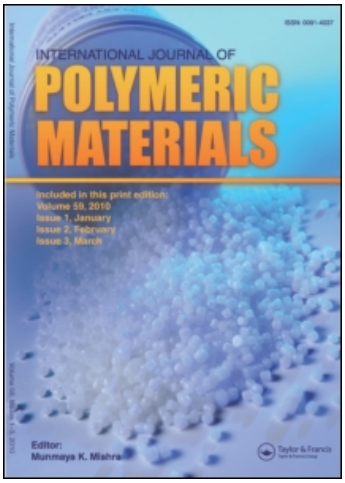

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PREPARATION OF A NOVEL SEMI-INTERPENETRATING POLYMER NETWORK (IPN) AND STUDY OF THE RELEASE DYNAMICS OF HUMAN BLOOD THROUGH THE IPN

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PREPARATION OF A NOVEL SEMI-INTERPENETRATING POLYMER NETWORK (IPN) AND STUDY OF THE RELEASE DYNAMICS OF HUMAN BLOOD THROUGH THE IPN

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A novel interpenetrating polymer network (IPN) of poly (ethylene glycol), poly(vinyl alcohol) and poly(acrylamide) was prepared and its potential for sorption and delivery of human blood was evaluated. The influence of chemical composition of the IPN on the release dynamics of blood was also investigated. On the basis of the Fick's equation the diffusional exponent (n) was evaluated for different IPN compositions and tentative mechanisms of blood transport were worked out. Effect of pH of the release medium on the released amount of blood was also studied.

Keywords: IPN, poly(vinyl alcohol), poly(ethylene glycol), blood, release, dynamics

INTRODUCTION

Macromolecular materials displaying unusually high affinity for water are often termed as hydrogels or fascinatingly called "intelligent polymers" or "smart polymers" [1]. The presence of water reservoir in these materials imparts them with a number of unique biophysical properties such as soft and rubbery nature, living tissue–like resemblance, low interfacial tension, etc. In addition, they also possess non-toxicity and good biocompatibility. All these characteristics of hydrogels enable them to be employed as potential biomaterials in a wide range of applications, such as artificial implants [2], burn-dressings [3], dialysis membranes [4], contact lenses [5], drug-delivery vehicles [6], etc.

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In a number of situations, physiologically active features have to be incorporated into hydrogels, such as controlled drug release [7], biosensors [8], bioreactors [9], tissue engineering [10], etc. In recent years much efforts have been invested in techniques to control loading and delivery of macro–molecular drugs such as peptides, enzymes, proteins, etc. [11, 12]. Controlled release of macromolecular drugs is not as easy as that of the low molecular weight drugs because of certain reasons. For instance, the molecular size of the macro drug is a decisive factor in hindering the diffusion and release from hydrophilic networks [13]. Another critical consideration, in particular in protein delivery from hydrogel system, is the potential for protein denaturation in the device [14]. One more problem is the retention of bioactivity of peptides and proteins when loaded into the polymeric hydrogel devices [15]. Thus, the area of controlled delivery of macromolecular drugs possess challenges and therefore, deserves, attention.

Blood serves as the principal transport system of the body, the heart furnishing the propulsive force. The most important quantitative functions of the blood are to bring oxygen and nutrients to the tissues and to carry away the waste products and deliver them to the excretatory organs – the kidney, lungs, biliary system of the liver, intestinal mucosa and skin. Blood also plays an important role in coordinating the activities of various tissues through distribution of hormones, in maintaining the pH and the oxidation-reduction potentials within narrow limits, in supplying defense against infection, and in guarding against hemorrhage.

Thus, looking to the great physiological significance of blood and realizing the need for designing a suitable vehicle for loading and release of macromolecular drugs, we in the present communication are reporting results on the synthesis of a novel type of ternary semi-IPN of polyvinyl alcohol (PVA), poly(ethylene glycol) and poly(acrylamide) (PAM), which shows potential to absorb blood into its network structure and deliver it into an aqueous release medium.

The reason for selecting PEG as one of the polymeric components of the IPN lies in the fact that PEG is known to have “stealth” properties, i.e. it can prevent the immunoreaction of the body to the biomaterial [16]. The presence of PEG also increases the stability of certain proteins or physically entrapped bioactive compounds entrapped into the matrix. The poly(vinyl alcohol) (PVA), on the other hand, is a linear polymer with inherent non-toxicity, non-carcinogenicity, good biocompatibility, and desirable physical properties such as rubbery or elastic nature and high degree of swelling in aqueous solutions. The polyacrylamide in crosslinked state has been extensively employed in hydrogel preparations for different purposes [17].

EXPERIMENTAL

Materials

Polyethylene glycol (PEG) (Mol.wt. 600) was obtained from Wilson Laboratories, Bombay, India and used as received. Polyvinyl alcohol (hot processed, Mot. Wt. 40,000, 98.6% hydrolyzed) was obtained from Burgoyne Burbidges and Co. India, and used without any pretreatment. Acrylamide (Research Lab, Poona, India) was crystallized twice from methanol (GR) and dried under vacuum over anhydrous silica for a week. N,N′-methylene bisacrylamide (MBA) (Central Drug House, Bombay, India) as a polymerization initiator. Human blood (hemoglobin 14.09/100 ml) was collected from a single donor and stored in a refrigerator.

All other chemicals used were of AR grade and bidistilled water was used throughout the experiments.

Preparation of IPN

The IPN was prepared by a free radical polymerization method as described in our earlier communications [18]. In brief, into a petridish (4−inch diameter, corning) were added PVA 3.0% w/v, AM 4% w/v, PEG 2.0% v/v, and KPS and MBA 0.04% w/v of each. The mixture (total volume 20 ml) was homogenized and kept at 80°C for 3 h so that the whole mass converted into a thin, white circular film.

