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DYNAMIC SWELLING BEHAVIOR OF POLYACRYLAMIDE BASED THREE COMPONENT HYDROGELS

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Key Words: Hydrogel, Acrylamide, Polyvinyl Pyrrolidone, Gelatin, Swelling

ABSTRACT

Three component polymeric thydrogels with greater water sorption properties were prepared of polyacrylamide, poly-vinyl-pyrrolidone, and gelatin by crosslinked polymerization method. The water uptake by hydrogel was greatly dependent on the composition of the hydrogel and external stimuli such as the presence of electrolytes and temperature of the system. The dynamics of the sorption process was investigated and found to be Fickian controlled. The hydrogels prepared were found to exhibit high anti-thrombogenic property than that possessed by the glass surface.

INTRODUCTION

In recent years, polymeric hydrogels, called biomaterials, have received considerable attention for use as specific sorbents and as support carriers in biomedical engineering [1-4]. Hydrogels are unique biomaterials which find extensive applications in medical science. The significant property for which they are

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known to form a novel class of material, is their capacity to imbibe high degree of water into their molecular structure [5]. Hydrogels are normally prepared by free radical polymerization of a hydrophilic vinyl monomers in the presence of a suitable crosslinking agent. To increase the swelling capacity of hydrogels, other polymeric components are normally introduced into the matrix, so that a proper balance between the swelling characteristics and mechanical properties of swollen hydrogels could be maintained.

The most common vinyl monomer which has been extensively employed in preparation of hydrogels is 2-Hydroxy Ethylmethacrylate (HEMA) [6-8]. The crosslinked homopolymers of HEMA along with different combinations of other monomers have been greatly employed to meet various situations like artificial implants, burn-dressings, cardiovascular devices, etc. [9-13]. There is quite a bit of literature on the work done on HEMA hydrogels, however, a fewer number of studies have been organized to focus at the synthesis of hydrogels with monomers other than HEMA [14-16]. Moreover, polymeric hydrogels composed of three component systems with good swelling behavior and mechanical strength are much fewer in number.

Thus, looking to the significant applications of hydrogels in biomedical fields, the present work consists of investigating the swelling characteristics of hydrogels containing an intimate mixture of crosslinked polyacrylamide, polyvinylpyrrolidone (PVP) and Gelatin and evaluating the blood compatibility of the end products. Our preliminary investigations on synthesis and swelling indicated that the hydrogels composed of the PVP, PAM and Gelatin showed the greatest swelling ratio and equilibrium swelling than those exhibited by two component hydrogels of any other compositions. This led us synthesize the three component polyacrylamide based hydrogels.

EXPERIMENTAL

Acrylamide (OttKemi, Bombay, India) was recrystallized from methanol and dried in vacuum over anhydrous silica for a week. Polyvinyl pyrrolidone (Burgoyne UR Bidges and Co., India) and Gelatin (Loba Chemie, India) were used without any pretreatment. N,N'-methylene bisacrylamide (MBA) (Central Drug House (P) Ltd, Bombay) was used as a crosslinking agent in free radical polymerization of acrylamide initiated by potassium persulphate (KPS) (Loba Chemie). Other chemicals used were of AR grade. Throughout the experiments doubly distilled water was used.

Method of Hydrogels Preparation

To a 25 ml doubly distilled water taken in a Petri-dish (corning) were added 0.75 g each of PVP and gelatin and 1.0 g of recrystallized acrylamide. The dish was heated gently, so as to prepare a homogeneous and transparent solution of the three polymer components. To this solution, were added 0.01 g of MBA and 0.05 g KPS and the the resulting solution was heated at 60°C for 2 minutes so that the whole solution solidified into a semi-transparent gel type material. This gel was placed in an oven at 110°C for 12 hours. By this prolonged heating, the gel converted into a solid thin film which was cooled and then stored in an air-tight container.

Swelling Experiments

For performing swelling experiments, a gravimetric method was adopted as followed in many similar studies [17, 18]. In brief, a pre-weighed piece of hydrogel film (0.5 cm × 0.5 cm × 0.038 cm) was poured into a fixed volume of doubly distilled water and allowed to swell. For monitoring the progress of the swelling process, the swollen piece was carefully taken out at definite time intervals and the excess was water removed by pressing the hydrogel in between the blotting papers and finally weighed in a sensitive balance (Anamed Electronic Balances, India, sensitivity up to 0.00019). The following swelling parameters were determined for the swollen hydrogels samples.

$$\text{Percent Equilibrium Water Content (EWC)} = \frac{\text{Weight of water}}{\text{Weight of dry gel}} \times 100$$

$$\text{Swelling Ratio (S.R.)} = \frac{\text{Weight of swollen gel}}{\text{Weight of dry gel}}$$

Blood Compatibility Studies

To judge the blood compatibility of hydrogels, the antithrombogenic property of hydrogel was compared with that of the glass by a method developed elsewhere [19, 20].

Prior to performing the compatibility tests, the hydrogel samples were hydrated in saline water (0.9% NaCl solution) at 30°C for 24 hours in a constant temperature bath. To these 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 (4M) to start the thrombus formation. The reaction was stopped at different time intervals by adding 4.0 ml dionized water and thrombus formed was separated by soaking in water for 10 minutes at room temperature and then fixed in 36% HCHO solution (2.0 ml) for another 10 minutes. This fixed clot was placed in water for 10 minutes and after drying, its weight was measured. The same procedure was repeated for the glass surface and other hydrogels and respective weights of thrombus formed were noted.

