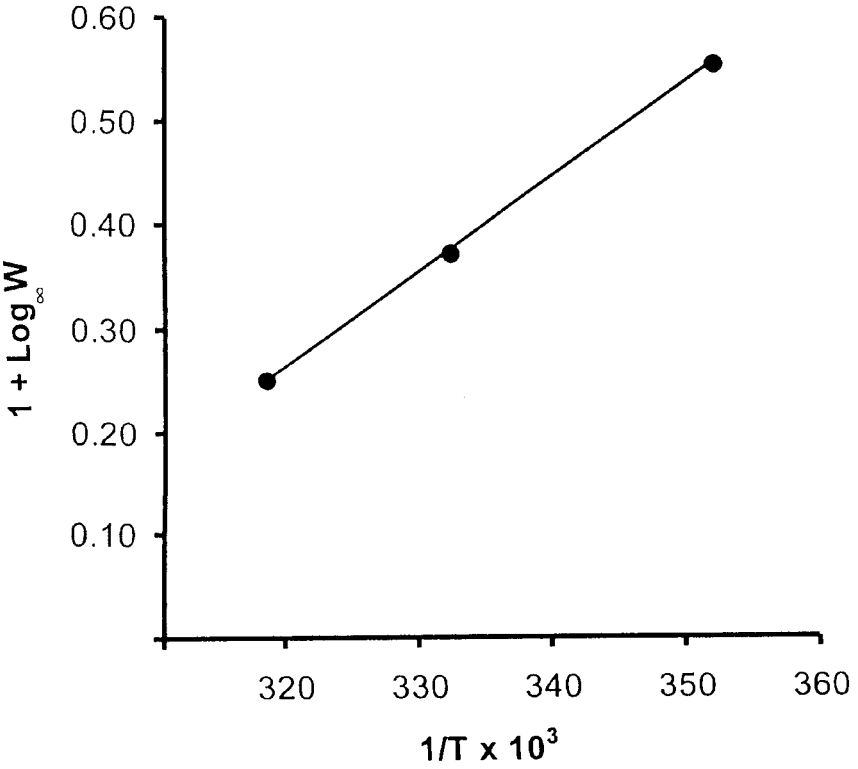

Figure 10. Plot drawn between $\ln W_\infty$ and $1/T$ for evaluating enthalpy of mixing (ΔH_m).

CONCLUSION

Inclusion of a hydrophilic polymer such as polyethylene glycol (PEG) into crosslinked matrix of polyHEMA produces an IPN which exhibits a significant increase in the water sorption capacity of the polyHEMA hydrogel. On increasing the PEG content beyond a critical value (3.45% v/v), the equilibrium water content is found to decrease, whereas on increasing the concentration of monomer (HEMA) and crosslinker (EGDMA) in the feed mixture of the IPN, the degree of swelling decreases. The equilibrium swelling was also found to depend on the previous history of the sample, i.e., a gel with a greater number of swell/dry cycle shows a lower equilibrium water content. The presence of solutes such as KI, urea, D-glucose, in the swelling medium also influence water sorption kinetics. An increase in EWC is noticed with KI while a decrease is observed with urea and D-glucose. The IPN also swells to a lesser degree in saline water and synthetic urine. The presence of salt ions (halide) also suppress the EWC but with thiocyanate ions an enhanced swelling is observed.

Table 5. Variation in Amounts of Blood Clot Formed on the Semi-IPN Surfaces of Different Compositions

PEG (g)	HEMA (mM)	EGDMA (mM)	Weight of Blood-Clot (mg)
0.33	32.9	0.53	28.2
0.56	32.9	0.53	20.6
0.89	32.9	0.53	12.0
1.34	32.9	0.53	10.6
0.33	41.1	0.53	24.4
0.33	49.3	0.53	18.0
0.33	57.5	0.53	14.6
0.33	32.9	1.16	30.2
0.33	32.9	1.59	32.4
0.33	32.9	2.12	34.0
Glass surface			38.6

The chemical architecture of the IPN also affects the water transport mechanism. It is found that increasing the PEG content in the IPN slightly shifts the water transport mechanism from Fickian to anomalous type, whereas increasing the HEMA content brings the mechanism towards a Fickian type. In the case of EGDMA, its increasing content in the hydrogel shifts the mechanism towards a non-Fickian type. An increase in temperature of the swelling medium results in a fall in the water sorption capacity of the IPN. It is also observed that increasing the PEG and HEMA content in the IPN makes the IPN surface more antithrombogenic while increasing the crosslinker results in a more thrombogenic hydrogel.

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