Upon swelling the IPNs for three days they turned into colorless and semi-transparent thick discs, which were then cut into several circular pieces, each of 2.0 cm diameter. The IPNs were further dried at room temperature for a week and stored in air−tight container.

Loading of Blood

The loading of a drug onto hydrogels is normally performed by two general methods. In one method, the hydrogel monomer is mixed with the drug, within the matrix [19]. In the second approach, the hydrogel is allowed to swell in the drug solution until equilibrium and then dried to obtain the release device. The latter method has some advantages over the first method as polymerization conditions may have deleterious effect on the drug properties and the difficulties in device purification after loading and polymerizations often remain.

In the present work the second method was adopted for blood loading. In brief, preweighed dry circular pieces of IPN were allowed

to swell in a blood reservoir for two weeks and then taken out, washed with bidistilled water and dried at room temperature for a week. The following equation was used to calculate the percent loading,

$$\text{Percent loading} = \frac{W_d}{W_o} \times 100 \quad (1)$$

where W_d and W_o are the weights (in g) of blood loaded and dry gel, respectively.

Swelling Measurements

Swelling measurements were made primarily by gravimetric means. The pre-weighted pieces of IPN samples were immersed in 25 ml of bidistilled water for a period of time, then removed after an appropriate interval, blotted free of surface moisture with filter paper, weighed in a sensitive balance, and then returned to the water. This procedure was repeated until the sample attained constant weight.

The following swelling parameters were determined for the swollen IPN samples.

$$\text{Swelling Ratio (S.R.)} = \frac{W_s}{W_d} \quad (2)$$

where W_s and W_d are the swollen and dry weights of the loaded hydrogels, respectively.

Release Experiments

Two pieces of dried and loaded IPNs were placed into a definite volume (15 ml) of bidistilled water taken as a release medium. After definite time intervals 5 ml of release medium was taken out and estimated for the released blood by recording its absorbance at 390 nm (Systronics, Model No. 106, India) and determining the amount of blood with the help of a calibration plot. The density of blood was determined by pyknometry and found to be 1.05.

Kinetic Analysis of Release Data

The dynamic release properties of a polymer include the rate of desorption of drug, the rate of approach to equilibrium release and the

transport mechanism controlling the desorption of drug. The potentiality of a drug delivery system is characterized on the basis of first 50–60% release performance of the device, as beyond this level therapeutically ineffective amounts of drug are present in the blood plasma. The rate of approach to equilibrium can be monitored by a diffusion coefficient, D, in the case of Fickian transport mechanism, which indicates the relative importance of diffusion and relaxation. The release of solute from a slab can be calculated from the following equation [20]:

$$\frac{M_t}{M_\infty} = 1 - \sum_{n=0}^{\infty} \left\{ \frac{8}{(2n+1)^2 \pi^2} \right\} \cdot \exp\left\{ \frac{-D(2n+1)^2 \pi^2 t}{4L^2} \right\} \tag{3}$$

Here, M_t is the mass of solute desorbed at time t, M_∞ is the mass desorbed at equilibrium, L is the initial film thickness and n is an integer. This equation can be reduced to a more simplified form as

$$\frac{M_t}{M_\infty} = 4\left(\frac{Dt}{\pi L^2}\right)^{1/2} \tag{4}$$

for $0 \leq M_t/M_\infty \leq 0.6$.

A more realistic view can be constructed about the release mechanism when the data are analyzed in the light of the following empirical expression [21].

$$\frac{M_t}{M_\infty} = k\, t^n \tag{5}$$

where M_t/M_∞ is the fractional release at time t and k is a rate constant and n is the kinetic (diffusional) exponent, respectively. Equation (5) is a phenomenological rate law where the kinetic exponent n provides insights into the type of mechanism that is operative and in general has a value b/w 0.5 and 1. When $n = 0.5$, the release is taken to be Fickian. When $n = 1$, the release is zero order, i.e. constant with time. In between these values, i.e. $0.5 < n < 1$, the release is considered to be anamolous. The closer n is to 1, the closer is the release pattern to steady state release. When $M_t/M_\infty = 0.5$, t is the half life, which is another significant parameter

in comparing systems. In light of Eq. (4) and (5) the release data will be analyzed.

RESULTS AND DISCUSSION

Network Studies

One of the most important structural parameters characterizing crosslinked polymer is M_c, the average molar mass between crosslinks, which is directly related to the crosslink density. The magnitude of M_c significantly affects the physical and mechanical properties of crosslinked polymers and its determination has great practical significance. Equilibrium swelling is widely used to determine M_c. Early research by Flory and Rehner laid the foundation for the analysis of equilibrium swelling. According to the theory of Flory and Rehner, for a perfect network

$$M_c = .5 - V_1 d_p \frac{(V_s^{1/2} - V_s/2)}{\ln(1 - V_s) + V_s + XV_s^2} \tag{6}$$

where M_c is the number average molar mass of the chain between crosslinks, V_1 is the molar volume (mL ml^{-1}, d_p is the polymer density (g mL^{-1}, V_s is the volume fraction of polymer in the swollen gel, and X is the Flory-Huggins interaction parameter between solvent and polymer [22].

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

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

where M_o is the molar mass of the repeating unit.

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

$$V_e = d_A N_A / M_c \tag{8}$$

The value of V_1, d_p and X were taken from related literature [23–25].

The values of M_c, q and V_e of the networks have been calculated and summarized in Table 1 for varying compositions in the IPN.

