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Psyllium and copolymers of 2-hydroxylethylmethacrylate and acrylamide-based novel devices for the use in colon specific antibiotic drug delivery

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Abstract

In order to utilize the psyllium husk, a medicinally important natural polysaccharide, to develop the hydrogels meant for the drug delivery, we have prepared psyllium 2-hydroxylethylmethacrylate (HEMA) and acrylamide (AAm)-based polymeric networks by using *N*,*N*′-methylenebisacrylamide (*N*,*N*′-MBAAm) as crosslinker and ammonium persulfate (APS) as initiator. The polymeric networks thus formed [psy-*cl*-poly(HEMA-*co*-AAm)] were characterized with FTIR and swelling studies which were carried out as a function of crosslinker concentration, time, pH and [NaCl] of the swelling medium. The swelling kinetics of the hydrogels and in vitro release dynamics of model drug (tetracycline hydrochloride) from these hydrogels has been studied for the evaluation of swelling mechanism and drug release mechanism from the hydrogels. The values of the diffusion exponent '*n*' have been obtained 0.5 for both swelling kinetics and drug release dynamics. This value shows that the Fickian type diffusion mechanism has occurred for the swelling of the polymers and for the release of drug from the polymers in different release mediums. The values of the initial diffusion coefficients (10.6×10^{-4}, 13.1×10^{-4}, 14.0×10^{-4}) cm^2/min, average diffusion coefficients (22.2×10^{-4}, 25.7×10^{-4}, 27.0×10^{-4}) cm^2/min and late diffusion coefficients (1.68×10^{-4}, 2.15×10^{-4}, 2.28×10^{-4}) cm^2/min for the release of tetracycline HCl respectively in distilled water, pH 2.2 buffer and pH 7.4 buffer from the drug loaded samples shows that in the initial stages, the rate of release of drug from the hydrogels is slow and rate of diffusion of drug increases with time.

Keywords: Drug delivery devices; Hydrogels; Psyllium; Release dynamics; Swelling kinetics

1. Introduction

In recent years, many research efforts have been made in the achievement of selective delivery of drugs into the colon following oral administration. Indeed, colonic release is regarded as a beneficial approach to the pharmacological treatment or prevention of widespread large bowel pathologies (Gazzaniga et al., 2006). For successful colon targeted drug delivery, a drug needs to be protected from degradation, release and/or absorption in the upper portion of the GI tract and then ensure abrupt or controlled release in the proximal colon (Asghar and Chandran, 2006). Hydrogels, specially based on the polysaccharides, have attracted considerable attention to act as smart candidates for the controlled release of therapeutic agents to the specific sites in the GI tract (Bromberg, 2005; Kosaraju, 2005). Different polysaccharides such as cellulose acetate (Dashora et al., 2006), chitosan (Gupta and Jabrail, 2006; Jaganathan and Vyas, 2006), sodium alginate (Sankalia et al., 2005) and guar gum (Chourasia and Jain, 2004a; Soppirnath and Aminabhavi, 2002)-based drug delivery devices have been reported. The rationale for the development of polysaccharide-based delivery systems for colon is the presence of large amount of polysaccharidases in the human colon, as the colon is inhabited by a large number and variety of bacteria, which secrete many enzymes (Chourasia and Jain, 2003, 2004b). The controlled release of active anti-microbial agents such as amoxicillin (Risbud and Bhonde, 2000; Risbud et al., 2000; de la Torre et al., 2003), metronidazole (Portero et al., 2002), oxytetracycline (Mi et al., 1997), vancomycin (Cerchiara et al., 2003) and tetracycline HCl (Bittner et al., 1999; Hejazi and Amiji, 2002, 2003) from the polymeric matrix to the

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GI tract have been carried out successfully by various workers. Biocompatible and non-toxic 2-hydroxylethylmethacrylate (HEMA) monomer has attracted a considerable attention to develop biomedical devices for the use in drug delivery (Tsou et al., 2005; Mahkam and Doostie, 2005).