RESULTS AND DISCUSSION

Mechanism of Water Uptake

The hydrogels prepared in the present study are the intimate mixtures of PVP, gelatin and crosslinked PAM chains bonded to one another through H-bonding and electrostatic type of forces as shown in Figure 1. The PAM chains were crosslinked with the crosslinking agent in the solution, where the macromolecules assume the most probable extended conformations. As a result, in the dehydrated state (xerogel) the end to end distance will be shorter and the polymer will have an overwhelming tendency to become solvated. These hydrogels have also been described as 'high free energy' or 'hungry' networks. Thus, the water molecules will penetrate the network through the free volume accessible to the entering water molecules and this situation is presented in Figure 1.

The state of water in such hydrogel systems has been a subject of investigation for many years [21]. A common, but important, aspect of all such studies has been to explore if there is an existence or non-existence of 'different states' or different types of water in homogeneous mixtures of water and amorphous polymer network. It has been revealed from differential thermal analysis and differential scanning calorimetry (DSC) measurements [22] that two states of water molecules are present in the hydrogel, (i) the water molecules close to the hydrophilic polymer chains and in some way 'bound' to the poymer, and (ii) free water molecules which are unbound to the network chains. The two states of water are separately shown in Figure 1.

Effect of Monomer on Swelling

Since the hydrogels prepared are polyacrylamide based, the effect of increasing concentrations of acrylamide on the swelling behavior of hydrogel has been observed by polymerizing acrylamide in 3.0-8.0% (w/v) concentration

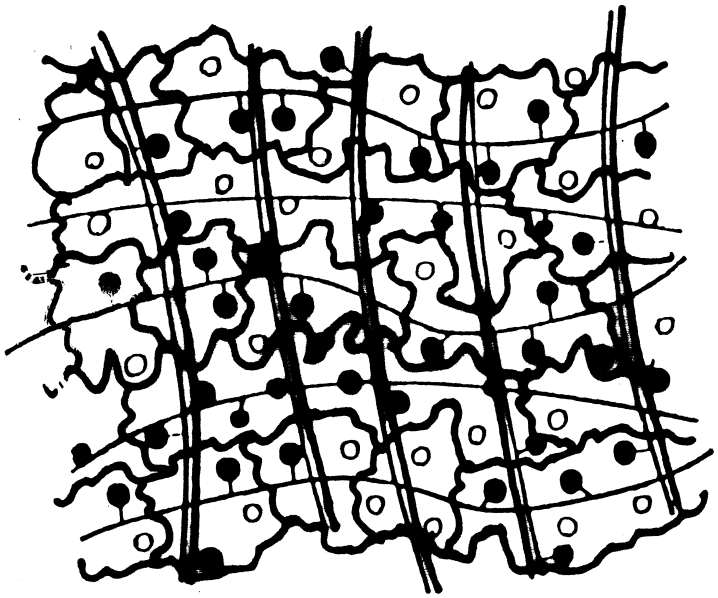

Figure 1. A model depicting the uptake of bound and unbound water molecules by the hydrogel. (●) bound water, (○) unbound water, (——) PVP chains, (||) gelatin chains and (∿∿) crosslinked PAM chains.

range. The results are depicted in Figure 2 which indicate that with an increasing concentration of monomer the swelling ratio and EWC of respective hydrogels decrease and the maximum swelling is obtained when the concentration of acrylamide is 3%. It has also been noticed that below 3% of acrylamide, the gel does not form at all. It is also found that the thickness of gel gradually increases with increasing acrylamide content in the gel.

The results can be explained by the fact that with increasing polymerizing monomer molecules in the system greater network of PAM chains are formed in the gel and thus the free volume accessible to water molecules significantly decreases and this accounts for low swelling ratio and EWC at higher monomer concentration.

It also reveals from Figure 2 that at lower monomer concentration, the equilibrium swelling is soon reached in comparison to swelling curves at higher monomer concentrations. The reason for this observation may be that at low acrylamide concentration, the network density of the hydrogel becomes quite low and, therefore, due to faster penetration of water molecules the saturation in swelling is achieved in shorter period.

