Casein Cross-linked Polyacrylamide Hydrogels: Study of Swelling and Drug Release Behaviour

S.K. Bajpai
Department of Chemistry, Government Science College (Autonomous), Jabalpur (M.P.), India

Received 21 June 1998; accepted 5 July 1999

ABSTRACT

The polymeric hydrogels composed of polyacrylamide and food protein casein have been synthesized for the purpose of studying their swelling and drug release behaviour. The two samples, differing in cross-linking ratio, show almost Fickian swelling behaviour (n=0.50) except the less cross-linked sample at pH 7.0 for which swelling exponent n was 0.62, thus showing non-Fickian swelling behaviour. The swelling parameters like diffusion exponent, penetration velocity, and diffusion coefficient have also been evaluated. The swelling behaviour of hydrogels is greatly affected by variation in pH of the external medium. These gels show maximum swelling at pH 7.0 and it decreases in both acid and alkaline range. This behaviour has been explained on the basis of osmotic swelling pressure theory, thus treating the hydrogel to be of ionic nature due to presence of protein casein. The release of model drug bromocresol green (BCG) has been studied as a function of temperature of the external medium, and it has been observed that the amount of drug released decreases beyond 40 °C. The purpose of undertaking the present work is to explore the possibilities of using casein the natural protein, as a drug delivery device so that like other natural polymers (collagen, guargum, gum arebica etc.) casein may also be used without causing any toxic effect in the human body system. These gels also undergo a number of reversible swelling-deswelling cycles.

Key Words: hydrogels, equilibrium swelling capacity, cross-linking, casein, polyacrylamide

INTRODUCTION

Hydrogels are water-swellable, three-dimensional polymeric networks possessing both the cohesive properties of solids and diffusive transport properties of liquid. They have been increasingly attracted to researchers and technologists due to their widespread applications in contact lenses [1], wound dressings [2], drug delivery systems [3, 4], controlled release of perfumes [5], adsorption of proteins [6] and metal ions [7] etc.

However, most of the research work on
polymer gels is mainly focused on five synthetic polymeric gels, thus neglecting the considerable variety of networks in natural polymers such as naturally occurring polysaccharides, proteins etc. Since the biological responses to polymer surfaces are complex, each polymer system should meet certain requirements for biomedical applications.

Biocompatibility of the material is critical, and for some applications biodegradability is desirable. The natural gels are ideal candidates for these biomedical applications. For example, they could be used to encapsulate the cultivate cells inside the gel, where the network will act as a semipermeable membrane allowing only growth factors to enter to aid the growth of the cells. The study of gels could be useful in the development of novel synthetic polymer networks that mimic natural gels [8], and a knowledge of the response of natural gels to the changes in the environment could be invaluable verifying the trends observed in the experimental behaviour of synthetic polymeric gels.

In recent past the researchers have focused their attention on studies related with synthesis, swelling behaviour and drug release analysis of naturally occurring polymeric hydrogels in the form of nanoparticles, thin films, microspheres etc. For example, collagen [9], chitosan [10] guar gum [11], agarose [12], gum arabica [13] have been successfully used as drug delivery devices for anticancer drugs, antibiotic drugs, colonic drugs, antimicrobial drugs, protein and peptide drug delivery respectively. In this connection, the author has already reported the swelling behaviour of hemoglobin cross-linked polyacrylamide hydrogels [14] and in continuation the present communication describes the analysis of swelling behaviour of casein cross-linked polyacrylamide hydrogels. The equilibrium swelling has been studied as a function of pH of the external solution. The model drug release behaviour of hydrogels has also been analyzed.

**EXPERIMENTAL**

**Materials**

The raw materials used have been described in Table 1. Acrylamide was recrystallized in methanol before use and other material were used as received. The doubly distilled water was used throughout the work.

