J Mater Sci: Mater Med (2008) 19:2771–2780
DOI 10.1007/s10856-008-3406-5

In vitro release dynamics of model drugs from psyllium and acrylic acid based hydrogels for the use in colon specific drug delivery

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Received: 9 July 2007 / Accepted: 6 February 2008 / Published online: 29 February 2008

Abstract Psyllium is medicinally important gel forming polysaccharides. Keeping in view, the pharmacological importance of psyllium and drug delivery devices based on hydrogels, psyllium, if suitably tailored to prepare the hydrogels, can act as the double potential candidates for the novel drug delivery systems. Therefore, it is an attempt to prepared psyllium and acrylic acid based pH sensitive novel hydrogels by using *N*,*N*′-methylenebisacrylamide (*N*,*N*-MBAAm) as crosslinker and ammonium persulfate (APS) as initiator for the use in colon specific drug delivery. The present paper discusses the swelling kinetics of the hydrogels and release dynamics of model drugs (tetracycline hydrochloride, insulin and tyrosine) from drug-loaded hydrogels, for the evaluation of the swelling mechanism and drug release mechanism from the polymeric networks .The effect of pH on the swelling kinetics and release pattern of drugs have been studied by varying the pH of the release medium. It has been observed that swelling and release of drugs from the hydrogels occurred through non-Fickian or anomalous diffusion mechanism in distilled water and pH 7.4 buffer. It shows that the rate of polymer chain relaxation and the rate of drug diffusion from these hydrogels are comparable.

1 Introduction

Recently, site specific, controlled and sustained drug delivery has become the standard in modern pharmaceutical design and an intensive research has been undertaken to achieving much better drug product effectiveness, reliability and safety. A number of polymeric based devices have been proposed to achieve drug delivery systems for efficient therapy. Among them, 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 [1–5]. It is desirable to target areas of the GI tract for the local treatment of local diseases such as colonic carcinomas or ulcerative colitis. Delivery of a drug molecule directly to its site of action may allow a reduction in dose, and consequently a reduction in potential systemic side effects, which are a major issue in the treatment of these conditions [6]. 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. In addition, polysaccharides are readily available, cheap, non-toxic and are biodegradable [7–11].

Hydrogels are three-dimensional polymeric networks those swell quickly by imbibing a large amount of water or de-swell in response to changes in their external environment. The volume phase transitions as a response to different stimuli make these materials interesting objects of scientific observations and useful materials for use in advanced biomedical technologies. These changes can be induced by changing the surrounding pH, temperature, ionic strength and electro stimulus [12–14]. The pH-sensitive hydrogels have a potential use in site-specific delivery of drugs to specific regions of the GI tract and have been prepared for low-molecular-weight and protein drug delivery [15–17]. The release of water soluble drug, entrapped in a hydrogels, occur only after water penetrates the network to swell the polymer and dissolve the drug,

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followed by diffusion along the aqueous pathways to the surface of the device. 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 [18–21]. Hydrogels exhibit a thermodynamic compatibility with water, which allows them to swell in aqueous media and have numerous applications, in particular, in the medical and pharmaceutical sectors. Hydrogels resemble natural living tissue more than any other class of synthetic biomaterials because of their high water contents and soft consistency, which is similar to natural tissue. Moreover, the high water content of the materials also contributes to their biocompatibility. Consequently, hydrogels can be used as contact lenses, membranes for biosensors, linings for artificial hearts, materials for artificial skin, and drug delivery devices [22–24]. The controlled release of peptides, low molecular weight drugs [25–28] and active anti-microbial agents (amoxicillin, metronidazole, oxytetracycline, vancomycin and tetracycline-HCl) [29–34] from the polymeric matrix have attracted growing interest in recent years following the development of new delivery systems which is able to overcome problems due to the acid environment and enzymatic degradation in the gastrointestinal tract.

Psyllium is the common name used for several members of the plant genus *Plantago* and its seeds are used commercially for the production of mucilage, which a white fibrous material, hydrophilic nature and forms the clear colorless mucilaginous gel by absorbing water [35]. Gel-forming fraction of the alkali-extractable polysaccharides composed of arabinose, xylose and traces of other sugars [36]. Psyllium has been reported as a medicinally active gel forming natural polysaccharide [37]. It has been used for the treatment of constipation, diarrhea, inflammation bowel diseases-ulcerative colitis, colon cancer, obesity in children and adolescents and high cholesterol. Psyllium supplementation has also improved blood sugar levels in some people with diabetes [37].

Keeping in view, the pharmacological importance of psyllium polysaccharides and drug delivery devices based on hydrogels, psyllium, if suitably tailored to prepare the hydrogels, can act as the double potential candidates for the novel drug delivery systems. Modification of the psyllium to develop the hydrogels is not much reported in the literature. Therefore, the present study is an attempt, to synthesize psyllium and poly(AAc) based hydrogels by using *N*,*N*-MBAAm as crosslinker and ammonium persulfate (APS) as initiator. This paper discusses the swelling kinetics of the hydrogels and release dynamics of model drugs (tetracycline hydrochloride, insulin and tyrosine) from these hydrogels in the different release medium for the evaluation of mechanism for the swelling of the hydrogels and mechanism for the release drugs from these hydrogels.

