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MODULATION OF IN VITRO RELEASE OF CRYSTAL VIOLET FROM A BINARY POLYMER HYDROGEL SYSTEM

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ABSTRACT

A macromolecular vehicle entrapping crystal violet (CV) as a model drug was developed by crosslink polymerization of acrylamide and styrene in the presence of a hydrophilic polymer poly(vinyl alcohol). The loaded polymer matrix was monitored for the controlled release of the crystal violet by a spectrophotometric method. The dynamics of the release process was investigated as a function of the composition of the gel and pH of the release medium. The mechanism of the release process was examined kinetically in terms of the quantitative parameters such as the diffusional exponent n and diffusion constant D evaluated using the Ficks equations.

Key Words: Polyvinyl alcohol; Poly(acrylamide-co-styrene); Crystal violet; Release; Kinetics

INTRODUCTION

The pharmaceutical applications of polymeric materials encompass many diverse areas. Perhaps the oldest examples are enteric coatings of orally ingested drugs and time-release (sustained release) preparations. Although coatings and compounding techniques can prolong the biological action

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of drugs, their rate of release is not uniform, or in other words, it is not "controlled." Similarly, the absorption of drugs administered parenterally may be prolonged by repository preparations providing for therapeutic effectiveness extending from 12 hours to several days, as for example with Penicillin G.

In contrast to the above, controlled drug delivery is aimed at providing not only sustained action but also constant, that is, ideally zero-order release rates in which the amount of drug released to the absorption site remains reasonably constant over prolonged periods of time.[1] Only some drug delivery systems can fulfill the later requirement, although, some repository preparations can remain therapeutically effective up to several days even without exhibiting zero-order kinetic release behavior. Among various natural and synthetic drug delivery systems, the most popular drug carriers are the hydrogels, which are three-dimensional networks of macromolecular chains possessing an extraordinary capacity of imbibing water into their internal structure. Hydrogels are very versatile materials.[2]

These polymers readily hydrate, absorb water, and swell quickly. Their hydrophilic nature and highly crosslinked structure render them a more suitable potential candidate for a controlled drug delivery system (CDDS). Hydrogels are hydrophillic macromolecular networks that, after swelling maintain their shape due to permanent links. Hydrogels may be impregnated with biologically active agents, such as antibiotics, enzymes, contraceptives, drug antagonists, anticoagulants, anticancer, etc., and may serve as a system for controlled release of the agent absorbed over a prolonged time period at a specific body site.[3,4] Hydrogels as biomaterials are favored due to the possibility of an interchange between the water they retain and body fluid, which is associated with biocompatibility. Drug delivery technologists usually tend to consider all hydrophillic delivery system as hydrogels. These polymers allow the preparation of a drug delivery system that results from a transition from glassy to rubbery state. A common feature is the swelling of the polymer that often results from the glassy rubbery transition of the dry form. This property is used in drug delivery controlled mechanism. CDDSs are being used with increased frequency in the treatment of many diseases.[5,6] Cases where long-term delivery and/or minimal fluctuation of plasma concentration of the drug are needed are when these systems mainly are used.

Polyvinyl alcohol hydrogels have been used in a number of biomedical applications including soft contact lenses,[7] implant,[8] and artificial organs,[9] and they also have gained wide pharmaceutical applications as drug delivery systems [10–13] because of their inherent toxicity, noncarcinogencity, good biocompatibility, and desirable properties such as a rubbery or elastic nature and a high degree of swelling in aqueous media.

All these and many more such applications are related fundamentally to the water sorption behavior of the hydrogels, which has been an area of

active and intensive research in the recent past.[14] The study of the swelling pattern of a hydrogel is important as this not only describes the amount of water contained within the hydrogels at equilibrium but also gives an insight into the network structure of the gel and the mechanisms of water transport processes.

Thus, realizing the contribution of PVA-based hydrogel systems to controlled drug delivery technology, we, in the present communication, are reporting results on the release kinetics of crystal violet (CV), a model drug, from a binary macromolecular system consisting of polyvinyl alcohol and poly(acrylamide-co-styrene).

EXPERIMENTAL

Materials

Polyvinyl alcohol (PVA) (hot processed M.wt = 40,000) was obtained from Burgoyne Burbidges and Co., Bombay, India, and was used without further purification. Acrylamide (AM, Research Lab, Poona, India) and Styrene (ST, Research Lab, Poona, India) were purified in order to remove the inhibitor. N,N′,Methylene bis acrylamide (MBA, Central Drug House Pvt. Ltd., Delhi, India) was used as a crosslinking agent and potassium persulphate (KPS, Loba Chemie Pvt. Ltd., Delhi, India) as polymerization initiator. Crystal Violet (CV) used as a model drug was obtained from E. Merck. Bidistilled water was used throughout the experiment.

Methods

The gels were prepared in a petri–dish (diameter 2′, Corning) by crosslink polymerization of acrylamide and styrene (3.75% w/v and 5.00% v/v), respectively, in the presence of polyvinyl alcohol (5.00% w/v). The polymerization was carried out at 80°C for 3 hours, and the gels so formed were dried at 60°C for 5 hours. They were further purified by equilibrating them in bidistilled water for 24 hours. The equilibrated swollen gels were dried at room temperature and cut into small pieces of equal weights (0.04 g).

The swelling experiments were performed gravimetrically as described in other communications.[15] The swelling ratio of the swollen gel was calculated by the following formula:

$$\text{Swelling Ratio} = \frac{\text{Weight of swollen gel}}{\text{Weight of dry gel}} \quad (1)$$

Release Experiments

For loading onto CV into the dried gels, small pieces (0.04 g) of dry gels were dipped into CV solution (1.0% w/v, specific density 0.98 g/cm^3 at 27°C) and equilibrated at 27°C for 24 hours. The loaded gels were dried at 50°C for 3 hours. The CV release experiments were carried out in double distilled water as release medium at 27°C by withdrawing 3 mL solution from the release medium at every 30 minutes. The contents were analyzed for CV spectrophotometrically (Systonics-106, India) at 560 nm and the samples were then returned into the release medium.

Kinetic Analysis of Release Data

An ideal CDDS is expected to maintain a constant, but effective, level of the drug in the blood plasma for a desirable period of time span. In most of the cases, the controlled release assessment of a device is made primarily on the basis of the first 50–60% release performance of the carrier as beyond this level therapeutically ineffective amounts of drug are present in the blood plasma. If a hydrogel film is equilibrated with a drug by soaking the hydrogel (xerogel) in an aqueous solution of the drug, the film can act as a vehicle for subsequent release of the drug when it is transferred to an aqueous sink. Release of a solute from a slab can be regarded as one-dimensional if it takes place predominantly from the two main surfaces and, thus, according to Crank:[16]

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

where M_∞ is the total drug content, M_t is the amount of drug released at time t, ℓ is the gel thickness, and n is an integer. This equation can be reduced to a simplified form still 99% accurate,

$$\frac{M_t}{M_\infty} = 4\left(\frac{Dt}{\pi\ell^2}\right)^{0.5} \tag{3}$$

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

A more realistic view can be constructed above the release mechanism when the release and swelling data are analyzed in light of the following equation:

$$\frac{M_t}{M_¥} = kt^n \tag{4}$$

where M_t/M_∞ is the fractional release at time t and k is a rate constant. The exponent n is an important indicator of the mechanism of transport and in

general has a value between 0.5 and 1.[17] 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 described as anomalous. The closer n is to 1, the closer is the release pattern to steady-state release. When $M_t/M_\infty 8$ is 0.5, t is in half-life, which is another extremely significant parameter in comparing systems. In light of Eqs. (3) and (4), the release data will be analyzed.