**Synthesis of Cross-linked Hydrogels**

A definite amount of casein powder was dissolved in NaOH solution and then acrylamide (AAm) and N,N'-methylene bisacrylamide (BIS) were added in definite amounts and mixed thoroughly, followed by addition of calculated quantities of potassium persulphate (KPS) and sodium metabisulphite (SMB). The total mixture was stirred well quickly to avoid lumping, poured into 10×75 mm test tubes and set aside undisturbed. The resulting smooth, semi-transparent cylindrical hydrogels were removed from the test tubes and then sliced into discs, washed with Tris-HCl buffer, pH 7.0, followed by acetone and water and dried, in a dust free glass chamber at room temperature. In all, two samples of hydrogels were prepared with different cross-linking ratio X (X = mol BIS/mol AAm). These samples will be denoted as Cas-PAAm X (2.1) and Cas-PAAm X (1.7) where number in the parentheses represent the cross-linking ratio in mol % (Table 2). Scheme 1 describes the formation of hydrogel in systematic way. In order to prepare the drug loaded gel, the calculated amount of model drug bromocresol green (BCG) was added to

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Name and description</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acrylamide (AAm)</td>
<td>Robert Johnson*</td>
</tr>
<tr>
<td>2</td>
<td>N,N'-Methylene bisacrylamide (BIS)</td>
<td>Central Drug House*</td>
</tr>
<tr>
<td>3</td>
<td>Casein powder</td>
<td>Loba Chemie Industries*</td>
</tr>
<tr>
<td>4</td>
<td>Potassium persulphate (KPS)</td>
<td>Loba Chemie Industries*</td>
</tr>
<tr>
<td>5</td>
<td>Sodium metabisulphite (MBS)</td>
<td>S.D. Fine Chemicals*</td>
</tr>
<tr>
<td>6</td>
<td>Bromocresol green (BCG)</td>
<td>Central Drug House*</td>
</tr>
</tbody>
</table>

Table 1. Raw materials employed and their source.
Casein solution of casein hydrogels. After the attainment of equilibrium the swelling capacity was calculated using the formula:

\[
\text{Grams of water per gram of gel} = \frac{W_e - W_0}{W_0}
\]  \hspace{1cm} (1)

Where \(W_e\) is the weight of the equilibrated hydrogel and \(W_0\) is the initial weight of the dry hydrogel.

The penetration velocity \((V)\) of buffer in each polymer was determined by weight gain method as reported elsewhere [15]. The penetration velocity was calculated from the slope of the initial portion of the penetrant uptake curve by using the equation:

\[
V = \frac{1}{2dA} \frac{dW_e}{dt}
\]  \hspace{1cm} (2)

where \(V\) denotes penetration velocity, \(dW_e/dt\) denotes the slope of the weight gain versus time curve, \(d\) denotes the density of water at 37 °C, and \(A\) denotes area of one face of the disc.

The mass uptake of the swelling solution \(M_t\) as a function of time \(t\) was analyzed according to the eqn (3) [16],

\[
\frac{M_t}{M_\infty} = k t^n
\]  \hspace{1cm} (3)

Eqn (3) could be used to find out the Fickian and non-Fickian absorption of water by hydrogel. \(M_\infty\) is the mass uptake of the solvent at equilibrium, \(k\) is a constant and \(n\) is the exponent describing the Fickian or anomalous swelling mechanism.

On taking natural log of eqn (3):

\[
\ln \left(\frac{M_t}{M_\infty}\right) = \ln k + n \ln t
\]  \hspace{1cm} (4)

The values of \(n\) and \(k\) were calculated from the slope and intercept of the plot of \(\ln M_t/M_\infty\) against \(\ln t\), respectively.

The diffusion coefficient \(D\) of solvent was calculated using the following equation [17]:

\[
D^* = \frac{k(\pi D^*)^2}{4}
\]  \hspace{1cm} (5)

**Scheme I**

the reaction mixture before adding sodium metabisulphite and potassium persulphate. There is no particular reason for selecting bromocresol green as a model drug because the purpose of study is just to have an understanding about the drug releasing capacity of the proposed hydrogel, so that it could be used as a model drug-releasing device in near future. The semi-transparent greenish hydrogel discs were obtained.

**Dynamic Swelling Studies**

Hydrogels were swollen to equilibrium in water at physiological temperature 37 °C. Equilibrium was attained in 20 h, and the approach to equilibrium was monitored by measurement of mass of the swollen hydrogels. After the attainment of equilibrium the swelling capacity was calculated using the formula:
Table 2. Composition of Cas-PAAm hydrogels.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>System</th>
<th>Composition (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cas</td>
</tr>
<tr>
<td>1</td>
<td>Cas-PAAmX(2.1)</td>
<td>4.0</td>
</tr>
<tr>
<td>2</td>
<td>Cas-PAAmX(1.7)</td>
<td>3.0</td>
</tr>
<tr>
<td>3</td>
<td>Cas-PAAmX(2.1)</td>
<td>4.0</td>
</tr>
<tr>
<td>4</td>
<td>Cas-PAAmX(1.7)</td>
<td>3.0</td>
</tr>
</tbody>
</table>

where, r is the radius of the gel disc.