2 Experimental

2.1 Materials and Method

Plantago psyllium mucilage (Psy) was obtained from Sidpur Sat Isabgol factory (Gujrat, India), acrylic acid (AAc) was obtained from Merck-Schuchardt, Germany, sodium hydroxide, Sodium potassium tartrate and Folin's reagents was obtained from Merck Mumbai-India. Ammonium persulphate (APS), copper sulphate and *N*,*N*′-methylenebis-acrylamide (NN-MBAAm) was obtained from S.D. Fine, Mumbai-India and were used as received. Insulin was obtained from the Torrent Pharmaceuticals Ltd. Indrad, Mehsana, India. L-Tyrosine was obtained from the Himedia Laboratories Pvt. Limited, Mumbai- India. Tetracycline hydrochloride was obtained from the Ind-Swift Limited, Chandigarh, India. Sodium carbonate was obtained from Ranbaxy, SAS Nagar Punjab-India.

2.2 Synthesis of Psy-*cl*-poly(AAc)

Reaction was carried out with 1 g of psyllium husk, 1.095×10^{-2} moles/l of APS, 6.94×10^{-1} moles/l of AAc, 16.20×10^{-3} moles/l of *N*,*N*-MBAAm in the aqueous reaction system at 65°C temperature for 2 h. Polymer thus formed was stirred for 2 h in distilled water and for 2 h in ethanol to remove the soluble fraction and then was dried in an oven at 40°C. The resultant polymeric network called thereafter Psy-*cl*-poly(AAc), was used to study the swelling kinetics of the hydrogels and release dynamics of the model drugs from the drug loaded hydrogels. Polymeric networks were synthesized by chemically induced polymerization through free radical mechanism. APS has generated the reactive sites, both on the psyllium and monomer, lead to the propagation of the reaction. In the presence of crosslinker *N*,*N*-MBAAm (CH_2=CHCONHCH_2NHCOCH=CH_2), because of its polyfunctionality four reactive sites formed in he presence of initiator and these sites can be linked both with the radical on the psyllium and on the poly(acrylic acid) or poly(AAc) form the three-dimensional networks i.e., Psy-*cl*-poly(AAc).

2.3 Swelling kinetics

Swelling kinetics of the polymeric networks was carried out in different pH solution by gravimetric method. Known weight of polymers was taken and immersed in excess of solvent for different time intervals at 37°C and then polymers were removed, wiped with tissue paper to remove excess of solvent, and weighed immediately. The difference in weight has given the gain in weight at different time intervals. The swelling of the hydrogels were also taken after 24 h.

2.4 Release dynamics of model drugs from Psy-*cl*-poly(AAc)

2.4.1 *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) and calibration graph was constructed. The concentration of the drug in the sample solution was read from the graph as the concentration corresponding to the absorbance of the solution. Three calibration graphs of each drug were made to determine the amount of drug release from the drug loaded polymeric matrix in different medium that is distilled water, pH 2.2 buffer and pH 7.4 buffer and these curves are respectively Using the straight line equation ($y = mx + c$), slope and intercept values were obtained in case of tetracycline HCl as (3.60815, 0.01937), (2.56661, 0.02625) and (2.98448, 0.01978), in case of insulin as (0.03838, −0.00107), (0.04778, 0.02879) and (0.05782, −0.00585), and in case of tyrosine as (10.77309, 0.06762), (14.81642, 0.11987) and (12.02782, −0.01092) respectively for distilled water , pH 2.2 buffer and pH 7.4 buffer.

2.4.2 *Drug loading to the polymer matrix and drug release from polymer matrix*

The loading of a drug onto hydrogels was carried out 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.

In vitro release studies of the drug were carried out by placing dried and loaded sample in definite volume of releasing medium at 37°C temperature. The amount of tetracycline hydrochloride released was measured spectrophotometrically as such but model drugs insulin and tyrosine were assayed by Lowry method [38]. The absorbance of the solution was measured at λ_{max}, (768.0, 753.0 and 758.0 nm) for insulin, at (765.0, 763.0 and 772.0 nm) for tyrosine and at (357.0, 358.0 and 361.0 nm) for tetracycline hydrochloride respectively for the release in distilled water, pH 2.2 buffer and pH 7.4 buffer after every 30 min in each case. The reagents and procedure for Lowry method is as follows:

2.4.3 *Reagents used and procedure for Lowry method and preparation of buffer solution*

Reagent A: Sodium carbonate (2% w/v) in 0.1 N Sodium hydroxide solution was prepared by dissolving 20 g of sodium carbonate and 4 g of sodium hydroxide in1 l of distilled water. Reagent B: Copper sulphate solution (1% w/v) was prepared by dissolving 1 g of copper sulphate (AR) in100 ml of distilled water.

Reagent C: Sodium potassium tartrate solution (2% w/v) was prepared by dissolving 2 g of the salt in 100 ml distilled water.

Reagent D: Alkaline copper reagent: 1 ml each of reagent B and C was mixed with 98 ml of reagent A and vortexed. This reagent was prepared freshly.

To 1 ml of the standard drug solution (insulin or tyrosine) or released drug sample solution were added 4 ml of reagent D and the contents were mixed. After 10 min of incubation at room temperature 0.4 ml of Folin's reagent was added and the contents were vortexed immediately. A reagent blank with 1 ml of distilled water (or buffer solution of respective pH) was also processed in same manner as described above. After 30 min of incubation at room temperature, the blue color developed was measured at λ_{max}. Calibration curve was constructed and computed to calculate the concentration of the insulin released from the sample. While calculating the concentration of these drugs in the unknown sample, the dilution factor has been taken into account [38].

Buffer solution of pH 2.2 was prepared by taking 50 ml of 0.2 M KCl and 7.8 ml of 0.2 N 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 0.2 N NaOH in volumetric flask to make volume 200 ml with distilled water [39].