RESULTS AND DISCUSSION

Dynamic Release Model

Swelling CDDSs have their own advantages over the bioerodible, biodegradable, osmotic, and diffusion controlled systems as in the former devices the release profile is intimately regulated not only by the external stimuli such as pH, temperature, and ionic strength of the medium, but also by the chemical architecture of the releasing system. In the present investigation, the release devices falls into a swelling controlled delivery systems that involve three consecutive steps: absorption of water into the polymeric matrix, dissolution of drug into the imbibed water, and finally the diffusion of the drug into the external release medium. More importantly, the release of the drug is basically determined by the process of relaxation of macromolecular chains and the diffusion of the entrapped drug molecules into the exterior medium.

From a morphological consideration, a hydrogel could be considered to be an intimate mixture of macromolecular chains bonded to one another via chemical crosslinks or a weak type of intermolecular forces. When a drug loaded xerogel comes in contact with a thermodynamically compatible solvent, relaxation of polymeric chains takes place. This happens when the characteristic glassy-rubbery temperature of the polymers is decreased below the temperature of the experiment. The dissolved drug diffuses into the external receiving medium crossing the swollen polymer layers formed around the matrix. In order to visualize the dynamics of the release process, a situation may be considered when a loaded xerogel is equilibrated with a still medium (Fig. 1). As the penetrant water molecules invade the hydrogel surface, a moving front is observed that clearly separates the unsolvated glassy polymer region ahead of the solvent front from the swollen and rubbery gel phase behind it.[18] Just ahead of the front, the presence of solvent plasticizes the polymer and causes it to undergo a glass to rubber transition. Now the following possibilities could arise:

(1) Provided that the glass transition temperature (T_g) of the polymer is well below the experimental temperature, the polymer will be in the rubbery state and polymer chains will possess greater segmental mobility thus allowing easier penetration of the release medium molecules into the gel matrix resulting in a subsequent release of entrapped CV molecules. This normally

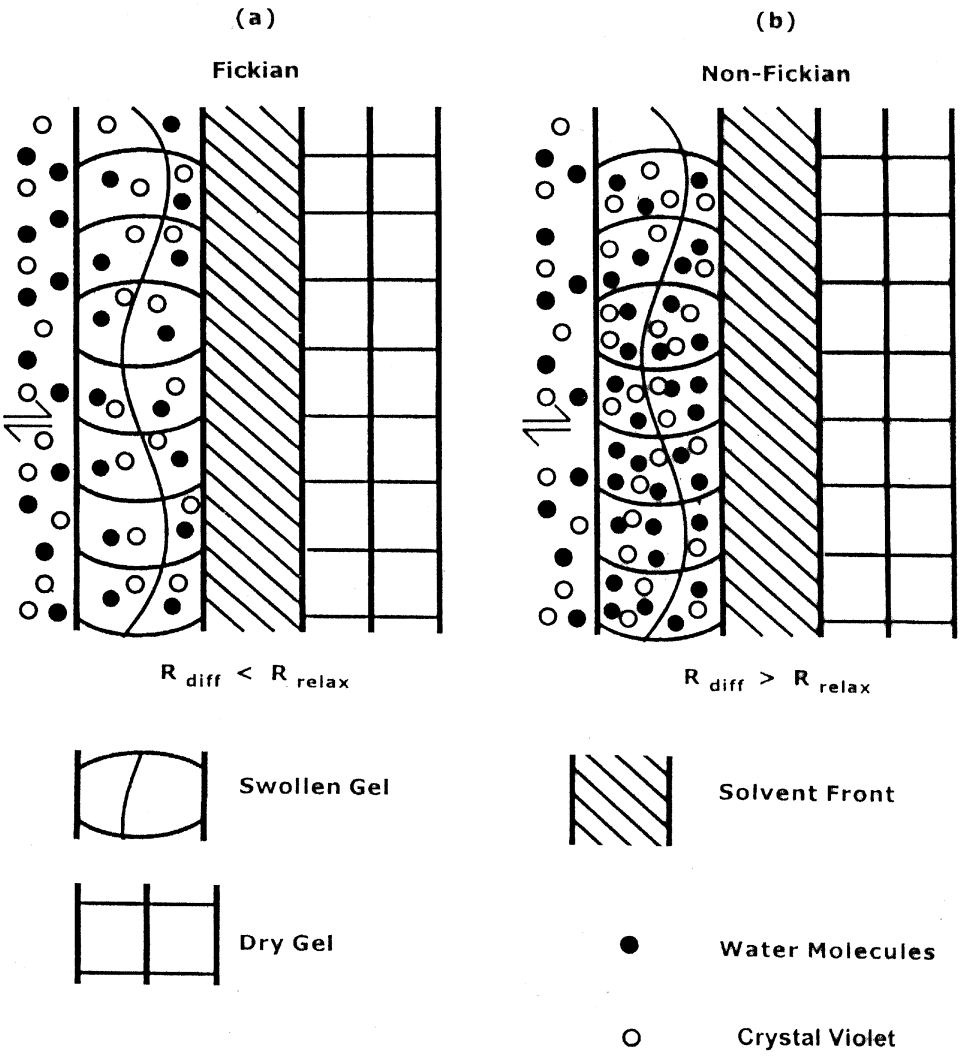

Figure 1. A model depicting the Fickian and non-Fickian release from a loaded hydrogel.

results in a Fickian release, which is characterized by a solvent and drug diffusion rate R_{diff}, slower than the polymer relaxation rate, R_{relax} ($R_{diff} \ll R_{release}$).

(2) If the experimental temperature is below the glass transition temperature, the polymer chains of the loaded device may not have sufficient segmental mobility to allow an immediate penetration of the solvent into the polymer core. Thus, the relaxation rate of polymeric chains becomes slower than those of the diffusion of the release medium molecules into the gel matrix and diffusion of the entrapped CV molecules into the release medium. This consequently results in a non-Fickian release, which includes Case 2 and

anamolous diffusion depending on the relative rates of diffusion of release medium and drug molecules and the chain relaxation (for Case 2, $R_{diff} \ll R_{relax}$ and for anomalous, $R_{diff} \sim R_{release}$).