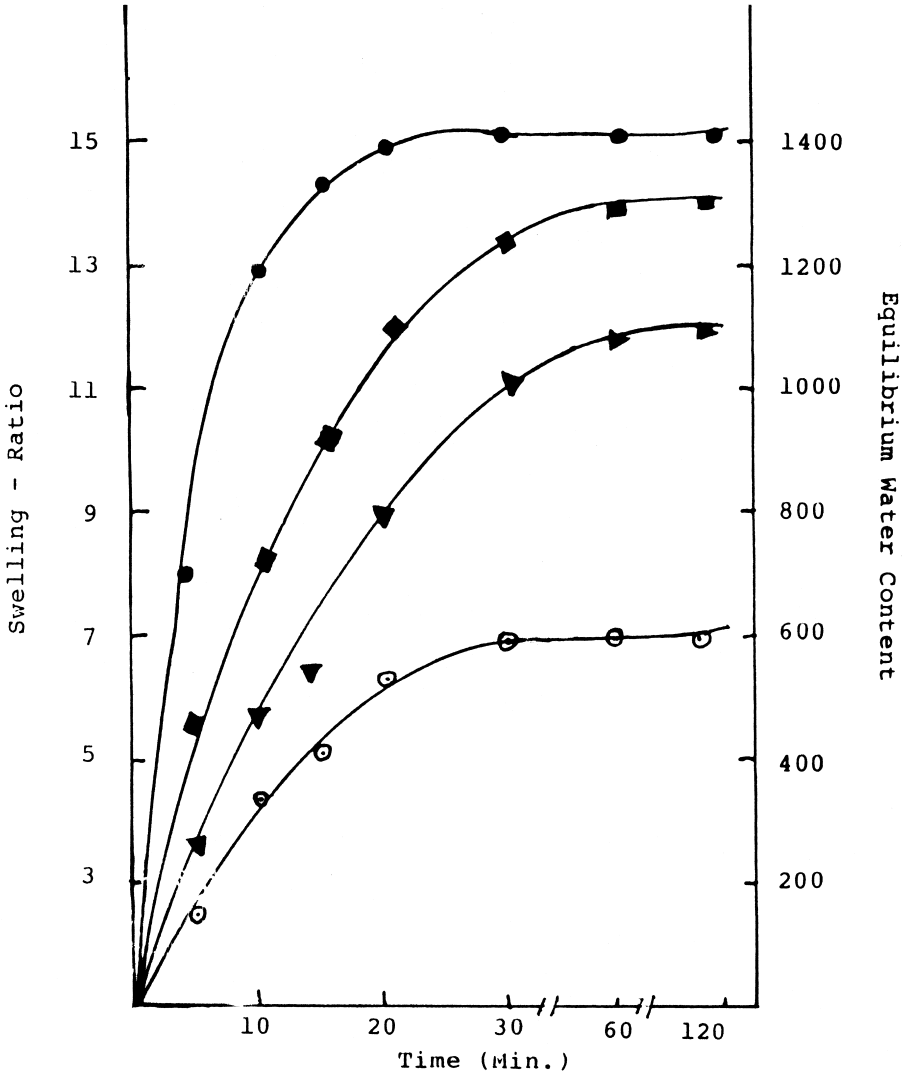

Figure 2. Effect of acrylamide content (percent w/v) of the hydrogel on its swelling behavior. (⊙) 8.0, (▲) 6.0, (■) 4.0 and (●) 3.0, PVP = 3.0, Gelatin = 3.0 at 30 ± 2°C.

Effect of PVP and Gelatin on Swelling

On increasing the concentrations of PVP in the range 2.0 to 8.0%. (w/v) in the polymerization system, it is found that initially the swelling ratio and EWC increase and, after the concentration of PVP solution reaches 3.0%, it

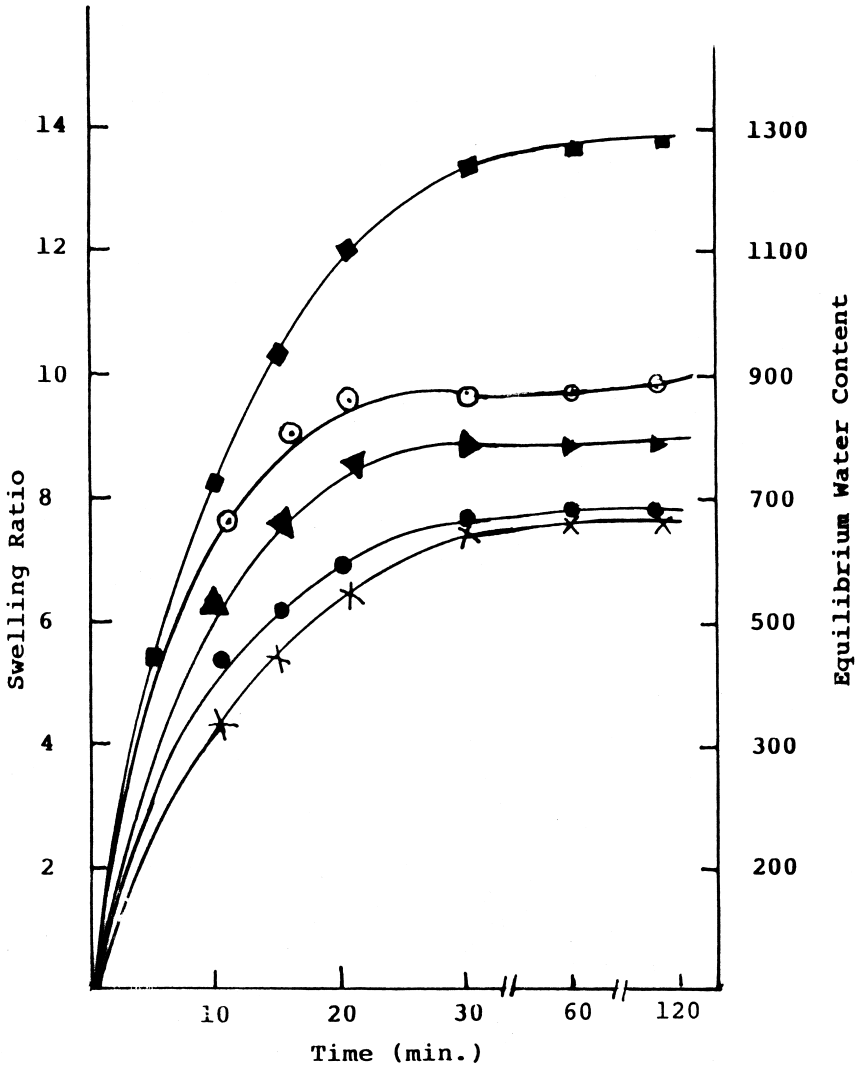

Figure 3. Variation between PVP content (percent w/v) of the hydrogel and its swelling behavior. (×) 8.0,(●) No PVP, (▲) 6.0, (⊙) 2.0, and (■) = 3.0, PAM = 1.0, Gelatin = 3.0 at 30 ± 0.2°C.

