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Synthesis and characterization of hydrogels based on grafted chitosan for the controlled drug release

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ABSTRACT

Temperature and pH-responsive hydrogels based on chitosan grafted with poly acrylic acid (PAAc), poly hydroxy propyl methacrylate (PHPMA), poly (vinyl alcohol) (PVA) and gelatin were prepared for controlled drug delivery. These stimuli-responsive hydrogels were synthesized by gamma irradiation technique. The degree of gelation was over 90% and increased as chitosan, AAc and PVA content increased, while the degree of gelation decrease with the increase of gelatin content. The equilibrium swelling studies of hydrogels prepared in various conditions were carried out in an aqueous solution, and the pH sensitivity in the range of 2–9 was investigated. An increase of swelling degree with an increase in the pH was noticed and showed the highest value at pH 9. Also antibiotic drug Oxttetracycline was loaded into the hydrogels and the release studies were carried out at different pH and temperature. The in vitro release profiles of the drug showed that, the release of the drug increased as the time, temperature and pH increased and reached to maximum after 48 h at pH 9. The prepared hydrogels were characterized by using SEM, FTIR, and DSC.

1. Introduction

The use of hydrogels as biomaterials has recently gained great important in view of low toxicity and high biocompatibility (Dinarvand & D'Emanuele, 1995; Hoffman, 1987). One of the advantages of the hydrogels lies in their capability of undergoing first-order phase transition under the change of some external parameters such as pH, temperature, ionic strength and electric fields (Kayaman, Kazan, Erarslan, Okay, & Baysal, 1998; Ozturk & Okay, 2002). Smart polymers are novel materials that operate under very mild aqueous conditions, and have the potential to provide a novel and cost-effective means to isolate valuable biomolecules and pharmaceuticals from agri-food and other raw materials. These smart polymers have vast potential applications in pharmaceutical technology and industrial biotechnology.

Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids. The polymeric hydrogels are prepared from a limited number of synthetic polymers and their derivatives such as copolymers of methacrylic acid, acrylamide and *N*-isopropylacrylamide (Chen & Hoffman, 1995; Holtz & Asher, 1997; Yoshida et al., 1995).

In recent years, considerable interest has been focused on modification of the most abundant naturally occurring polysaccharides such as cellulose, starch and alginates by grafting technique. In particular, chitosan has been largely evaluated as a potential polymer for drug administrated orally because of its cationic nature and high charge density in a solution. Moreover it is acknowledged that chitosan posses good mucoadhesive properties (Fumio et al., 2003) thus sustained release and improved bioavailability of drugs can be achieved by prolonging the residence time of drug carriers at the absorption site. The hydrophilicity of chitosan, due to presence of amino and hydroxyl functional groups in its repeat unit, makes the polymer soluble in dilute acidic solutions and yield a rubbery hydrogel in water.

On the other hand, poly (vinyl alcohol) (PVA), has several desirable physical properties such as elasticity and high hydrophilicity (Kurkuri & Aminabhavi, 2004; Schellekens & Bastiansen, 1991), making it appropriate to blend with other polymers such as chitosan. Blending of chitosan with PVA would produce a biodegradable polymer blend system that can be used in controlled release (CR) of drugs (Kurkuri & Aminabhavi, 2004; Miya, Iwamoto, & Mima, 1984; Muzzarelli, Jeuniaux, & Gooday, 1986).