2.4.4 *Mechanism of drug release from polymer matrix*

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 [40]. The diffusion of water molecule and drug from the hydrogels have been classified into three different types based on the relative rates of diffusion and polymer relaxation [41, 42]. In the case of water uptake, the weight gain, M_s, is described by the following empirical equations:

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

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. Ritger and Peppas showed that the above power law expression could be used for the evaluation of drug release from swellable systems. In this case, M_t/M_∞ replace M_s in above equation to give

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

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. When the plot is drawn between ln M_t/M_∞ and ln t, the slope of the Plot gives the value of 'n' and intercept will tell about 'k'. This equation applies until 60% of the total amount of drug is released. It predicts that the fractional release of drug is exponentially related to the release time and it adequately describes the release of drug from slabs, spheres, cylinders and discs from both swellable and non-swellable matrices. Fick's first and second laws of diffusion adequately describe the most diffusion processes. For cylindrical shaped hydrogels the integral diffusion is given in simple Eq. 3 by Ritger and Peppas [41, 42]

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

where (M_t/M_∞) is the fractional release and M_t and M_∞ is drug released at time 't' and at equilibrium respectively, D is the diffusion coefficient and ℓ is the thickness of the sample. In Eq. 3 the slope of linear plot between (M_t/M_∞) and $t^{1/2}$ yield diffusion coefficient D. Therefore, initial diffusion coefficient D_i can be evaluated from the slope of the plot. The average diffusion coefficient D_A may also be calculated for 50% of the total release by putting $M_t/M_\infty = 0.5$ in the Eq. 3, which finally yields 4

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

where $t^{1/2}$ is the time required for 50% release of drug. Late diffusion coefficients (D_L) can be calculated using the late-time approximation as described by Peppas given in Eq. 5.

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

The slope of the plot between $\ln(1-M_t/M_\infty)$ and t is used for the evaluation of D_L.

3 Results and discussion

3.1 Characterization

Polymers were characterized by FTIR spectroscopy and FTIR spectra of polymers were recorded in KBr pellets on Nicolet 5700FTIR THERMO to study the modification of the psyllium (Fig. 1a, b). IR absorption bands due to C=O stretching has been witnessed at 1718.2 cm^{-1} in psy-*cl*-poly (AAc) apart from usual peaks in the psyllium.

3.2 Swelling kinetics of hydrogels

Hydrogels exhibit a thermodynamic compatibility with water, which allow them to swell in aqueous media. The pH of swelling medium has a significant effect on water uptake of these hydrogels. In order to study the effect of pH on water uptake by the polymers, swelling studies were carried out in distilled water, pH 2.2 buffer and pH 7.4 buffer at 37°C. The amount of water uptake by the polymer matrix up to 300 min was studied after fixed interval of 30 min and results thus obtained are shown in Fig. 2a and b. It has been observed from the Fig. 3a that amount of water uptake per grams of the gel in pH 2.2 buffer and distilled water was lesser than the pH 7.4 buffer. 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 was also taken after 24 h to get the value for equilibrium swelling. Percent swelling 362.5%, 331.0% and 410.5% has been obtained respectively in distilled water, pH 2.2 buffer and pH 7.4 buffer at 37°C. These values indicates that the equilibrium swelling is higher in high pH solution for the same above-mentioned reason. It is also observed from the Fig. 3b that the 50% of the total release occurred in 300, 300, 210 min respectively in distilled water, pH 2.2 buffer and pH 7.4 buffer. This observation indicated that the rate of swelling is faster in pH 7.4 buffer as compared to the other medium.

The values of diffusion exponent 'n' and gel characteristic constant 'k' for the swelling of polymers in different pH have been evaluated from the slope and intercept of the plot ln Mt/M_∞ versus ln t (Fig. 2c) and results are presented in the Table 1. From the values of the diffusion exponent 'n' (0.55, 0.58, 0.55) and gel characteristic constant 'k' (2.13×10^{-2}, 1.75×10^{-2} and 2.55×10^{-2}) respectively in distilled water, pH 2.2 buffer and pH 7.4 buffer, it has been observed that swelling kinetics follows non-Fickian diffusion mechanism for the swelling of polymeric matrix. The values of initial diffusion coefficients and late diffusion coefficient were observed to be less than the value of average diffusion coefficient which reflects that during initial and late stages, the penetration of water into the polymeric matrix was slow (Fig. 2d, e) and Table 1). The values for the diffusion coefficient are presented in the Table 1.

3.3 Release dynamics of model drugs from drug loaded hydrogels

3.3.1 Release dynamics of tetracycline hydrochloride

The release of water-soluble drug, entrapped in a hydrogels, occur only after water penetrates the network to swell the polymer and dissolve the drug, followed by diffusion along the aqueous pathways to the surface of the device. The release of drug is closely related to the swelling characteristics of the hydrogels, which in turn, is a, key