decreases significantly (Figure 3). The reason for the observed behavior is that in the initial range of increasing PVP concentrations due to the hydrophilic nature of the PVP polymer, greater number of water molecules will be bound to the PVP chains and swelling increases. However, beyond a critical concentration of PVP the network density of hydrogel increases so much that the gel become

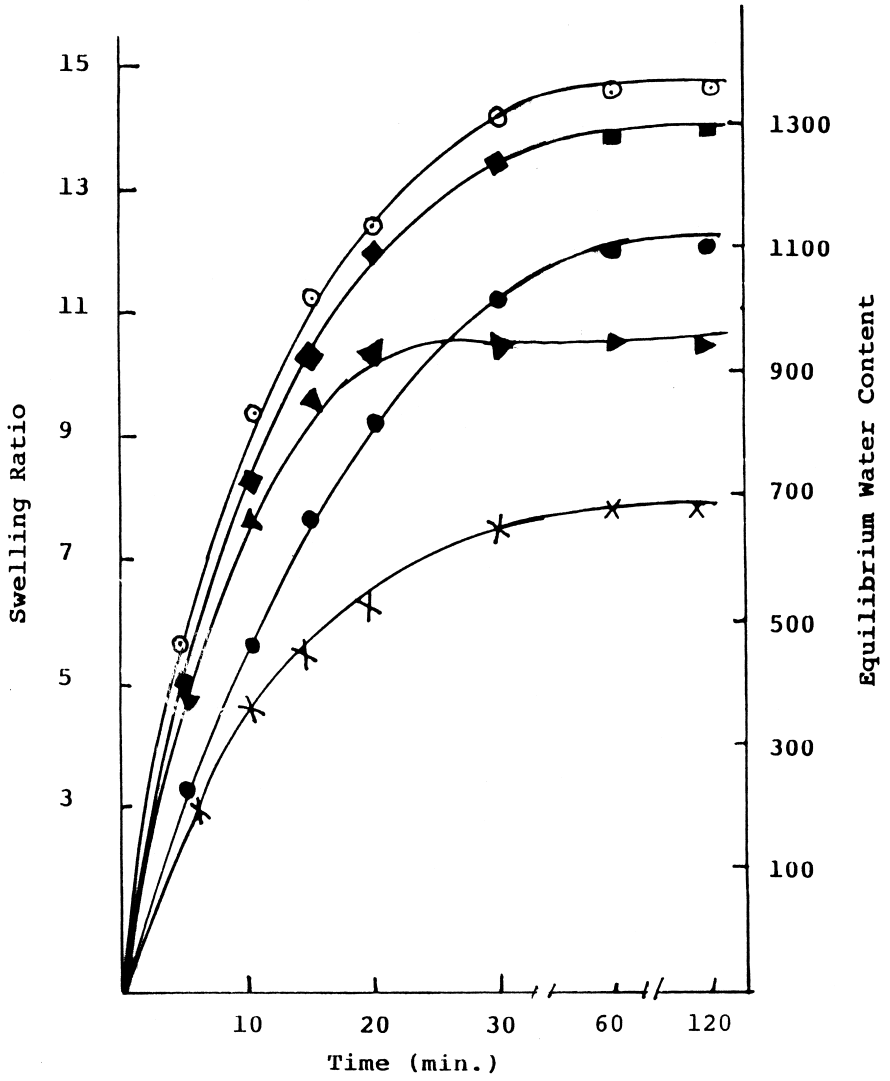

Figure 4. Effect of Gelatin content (percent w/v) of the hydrogel on its swelling behavior. (×) 1.6, (●) 6.0, (▲) 8.0, (■) 3.0, (⊙) No gelatin, PAM = 4.0, PVP = 3.0 at 30 ± 0.2°C.

compact and the penetration of water molecules into the IPN becomes difficult. This obviously results in a lower swelling of the hydrogel.

A similar type of swelling behavior has been noticed when the concentration of gelatin varies between 1.6-6.0% (w/v) as shown in Figure 4. This clearly reveals from Figure 4 that at 3.0% of gelatin concentration, a maximum

swelling is observed, whereas below and above 3.0% (w/v) concentration, the swelling is less due to insufficient and excess number of gelatin molecules in the hydrogel, respectively.

Effect of Crosslink Density on Swelling

The influence of crosslinking on swelling of the hydrogel has been investigated by varying the amount of N,N' MBA in the range 0.02-0.28% (w/v) in polymer solution mixtures. The results indciate that the swelling ratio and EWC gradually decrease with increasing amount of the crosslinker. The reason is quite obvious as increase in degree of crosslinking reduces the free volume of the hydrogel network and thus lesser number of water molecules enter the gel. Moreover, increased crosslinks in the gel also make the network chains more stiff so there is no chain relaxation on swelling and this explains why the swelling is low at higher N,N' MBA concentrations.

It was also observed that below 0.02% (w/v) of MBA concentration, the gels prepared showed remarkably good swelling but were very weak in strength in the swollen state and, therefore, were discarded.