Both of the release possibilities are depicted in Fig. 1.

Effect of Drug Loading on Released CV

There are two general methods for loading of hydrogels as drug carriers. In one method, the hydrogel monomer is mixed with a drug, an initiator, with or without a crosslinker, and allowed to polymerize, trapping the drug within the matrix.[19] In the second approach, a preformed hydrogel is allowed to swell to equilibrium in a suitable drug solution. The drug-loaded hydrogel is dried, and the device is obtained. The latter method has some advantages over the first method because polymerization conditions may have deleterious effects on drug properties and the difficulties in device purification after loading the polymerization often remain.

In the present study, the latter method of loading was followed, which involved swelling of preweighed pieces of the gel into the CV solution of concentration ranging from 5 to 20 mg/mL. The loaded gels were allowed to release the entrapped CV into a definite volume of the medium. The results are depicted in Fig. 2, which clearly indicate that the amounts of released CV gradually increase with increasing percent loading. The observed increase in the release rate may be attributed to the fact that a larger loading of the gel facilitates a faster movement of the solvent front that penetrates the surface of the loaded gel slab.[20]

Another reason for the observed higher release rate at higher loading could be that as CV is a charged molecule (Fig. 3), a larger percent loading of CV in the hydrogel will cause a greater repulsive force within the gel matrix, thus resulting in a faster relaxation of macromolecular chains. This obviously brings about a greater release rate.

Effect of PVA on Released CV

Drug release from swellable matrix tablets is based on the glassy–rubbery transition of the polymer, which occurs as a result of water penetration into the matrix. Whereas interactions between water, polymer, and drug are the primary factors in release control, various formulation variables influence the drug release rate to a greater or lesser degree.

According to Ford and coworkers [21–23] and Xu and Sunada,[24] the most important factor affecting the rate of release from polymer matrices is the drug:polymer ratio. In the present investigation, the effect of PVA content of the device on the release profile of CV has been studied by varying the concentration of PVA in the range 2.5 to 7.5% w/v. The results are displayed

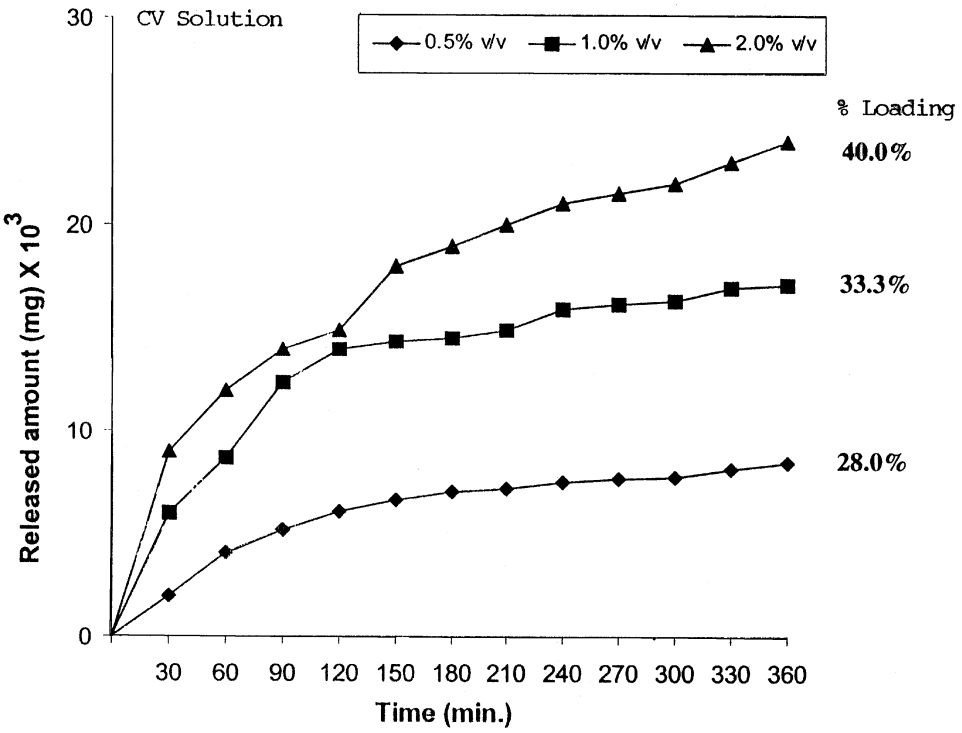

Figure 2. Release profiles of crystal violet from hydrogels loaded to different extents.

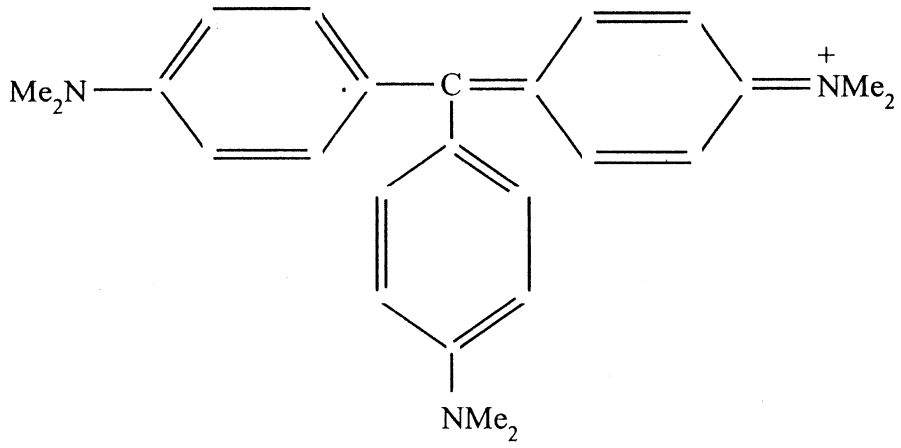

Figure 3. Molecular structure of crystal violet.

in Fig. 4, which reveal that the percent release of CV increases with decreasing PVA content of the gel.

The results can be explained on the basis of the swelling behavior of the hydrogel as shown in Fig. 5. It is clear from the figure that the swelling ratio decreases with increasing PVA content of the gel. The observed decrease in swelling is due to the fact that increasing PVA results in a greater density of the macromolecular network, which inhibits diffusion of penetrant water molecules into the gel matrix. Thus, a lower swelling of the loaded gel will consequently result in a lower amount of the released CV. It is also obvious now that since increasing PVA content results in a lower degree of swelling of the gel, it will also cause a lower percent loading of the CV into the gel, which, in turn, slows down the released amounts of the drug.