TABLE 1 Network Parameters of the IPNs of Different Compositions

PEG	PVA	AM	MBA			
% v/v		% v/v		M_c	$q \times 10^3$	$V_e \times 10^{-20}$
1.0	3.75	5.0	0.05	7664	9.2	0.75
4.0	3.75	5.0	0.05	3602	19.7	1.60
6.0	3.75	5.0	0.05	3001	21.8	1.82
2.5	2.5	5.0	0.05	5517	12.8	1.04
2.5	5.0	5.0	0.05	5400	16.8	1.82
2.5	7.5	5.0	0.05	2124	33.4	2.72
2.5	3.75	3.75	0.05	7525	9.4	0.76
2.5	3.75	7.5	0.05	7369	9.6	0.79
2.5	3.75	10.0	0.05	3602	19.7	1.60
2.5	3.75	5.0	0.10	4075	17.4	1.42
2.5	3.75	5.0	0.20	3602	19.7	1.60
2.5	3.75	5.0	0.30	2780	25.5	2.08

Dynamic Release Model

The IPN, in the present case, could be regarded as an intimate network of macromolecular chains bonded to each other via chemical crosslinkings or weak intermolecular forces. In addition, the diffusion of the blood through the IPN is regulated by the processes of diffusion of blood component molecules to the release medium and relaxation of macromolecular chains. These processes basically determine the dynamic nature of release process. The release process could be realized by considering the situation when the IPN contacts a thermodynamic compatible solvent. As the penetrant solvent invades the IPN surface a moving front is observed that clearly separates the unsolvated glassy polymer region ahead of the front from the swollen and rubbery gel phase behind it [26]. Just ahead of the front, the presence of solvent plasticizes the polymer and causes it to undergo a glass to rubber transition [27]. Now the following possibilities could arise:

(i) If the glass transition of the polymer (T_g) is well below the experimental temperature, the polymer will be in the rubbery state and the polymer chains will have a greater mobility that allows an easier penetration of the solvent [28]. This clearly results in a Fickian diffusion (Case I) that is characterized by the solvent diffusion rate, R_{diff}, slower than the polymer relaxation rate, R_{relax}($R_{diff} \ll R_{relax}$).

(ii) If the experimental temperature is below T_g, the polymer chains may not be sufficiently mobile to permit immediate penetration of the solvent in the polymer case. This gives rise to non-Fickian diffusion process, which includes case II diffusion and anamolous diffusion

depending on the relative rates of diffusion and chain relaxation (for Case II, $R_{diff} \gg R_{relax}$ and for anamolous $R_{diff} \sim R_{relax}$).

Both the possibilities of diffusional and relaxation controlled release process of the hydrogel are modelled in Fig. 1(a) and 1(b), respectively.

Effect of Gel Composition on Blood Loading

The total blood content that is loaded in the three-dimensional IPN matrix depends on the potentiality of the gel to imbibe the blood when placed in the blood reservoir and this, in turn, depends on the chemical architecture of the IPN.

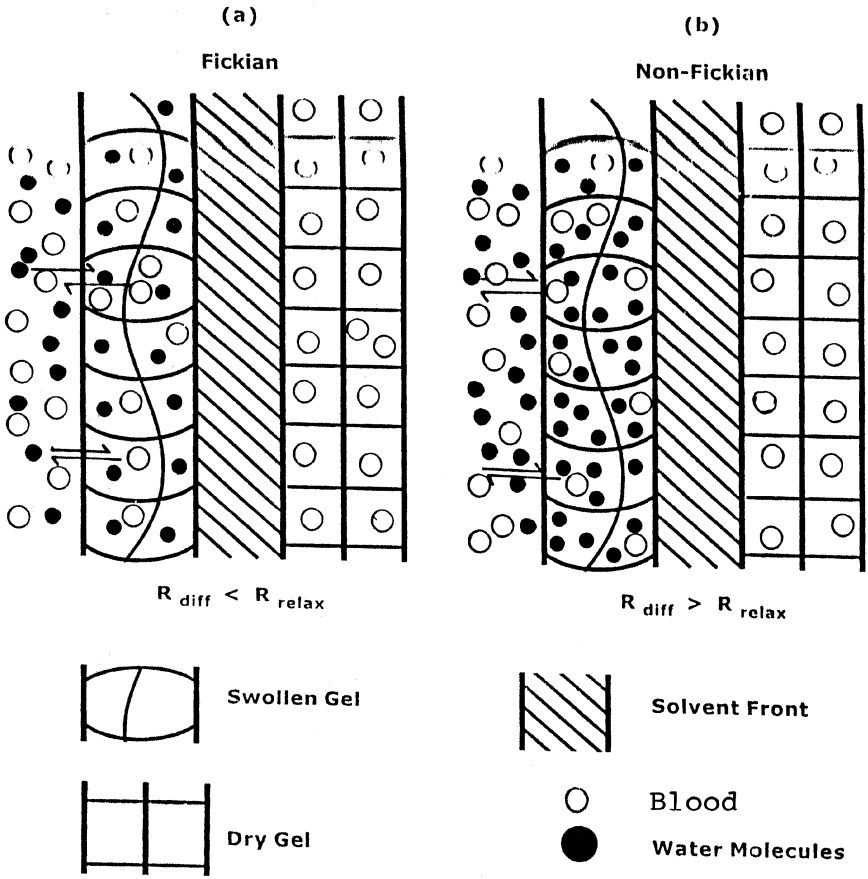

FIGURE 1 A hypothetical model of the IPN depicting the blood-transport mechanism (a) Fickian, and (b) non-Fickian.

The IPNs of different compositions were prepared by varying the amounts of PEG, PVA, AM and MBA in the feed mixture and the blood was loaded by equilibrating them in blood reservoir for two weeks. The effect of composition of the gel on the amount of loaded blood is shown in Fig. 2. The results clearly indicate that the composition of the IPN has a pronounced effect on the percent loading of blood. The results can be explained as follow:

When the amount of PEG is made to increase in the feed mixture in the range 1.0 to 6.0 v/v, there is observed a fall in the percent loading of blood. The result so obtained may be explained by the fact that on increasing the concentration of PEG, there is an increase in the number of PEG chains, thereby decreasing the mesh size of the free volumes available in between the macromolecular chains, which hinder the penetration of the giant blood component molecules into the network structure of the IPN. This ultimately results in a fall in the percent loading of the blood.