Dynamics of Swelling

For monitoring the progress of the swelling of gels, various gels of varying compositions were prepared and the water uptake at different time intervals was determined gravimetrically. For the kinetic analysis of the results, the 'Fick's law' [23, 24] can be applied as an approximation as the diffusion of water molecules through the edges may be neglected. According to this law,

$$4\,(D_t / \pi l^2)^{1/2} = W_t / W_\infty \qquad (1)$$

where W_t and W_∞ represents the water uptake at time t and at infinite time, respectively, D is the diffusion coefficient and l is the average thickness of the film.

The results are depicted in Figure 5 which indicates the fractional uptake of water at different time intervals for varying compositions of gels. The diffusion constants calculated according to Equation 1 are summarized in Table 1 which clearly reveals that the penetration of water molecules into the hydrogel network is a function of the network structure. It also implies from the Table that the value of diffusion constant is significantly affected when there is a change in the concentration of the PVP and gelatin in the hydrogel rather then the change brought about by the acrylamide variation in the hydrogel.

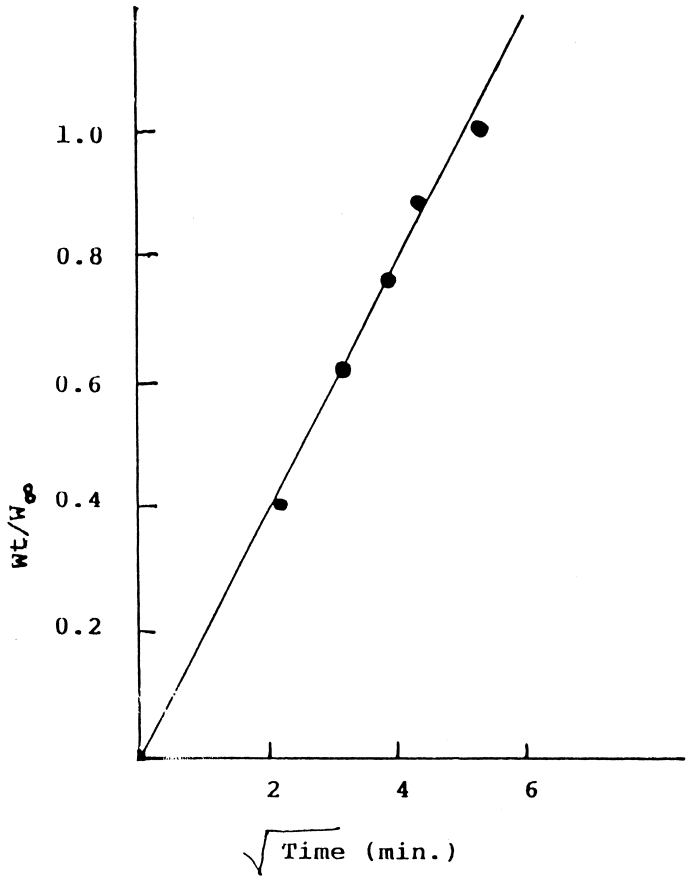

Figure 5. A representative plot drawn between W_t/W_∞ and $\sqrt{t}$ for evaluating the diffusion constant (D). PAM = 6.0, PVP = 3.0 and Gelatin = 3.0 (all in percent w/v) at fixed 30 $\pm$ 0.2°C.

In order to have a more realistic insights into the swelling process, the following exponential equation can give rise to more quantitative information,

$$\frac{W_t}{W_\infty} = k\, t^n \qquad (2)$$

where k is a characteristic constant of the gel, n is a characteristic exponent of the mode of transport of the penetrant. On taking logarithm of the above equation, we get

TABLE 1. Data Showing the Kinetic Parameters of the Swelling of Different Hydrogels of Varying Compositions

S.No.	Hydrogel composition			Diffusion constant $D \times 10^{11}$ m^2s^{-1}	η
	[Acrylamide]	[PVP]	[Gelatin]		
	percent (w/v)				
1.	4.0	3.0	3.0	1.71	0.50
2.	6.0	3.0	3.0	1.83	0.60
3.	8.0	3.0	3.0	2.10	0.60
4.	4.0	6.0	3.0	2.21	0.50
5.	4.0	8.0	3.0	0.89	0.54
6.	4.0	3.0	6.0	2.47	0.50
7.	4.0	3.0	8.0	1.48	0.73

$$\log \frac{W_t}{W_\infty} = \log k + n \log t \quad (3)$$

It is known that the numerical value of n decides the nature of the water diffusion process. If n = 0.5 then the diffusion process is rate limiting and it follows Fickian kinetics and on the other hand, when n varies between 0.5 and 1, it indicates that the desorption process is non-Fickian in nature. In the present studies, the plot drawn according to Equation 3 is shown in Figure 6 and the values of n and k are presented in Table 1. It is clear from the data that the process of diffusion is Fickian in nature for definite compositions of the hydrogel only.