On the other hand, psyllium has been reported as a gel forming medicinally active natural polysaccharide and has been used for the treatment of constipation, diarrhea, inflammation bowel diseases—ulcerative colitis, colon cancer, high cholesterol and diabetes (Singh, 2007). Oral sustained release gastroretentive dosage developed from psyllium husk, HPMC K100M and, crosspovidone has offered improved bioavailability of medications that are characterized by a narrow absorption window (Chavanpatil et al., 2005, 2006). When psyllium has been administered with ethinyloestradiol, the extent of ethinyloestradiol absorbtion increased slightly and the rate of absorption has decreased (Garcia et al., 2000). Succinic acid and tartaric acid treated psyllium has showed superior swelling and release profile of diltiazem HCl as compared to untreated powder. The release of drug from the modified formulation occurred in very controlled and sustained manner (Gohel et al., 2000, 2003). When the drug is loaded into the hydrogels by equilibrium swelling in the drug solution, drug release from the swollen gel follows Fick's law. This is known as Fickian diffusion mechanism. In this diffusion mechanism the rate of diffusion of drug from the polymer matrix is very less as compared rate of relaxation of polymer chains (Peppas and Korsmeyer, 1987).

Keeping in view, the pharmacological importance of gel forming psyllium polysaccharides and need to develop the colon specific drug delivery devices, psyllium, if suitably tailored to prepare the hydrogels, can act as the potential candidate for the novel drug delivery systems. Therefore, the present study is an attempt, to synthesize psyllium, poly(HEMA) and poly(AAm)-based hydrogels by using *N*,*N*′-MBAAm as crosslinker and ammonium persulfate (APS) as initiator. The polymeric networks thus formed were called as [psy-*cl*-poly(HEMA-*co*-AAm)] hydrogels thereafter, and were characterized by FTIR and swelling studies. The swelling responses of the hydrogels were studied as a function of time, pH and [NaCl] of the swelling medium. The release dynamics of tetracycline hydrochloride from hydrogels was also studied for the evaluation of the release mechanism and diffusion coefficients.

2. Experimental

2.1. Materials and method

Plantago psyllium mucilage was obtained from Sidpur Sat Isabgol factory, Gujrat, India. Hydroxyethylmethacrylate (HEMA) and acrylamide (AAm) were obtained from Merck-Schuchardt, Germany. Ammonium persulfate and *N*,*N*′-methylenebisacrylamide (*N*,*N*′-MBAAm) were obtained from S.D. Fine, Mumbai, India, and were used as received. Tetracycline hydrochloride was obtained from the Ind-Swift Limited, Chandigarh, India.

2.2. Synthesis of psy-cl-poly(HEMA-co-AAm)

Reaction was carried out with 1 g of psyllium husk, definite concentration of APS, definite concentration of monomers and crosslinker in the aqueous reaction system at 65 °C temperature for 2 h. Polymers thus formed [psy-*cl*-poly(HEMA-*co*-AAm)] were stirred for 2 h in 1:1 mixture of distilled water methanol to remove the soluble fractions in the polymers and were than dried in oven at 40 °C. The optimum reaction parameters were evaluated for the synthesis of [psy-*cl*-poly(HEMA-*co*-AAm)] by varying [APS] (from 4.38×10^{-3} to 21.9×10^{-3} mol/L), [HEMA] (from 0.33×10^{-1} to 8.23×10^{-1} mol/L) and [AAm] from (2.81×10^{-1} to 14.07×10^{-1} mol/L). During evaluation of these conditions, concentration of crosslinker was kept constant in each case, i.e. 32.40×10^{-3} mol/L. These reaction parameters were evaluated on the basis of the morphology and swelling studies after 24 h in distilled water. At these optimum reaction parameters (i.e. 1 g of psyllium, 4.38×10^{-3} mol/L of APS, 8.23×10^{-1} mol/L of HEMA, 14.07×10^{-1} mol/L of AAm), to study the effect of crosslinker variation on the structure of three-dimensional networks and thereafter on the swelling kinetics of these polymers, different polymeric networks were synthesized by varying [*N*,*N*′-MBAAm] (from 6.49×10^{-3} to 32.40×10^{-3} mol/L). The polymers used to study the effect of nature of swelling media on swelling kinetics and to study the release dynamics of the tetracycline hydrochlorides were prepared with 1 g of psyllium, 4.38×10^{-3} mol/L of APS, 8.23×10^{-1} mol/L of HEMA, 14.07×10^{-1} mol/L of AAm and 25.95×10^{-3} mol/L of *N*,*N*′-MBAAm.