Similar type of results have been observed when the hydrophilic polymers PVA increases in the feed mixture in the range 2.5 to 7.5% w/v. The observed fall in the percent loading of blood may be attributed to the reason that increasing the number of PVA chains in the hydrogel produces a more compact arrangement of macromolecular chains which contain small sized free volumes within the

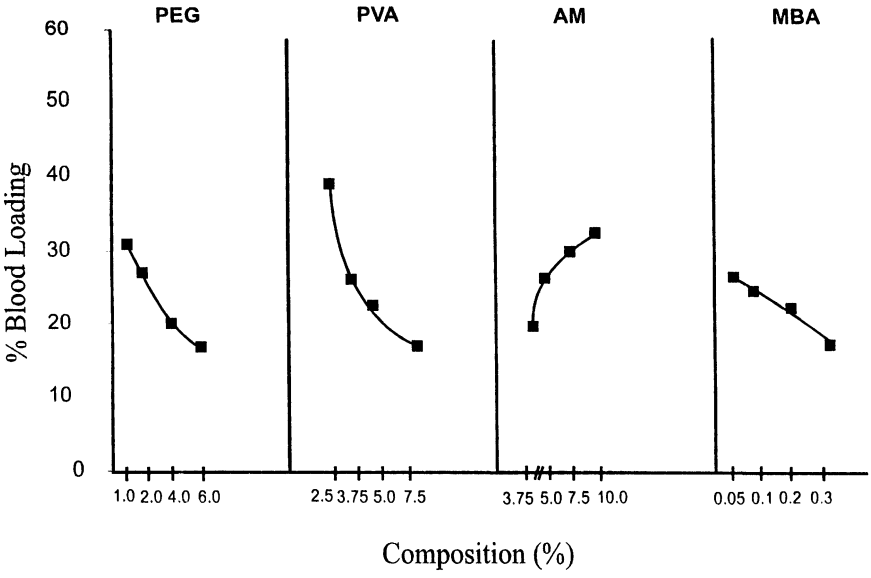

FIGURE 2 Effect of composition of the IPNs on percent loading of blood.

gel. Thus, blood component molecules are prevented from entering the IPN leading to a lower percent loading.

A reverse trend is noticed when the hydrophilic acrylamide increases in the feed mixture in the range 3.75 to 10.0% w/v. The results reveal that the percent loading of the blood increases in the above mentioned range of acrylamide. The results so obtained can be explained by the fact that increasing acrylamide content in the gel not only increases the number of crosslinked polyacrylamide chains but also increases the length of the chains, which as a result produces larger mesh sizes of the free volume in between the chains. This results in a higher percent loading of the blood.

The influence of crosslinking on the swelling behavior of the IPN was investigated by using different amounts of crosslinking agent (MBA) in the hydrogel preparation. When MBA was used in the feed mixture in the concentration range 0.05 to 0.3% w/v and the resulting IPNs loaded with blood, a drastic fall in the percent loading was observed with increasing MBA content of the gel. A plausible explanation for this is that greater number of crosslinks squeeze the free volumes available between the chains of macromolecular network and, as a result, less amount of blood is loaded into the gel.

Evidence of Blood Loading and Release

It is clearly depicted in the photograph of Fig. 3 that whereas the unloaded IPN is semi transparent in appearance, the loaded one is dark red. In order to further confirm the nature of the released fractions, the visible spectra of a diluted solution of blood (0.01% v/v) was recorded on a visible spectrophotometer in 400 to 700 nm range and compared to that of the released fractions. As depicted in Fig. 4 both the spectra show almost identical absorption peaks, thus confirming the release of the blood from the loaded IPN's.

Effect of Blood Loading on its Release

An important aspect in the use of hydrogels as drug vehicles is the effect of drug loading level on the rate of drug release. To achieve higher drug loadings, it is necessary to use either highly concentrated feed solutions or to apply repeated soaking of the gels in drug solutions and drying.

In the present work, the second method was adopted to study the amount of blood that was loaded, each time when the hydrogel matrix was repeatedly loaded and dried. The loaded gels were released in distilled water (15 ml) and the results obtained are depicted in Fig. 5.

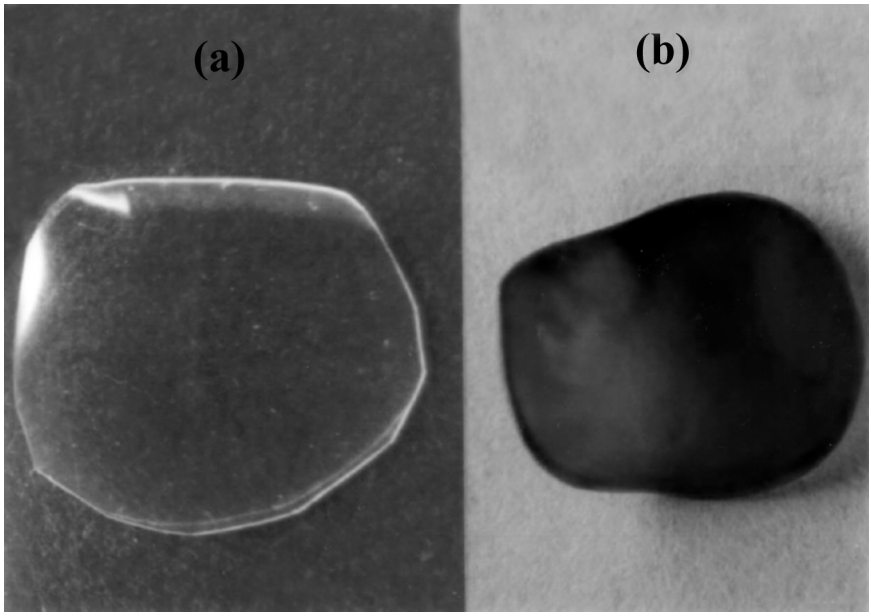

FIGURE 3 A photograph clearly depicting the difference between (a) unloaded and (b) loaded IPNs.