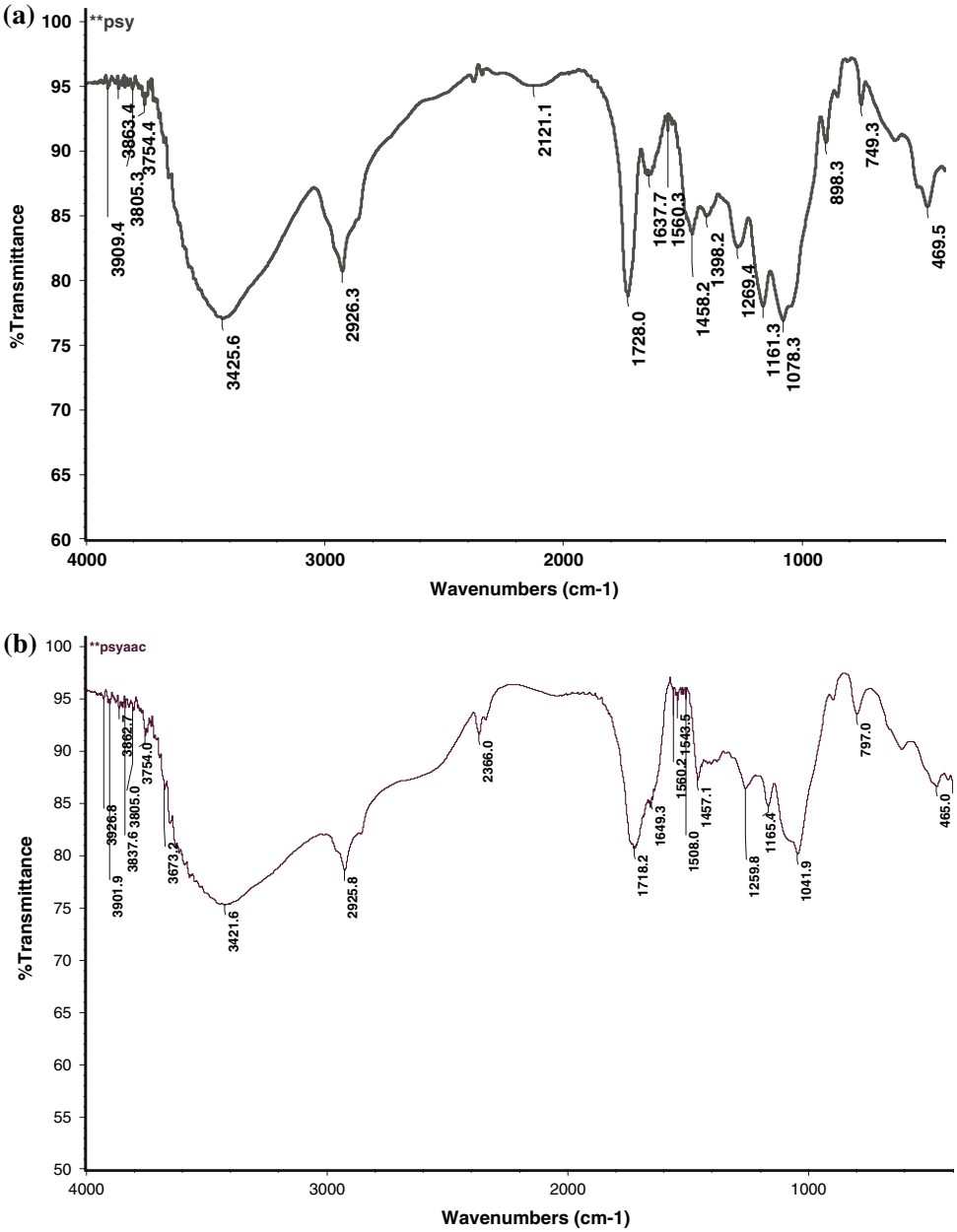

Fig. 1 FTIR of (**a**) psyllium and (**b**) FTIR of psy-*cl*-poly(AAc)

function of chemical architecture of the hydrogels. In the present case, the release profile of tetracycline hydrochloride from per grams of the drug-loaded hydrogels has been investigated in different release medium and shown in the Fig. 3a–e. It has been observed from the Fig. 4a that the amount of drug release increases with time and amount release in pH 7.4 buffer is higher than and distilled water and pH 2.2 buffer. This observation is explained on the basis of the swelling of the hydrogels and corresponding to the swelling of the hydrogels. The swelling of hydrogels [psy-*cl*-poly(AAc] increases when the pH of the medium changes from pH 2.2 to pH 7.4 At lower pH the $-CO_2H$ groups does not ionized and keep the network at its collapsed state. At high pH values, it gets partially ionized, and the charged $-COO^-$ groups repel each other, leading to the higher swelling of the polymer and resultant to more drug release. In pH 2.2 buffer higher amount of release may be due to the more solubility of the drug in this medium is expected. The release of drug quicker in pH 7.4 buffer is also supported from the figures of percent cumulative release (Fig. 4b). 50% of the total release of drug occurred in 158, 190 and 241.8 min respectively in releasing medium of pH 7.4 buffer, pH 2.2 buffer and distilled water. The values of diffusion exponent '*n*' and gel characteristic constant '*k*' for the release dynamics of tetracycline hydrochloride in different pH have been evaluated from the slope and intercept of the plot ln Mt/M_∞ versus ln t (Fig. 3c) and results are presented in the