2.3. Characterization

Psyllium and psy-*cl*-poly(HEMA-*co*-AAm) polymers were characterized by the FTIR spectroscopy and swelling studies. FTIR spectras of polymers were recorded in KBr pellets on Nicolet 5700FTIR (THERMO) and swelling studies were carried out by gravimetric method.

2.4. Swelling studies

Swelling studies of the polymeric networks were carried out in aqueous medium by gravimetric method in triplicate. Known weight of polymers were taken and immersed in excess of solvent for 24 h at fixed temperature to attain equilibrium swelling and then polymers were removed, wiped with tissue paper to remove excess of solvent, and weighed immediately. The difference in the weight of the polymer after swelling has showed the amount of water taken by the polymers. Swelling behavior of the polymeric networks were studied as function of time, pH and [NaCl] and swelling was taken as the difference of initial and final weight of polymers after fixed interval.

2.5. Release dynamics of the drug

2.5.1. Preparation calibration curves

In this procedure, the absorbance of a number of standard solutions of the reference substance at concentrations

encompassing the sample concentrations were measured on the UV–Visible Spectrophotometer (Cary 100 Bio, Varian) at wavelength 358, 357 and 360 nm respectively in distilled water, pH 2.2 buffer and pH 7.4 buffer respectively and calibration graphs were constructed. The Beer's law is obeyed up to 0.02, 0.01 and 0.02 mg/mL of the drug solution in distilled water, pH 2.2 buffer and pH 7.4 buffer respectively. The method is quite sensitive; as little as 0.002 mg/mL of the drug can be determined in each case (the molar extinction coefficient values respectively are 2.81×10^4, 5.69×10^4 and 3.25×10^4 L mol^{-1} cm^{-1}). The color is stable for at least 25 h in all the cases.

2.5.2. Drug loading to the polymer matrix

The loading of a drug onto hydrogels was carried out in triplicate by swelling equilibrium method. The hydrogels were allowed to swell in the drug solution of known concentration for 24 h at 37 °C and than dried to obtain the release device.

2.5.3. Drug release from polymer matrix

In vitro release studies of the drug have been carried out in triplicate by placing dried and loaded sample in definite volume of releasing medium at 37 °C temperature. The amount of tetracycline HCl released was measured spectrophotometrically by taking the absorbance of the solution after every 45 min at wavelength 358, 357 and 360 nm respectively for release in distilled water, pH 2.2 buffer and pH 7.4 buffer. The drug release was measured after fixed interval of time and release dynamics of model drugs were studied.

2.5.4. Preparation of buffer solution

Buffer solution of pH 2.2 was prepared by taking 50 mL of 0.2 M KCl and 7.8 mL of 0.2N HCl in volumetric flask to make volume 200 mL with distilled water. Buffer solution of pH 7.4 was prepared by taking 50 mL of 0.2 M KH_2PO_4 and 39.1 mL of 0.2N NaOH in volumetric flask to make volume 200 mL with distilled water (Pharmacopoeia of India, 1985).

3. Results and discussion

Polymeric networks have been synthesized by chemically induced polymerization through free radical mechanism. APS has generated the reactive sites on the psyllium, monomers and crosslinker. The crosslinker *N*,*N*′-MBAAm has four reactive sites which have formed linkage with the radical generated on the psyllium, poly(HEMA) and poly(AAm) and have produced three-dimensional networks, i.e. [psy-*cl*-poly(HEMA-*co*-AAm)]. These networks have been used to study the swelling kinetics of the polymers and in vitro release dynamics of the model drugs.

3.1. Mechanisms and mathematical modeling of drug release from polymer matrix

Based on the relative rate of diffusion of water into polymer matrix and rate of polymer chain relaxation, swelling of the polymers and the drug release profiles from the swelling polymer have been classified into three types of diffusion mechanisms (Alfrey et al., 1966; Peppas and Korsmeyer, 1987). These mechanisms are Case I or Simple Fickian Diffusion, Case II Diffusion and Non-Fickian or Anomalous Diffusion (Ritger and Peppas, 1987a,b). Although there are a number of reports dealing with mathematical modeling of drug release from swellable polymeric systems, no single model successfully predicts all the experimental observations (Brannon-Peppas and Peppas, 1989; Korsmeyer et al., 1986; Lee, 1980). Since most complex models do not yield a convenient formula and require numerical solution techniques, the generalized empirical equations has been widely used to describe both the water uptake through the swellable glassy polymers and the drug release from these devices. In the case of water uptake, the weight gain, M_s, is described by Eq. (1)