The figure clearly reveals that the amount of released blood increases with increasing percent loading. The results are quite expected as the larger the initial load, the faster the movement of the solvent front penetrating the surface of the loaded gel [29]. A higher loading of the blood into the IPN may also facilitate relaxation of macromolecular chains of the gel network and, thus, a larger swelling of loaded IPN is also expected in the release medium, which will obviously result in a greater amount of released blood.

Effect of PEG on Released Blood

On varying the amount of PEG in the concentration range of 1.0 to 6.0% v/v in the feed mixture, the release profiles of blood are influenced. The results are depicted in Fig. 6, which indicates that the amount of released blood decreases with increasing concentration of PEG in the fed mixture of the IPN. The observed release results can be explained on the basis of two points, firstly the swelling of the loaded IPN in aqueous reservoir, and secondly the percent loading of the blood on the IPNs.

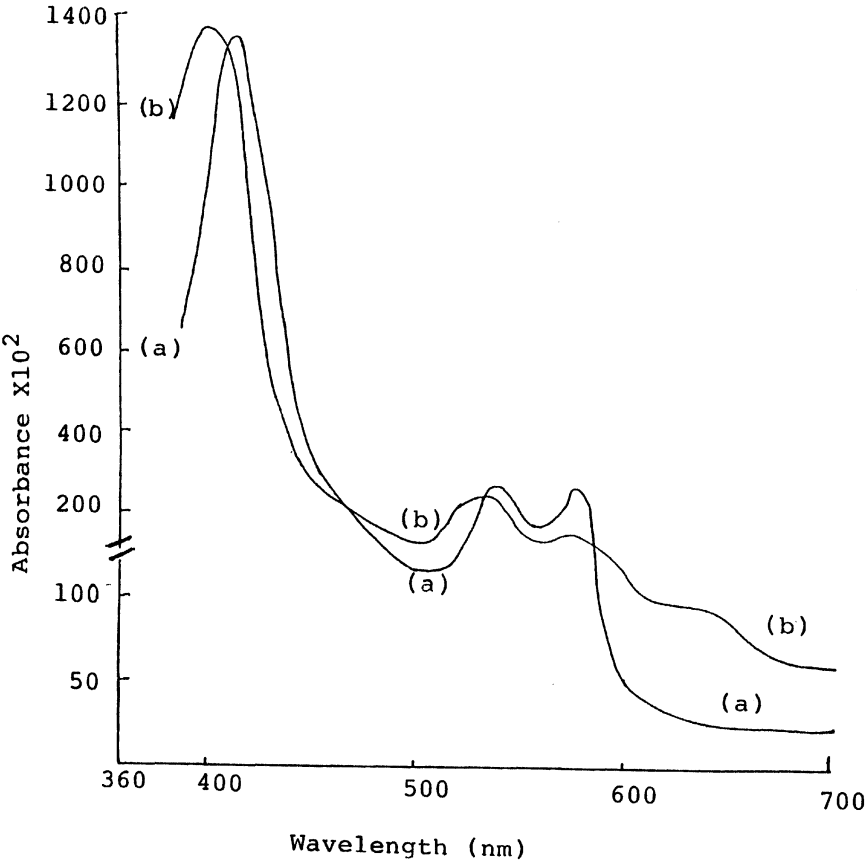

FIGURE 4 Spectra recorded in the range of 390–700 nm of (a) diluted solution of blood, (b) released fraction in aqueous medium.

The swelling results (not shown) imply that the swelling ratio increases with the increase in the concentration of PEG. These results are just opposite to those of blood release and can be explained as follows.

The reason for the observed increase in the swelling ratio with increasing PEG content of the IPN is quite apparent as PEG is a hydrophilic monomer and has distinct water associating property [30]. Obviously, its increasing proportion in the IPN composition will result in a greater swelling of the hydrogel. However, a reverse trend is observed in the case of percent loading and thereby its release. The observed fall may be attributed to the reason that with the increasing PEG content in the IPN the network density of the IPN may increase,

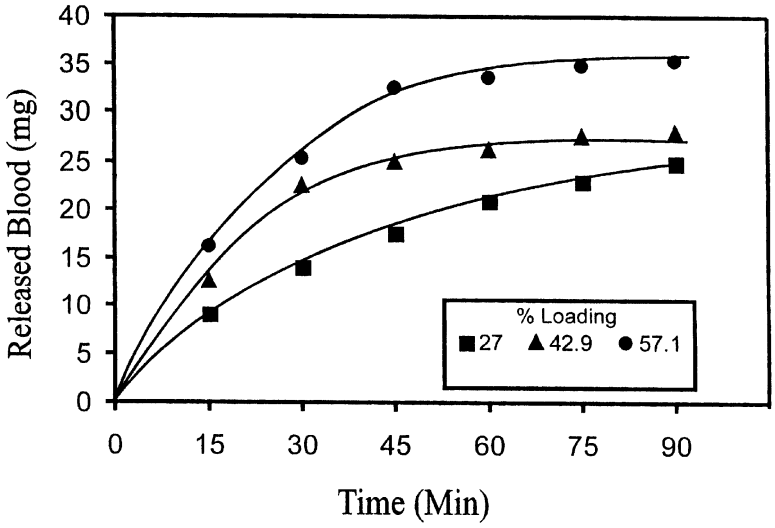

FIGURE 5 Release profiles of IPN's loaded with different percent of blood.