To study the swelling behaviour of the hydrogels in medium of different pH, two pieces of preweighed hydrogels were placed in buffer solution of required pH and allowed to equilibrate. Mass measurements of the hydrogels were taken at different time intervals to monitor the attainment of equilibrium, and swelling capacities (water sorbed per g of gel) were determined. In each case the final water content was determined for two pieces of hydrogels. Good agreement was found in the degree of swelling for both pieces, each having the same history, the average of two determinations being used for calculations.

In order to study the reversibility of the swelling process, the hydrogel samples were allowed to equilibrate in water and then placed in 2 M NaCl solution, which caused the gel to deswell. The deswelling was then followed by weighing the gel at various time intervals. The reversibility of swelling and deswelling was determined using the same samples for consecutive swelling and deswelling experiments. The degree of swelling has been expressed as the swelling ratio, the ratio of final weight of the gel to initial weight of the gel.

In another set of experiments, completely dried hydrogel was allowed to equilibrate in water and after attainment of the equilibrium it was dried again. The dried hydrogel, was further allowed to swell in water, and then this process of drying and swelling was repeated a number of times.

In order to study the drug release analysis, the drug-loaded hydrogels were placed in external medium at pH 7.0 and the absorbance of the solution was measured (Systronix, India) at definite time intervals. The amount of active ingredient released \( M_t \) at a time \( t \) was determined using Beer-Lambert law. The total amount of drug incorporated in the disc was taken as \( M_e \).

RESULTS AND DISCUSSION

Dynamic Swelling Studies

A critical analysis of the swelling process reveals that there are two underlying molecular processes: penetration of the solvent molecules into the void spaces in the network and subsequent stretching or relaxation of the network segments. The fundamental equation \( M_t/M_e = kt^n \) defines the following three situations:

- For a perfectly Fickian process where the rate of solvent penetration is the slowest and hence is the rate limiting step, the value of \( n=0.50 \).
- When the penetration velocity is far greater than the chain relaxation rate, the solvent uptake is proportional to time, i.e., \( n=1.0 \) (This is often called relaxation-controlled case-III transport) [18].
- When both the diffusion and polymer relaxation control the overall rate of water uptake, the diffusion mechanism is non-Fickian i.e., \( 0.5 < n < 1.0 \).

The values of swelling exponent \( n \) for the swelling of two hydrogel samples i.e., Cas-PAmX (2.1) and Cas-PAmX (1.7) in double distilled water at pH 7.0 at 37 °C were determined with the help of eqn (4) and are shown in Table 3. It is clear from the Table 3 that the two samples show Fickian swelling behaviour (\( n=0.50 \)) at all pH of the external medium with the exception of sample Cas-PAmX(1.7) showing non-Fickian swelling at pH 7.0 (\( n=0.61 \),
Table 3. Swelling parameters of Cas-PAAmX hydrogels at different pH over a period of 20 h with a temperature = 37 °C.