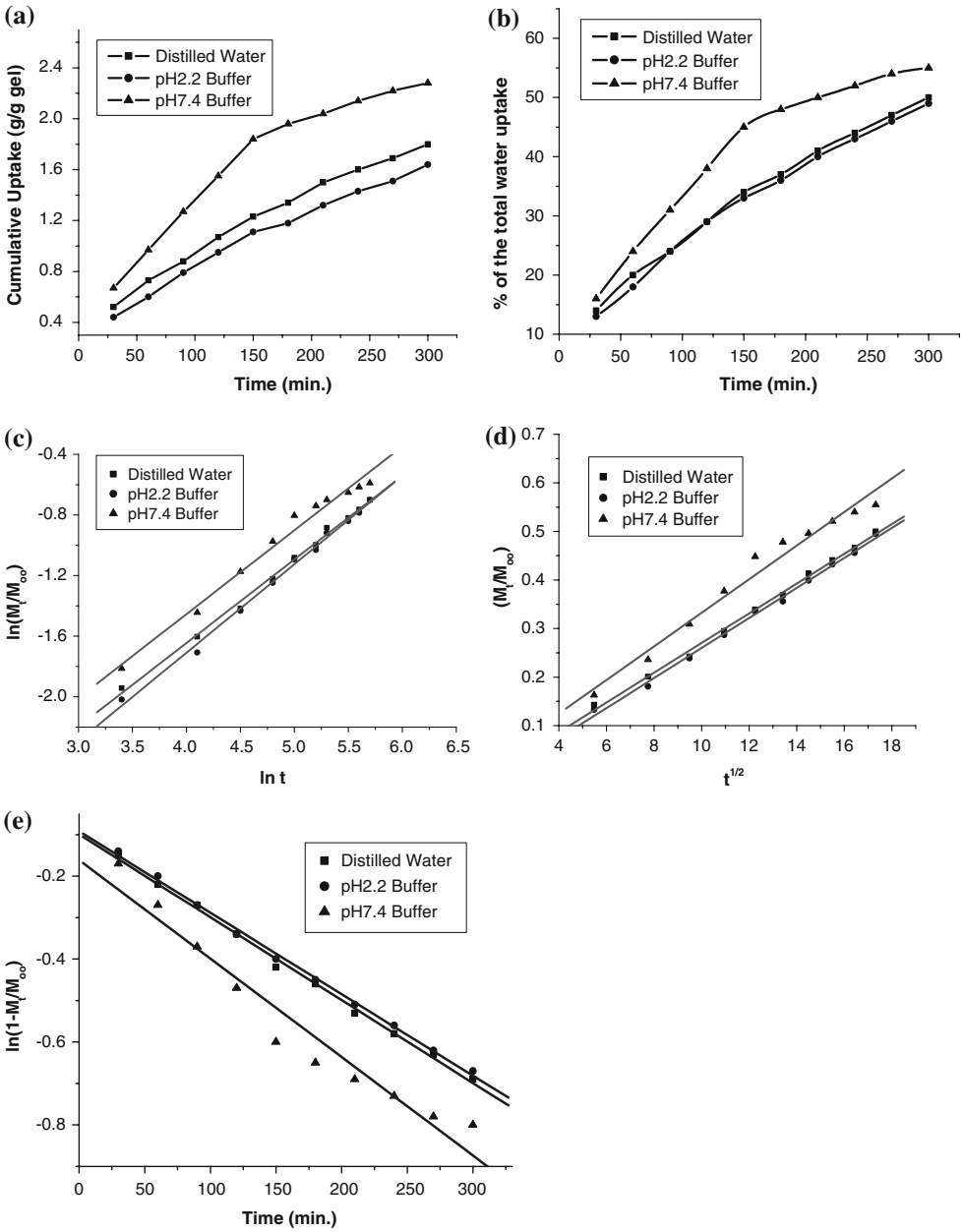

Fig. 2 (**a**) Swelling kinetics of the Psy-*cl*-poly(AAc) hydrogels different medium at 37°C (**b**) Percentage of the total swelling of the hydrogels with time (**c**) Plot of $\ln(M_t/M_\infty)$ versus $\ln\ t$ to evaluate the diffusion exponent '*n*' and gel characteristic constant '*k*' for the swelling of hydrogel (**d**) Plot of (M_t/M_∞) versus $t^{1/2}$ for the evaluation of initial and average diffusion coefficients for the swelling of hydrogel (**e**) Plot of $\ln(1-Mt/M_\infty)$ versus time for the evaluation of late diffusion coefficient for the swelling of hydrogel

Table 2. It is clear from the Table 2 that diffusion exponent '*n*' have 0.52, 0.57 and 0.61 values and gel characteristic constant '*k*' have 2.86×10^{-2}, 2.46×10^{-2} and 2.25×10^{-2} values in distilled water, pH 2.2 buffer and pH 7.4 buffer respectively. As the values of '*n*' are between 0.5 and 1.0 for the release of for the release of tetracycline which indicates a non-Fickian or anomalous diffusion mechanism for the release of drug from the polymer matrix in these mediums. In this type of diffusion mechanism, the rate of polymer chain relaxation and the rate of drug diffusion from these hydrogels are comparable. The values of the average diffusion coefficient for the release of tetracycline hydrochloride was observed to be higher than the values of the initial and late time diffusion coefficient in each release medium indicating that in the start, late stages of the diffusion of the drug from the polymeric matrix is faster (Fig. 3d and e, Table 2).

3.3.2 Release dynamics of insulin

The release dynamics of insulin from the polymer matrix is shown in Fig. 4a–e. Here, it has been observed from the Fig. 4a that the amount of insulin release per gram of the gel is higher in distilled water and pH 7.4 buffer as compared to the pH 2.2 buffer. This observation is again explained on the basis of the swelling of the hydrogels as discussed above. 50% of the total release of drug occurred in 210, 608 and 210 min respectively in releasing medium