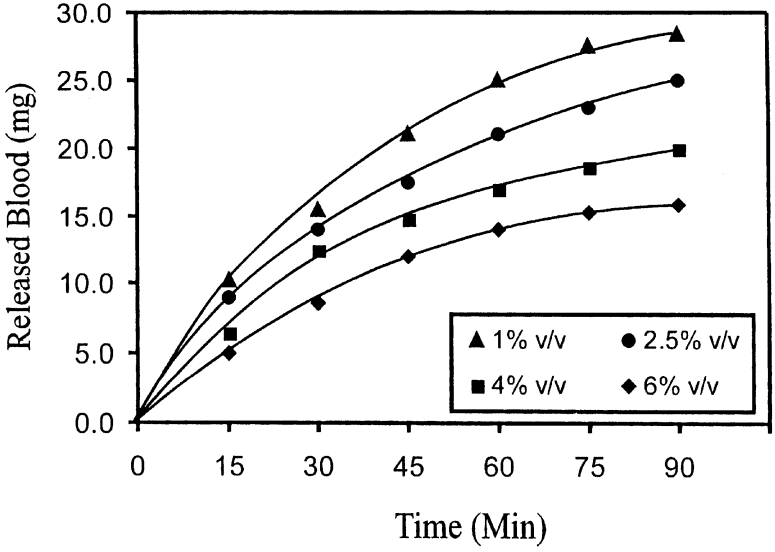

FIGURE 6 Effect of PEG content of the IPNs on released amount of blood, [PVA] = 3.75% w/v, [AM] = 5.0% w/v, [MBA] = 0.05% w/v, % Blood loading = 27.0.

which decreases the mesh size of the free volumes between the network chains and this obstructs the penetration of the giant blood molecules into the network structure of the IPN.

Effect of PVA on Released Blood

Incorporation of PVA, a hydrophilic polymer, into the macromolecular network is expected to enhance water sorption capacity of the IPN, which, in turn, will facilitate release of the entrapped blood. In the present investigation, the amount of PVA in the feed mixture has been varied in the range 2.0 to 6.0% w/v and the release profiles of resulting compositions are displayed in Fig. 7. It is clearly revealed from the figure that with increase in PVA content both the release rate and released amounts of blood increase. The results can be attributed to the fact that increasing PVA in the gel results in greater hydrophilicity of the network, which in turn shows greater swelling and, therefore, percent loading of the gel. Thus, because of greater percent loading of the blood, the release rate and released amounts of blood increase with increasing PVA content in the gel.

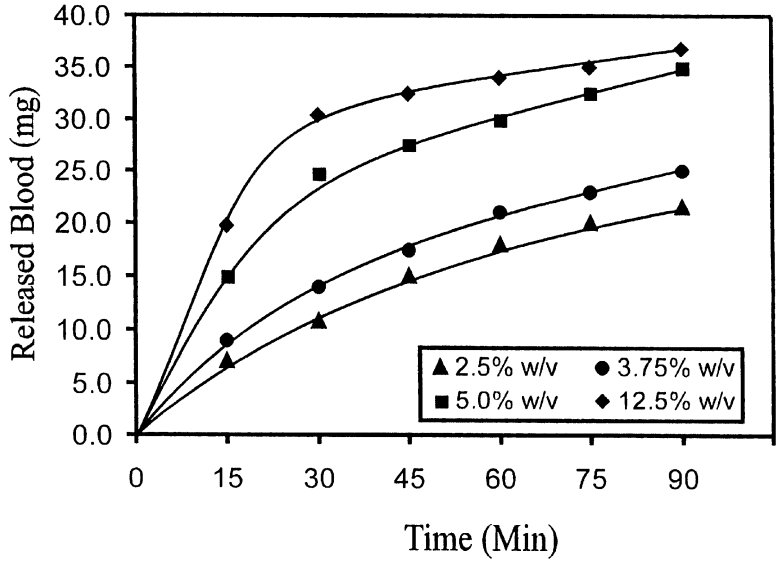

FIGURE 7 Variation in released amount of blood with varying PVA content of the IPNs, [PEG] = 2.5% v/v, [AM] = 5.0% w/v, [MBA] = 0.05% w/v, % Blood loading = 27.0.

Effect of Acrylamide on Released Blood

Since the IPNs prepared are acrylamide based, the effect of increasing concentrations of acrylamide on the release of blood has been observed by employing AM in the concentration range 3.75 to 10.0% w/v. The results are depicted in Fig. 8, which indicates that with increasing concentration of the monomer the amounts of the released blood from the respective IPNs also increase. Also, the swelling results show a sharp rise in the SR with increasing concentration of AM. The swelling results, thus obtained, are in good agreement with the percent loading results.

The swelling results can be explained by the fact that with increasing concentration of the hydrophilic monomer molecules in the system, a greater number of water molecules will be bound to the PAM chains, which results in an increased swelling.

The above discussion clearly reveals that with an increase in the AM content in the hydrogel, the released amount of blood from these polymeric devices also increases. This rise is due to the greater percent loading, which has already been explained on the basis of the increased mesh sizes of the free volumes available within the gel network. Thus, a hydrogel with greater loading favors a greater release.