Gelatin is also biocompatible protein, and when it takes in living body, it shows low antigenicity and very high bioabsorptivity. The three-dimensional gel network of gelatin is composed of microcrystallites interconnected with amorphous regions of randomly coiled segments and it has the characteristics, such as heat reversibility (Achet & He, 1995; Arvanitoyannis, Nakayama, & Aiba, 1998). The predominant property of gelatin would be the sol–gel transition under aqueous condition. The membranes between

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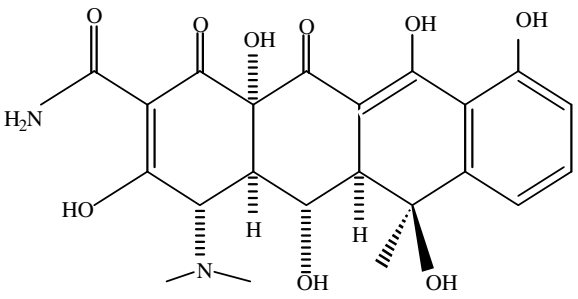
chitosan and gelatin having so many biomedical applications have been reported (Kolodziejska, Piotrowska, Bulge, & Tylingo, 2006).

In this study the preparation of temperature and pH responsive hydrogel based on chitosan grafted with PAAc, PHPMA, PVA and gelatin of different molar ratio and the effect of gamma radiation were investigated. The drug release characteristics of the prepared hydrogel were studied using Oxttetracycline, as example of antibiotic drug. Also the effect of hydrogel composition and radiation dose on the release rate of Oxttetracycline were examined.

2. Experimental

- Chitosan, powder was supplied by Fluka Chemical, acetylation degree 14%. Average molecular weight 70,000 kDa.
- PVA powder of molecular weight 17,000 kDa and saponification degree of 99.85% was supplied by D-MID GEL Co. Koysna, Monfiya, Egypt.
- Gelatin from bovine was supplied by Sigma–Aldrich nearly 225 Bloom.
- Acrylic acid (AAc) was purchased from Acros chemical company USA and hydroxy propyl methacrylate (PHPMA) from Merck – Schuchardt. Germany.
- Drug (Oxttetracycline) was supplied by National organization for drug control and research, Giza, Egypt.



Oxttetracyline

- All other chemicals were of reagent grade.

2.1. Graft copolymerization

A 1% (w/v) chitosan stock solution was prepared in 2% (w/v) acetic acid aqueous solution. A 1% (w/v) gelatin stock solution was prepared by dissolving in bidistilled water. AAc, PHPMA and PVA monomers, which were used in different molar ratio according to Table 1 were added to this solution and stirred until complete homogenization. The resulting solutions were transferred to petri dishes and subjected to γ-radiation at different doses of 10, 15, 20 kGy.

Resultant films that formed were removed from petri dishes. Then extracted in soxhlet for a 6-h reflux using distilled water as a solvent to remove the homopolymer or non-reacted monomers. Finally, the membranes were dried at room temperature on Teflon.

Table 1
Formula codes of different composition

Chitosan	PVA	HPMA	AAc		Code
1	1	1	1		Cs 1
2	–	1	1		Cs 2
2	1	–	1		Cs 3
1	1	–	2		Cs 4
1	2	–	1		Cs 5
1	2	1	–		Cs 6
			Gelatin	AAc	
2	–	–	1	1	Cs 7
1	1	–	2	1	Cs 8
–	1	1	1	1	Cs 9

2.2. Swelling measurement

The pre-weight (W_d) dry hydrogels of different compositions were placed into double distilled water and left to reach equilibrium swelling for 24 h, at room temperature and pH 7. The swollen hydrogels were then removed from water and whipped with filter paper then weighed as soon as possible (W_s).

The swelling percent (S%) was calculated from the following equation:

$$S\ (\%) = \frac{(W_s - W_d)}{W_d} \times 100$$

where W_d and W_s represent the dry and swollen hydrogel, respectively.

2.3. Drug loading and release experiment

Oxttetracycline was used as a model drug for drug loading and release experiment. The dry hydrogels (0.1 g) were equilibrated in vials filled with 25 ml of aqueous solution of Oxttetracycline (1000 ppm) at 4 °C.

After incubation, the samples were removed from the solution and rinsed in cold distilled water. The release of Oxttetracycline experiments were carried out by transferring previously incubated drug-loaded hydrogels into 50 ml of distilled water at various pHs, which was adjusted by acetic acid and sodium carbonate at 37 °C.