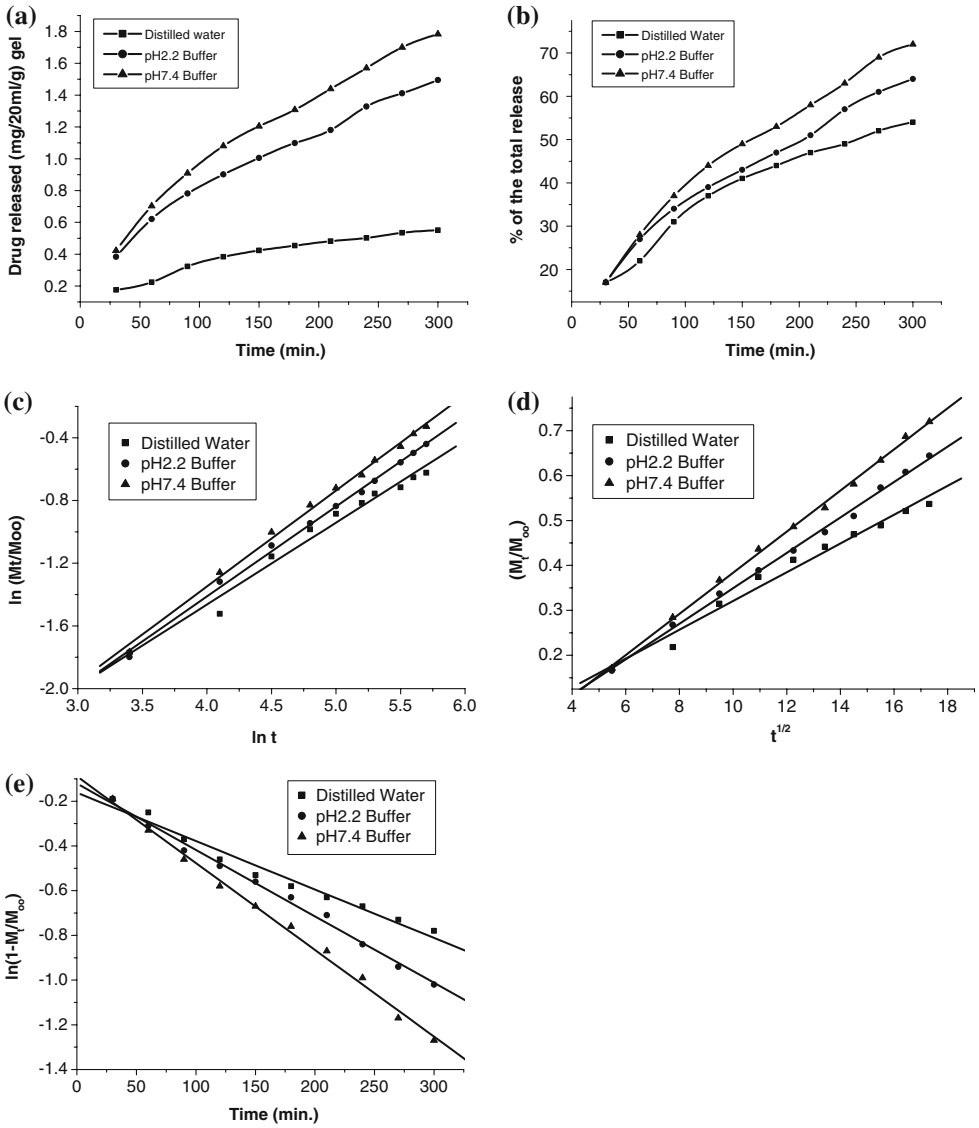

Fig. 3 (**a**) Release dynamics of tetracycline HCl from drug loaded samples of Psy-*cl*-poly(AAc) in different medium at 37°C (**b**) Percentage of the total release with time from drug loaded hydrogels (**c**) Plot of ln(M_t/M_∞) versus ln t to evaluate the diffusion exponent '*n*' and gel characteristic constant '*k*' for the release mechanism of tetracycline HCl from the drug loaded hydrogels (**d**) Plot of (M_t/M_∞) versus $t^{1/2}$ for the evaluation of initial and average diffusion coefficients for the release dynamics of the tetracycline HCl from the drug loaded hydrogels (**e**) Plot of ln(1-M_t/M_∞) versus time for the evaluation of late diffusion coefficient for the release dynamics of tetracycline HCl from the drug loaded hydrogels

Table 1 Results of diffusion exponent '*n*', gel characteristic constant '*k*' and various diffusion coefficients for the swelling kinetics of hydrogels samples of Psy-*cl*-poly(AAc)

Swelling medium	Diffusion exponent '*n*'	Gel characteristic constant '*k*' × 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	0.55	2.13	5.18	9.72	0.86
pH 2.2 buffer	0.58	1.75	5.04	9.55	0.83
pH 7.4 buffer	0.55	2.55	6.83	12.01	1.05

of pH 7.4 buffer, pH 2.2 buffer and distilled water. This observation is very important for developing the colon specific drug delivery systems and it has been observed from the rate of release and release trends that the release of insulin has occurred only at higher pH which corresponds to the colon. It is clear from the (Fig. 4c) Table 2 that diffusion exponent '*n*' have 0.54, 0.32 and 0.58 values and gel characteristic constant '*k*' have 2.69×10^{-2}, 6.32×10^{-2} and 2.15×10^{-2} values in distilled water, pH 2.2 buffer and pH 7.4 buffer respectively. The values of '*n*' indicates a non-Fickian or anomalous diffusion mechanism for the release of insulin from the polymer matrix in distilled water and pH 7.4 buffer. The values of the average diffusion coefficient for the release of insulin is higher than the values of the initial and late time diffusion coefficient in each release medium indicating that in the start, late stages of the diffusion of the drug from the polymeric matrix is faster (Fig. 4d and e, Table 2).