Temperature Effect on Swelling

For investigating the effect of temperature on swelling ratio, the water uptake experiments were performed in the range 10° to 40°C as shown in Figure

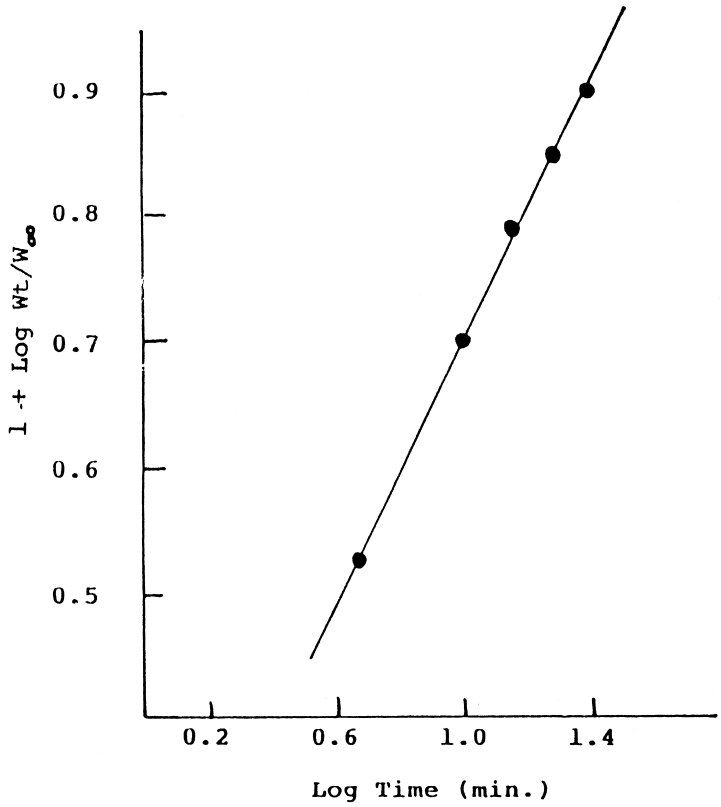

Figure 6. A representative plot drawn for evaluating the value of η (Equation 3) for the hydrogel of composition as mentioned in Figure 5.

7. The results indicate that the swelling ratio increases with increasing the temperature of the medium. Moreover, it also implies from the Figure that the initial rate of swelling, as well as the equilibrium swelling, are not significantly affected when the temperature exceeds the room temperature. On the other hand, the swelling curve at lower temperature (10°C) shows a much lower swelling rate and equilibrium swelling. The observed results can be explained by the fact that when the temperature increases from lower (10°C) to a room temperature range, then due to an increased segmental mobility of hydrogel chains, the water sorption capacity increases significantly. However, on increasing the temperature of the swelling medium beyond the room temperature, the hydrogel chains must have acquired complete relaxation so that with a further increase in temperature, they do not loosen and, as a consequence, no appreciable change in swelling

behavior could be observed at a higher temperature. To analyze the temperature effect, the Gibbs-Helmoholtz equation can be applied [25],

$$\frac{d \ln(w_\infty)}{d(1/T)} = -\Delta H_m/R \quad (4)$$

where R is a gas constant and ΔH_m is the enthalpy of mixing between the dry polymer and an infinite amount of water. When W_∞ is plotted against reciprocal of the swelling temperature (1/T), a straight line with a negative slope is obtained (Figure 8) which means an exothermic process.

The value of ΔH_m is calculated to be 0.97 KJ/mole. We have also investigated the effect of swelling temperature on the diffusion constants as summarized in Table 2 and it reveals that the diffusion constants increase with increasing temperature. An Arrhenius Equation 5 can be applied to the experimental data:

$$D = D_o \exp(-E_D/RT) \quad (5)$$

where E_D is the apparent activation energy for the diffusion process. The value of activation energy has been calculated to be 0.25 KJ/deg/mole from the above equation.

Such a low value of activation energy for diffusion of water molecules certainly points out a greater water uptake by the hydrogel and hence, this provides support to the high water sorption quality of the hydrogel.

Electrolyte Effect

It is well recognized that a balance between the osmotic pressure and the polymer elasticity sets the physical dimensions of the swelling hydrogels [26]. The osmotic pressure results from a net difference in concentration of mobile ions between the interior of gel and exterior solution. For ionic polymer gels, such as polyacrylic acid, fixed negatively charged acrylic acid groups attract hydrated counter ions which tend to expand the gel, while the conformational entropy elasticity of the crosslinked polymer chains oppose this expansion. Increasing the ionic concentration of the bathing medium reduces the mobile ion concentration difference between the polymer gel and the external solution (osmotic swelling pressure) and, thereby reduces the gel volumes, i.e., results in a shrinkage of the gel.