Another explanation of the observed decrease in percent release may be that as the PVA is a viscous polymer, an increase in polymer concentration

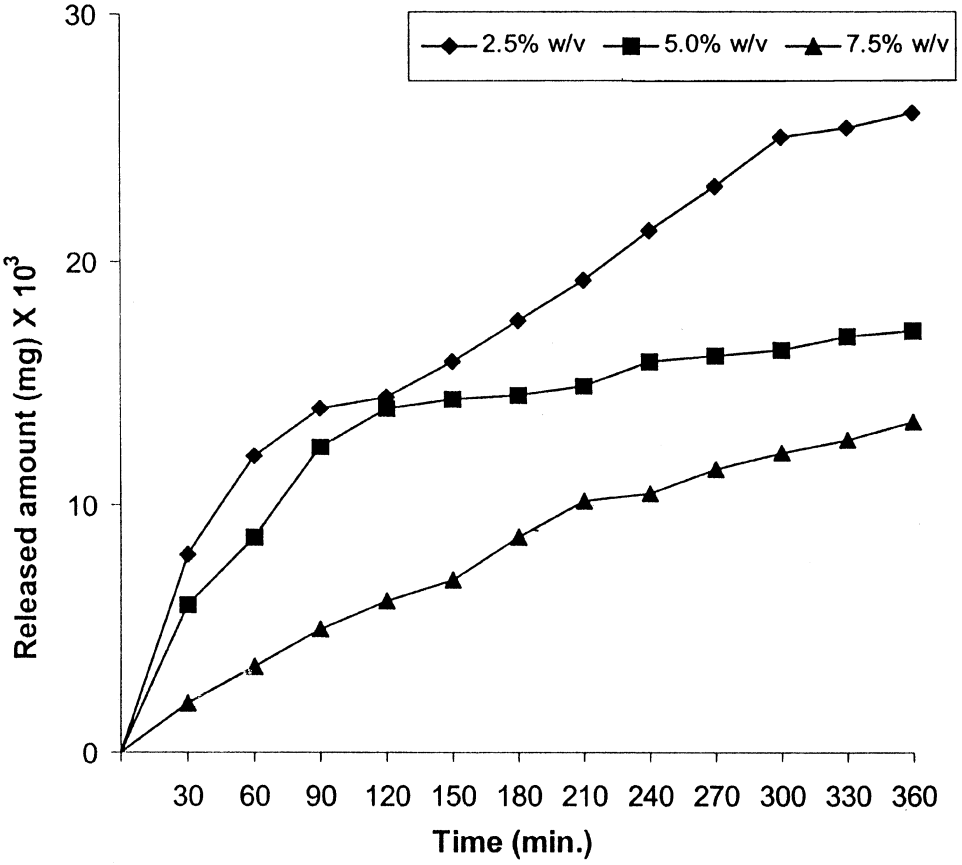

Figure 4. Effect of increasing polyvinyl alcohol (PVA) content of the hydrogel on the release profiles of crystal violet.

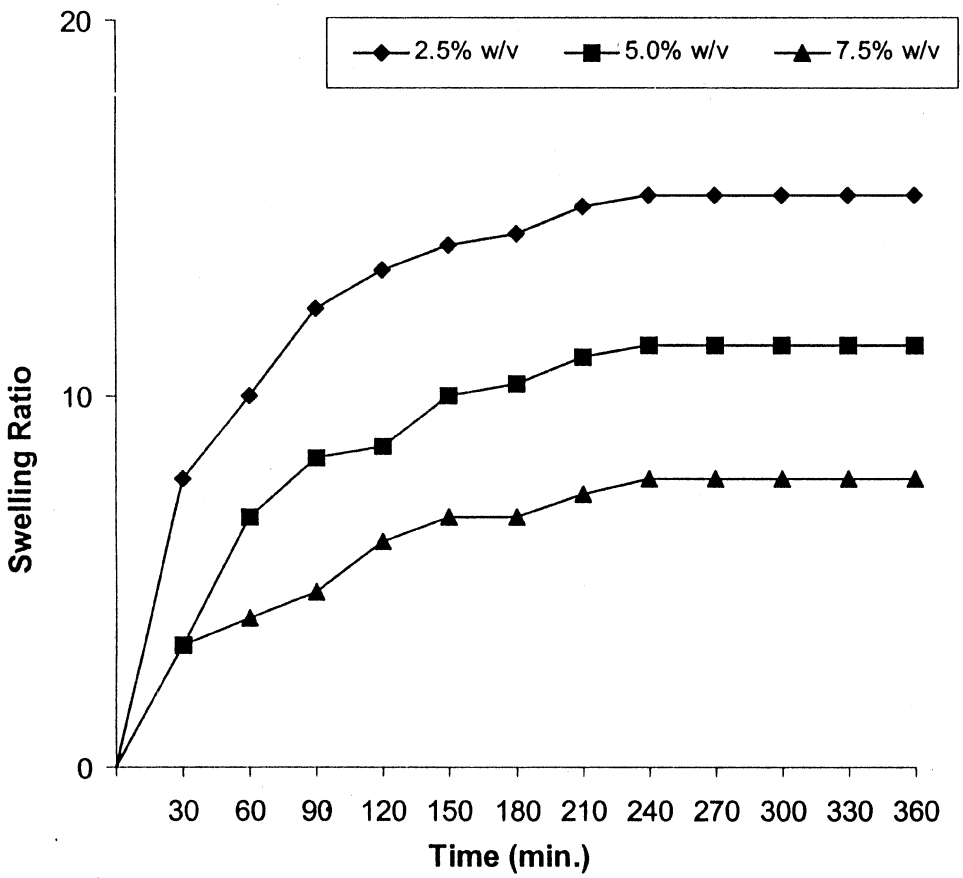

Figure 5. Swelling ratio vs time curves for the hydrogels with varying content of polyvinyl alcohol.

causes an increase in the viscosity of the gel, as well as the formation of a gel layer with a longer diffusional path. This could cause a decrease in the effective diffusion coefficient of the drug and, therefore, a reduction in the drug-release rate.

Effect of Monomers on Released CV

The influence of hydrophilic monomer acrylamide on the release profile of the hydrogel has been investigated by varying the composition of the monomer in the feed mixture in the range 2.5 to 6.25% w/v. The results (Fig. 6) of the release study indicate that with increasing the acrylamide content in the range 2.5 to 3.75% w/v, the released amount of CV increases, while beyond 3.75% w/v, there is observed a fall in the released amount. An

identical pattern of results were also obtained for the swelling behavior of the gel (Fig. 7). The results could be explained by the fact that since acrylamide is a hydrophilic monomer, its increasing proportion in the gel will result in a greater hydration of the network and, therefore, the swelling and, as a consequence, the released amount of the drug will increase in the initial increasing concentration range of acrylamide. However, beyond the acrylamide content of 3.75% w/v, the number of polyacrylamide segments becomes so large that both the diffusion of water and drug molecules through the network and relaxation of macromolecular segments become restrained thus bringing about a fall in the swelling of the gel, as well as in the released amount of CV.