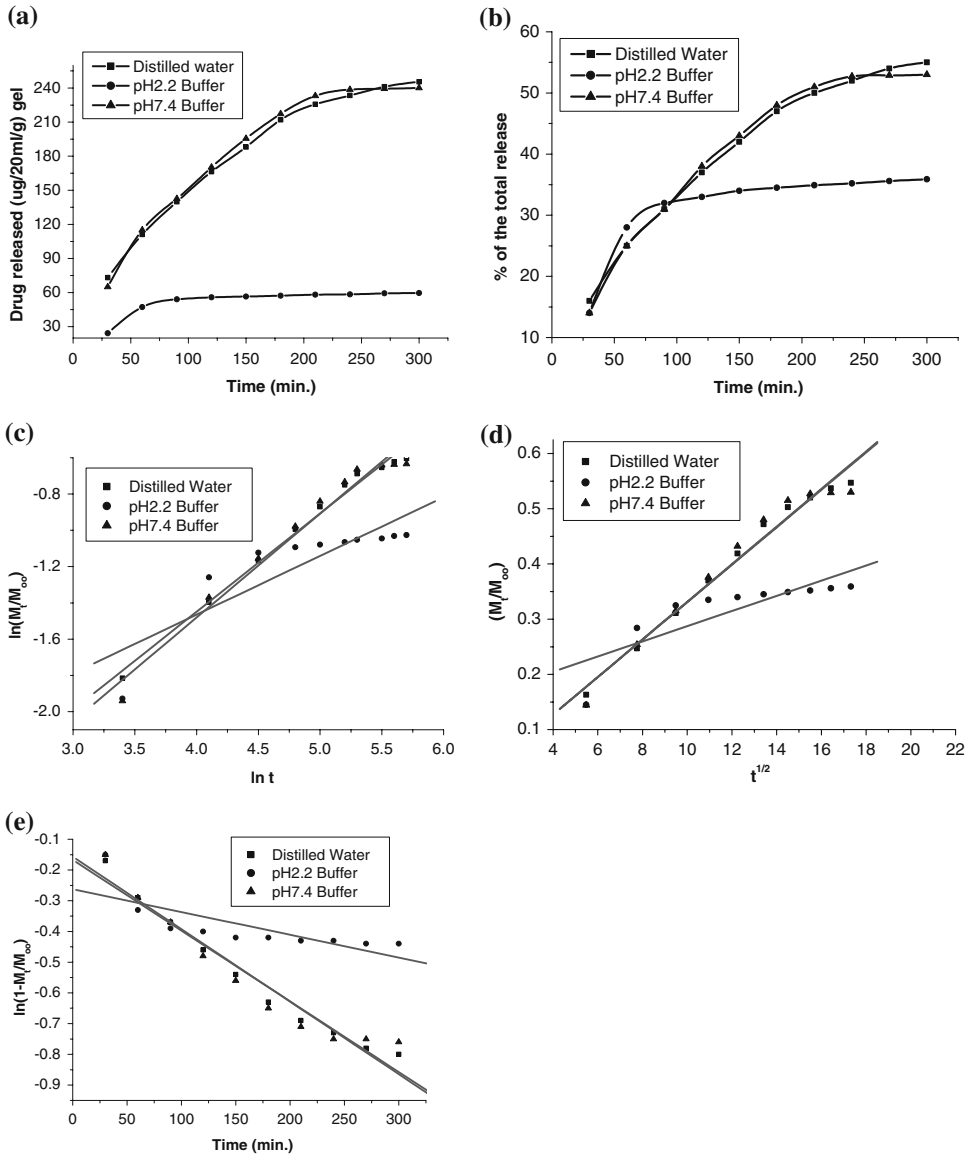

Fig. 4 (**a**) Release dynamics of insulin from drug loaded samples of Psy-*cl*-poly(AAc) in different medium at 37°C (**b**) Percentage of the total release with time from drug loaded hydrogels (**c**) Plot of $\ln(M_t/M_\infty)$ versus ln t to evaluate the diffusion exponent '*n*' and gel characteristic constant '*k*' for the release mechanism of insulin from the drug loaded hydrogels (**d**) Plot of (M_t/M_∞) versus $t^{1/2}$ for the evaluation of initial and average diffusion coefficients for the release dynamics of the insulin from the drug loaded hydrogels (**e**) Plot of $\ln(1-M_t/M_\infty)$ versus time for the evaluation of late diffusion coefficient for the release dynamics of insulin from the drug loaded hydrogels

Table 2 Results of diffusion exponent '*n*', gel characteristic constant '*k*' and various diffusion coefficients for the release of model drugs from drug loaded samples of Psy-*cl*-poly(AAc)

Drug in releasing medium	Diffusion exponent '*n*'	Gel characteristic constant '*k*' × 10^2	Diffusion coefficients (cm^2/min)		
			Initial $D_i \times 10^4$	Average $D_A \times 10^4$	Late time $D_L \times 10^4$
Tetracycline hydrochloride					
Distilled water	0.52	2.86	3.06	6.00	0.516
pH 2.2 buffer	0.57	2.46	4.44	6.59	0.690
pH 7.4 buffer	0.61	2.25	6.76	7.93	0.986
Insulin					
Distilled water	0.54	2.69	3.45	6.43	0.56
pH 2.2 buffer	0.32	6.32	0.57	3.69	0.53
pH 7.4 buffer	0.58	2.15	3.45	6.43	0.55
Tyrosine					
Distilled water	0.6	2.16	3.91	6.43	0.615
pH 2.2 buffer	0.3	5.09	0.27	3.66	0.128
pH 7.4 buffer	0.65	1.67	5.63	7.19	0.806