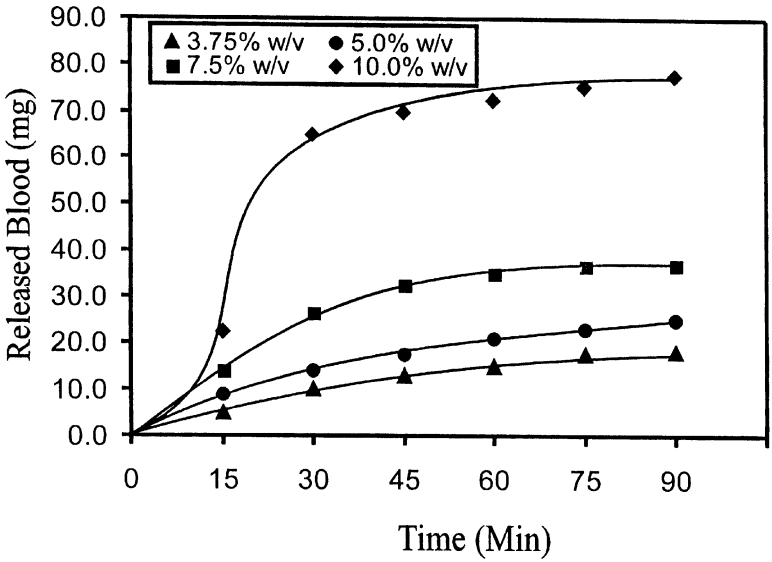

FIGURE 8 Effect of AM content of the IPNs on the released amounts of blood, [PEG] = 2.5% v/v, [PVA] = 3.75% w/v, [MBA] = 0.05% w/v, % Blood loading = 27.0.

Effect of Crosslinker on Released Blood

For monitoring the effect of crosslinker on the swelling and release behavior of the IPN, swelling behavior of the feed mixture was charged with varying concentration of the crosslinker in the concentration range 0.05 to 0.3% (w/v). The results (not shown) reveal that the amount of released blood decreases with increasing MBA in the feed mixture. The reason is quite obvious as increase in the degree of crosslinker reduces the free volume of the hydrogel network and, thus, less numbers of water molecules enter the gel from the release medium. This effect also hinders the diffusion of larger components of blood from within the IPN to the release medium and hence a drastic fall in the released blood is observed. Similar type of results have also been reported by other workers [31].

The release results thus obtained are in good agreement with the percent loading and swelling observations. The effect of the crosslinker on the percent loading has been already explained on the basis of the decreased mesh sizes available within the gel network, which results in the low loading of blood. A decrease in the SR with increasing MBA content is observed in the IPN. A plausible explanation is that increasing the crosslinker in the IPN lowers the average molecular weight of polymer chains (Table 1) between the crosslinks and consequently reduces the free volumes accessible to penetrant water molecules. This, therefore, results in a suppressed swelling of the IPN.

Effect of pH on Released Medium

pH–sensitive IPNs have great practical significance and new drug delivery systems in response to changes in pH of the release medium are currently being explored [32] to improve therapeutic efficiency and reduce and eliminate side effects of oral controlled drugs. It is also being attempted to deliver drugs to specific regions of the gastrointestinal (GI) tract by making utilization of pH changes within the GI tract.

In the present investigation, the effect of pH on release behavior of blood–loaded gels has been studied by varying pH of the release medium in the range 0.3 to 11.0. The release results, displayed in Fig. 9, indicate that whereas the released amount of blood decreases in the pH range 3.0 to 9.0, an increase in release rate is observed beyond pH 9.0 and the released amount attains an optimum value at pH 11.0. The results can be explained by the fact with increasing pH of the release medium the amide groups of PAM chains of the gel undergo

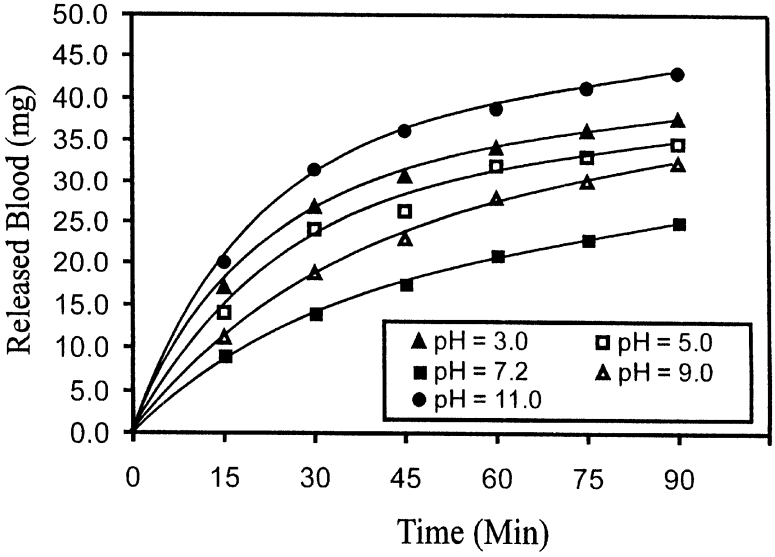

FIGURE 9 Effect of pH of the release medium on the release amounts of blood.

increasing hydrolysis and therefore produce repulsive forms among the network chains. Because of the existing repulsive forces the network chains undergo rapid relaxation, thus permitting an easier entrance to water molecules from the release medium into the gel matrix and subsequently favoring faster diffusion of blood from within the loaded matrix into the release medium. Similar type of results have also been reported by other workers [33].