$$M_s = kt^n \tag{1}$$

where k and n are constant. Normal Fickian diffusion is characterized by $n = 0.5$, while Case II diffusion by $n = 1.0$. A value of n between 0.5 and 1.0 indicates a mixture of Fickian and Case II diffusion, which is usually called Non-Fickian or Anomalous Diffusion (Alfrey et al., 1966). Ritger and Peppas showed that the above power law expression could be used for the evaluation of drug release from swellable systems (Ritger and Peppas, 1987a,b). In this case, M_t/M_∞ replace M_s in above equation to give Eq. (2). For cylindrical shaped hydrogels, the initial diffusion coefficients (D_i), average diffusion coefficient D_A and late diffusion coefficients has been calculated from Eqs. (3)–(5) respectively (Ritger and Peppas, 1987a,b).

$$\frac{M_t}{M_\infty} = kt^n \tag{2}$$

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

$$D_A = \frac{0.049\ell^2}{t^{1/2}} \tag{4}$$

$$\frac{M_t}{M_\infty} = 1 - \left(\frac{8}{\pi^2}\right) \exp\left[\frac{(-\pi^2 D_t)}{\ell^2}\right] \tag{5}$$

where M_t/M_∞ is the fractional release of drug in time t, 'k' is the constant characteristic of the drug–polymer system, and 'n' is the diffusion exponent characteristic of the release mechanism. M_t and M_∞ is drug released at time 't' and at equilibrium respectively, D is the initial diffusion coefficient and 'ℓ' is the thickness of the sample. $t^{1/2}$ is the time required for 50% release of drug.

The values of diffusion coefficients have been evaluated for the swelling of the polymers and for the release of the drug from the polymers and results are presented in Tables 1–3.

3.2. Characterization

Psyllium psy-*cl*-poly(HEMA-*co*-AAm) were characterized by FTIR and swelling studies.

Table 1
Results of diffusion exponent '*n*', gel characteristic constant '*k*' and various diffusion coefficients for the swelling kinetics of psyllium-*cl*-poly(HEMA-*co*-AAm) hydrogels prepared with different [*N*,*N*′-MBAAm]

Hydrogels prepared with different [*N*,*N*′-MBAAm] ($\times 10^3$ mol/L)	Diffusion exponent, '*n*'	Gel characteristic constant, '*k*' $\times 10^2$	Diffusion coefficients (cm^2/min)		
			Initial, $D_i \times 10^4$	Average, $D_A \times 10^4$	Late time, $D_L \times 10^4$
6.49	0.5	2.787	9.73	22.5	1.81
12.97	0.5	3.004	8.23	19.3	1.62
19.46	0.5	3.145	8.04	18.9	1.58
25.95	0.5	3.177	7.67	19.2	1.54
32.43	0.5	2.947	8.94	22.1	1.79

Table 2
Results of diffusion exponent '*n*', gel characteristic constant '*k*' and various diffusion coefficients for the swelling kinetics of psy-*cl*-poly(HEMA-*co*-AAm) in different medium

Swelling medium	Diffusion exponent, '*n*'	Gel characteristic constant, '*k*' $\times 10^2$	Diffusion coefficients (cm^2/min)		
			Initial, $D_i \times 10^4$	Average, $D_A \times 10^4$	Late time, $D_L \times 10^4$
Distilled water	0.5	2.132	8.31	19.1	1.57
pH 2.2 buffer	0.5	2.032	9.22	21.5	1.63
pH 7.4 buffer	0.5	2.219	9.38	21.7	1.77
0.9% NaCl	0.5	2.469	7.57	19.4	1.47

Table 3
Results of diffusion exponent '*n*', gel characteristic constant '*k*' and various diffusion coefficients for the release of tetracycline HCl from drug loaded samples of psy-*cl*-poly(HEMA-*co*-AAm) in different pH medium

Drug in releasing medium	Diffusion exponent, '*n*'	Gel characteristic constant, '*k*' $\times 10^2$	Diffusion coefficients (cm^2/min)		
			Initial, $D_i \times 10^4$	Average, $D_A \times 10^4$	Late time, $D_L \times 10^4$
Distilled water	0.540	2.962	10.6	22.2	1.68
pH 2.2 buffer	0.522	2.745	13.0	25.7	2.15
pH 7.4 buffer	0.530	2.696	14.0	27.0	2.28