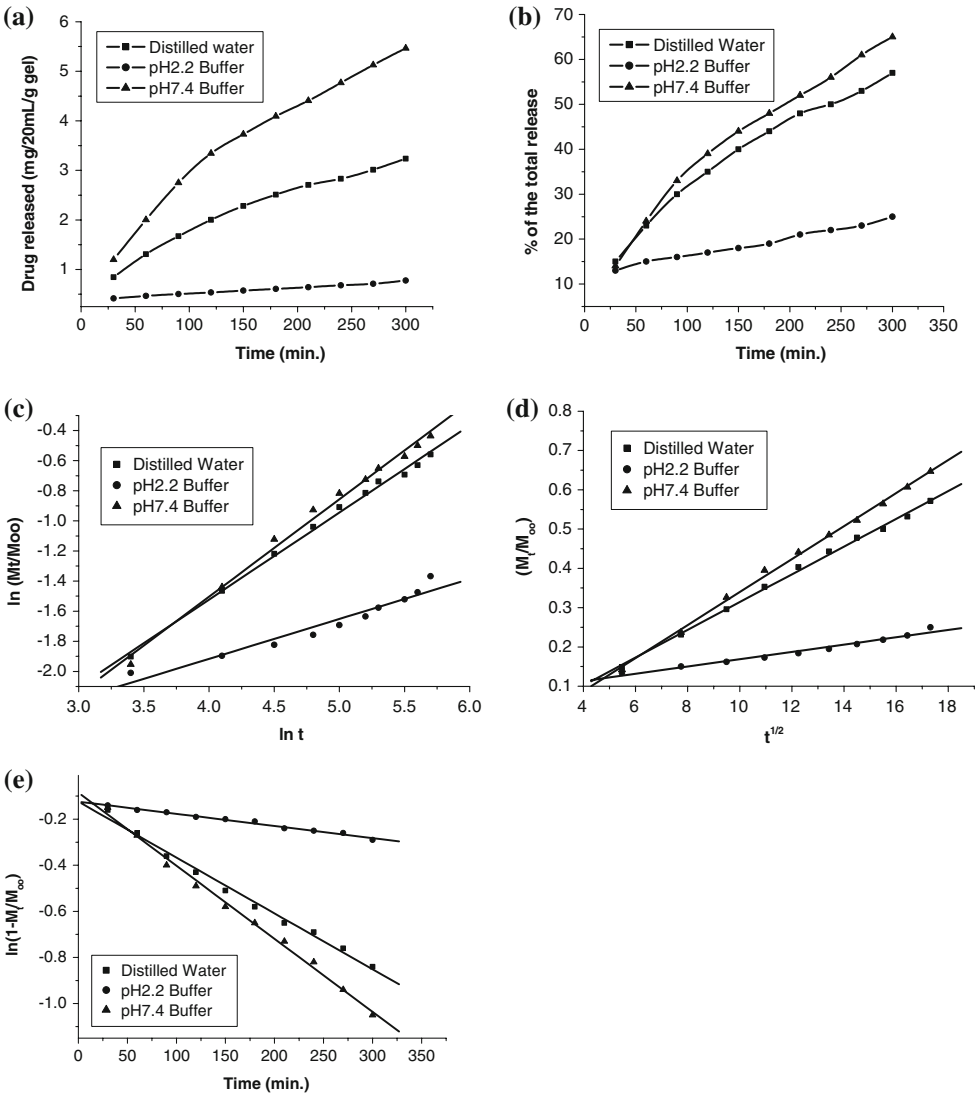

Fig. 5 (**a**) Release dynamics of tyrosine from drug loaded samples of Psy-*cl*-poly(AAc) in different medium at 37°C (**b**) Percentage of the total release with time from drug loaded hydrogels (**c**) Plot of $\ln(M_t/M_\infty)$ versus ln t to evaluate the diffusion exponent 'n' and gel characteristic constant 'k' for the release mechanism of tyrosine from the drug loaded hydrogels (**d**) Plot of (M_t/M_∞) versus $t^{1/2}$ for the evaluation of initial and average diffusion coefficients for the release dynamics of the tyrosine from the drug loaded hydrogels (**e**) Plot of $\ln(1-M_t/M_\infty)$ versus time for the evaluation of late diffusion coefficient for the release dynamics of tyrosine from the drug loaded hydrogels

3.3.3 Release dynamics of tyrosine

The release pattern of tyrosine is also similar to the release pattern of insulin and shown in Fig. 5a–e. Amount of tyrosine release per gram of the gel is higher in distilled water and pH 7.4 buffer as compared to the pH 2.2buffer (Fig. 5). 50% of the total release of drug in this case occurred in 192.10, 677.88 and 240.25 min respectively in releasing medium of pH 7.4 buffer, pH 2.2 buffer and distilled water. The diffusion exponent 'n' have 0.6, 0.3 and 0.65 values and gel characteristic constant 'k' have 2.16×10^{-2}, 5.09×10^{-2} and 1.67×10^{-2} values in distilled water, pH 2.2 buffer and pH 7.4 buffer respectively (Fig. 5c). The values of 'n' indicates a non-Fickian or anomalous diffusion mechanism for the release of tyrosine from the hydrogel in distilled water and pH 7.4 buffer. The values of the average diffusion coefficient for the release of tyrosine is also higher than the values of the initial and late time diffusion coefficient in each release medium. These values are obtained from the Fig. 5d–e and presented in Table 2.

4 Conclusion

It is concluded from the foregone discussion that hydrogels developed from modification of psyllium can act as colon specific drug delivery devices, indicated from the swelling kinetics and drug release profile of model drug in different release medium. These hydrogels may be useful for the colon-specific delivery of proteins/ amino acids/antibiotics. It is also been concluded from the drug release dynamics that the drug released through the polymeric matrix follows non-Fickian diffusion mechanism in pH 7.4 buffer solution and distilled water for which, the rate of drug diffusion and rate of polymer chain relaxation are comparable.

Therefore, drug release depends on two simultaneous rate processes, water migration into the device and drug diffusion through continuously swelling hydrogels. In each release medium, the average diffusion coefficient has been observed more as compare to the initial and late time diffusion coefficient.

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