Analysis of Dynamic Release Data

(i) Kinetics of Swelling Process

The swelling rate of hydrogels commonly follows second-order kinetics where the swelling rate is directly proportional to the quadratic of the remaining hydration capacity [34]

$$\frac{\mathrm{d}}{dt}\mathrm{S_R} = \mathrm{k_{S_R}}[\mathrm{S_{RX}} - \mathrm{S_R(t)}]^2 \tag{9}$$

Here S_{RX} is the maximum swelling capacity (in percent) of the hydrogel at equilibrium and K_{SR} is a kinetic rate constant for the swelling process. Integrating Eq. (9) yields, after rearrangement

TABLE 2 Second Order Kinetic Parameters Obtained from a Linear Regression of Plots made According to Eq. (10) for the Swelling of IPNs of Different Compositions

PEG	PVA	AM	MBA		
% v/v		% v/v		$k_{SR} \times 10^9$	S_{RX}(%)
1.0	3.75	5.0	0.05	4.0	769
4.0	3.75	5.0	0.05	1.5	476
6.0	3.75	5.0	0.05	1.4	470
2.5	2.5	5.0	0.05	7.2	588
2.5	5.0	5.0	0.05	8.4	625
2.5	7.5	5.0	0.05	1.5	769
2.5	3.75	3.75	0.05	9.4	1886
2.5	3.75	7.5	0.05	2.8	769
2.5	3.75	10.0	0.05	2.6	500
2.5	3.75	5.0	0.10	17.0	769
2.5	3.75	5.0	0.20	8.0	500
2.5	3.75	5.0	0.30	6.1	384

$$\frac{1}{S_R} = \frac{1}{S_{RX}} \cdot t + \frac{1}{k_{S_R} S_{RX}^2} \tag{10}$$

The above equation clearly reveals that the plot of t/S_R versus time for the gel should be linear and, if so, follows a second order kinetics. The value of the kinetic constants (k_{SR} are presented in Table 2 for various compositions of the hydrogel. The observed kinetic constants support the qualitative swelling results.

(ii) Mechanism of Blood Transport

It is known that the release process basically results from the swelling of the loaded hydrogel in the release medium. In the present study the release data have been treated by Eq. (4) and (5) and the evaluated kinetic parameters have been summarized in Table 3. Now the summarized data could be analyzed to give some information about the mechanism of the release process as explained below:

When the amount of PEG increases in the concentration range 1.0 to 6.0% v/v in the feed mixture of the loaded IPN, the diffusional exponent n decreases from nearly Case II transport to Fickian transport as shown in Table 3. This clearly implies that with increasing PEG in the IPN, the blood transport shifts from relaxation controlled to diffusion controlled mechanism. This appears justified also, as increasing PEG chains in the IPN increases density of the network, thus resulting in a slower diffusion of blood from within the gel matrix into the outer release medium. This is further confirmed by the decreasing values of diffusion constant with increasing PEG content.

TABLE 3 Data Showing the Kinetic Parameters of the Release of the Blood through the IPNs of Different Compositions

PEG % v/v	PVA	AM	MBA	n	$D \times 10^5\ cm^2 min^{-1}$	Release mechanism
		% w/v				
1.0	3.75	5.0	0.05	0.98	3.4	Case II
4.0	3.75	5.0	0.05	0.58	1.0	Anomalous
6.0	3.75	5.0	0.05	0.52	0.84	Fickian
2.5	2.5	5.0	0.05	0.92	1.3	Anomalous
2.5	5.0	5.0	0.05	0.72	0.92	Anomalous
2.5	7.5	5.0	0.05	0.51	0.84	Fickian
2.5	3.75	3.75	0.05	1.0	0.13	Case II
2.5	3.75	7.5	0.05	0.52	0.31	Fickian
2.5	3.75	10.0	0.05	0.48	0.54	Less Fickian
2.5	3.75	5.0	0.10	0.58	8.7	Anomalous
2.5	3.75	5.0	0.20	0.76	2.7	Anomalous
2.5	3.75	5.0	0.30	1.01	0.13	Case II

On increasing the concentration of PVA in the feed mixture of the IPN in the range 2.5 to 7.5% w/v, the amount of released blood is found to increase while a decrease is observed in the diffusional exponent n from anomalous to a Fickian value. This, in other words, indicates that the release process changes from relaxation controlled to diffusion controlled. The observed shift may be explained by the fact that increasing number of PVA chains in the IPN increases the compactness of the network which, in turn, slows down the diffusion of blood from the IPN.

It is also implied by Table 3 that when the concentration of AM is raised in the feed mixture of the IPN from 3.75 to 10.0% w/v, the amounts of blood released gradually decrease. It is also observed that the diffusional exponent n also decreases from a Case II to Fickian value. This suggests that the release process shifts from a relaxation controlled to diffusion controlled mechanism. The observed results can be explained by the fact that increasing AM results in a greater number of PAM chains in the IPN. This widens the mesh sizes of the free volumes available between the network chains and facilitate the relaxation process, thus making the release process as diffusion controlled.

On increasing the amount of crosslinker (MBA) in the concentration range 0.05 to 0.30% w/v in the IPN the diffusional exponent n is found to increase in the anamolous range and finally attains a Case II value of unity. The increase observed in n implies an increasing relaxation–controlled nature of the release process.

CONCLUSIONS

The semi IPN prepared by polymerizing acrylamide in the presence of PEG and PVA shows a fair potential to absorb human blood and release it into a aqueous release medium. The loading of blood into the IPN is greatly influenced by the chemical composition of the gel. It is found that with increasing PEG and PVA contents in the IPN, the percent loading decreases, while with increasing AM an increase in blood loading is noticed. It is also found that a greater loading is obtained with repeated loading process and subsequently greater amounts of blood are released.

The release profiles of blood are quite sensitive to the chemical architecture of the IPN. For instance, a decrease in release rate is observed when the IPN contains increasing amounts of PEG, AM and MBA. On the other hand, an IPN with more PVA displays a faster and greater release of blood.

The IPN's are also quite responsive to pH of the release medium. It is noticed that the amount of released blood decreases up to pH 9.0, while beyond this pH an increase in blood release is observed with an optimum release at pH 11.0.

The dynamic release process is found to obey second order kinetics. It is found that the mechanism of blood transport is affected by the chemical composition of the IPN. When the PEG, PVA and AM content increase in the IPN, the release process shifts from non Fickian type, thus indicating a shift from relaxation to diffusion controlled blood release mechanism.

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