The use of a hydrophobic segment in hydrogel preparation has become increasingly popular because of the new trends particularly in the field of contact lenses that involves hydrophobic microdomains in the optical material for improved permeability of oxygen without drastic loss of transparency

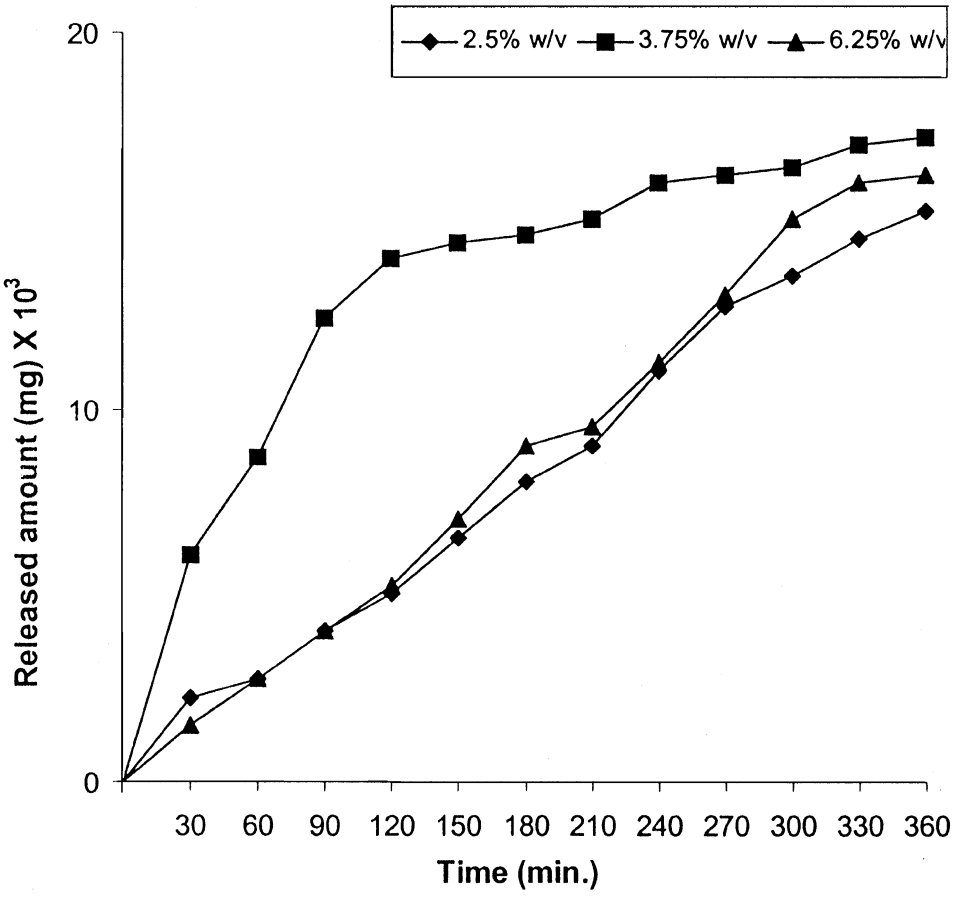

Figure 6. Effect of acrylamide content of the hydrogel on the release profiles of crystal violet.

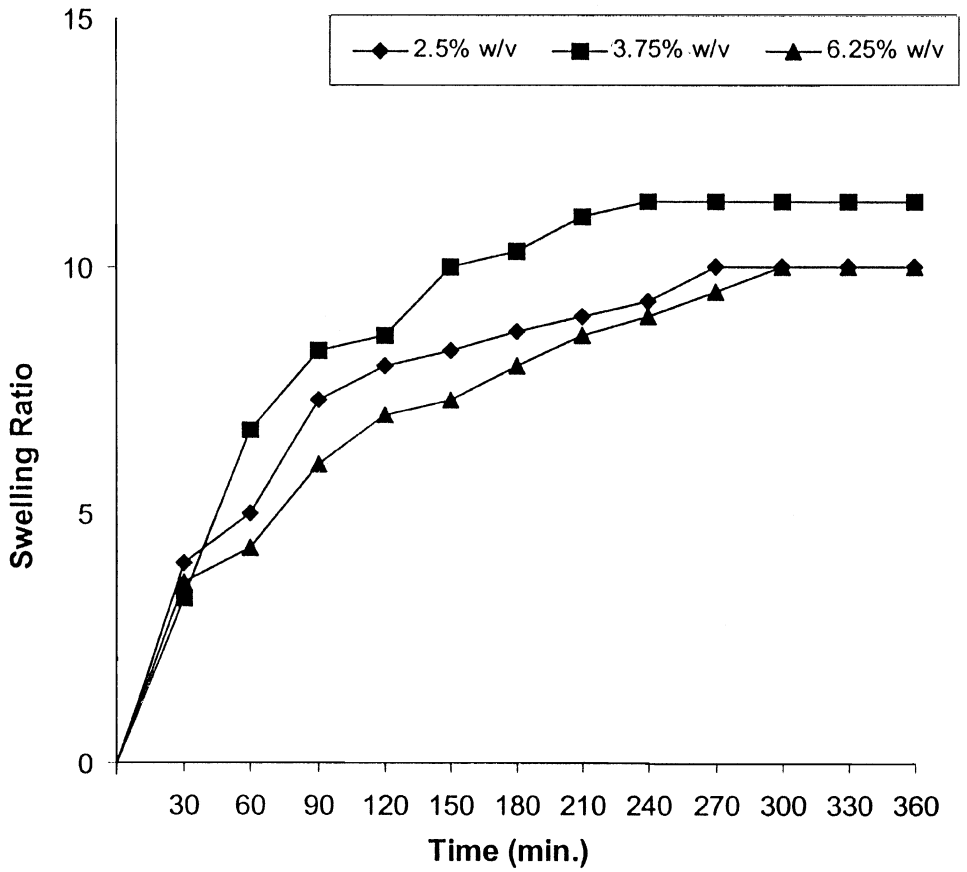

Figure 7. Influence of acrylamide content of the hydrogels on their swelling pattern.

and other optical properties. The introduction of a hydrophobic component into a hydrogel system greatly affects the organization of water elements within the gel and, consequently, affects its other allied properties.[25] In the present work, the concentration of styrene, a hydrophobic monomer, has been varied in the range 2.5 to 7.5% v/v in the feed mixture, and its effect on the drug release profile has been investigated. The results are depicted in Fig. 8, which reveal that the released amount of CV increases with increasing styrene proportion in the gel. The observed increase may be explained by the fact that increasing numbers of polystyrene segments in the gel produces larger mesh sizes of the free volumes within the network, and this results in a greater entrapment of the CV molecules within the device.

It is also worth mentioning that the bulky size of the phenyl ring in styrene molecules the steric factors facilitate the relaxation process of polystyrene segments of the gel, and this results in an increasing amounts of the released CV.