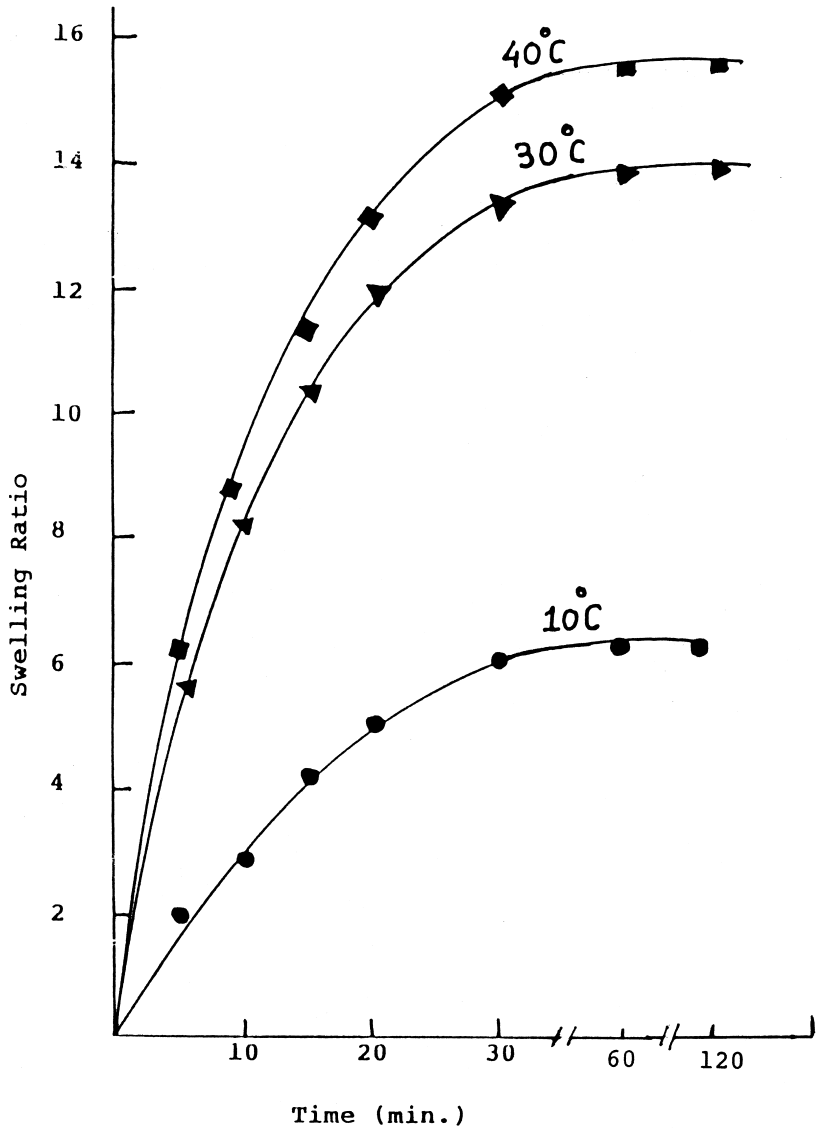

Figure 7. Variation of swelling ratio of the hydrogel with temperature of the external solution. The composition of gel is same as in Figure 5.

Although several different types of models such as thermodynamic, mechanochemical, and scaling theories have been developed which predict the equilibrium swelling response of ionic hydrogels to changes in ionic strengths [27], however, Donnan equilibrium theory can well interpret the results. Thus, according to the theory of swelling equilibrium, when a gel contacts a liquid,

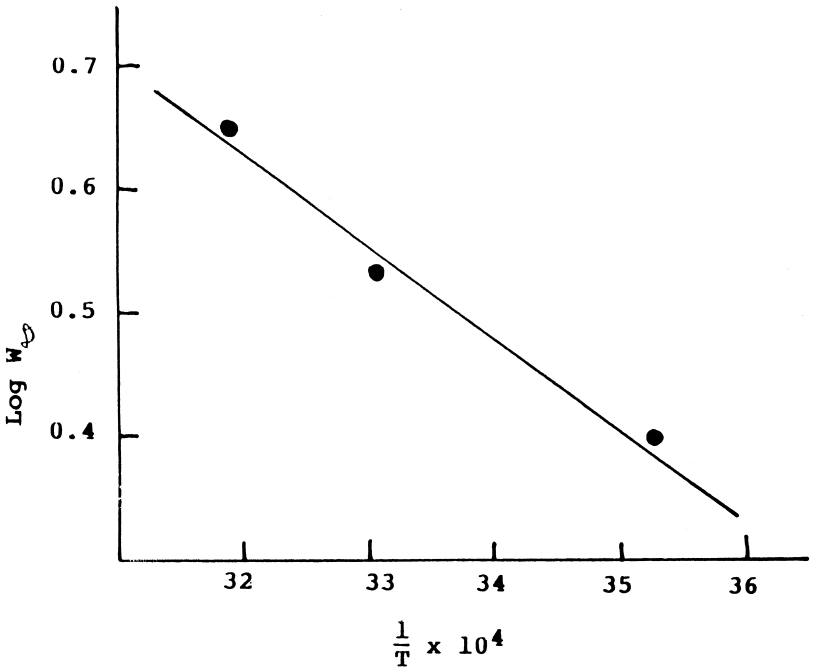

Figure 8. A plot between ln W_∞ and 1/T for evaluating ΔH_m for the hydrogel of composition as same as in Figure 5.

TABLE 2. Amounts of the Blood-Clot Formed on Various Surfaces and Respective Swelling Ratio of Hydrogels

Surface	Swelling Ratio	Wt. of clot (mg)
Gelatin – PAM	7.6	10.0
PVP – PAM	14.2	20.0
PVP – Gelatin – PAM	13.4	21.4
Glass	–	70.0

then the solvent chemical poential μ, in both the gel and solution phases must be equal at equilibrium,

$$\Delta\mu_1^{\,g} = \Delta\mu_1^{\,s} \tag{6}$$

where the superscripts g and s denotes the gel and solution phases, respectively. In terms of the osmotic pressure π, above Equation 6 can be written as:

$$\pi = \frac{-(\mu_1^{\,g} - \mu_1^{\,s})}{V_1} = 0 \tag{7}$$

where V_1 is the molar volume of solvent. Osmotic pressure π of the gel determines whether the gel will expand or shrink, when non-zero, π provides a driving force for gel volume change. In the case of an ionic system, the osmotic pressure π is mainly contributed by π ions which is caused by the concentration difference of counterions between the gel and the outer solution. Now, neglecting ion-ion, ion-solvent and ion-polymer interaction, we can write:

$$\pi_{ion} = RT\,\Sigma_i\,(C_i^{\,g} - C_i^{\,s}) \tag{8}$$

where C_i is the mobile ion concentration of species i. The equation (8) clearly implies that the larger the difference of the ionic concentration between the gel and solution, the greater the swelling.