3.2.1. Fourier transform infrared spectroscopy

FTIR spectra of psyllium and polymeric networks psy-*cl*-poly(HEMA-*co*-AAm) were recorded to study the modification of the psyllium and are presented in Fig. 1a and b respectively. The broad absorption bands at 3428 cm^{-1} are due to –OH stretching indicates the association in the modified psyllium. In case of crosslinked polymer IR absorption bands at 1728 cm^{-1} due to C=O stretching of the ester, at 1663.9 cm^{-1} due to C=O stretching of the amide I and at 1617.7 due to N–H bending of amide II band were observed apart from usual peaks in psyllium.

3.2.2. Swelling kinetics of hydrogels [psy-cl-poly(HEMA-co-AAm)]

Swelling behavior of psy-*cl*-poly(HEMA-*co*-AAm) was studied as a function of [*N*,*N*′-MBAAm] in the polymer matrix, time, pH and [NaCl] of the swelling medium.

3.2.2.1. Swelling as a function of crosslinker concentration. In order to study the effect of crosslinker concentration in the polymers on water uptake behavior of psy-*cl*-poly(HEMA-*co*-AAm), the polymers have been prepared with different [*N*,*N*′-MBAAm]. The amount of water uptake by the polymer matrix at 37 °C has been studied after fixed interval of 30 min for 300 min and after that the equilibrium swelling has been

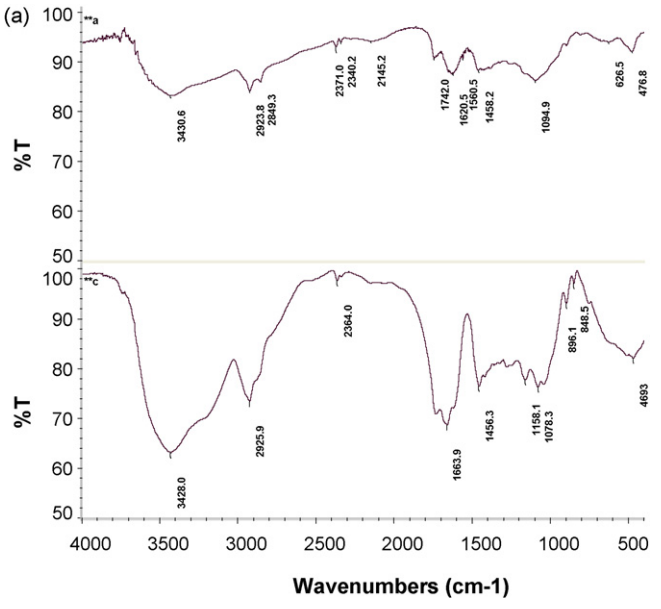

Fig. 1. FTIR of (a) psyllium and (b) psy-*cl*-poly(HEMA-*co*-AAm).

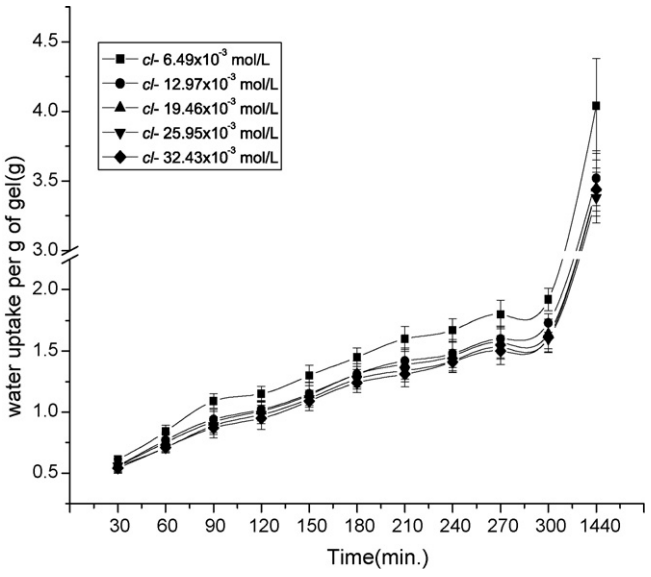

Fig. 2. Swelling kinetics of psy-*cl*-poly(HEMA-*co*-AAm)-based hydrogels prepared with different [*N*,*N*′-MBAAm].