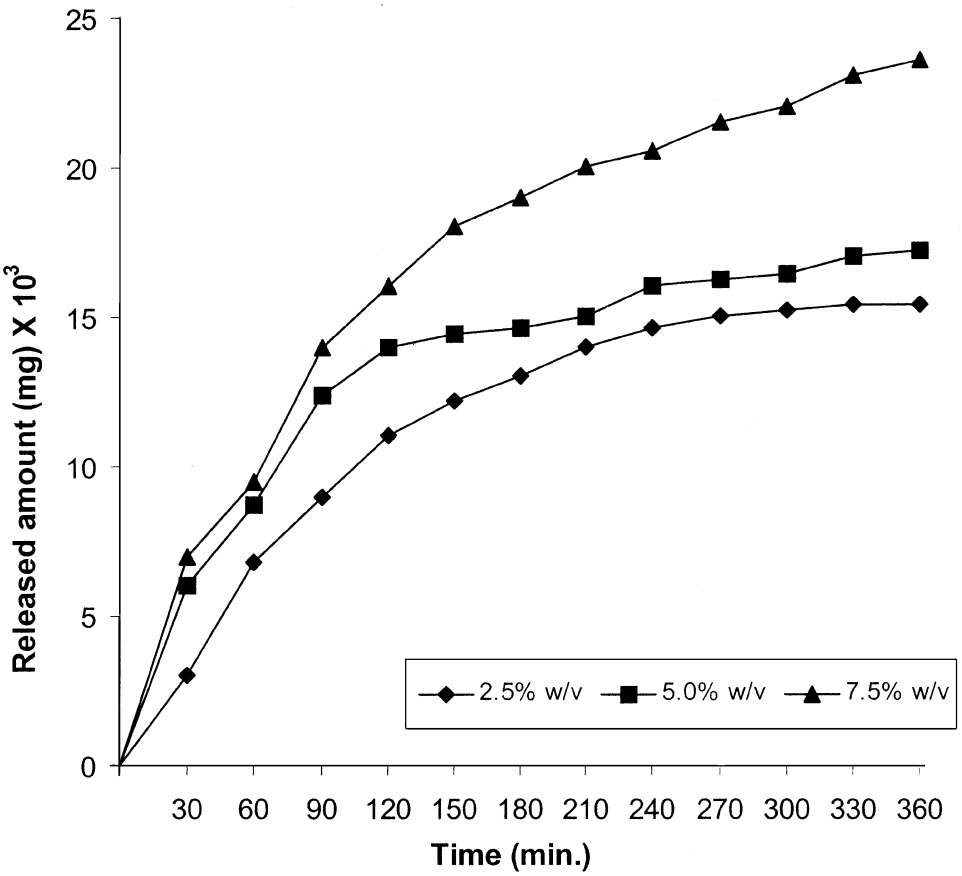

Figure 8. Effect of styrene content of the hydrogel on the release profiles of crystal violet.

Effect of Crosslinker on Released CV

In swelling CDDS, the release profile could be moderately and desirably changed by incorporating varying amounts of crosslinker in the feed mixture of the gel. It is a common belief that the degree of crosslinking has a direct control over the swelling characteristics of the hydrogel. Some authors [26] notice that the crosslink density affects the glass transition temperature of the polymer which, in turn, influences the swelling pattern of the gel.

In the present work, the effect of crosslinker (N,N′-methylene-bis-acrylamide) on the release kinetics of CV has been investigated by varying the concentration of the crosslinker in the range 0.05 to 0.20% w/v in the feed mixture of the gel. The results are presented in Fig. 9, which imply that the released amount of CV decreases with increasing crosslinker in the gel. The results can be explained by the fact that increasing numbers of crosslink

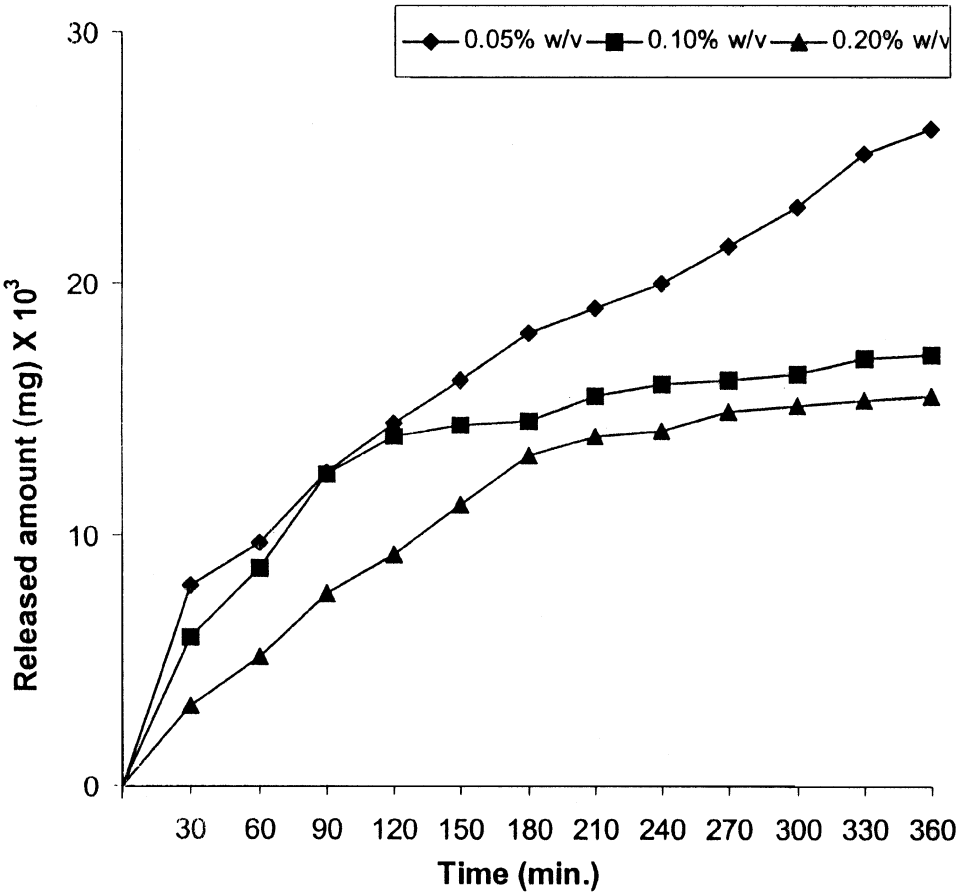

Figure 9. Release profiles of crystal violet from hydrogels containing varying amounts of crosslinker (N,N′-methylene bis acrylamide).

points in the gel reduce the mesh size of the free volumes available between the macromolecular chains of the network, and this obviously reduces the swelling of the hydrogel and, as a consequence, the drug release also. It is, however, also likely that increasing crosslink density of the network makes the hydrogel comparatively rigid and, therefore, the relaxation of polymer chains becomes difficult, which brings about in slow sorption of water molecules and subsequently lower release of CV. Similar type of results have also been reported by other workers.[27]