<table>
<thead>
<tr>
<th>pH</th>
<th>System</th>
<th>Equilibrium swelling capacity</th>
<th>Penetration velocity</th>
<th>n</th>
<th>k</th>
<th>Diffusion coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>H₂O:gel (g/g)</td>
<td>V x 10^6 (cm/s)</td>
<td></td>
<td></td>
<td>D x 10^6 (cm²/s)</td>
</tr>
<tr>
<td>2.0</td>
<td>Cas-PAAmX(2.1)</td>
<td>1.10</td>
<td>0.98</td>
<td>0.11</td>
<td>0.18</td>
<td>1.78</td>
</tr>
<tr>
<td></td>
<td>Cas-PAAmX(1.7)</td>
<td>1.86</td>
<td>1.67</td>
<td>0.20</td>
<td>0.28</td>
<td>2.86</td>
</tr>
<tr>
<td>4.0</td>
<td>Cas-PAAmX(2.1)</td>
<td>3.61</td>
<td>2.17</td>
<td>0.32</td>
<td>0.27</td>
<td>3.04</td>
</tr>
<tr>
<td></td>
<td>Cas-PAAmX(1.7)</td>
<td>4.92</td>
<td>3.06</td>
<td>0.42</td>
<td>0.40</td>
<td>4.26</td>
</tr>
<tr>
<td>7.0</td>
<td>Cas-PAAmX(2.1)</td>
<td>6.19</td>
<td>5.02</td>
<td>0.56</td>
<td>0.41</td>
<td>4.29</td>
</tr>
<tr>
<td></td>
<td>Cas-PAAmX(1.7)</td>
<td>7.82</td>
<td>6.08</td>
<td>0.61</td>
<td>0.57</td>
<td>6.81</td>
</tr>
<tr>
<td>9.0</td>
<td>Cas-PAAmX(2.1)</td>
<td>5.20</td>
<td>3.15</td>
<td>0.49</td>
<td>0.38</td>
<td>4.01</td>
</tr>
<tr>
<td></td>
<td>Cas-PAAmX(1.7)</td>
<td>6.15</td>
<td>4.87</td>
<td>0.55</td>
<td>0.47</td>
<td>5.01</td>
</tr>
</tbody>
</table>

thus following transport mechanism with a chain relaxation contribution.

**Effect of pH**

The swelling behaviour of hydrogels is greatly affected by variation in pH of the external solution as depicted in Figure 1. The results so obtained are quite different from those obtained in the case of gelatin - swelling was found to decrease with increase in pH of polyacrylamide hydrogels [19], where the equilibrium the external solution. It is clear from the Figure 1 that the equilibrium swelling capacity increases with rise in pH of the external solution, attains maximum value at pH 7.0, and then starts decreasing, as the pH goes in the alkaline range. It is also clear from the figure that swelling is suppressed to a greater extent in the acidic range as compared to the alkaline one.

In order to explain the observed experimental findings, two possible theories may be proposed. First theory is based on the formation of a complex structure in the polymer matrix through H-bonding interactions between -COOH and -CONH₂ groups due to hydrolysis of amide groups of polyacrylamide in the polymer matrix [20]. This theory clearly implies that the variation in swelling behaviour of Cas-PAmX hydrogels must be due to possible hydrolysis of polyacrylamide and hence it should play a key role in governing pH dependent swelling behaviour.

Now, in order to verify the above theory, hydrogels of polyacrylamide, with the same cross-linking ratio, were prepared in absence of other component casein. When these gels were put in various buffer solutions of different pH, the swelling was found to be almost the same for all pH values. If the above proposed theory were correct then the hydrogels of cross-linked polyacrylamide should have shown the similar pH dependent behaviour as observed with Cas-PAAmX hydrogels. This clearly verifies that no such complex structure formation takes place within the polymer matrix and obviously polyacrylamide does not play any role in governing the observed pH - effect. Therefore it must be the
other component of polymer matrix, namely casein, which should play the key role in the explanation of observed behaviour.

After failure of the above theory we now proceed for the other theory, according to which the swelling behaviour of ionic hydrogels in dilute electrolyte solution is mainly due to osmotic swelling pressure between the gel phase and external solution. At the moment, the above theory seems to be quite fit for the present study because casein, one of the components of the hydrogel, is a polyelectrolyte containing charged and dissociable groups along the macromolecular chain.

The kinetic swelling behaviour of an ionic hydrogel depends upon mass transfer limitations, Donnan equilibrium considerations, ion exchange and ionic interactions [21]. When such an ionic hydrogel is immersed in a high dielectric constant medium, these ionic moieties will dissociate and create an overall charge density along the chains, as well as a high concentration of mobile ions in the gel. As compared to the non-ionic gel behaviour, this ionic character will introduce two "new player" forces in the system: the osmotic pressure resulting from difference in ion concentrations between the swollen gel and the external solution i.e., \( \pi_{\text{ion}} \) (for "macroscopic" electroneutrality reasons, mobile ions belonging to the gel can not leave it and hence minimization of this osmotic pressure can only be achieved through dilution of the network charge density i.e., swelling) and the net charge density along the chains will generate some electrostatic repulsion (i.e., coulombic forces) between chain segments \( \pi_{\text{elec}} \). The resulting expansion of the network will contribute to the overall swelling behaviour [22]. It has been shown by theoretical calculations and experimental results that \( \pi_{\text{elec}} \) is typically similar than \( \pi_{\text{ion}} \).