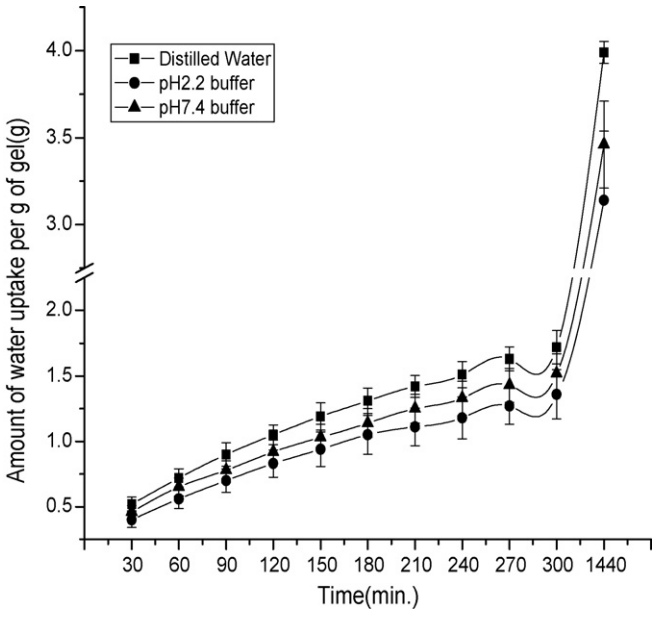

Fig. 3. Swelling kinetics of psy-*cl*-poly(HEMA-*co*-AAm)-based hydrogels in different medium at 37 °C.

taken after 24 h and results thus obtained are shown in Fig. 2. It has been observed from Fig. 2 that amount of water uptake by per gram of gel increases with increase in time and decreases with increase in crosslinker concentration in the polymer matrix. Further after 24 h swelling, it has been observed that maximum water uptake (4.04 ± 0.34) g/g of gel occurred for the polymer prepared with 6.49×10^{-3} mol/L of the *N*,*N*′-MBAAm and water uptake decreased to (3.38 ± 0.18) g/g of gel for the polymer prepared with 25.95×10^{-3} mol/L of the *N*,*N*′-MBAAm. This is probably due to increased extent of crosslinking of polymeric chains in hydrogels that leads to decrease in pore size and decreasing water up taking capacity of hydrogels. The decrease in swelling with increase in crosslinker agent in the hydrogels has been observed by Das et al. when they have crosslinked guar gum glutaraldehyde (Das et al., 2006). The values of diffusion exponent '*n*' and gel characteristic constant '*k*' have been evaluated from the slope and intercept of the plot $\ln M_t/M_\infty$ versus $\ln t$ and results are presented in Table 1. It is clear from the table that value of the '*n*' is 0.5, which indicates that Fickian type diffusion mechanism occurred for the diffusion of water molecules in the polymer matrix prepared with different crosslinker concentration. Diffusion coefficient values are presented in Table 1. It has been observed from the table that the values obtained for the average diffusion coefficient (D_A) are higher than the initial (D_i) and late diffusion coefficient (D_L).

3.2.2.2. Swelling as a function of pH and [NaCl]. In order to study the effect of pH on water uptake by the psy-*cl*-poly(HEMA-*co*-AAm) hydrogels, swelling studies have been carried out in distilled water, pH 2.2 buffer and pH 7.4 buffer for 24 h at 37 °C. The amount of water uptake by the polymer matrix after fixed interval of 30 min up to 300 min has been studied and results thus obtained are shown in Fig. 3. It has been observed from the figure that amount of water uptake by per gram of gel increases with increase in time and amount of water uptake has been observed to be more in pH 7.4 buffer and in distilled water as compared to the pH 2.2 buffer. Further after 24 h swelling, it has been observed that water uptake in pH 7.4 buffer solution $[(3.46 \pm 0.2)$ g/g of gel] is higher than pH 2.2 buffer solution $[(3.14 \pm 0.39)$ g/g of gel] (Fig. 3). This is attributed to the reason that partial hydrolysis leads to the generation of new water interaction centers and especially new ion dipole interactions in the polymer chains, leading to the significant changes in the water uptake of these hydrogels. The swelling of microgels prepared by polyacrylamide-grafted guar gum increased when the pH of the medium changed from acidic to alkaline (Soppimath et al., 2001). To study the effect of salt concentration on the swelling of the psy-*cl*-poly(HEMA-*co*-AAm) hydrogels, swelling has been carried out in 0.9% NaCl solution for 24 h at 37 °C (Fig. 4). It has been observed from the figure that amount of water uptake