Effect of pH on Released CV

The development of drug delivery systems capable of selective release of drugs in the colon has received much attention.[28] The major therapeutic ap-

plications that can be found for oral colon-specific delivery are the treatment of local disorders in the colon and the delivery of peptide and protein drugs. The colon is considered a less hostile environment (i.e., suitable as an absorption site for the drug because of less diversity and intensity of digestive enzymes) than the stomach and the small intestine.[29] The colon has a long retention time and is highly responsive to desorption enhancers.[30]

To improve therapeutic efficiency and reduce or eliminate side effects of oral controlled drugs, it is reasonable to delivery drugs to specific regions of the gastrointestinal (GI) tract. Various compounds have been targeted to the colon in the form of prodrugs.[31] However, a more universal drug delivery system, which is not drug specific, is desirable. Several methods of targeting the specific regions have been used or proposed. Two of these, i.e., utilization of pH changes within the GI tract [32] and exploitation of bacterial enzymes localized within the colon [33] are of current interest in CDDSs.

In the present investigation, the release dynamics of the drug has been observed under varying pH conditions as found in the GI tract (Table 1). The results are depicted in Fig. 10, which indicate that with increasing pH of the release medium, the amounts of released CV decrease. The results can be explained on the basis of the degree of swelling of the loaded hydrogels. In the basic pH range, because of a limited swelling of the gel, the CV molecules diffuse out into the release medium with difficulty and, therefore, a lower release rate is noticed. While in the acidic pH range, a greater swelling of the loaded hydrogel allows faster diffusion of the entrapped CV molecules into the external medium. A similar type of results have also been noticed by other workers.[34]

It is worth mentioning here that we have noted an opposite swelling trend of unloaded and loaded gel, i.e., whereas the swelling ratio of the unloaded gel increases with increasing pH of the medium, there is found a just reverse type of result for loaded hydrogel. The reason could be that the loaded polymer hydrogel already has extended chains and thus sorption of water molecules produces a smaller chain extension in the unloaded hydrogel. Moreover, in basic medium, the diffusion of OH^- ions from the release

Table 1. pH's of Various Human Body Fluids

Human body fluids	pH
Saliva (in mouth)	6.7
Stomach (gastric juice)	1.0
Small intestine	
(i) Deudenum (bile duct)	8–8.6
(ii) Pancrease (pancreatic duct)	7.5–8.0

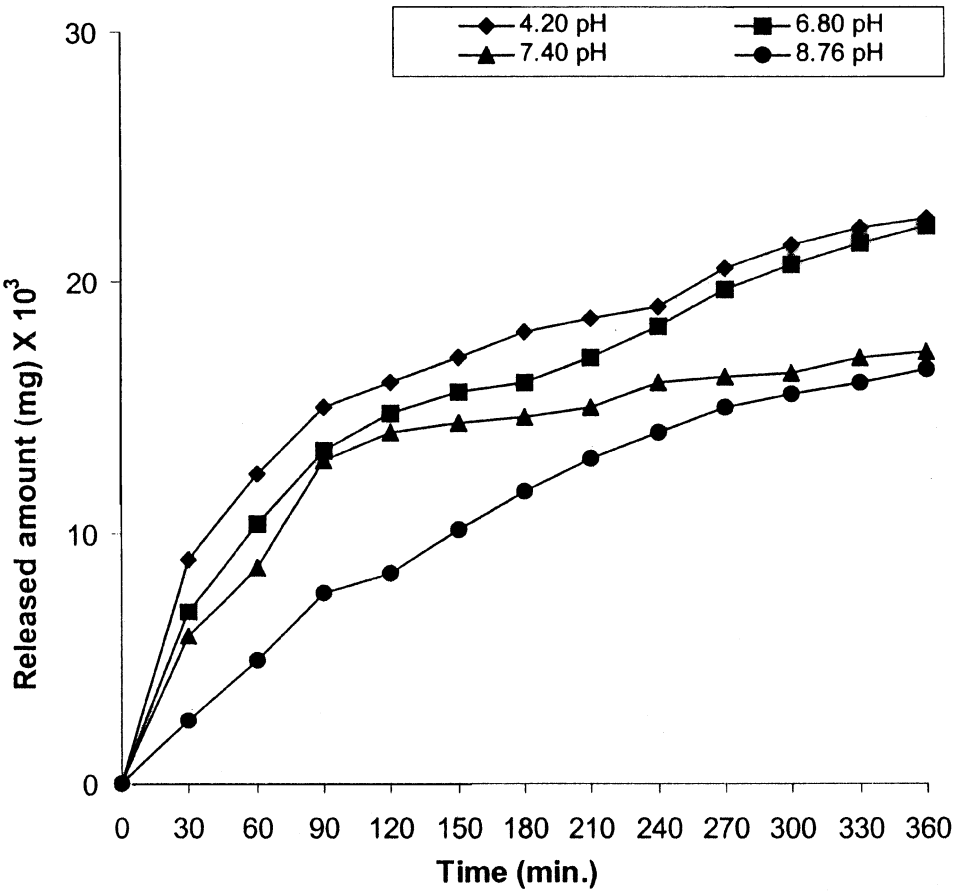

Figure 10. Effect of pH of the release medium on the release profiles of crystal violet.

medium into the loaded gel matrix could nullify the positively charged CV molecules thus causing a contraction in the gel network, while in acidic medium the diffusion of H^+ ions into the loaded gel enhance the positive charge within the network thus causing repulsion and subsequently a relaxation of macromolecular chains of the gel. This will obviously result in a greater swelling of the loaded gel in acidic media that then brings about a faster release of the entrapped drug. Both the situations may be modeled as shown in Fig. 11.

Analysis of Kinetic Data

It is a well established fact that the phenomenon of controlled drug release is basically ruled by the water sorption process that a loaded hydrogel

undergoes when immersed into a suitable solvent. The swelling of the gel could be due to the hydration of the polymer, which results in a rapid decrease in its glass transition temperature (T_g) to the temperature of the dissolution medium. Macroscopically, there is a relaxation response of the polymer chains due to stress induced by the presence of the dissolution solvent. This results in an increase in the radius of gyration and end-to-end distances of the polymer chains, causing a significant increase in the molecular volume of the hydrated polymer.[35] This reduces the free volume due to the presence of the micropores, which may manifest itself as a shift in the drug release mechanism.