For a weakly charged polymer network in a dilute electrolytic solution, the osmotic swelling pressure \( \pi_{\text{ion}} \) is given as:

\[
\pi_{\text{ion}} = RT\Sigma(C_i^c - C_i^s)
\]  

(6) where \( C_i^c \) and \( C_i^s \) are the molar concentrations of counter ions in the gel and solution phase respectively, \( R \) is general gas constant and \( T \) is the absolute temperature.

K-casein is an amphiphilic protein which has two identifiable regions: amino acids 1–105 containing predominantly hydrophobic residues and 106–169 containing hydrophilic charged amino acid residues. It is the latter portion that contributes towards the hydrophilic nature of casein. In addition, oligosaccharide chains consisting of sialic acid, galactose and N-acetylgalactosamine are grafted onto threonine at positions 131 and 135 in the amino acid sequence. This also contributes to the hydrophilicity of this portion of K-casein.

Since the synthesis of hydrogel involves the dissolution of casein in 0.1 N NaOH, the hydrogel contains undiffusible –COO\(^{-}\) groups along the macromolecular chain and a high concentration of mobile counter ions in the gel phase. When this hydrogel is placed in the doubly distilled water at pH 7.0, obviously the difference \( C_i^c - C_i^s \) becomes very large, thus resulting in a high osmotic swelling pressure \( \pi_{\text{ion}} \) and ultimately high degree of swelling. The mutual repulsion of –COO\(^{-}\) groups along the macromolecular chain also promotes the swelling.

When the hydrogel is placed in the buffer solution of pH 4.0, the dissociation of –COOH groups present along the macromolecular chain is suppressed and hence concentration of counter ions inside the gel phase i.e., \( C_i^c \) decreases and hence \( C_i^c - C_i^s \) becomes comparatively small. Moreover, since the pH of external solution is just below the isoelectric pH of the casein (i.e., 4.6), –NH\(_2\) groups present along the casein molecules also get protonated to a little extent. In this way the mutual attraction between the two oppositely charges groups –NH\(_2\) and –COO\(^{-}\) also causes the polymer segments to contract (\( \pi_{\text{elec}} \)). Both of these factors cause a decrease in the degree of swelling.

In the case of pH 2.0 of external solution the dissociation of COOH groups is suppressed to such a great extent that the difference \( C_i^c - C_i^s \) becomes extremely small. Therefore minimum swelling is observed. Here it is worth mentioning that the swelling observed at this pH is mainly due to the electrostatic repulsion between the similarly charge
groups along the segment. Moreover some contribution of hydrophilic tendency of polyacrylamide should also be taken into account.

In the alkaline range although the dissociation of $-\text{COOH}$ is complete, thus providing a large number of counter ions in the gel phase but at the same time there exists a higher concentration of $\text{Na}^+$ and $\text{OH}^-$ ions in the external solution. As a result the difference $C^s_1 - C^i_1$ becomes small thus resulting in decrease in osmotic swelling pressure as well as extent of swelling. However the suppression in the degree of swelling in alkaline medium is not to such a great extent as found in the acidic medium. This may be contributed to the fact that in alkaline medium the mutual repulsion among $-\text{COO}^-$ groups is more predominant.

The values of swelling exponent $n$ at different pH of the external solution (Table 3) also support the proposed mechanism.

**Reversibility of Hydrogel Swelling**

The ability of hydrogel to undergo several cycles of swelling and deswelling is shown in Figure 2a,b. It can be seen from Figure 2a that after the first cycle the gel did not achieve its original swollen state and in all the following cycles it swelled back to its previous swollen state. Since the virgin gel was used without any prior washing, some salt might have been present which could have leached out upon deswelling, thus reducing the degree of successive swelling.

When the freshly prepared gel is placed in the doubly distilled water at pH 7.0, the swelling occurs to maximum in accordance with the Donnan-membrane equilibrium. Now when this swollen gel is placed in 2 M NaCl solution, the concentration of osmotically active ions in the external solution becomes high and hence this results into diffusion of water molecules from gel phase into outer solution, thus causing the gel to deswell. Due to reversibility and rapidity of swelling, the gel could be considered as a mechanochemical system in which chemical ionization energy could be transformed directly into mechanical energy [23].