In the present study, the electrolyte effect has been observed by adding uni-univalents salts to the external solution in the concentration range 0.01 M to 0.1 M. The results are depicted in Figure 9 which reveal that in the concentration range 0.01 M to 0.02 M of the added salts, the swelling ratio decreases and beyond 0.02 M concentration the swelling again increases. The initially observed decrease in the swelling is in agreement with the theoretical prediction that, due to an increase in the salt concentration in the outer solution the osmotic pressure will also decrease and as a consequence de-swelling of the hydrogel will be observed. The observed decrease in swelling has been noticed by many workers [28].

The interesting point that has been noticed in the present investigation is that the swelling ratio increases beyond 0.02 M salt concentration. A similar type of increase has also been reported by Baker and colleagues [29] in ampholytic and non-ionic acrylamide based hydrogels. This increase, in the present case

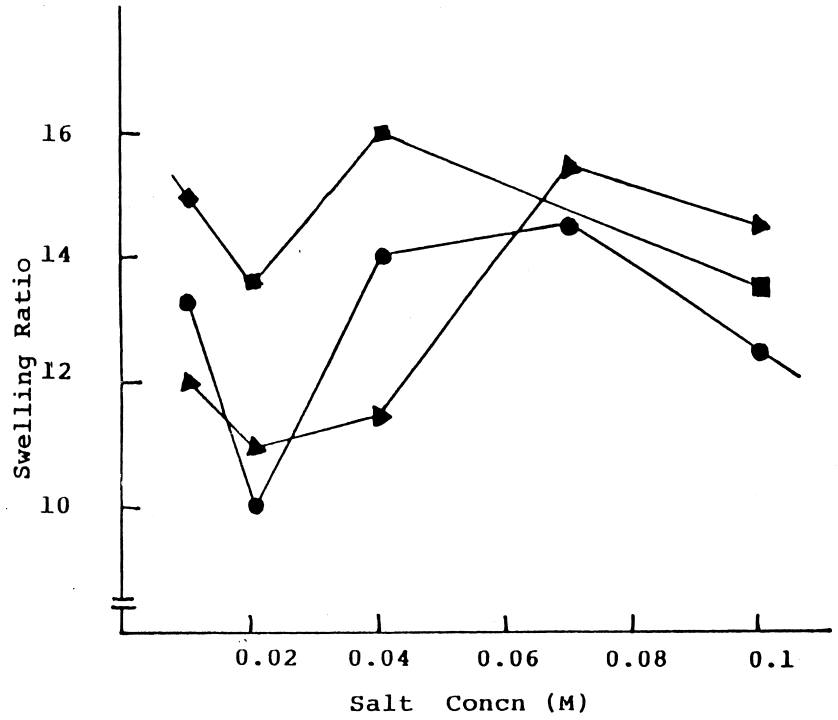

Figure 9. Variation in swelling ratio of the hydrogel with concentration of the salts added to the outer solution. (●) KI, (▲) KBr, and (■) KCl. Composition of gel is same as in Figure 5, 30 ± 0.2°C.

may be attributed to the fact that the osmotic pressure (π) also depends on the ion polymer interaction and, therefore, the difference in ion concentration ($c_1^g - c_1^s$) in Equation 8 alone cannot predict the dependence of π on salt concentration. Thus, beyond the salt concentration 0.02 M, the ions may interact with the PVP chains which are well known to exhibit ion-bonding property [30]. Thus, the binding of ions to the PVP chains results in an increased gap in concentrations of mobile ions in the gel and the external swelling of the gel network. However, after an optimum binding of the ions to PVP chains, a further increase in salt concentration will lead to a de-swelling of the gel as clearly shown in Figure 9.

When the relative effects of Cl^- and Br^- ions are compared then it is found that Br^- ions are more influential in causing depression in the swelling of hydrogels then that by the Cl^- ions in the same concentration range. The results can be explained by the fact that due to a smaller size of Cl^- ions they can more

easily diffuse across the gel membrane and thus will cause less decrease in osmetic pressure then what the Br^- ions will bring about.

Blood Compatibility

A major requirement for any hydrogel to be proven as a suitable biomaterial is that it must have a good blood compatibility and high swelling ratio. To judge the anti-thrombogenic potential of the hydrogel, we have compared the weights of the blood-clots formed when various hydrogels and cleaned glass surfaces are exposed to static blood as described in the experimental part. The results are presented in Table 2, which clearly indicate that the three component hydrogel shows a maximum swelling ratio and a minimum blood-clot weight than any other compositions. Moreover, hydrogel blood interaction has lower thrombogenic potential than the glass-blood has and this may be due to the high water content and hydrophilic nature of the polymers contained in the hydrogel.

CONCLUSION

The study of swelling behavior of three component hydrogels indicates that the maximum swellable hydrogel is obtained when crosslinked polyacrylamide, polyvinylpyrrolidone, and gelatin are present in a definite proportion in the hydrogel. It also reveals from the measurements that beyond the optimum swelling composition of the gel, the swelling ratio and equilibrium water content decrease appreciably with further increase in concentration of the gel constituents. For some definite compositions of the gel, the swelling process follows Fickian behavior. The swelling is also found to increase with an interesting temperature of the swelling medium in the range 10–40°C. The low value of energy of activation of the diffusion of water molecules supports a much greater swelling of the hydrogels. The swelling behavior is quite sensitive to the concentration of ions in the outer solution and shows interesting variations with the added salts concentration. The hydrogels prepared also exhibited good blood compatibility as evident from the clot formation studies.

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