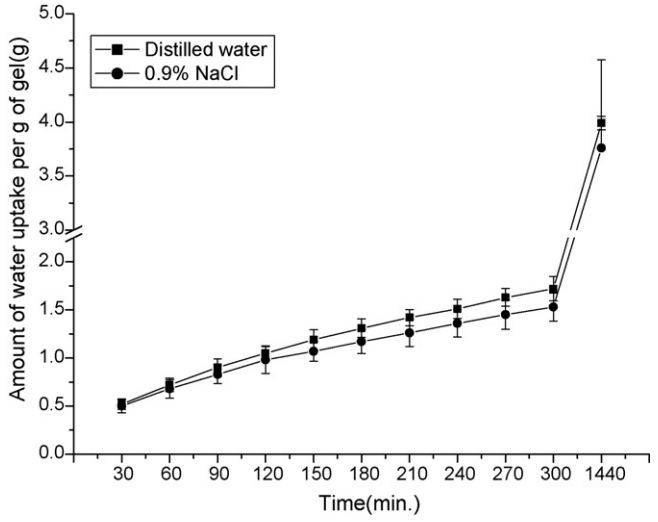

Fig. 4. Swelling kinetics of psy-*cl*-poly(HEMA-*co*-AAm)-based hydrogels in 0.9% NaCl solution at 37 °C.

by per gram of gel decreases in solution of NaCl. Further, maximum water uptake after 24 h swelling has been observed more in distilled water [(3.99 ± 0.06) g/g of gel] as compared to salt solution [(3.76 ± 0.8) g/g of gel]. Hydrogels do not swell appreciably in the presence of electrolyte salts due to ex-osmosis as even the swollen hydrogels shrink dramatically in the presence of salts.

The values of diffusion exponent '*n*' and gel characteristic constant '*k*' for the swelling of polymers in different pH and salt solution have been presented in Table 2. It is clear from the table that value of the '*n*' is 0.5, which indicates that Fickian type diffusion mechanism occurred for the diffusion of water molecules in the polymer matrix in different pH buffer and in salt solution. Fickian diffusion occurs when the rate of diffusion of water molecules in the polymer matrix is much less as compare to the rate of polymer chain relaxation and the same is occurring in the present studies. Diffusion coefficient for the swelling of polymers in different pH buffer and in salt solution is presented in Table 2. It has been observed from the table that the values obtained for the average diffusion coefficient (D_A) were higher than the initial (D_i) and late diffusion coefficient (D_L). It has been observed from the table that the values obtained for the average diffusion coefficient (D_A) are higher than the initial (D_i) and late diffusion coefficient (D_L). It means in the start and in the later stages of the swelling, the rate of diffusion of water molecules from the polymer matrix is slow.

3.3. Release dynamics of the drugs

The release profile of tetracycline hydrochloride from per gram of the drug loaded hydrogels in different pH buffer has been shown in Fig. 5. It has been observed from the release profile that the amount of drug released from the per gram of the gel is observed to be higher in distilled water and pH 7.4 buffer solution as compared to the release of drug in pH 2.2 buffer solution. Fifty percent of the total release of the drug in distilled water, pH 7.4 buffer and in pH 2.2 buffer respectively occurred in 270, 225 and 270 min. Maximum release of drug (2.19 ± 0.2) mg/20 mL/g of the gel has occurred in distilled water after 24 h. Similar observation has been made by Soppimath et al. where they have observed relatively quicker in pH 7.4 buffer than observed in 0.1N HCl (Soppimath et al., 2001). The release of drug is closely related to the swelling characteristics of the hydrogels, which in turn, is a, key function of chemical architecture of the hydrogels. At lower pH values the $-CONH_2$ groups of the polymeric matrix do not ionize and keep the polymeric network at its collapsed state. At higher pH values, these get partially ionized, and the charged $-COO^-$ groups repel each other, leading to the higher swelling of the polymer and resultant into increase in drug diffusion from the polymeric network, which otherwise is immobilized in the glassy polymer. The values of diffusion exponent '*n*' and gel characteristic constant '*k*' for the swelling of polymers in different pH is presented in Table 3. It is clear from the table that value of the '*n*' has been obtained 0.5 in each release medium, which indicates that Fickian type diffusion mechanism occurred for the diffusion of drug from the polymer matrix in different pH buffer. In Fickian diffusion the rate of diffusion of drug from the polymer matrix is much less as compared to the rate of polymer chain relaxation and the same is occurring in the present studies. Diffusion coefficient for the release of drug from the polymer matrix in different pH buffer is presented in Table 3. It has been observed from the table that the values obtained for the average diffusion coefficient (D_A) were higher than the initial (D_i) and late diffusion coefficient (D_L). It means in the start and in the later stages of the drug release rate of diffusion of drug from the polymer matrix is slow.