It is also clear from the Figure 2b that when completely dried gel is placed in water it attains almost maximum swelling in every cycle. This shows that during the swelling process the gel does not undergo any irreversible structural change and hence

![Figure 2](image-url)
it swells back to maximum when placed in water.

During swelling, the shape of the gel sample followed a repeatable pattern. Initially a swelling front moved inward separating the swollen surface layer and the unswollen inside core. As a result, the sample assumed a dumbbell shape. Observation through an optical microscope showed the presence of stresses. The surface of the gel was full of cracks which disappeared after a while, yet the dumbbell shape was maintained, although it gradually changed back to cylindrical shape. This behaviour was observed during the swelling of all samples including dried samples. Similar observations were reported by Tanaka et al. as mechanical instabilities during the swelling of polyacrylamide gel beads. It is concluded that the thin swollen layer would be in mechanical constraint due to the free outer surface and fixed inner surface. Hence two opposing forces, one forcing the gel to swell and the other to remain unswollen would be resolved depending upon the osmotic pressure developed.

Drug Release Analysis
The model drug release behaviour of Cas-PAAmX hydrogels has been studied as a function of temperature of the external medium. When the drug loaded hydrogel is placed in the double distilled water at pH 7.0 at 37 °C, water diffuses into the polymer matrix owing to the swelling osmotic pressure. The penetrant molecules diffuse into the gel and displace the drug particles which ultimately diffuse out of the device due to increased chain relaxation. It was observed that initial rate of drug release was higher which may be contributed to the fact that when gel is placed in solvent, the outermost surface of the polymer matrix immediately comes in contact with it and the solvent diffuses into the gel phase, followed by release of drug. Similar observations have also been reported elsewhere.

Figure 3 describes the effect of temperature on drug releasing capacity of drug loaded hydrogel with the cross-linking ratio 2.1 and 1.7 mol %. Here the amount of drug released in a period of 20 h has been plotted against the temperature of the external solution. It is clear from the figure that there is an increase in the amount of drug delivered up to 40 °C, and then it decreases. Initially the observed decrease in the amount of drug released beyond 40 °C was thought to be due to formation of some complex structure between the amide groups and carboxylic groups, which were produced due to possible hydrolysis of polyacrylamide. However, when the same experiment was conducted with the drug loaded hydrogel of cross-linked polyacrylamide alone, the theory proved to be wrong, as there was no decrease in the amount of drug released beyond 40 °C. This clearly showed that no such complex structure formed inside the polymer matrix. In fact, an increase in temperature from 25 to 40 °C shows a higher and faster drug release due to the extensive swelling and chain relaxation. An increase in temperature beyond 40 °C shows a decrease in drug release due to decrease in solubility of casein.

Effect of Cross-linking
The degree of cross-linking of a hydrogel network plays a significant role in controlling its swelling behaviour. In the present study, two hydrogel samples with the cross-linking ratio in mol % 2.1 and 1.7 have been used, of which sample Cas-PAAmX (1.7) showed a greater swelling tendency than the other one (Figure 1). This behaviour of hydrogels is very
common and may be attributed to the fact that by increasing molar percent of cross-linker to monomer (i.e., lightly to highly cross-linked) the number of efficient cross-links per unit volume increases with the result that there is less free volume or room available to accommodate solvent, and hence degree of swelling decreases.

CONCLUSION

The swelling behaviour of casein cross-linked polyacrylamide hydrogels has been found to be pH-dependent and it favours the medium with neutral pH 7.0. This effect could be explained well on the basis of osmotic swelling pressure theory. These gels also undergo a number of reversible swelling-deswelling cycles while maintaining their structural integrity. The pH-dependent and reversible swelling behaviour could be very useful in the development of artificial muscle or physiologically sensitive drug delivery systems and extraction of biocomponents from dilute solutions by a modified gel filtration technique.

The drug loaded gels release the drug over a period of 24 h and hence there is some possibility of using these gels in the case of short term drug delivery applications where an immediate or fast relief is needed. The non-toxic nature of casein is also a favourable factor for its possible use as drug delivery device. In brief, the aim of the proposed study to look for the possibilities of using casein as a material for drug delivery devices has been achieved to some extent.

REFERENCES