Thus, to investigate the influence of the composition of the gel on the release mechanism Eqs. (3) and (4) have been utilized as discussed below:

When the concentration of PVA increases in the range 2.5 to 7.5% w/v in the feed mixture, the diffusional exponent (n) increases from a Fickian release value to anomalous type of non-Fickian release value as evident from the data summarized in Table 2. In other words, this reveals a shift of release mechanism from diffusion controlled to relaxation controlled release process. The observed trend is obvious and can be explained by the fact that increasing PVA content in the gel causes an increase in crowding of the macromolecular chains within the gel matrix and, therefore, slows down the relaxation rate of polymeric chains. This clearly changes the release mechanism from diffusion to relaxation controlled. Khan and Zhu,[36] in a study of ibuprofen release from a hydrophilic matrix, observed a shift of release mechanism from anomalous to Case 2 release, and they attributed this due to

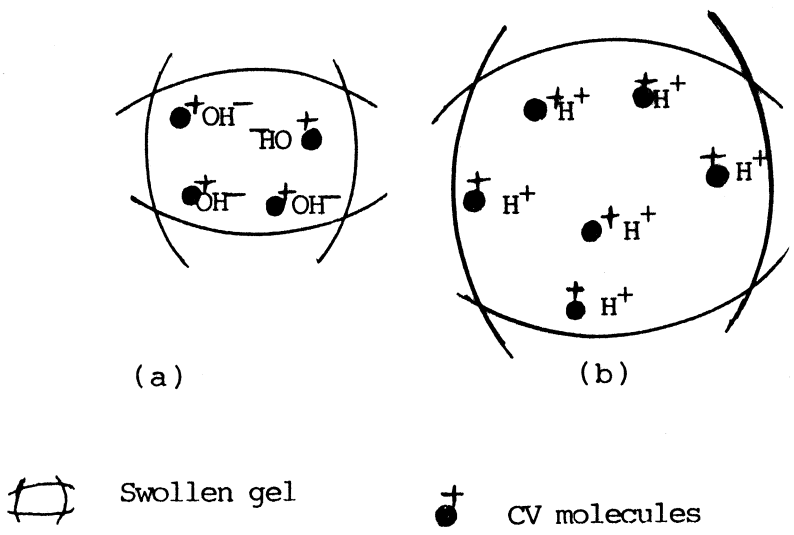

Figure 11. A model depicting the release of crystal violet from the loaded hydrogel in: (a) basic and (b) acidic release media.

Table 2. Data Showing the Kinetic Parameters of the Release of CV from Hydrogels of Varying Compositions

S. No.	Hydrogel Composition %					DX10^7		Release Mechanism
	PVA	AM	S	MBA	pH	n	cm^2s^{-1}	
1.	2.5	3.75	5.0	0.10	7.4	0.50	2.53	Fickian
2.	5.0	3.75	5.0	0.10	7.4	0.62	2.68	Anomalous
3.	7.5	3.75	5.0	0.10	7.4	0.75	5.60	Anomalous
4.	5.0	2.5	5.0	0.10	7.4	0.55	1.15	Anomalous
5.	5.0	3.75	5.0	0.10	7.4	0.62	2.68	Anomalous
6.	5.0	6.25	5.0	0.10	7.4	0.85	1.01	Anomalous
7.	5.0	3.75	2.5	0.10	7.4	0.50	1.47	Fickian
8.	5.0	3.75	5.0	0.10	7.4	0.62	2.68	Anomalous
9.	5.0	3.75	7.5	0.10	7.4	0.22	5.47	Anomalous
10.	5.0	3.75	5.0	0.05	7.4	0.50	1.36	Fickian
11.	5.0	3.75	5.0	0.10	7.4	0.62	2.68	Anomalous
12.	5.0	3.75	5.0	0.20	7.4	0.65	3.07	Anomalous
13.	5.0	3.75	5.0	0.10	4.12	0.50	1.77	Fickian
14.	5.0	3.75	5.0	0.10	6.8	0.57	1.97	Anomalous
15.	5.0	3.75	5.0	0.10	7.4	0.62	2.68	Anomalous
16.	5.0	3.75	5.0	0.10	8.7	0.66	5.47	Anomalous

a reduction in regions of low microviscosity and the closing of micropores in the swollen loaded polymer. However, we did not notice such a finding in our case.

On increasing acrylamide content in the copolymer poly(acrylamide-co-styrene) of the hydrogel in the range 2.5 to 6.25% w/v (in the feed mixture), the diffusional exponent n is found to increase in the non-Fickian range. As implied by the data in Table 2, the release mechanism shifts from low to high anomalous nature, thus, becoming more and more relaxation controlled with increasing acrylamide content. The observed results can be explained by the fact that increasing hydrophilic segments in the copolymer of hydrogel, the degree of hydration increases, which results in a restrained mobility of the copolymeric segments. This brings about in a relaxation-controlled release mechanism.

In a similar way, increasing styrene content in the gel in the range 2.5 to 7.5% v/v, there has been noticed a rise in the value of diffusional exponent from a Fickian value to non-Fickian value (Table 2). The observed shift of release mechanism from Fickian to anamolous type, i.e., from diffusion to relaxation controlled can be attributed to the fact that with increasing hydrophobicity, the dispersion and steric forces become prominent in the hydrogel and thus permit a restricted mobility to the macromolecular chains. This obviously results in a relaxation controlled release of the entrapped CV drug.

We have also studied the effect of crosslink density of the polymer as the release mechanism of the loaded gel. This has been achieved by employing the crosslinker (MBA) in the concentration range 0.05 to 0.20% w/v in the feed mixture. The data presented in Table 2 indicate that the diffusional exponent n increases from a Fickian value to anomalous value. This is quite expected, also, as on increasing the degree of crosslinking of the gel, the gel matrix becomes increasingly compact, and this definitely restricts the relaxation of the macromolecular chains.

A similar type of shift of release mechanism from a Fickian value to a anamolous value has been observed with increasing pH of the release medium from pH 4.12 to 8.70. The results clearly reveal that with increasing basicity of the medium, the relaxation of the network chains of the loaded gel becomes slow and slower, thus making the release mechanism as relaxation controlled.

The diffusion constants (D) calculated with Eq. (3) have also been summarized in Table 2.

CONCLUSION

The hydrogel of PVA and poly(acrylamide-co-styrene) presents a drug delivery system that could release the entrapped model drug crystal violet over a period of 6 hours. The release profiles are greatly influenced by the chemical architecture of the gel and pH of the release medium. It is found that increasing the drug to polymer (PVA) ratio in the loaded hydrogel decreases the amounts of the released CV. Whereas the released amount of CV increases initially with increasing acrylamide content of the gel, there is found a drop in the released amount with further increase in acrylamide proportion in the feed mixture of the gel. In the case of hydrophobic monomer styrene, the released CV constantly decreases. The crosslinking agent substantially reduces the released amounts of CV when the concentration of MBA increases in the feed mixture. Similarly, the release of CV is found to increase with increasing acidity of the release medium.

The drug release mechanism is found to shift with changing compositions of the gel. It is noticed that with increasing proportions of PVA, styrene and crosslinker in the gel, and pH of the release medium, the drug release mechanisms shift from Fickian to anomalous type. In the case of acrylamide variation in the gel, the release mechanism remains in the non-Fickian region thus changing from a less anomalous to more anomalous type.

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