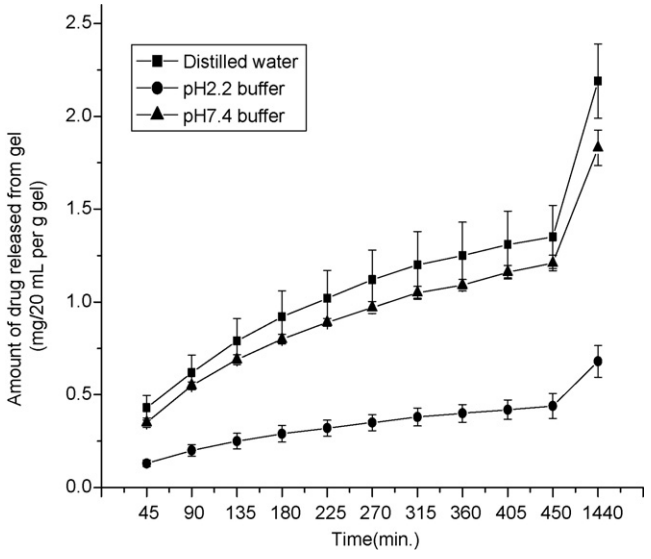

Fig. 5. Release profile of tetracycline HCl from drug loaded psy-*cl*-poly(HEMA-*co*-AAm) hydrogels in different medium at 37 °C.

It has been observed from the above mentioned findings that the swelling of the hydrogels, developed from the modification of psyllium polysaccharides, affects the release profile of the drugs from these hydrogels. Swelling of the hydrogels and release of drugs from these hydrogels has been observed pH responsive. The swelling of the hydrogels has been observed more at higher pH which corresponds to the pH of the colon and hence the colon specific delivery of therapeutic agents can be expected. The main importance of the present work is the modification of psyllium polysaccharides for developing the novel hydrogels (drug delivery systems) which have double potential to deliver the therapeutic agent. In literature double potential drug delivery devices has not been reported and the potential of the psyllium has not been explored. Here the double potential of the drug delivery device is based on the fact that psyllium polysaccharide itself is the therapeutic agent for the treatment of diabetes mellitus, ulcerative colitis and colon cancer, and, if the same drug which otherwise is used for the cure of these problems, when released from the drug loaded polymeric matrix developed from the psyllium will be act with double potential. These hydrogels will be effective in enhancing drug targeting specificity, lowering systemic drug toxicity, improving treatment absorption rates, and providing protection for pharmaceuticals against biochemical degradation. At the same time this drug will release in controlled and sustained manner from these polymeric matrices.

4. Conclusion

It is concluded from the foregone discussion that the swelling of the modified psyllium-based hydrogels is affected by the composition of the hydrogels and pH of the swelling medium. The swelling of the polymers has decreased with increase in crosslinker concentration in the polymers and has increased with increase in the pH of the swelling medium. It is also concluded that the release of drug from the polymer matrix increases with increase in pH of the releasing medium. As the pH of the colon is also higher so these hydrogels can act as colon targeted drug delivery systems indicated from swelling and release response of the hydrogels in the different medium. Further, the Fickian type diffusion mechanism has occurred for the diffusion of drug molecules from the hydrogels, in this diffusion mechanism the rate of diffusion of drug from the polymer matrix is much less as compared to the rate of polymer chain relaxation.

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