At various time interval 3 ml of drug solution were taken to measure drug concentration by using Shimadzu UV Spectrophotometer at 450 nm. The release percent of Oxttetracycline was calculated from the following equation:

$$\text{Release}\ (\%) = \frac{W_t}{W_\infty} \times 100$$

where W_t is the weight of released Oxttetracycline at time t and W_∞ is the total adsorbed Oxttetracycline in the gel structure.

2.4. Measurement of gel content

To measure the gel content, the irradiated hydrogel samples were placed in 200 mesh stainless steel net and washed with distilled water three times after extraction in distilled water at 80 °C for 24 h. The remaining gel was dried to constant weight. Gel content was measured gravimetrically as following:

$$\text{Gelation}\ (\%) = \frac{W_d}{W_o} \times 100$$

Where W_d is the weight of dry gel after extraction and W_o is the initial weight of dry gel.

2.5. Fourier transform infrared (FTIR) measurement

FTIR spectra were recorded on a Mattson 1000 FTIR spectrophotometer product of Unicam Ltd., England. About 2 mg of the sample were grounded thoroughly with KBr and pellets were prepared using hydraulic press under a pressure of 600 kg/cm^2.

2.6. Differential scanning calorimetry (DSC)

DSC thermograms of pure chitosan, PVA, PAAc and prepared hydrogel were recorded by using Shimadzu DSC system of type DSC–50, with heating rate of 10 °C/min from ambient temperature up to 600 °C.

2.7. Scanning electron microscopy

SEM images of the dry and drug-loaded hydrogel were recorded using JEOL SEM–25 (Japan) at the required magnification.

3. Results and discussion

In this study graft copolymerization of PAAc, PHPMA, PVA and gelatin onto chitosan was carried out using gamma irradiation. Formulations were prepared by varying the comonomer ratio of chitosan with PVA, PAAc, PHPMA and gelatin as shown in Table 1.

The hydrogels Cs 1–Cs 6 were prepared at three different radiation dose 10, 15, and 20 kGy, whereas Cs 7–Cs 9 were only prepared at radiation dose 20 kGy.

3.1. Degree of gelation

Table 2 shows the degree of gelation of chitosan grafted with PAAc, PHPMA, PVA and gelatin from various compositions shown in Table 2 at various irradiation doses. It was found that the degree of gelation was over 90% and increased as the content of PVA, PAAc and chitosan increased or in the absence of PHPMA. Also its noticed that slightly change occur in gelation (%) with increasing irradiation dose.

This is may be due to that chitosan have large quantities of amino groups in its chains thus a polyelectrolyte complex with higher electrostatic attraction was formed with PAAc, PVA and gelatin. Also, high degree of gelation may be due to the degree of breaking and crosslinking of the double bond located in the vinyl monomers by irradiation (Shem & Nho, 2003).

3.2. Swelling behaviour

From Table 3 it is found that the difference in the network structure and composition ratio of the prepared hydrogels yields different swelling percent in the employed media. From the results shown in Table 3 it can be seen that low swelling (%) in the presence of PHPMA Cs 1 and Cs 2. This is due to its hydrophobic nature, where most of the hydrophobic segments of the chain tend to be aggregate, and therefore the water form hydrogen-bonded with the polar groups is preferentially accumulate on the periphery, giving rise to a less swollen hydrogel (Pascual, Castellano, Vazquez, Gurruchaga, & Goni, 1996). Also it is found that the swelling degree increased as chitosan, PAAc and PVA increased (Cs 3, Cs 4 and Cs 5) and decreased in absence of PAAc (Cs 6).

In case of hydrogel samples Cs 7, Cs 8 and Cs 9 the decrease of swelling (%) with the decrease of Chitosan content and increase of gelatin content is due to the high hydrophilicity of chitosan compared to the gelatin.

Table 3
Effect of hydrogel composition on swelling (%) after 24 h at 20 kGy, pH 9 and 25 °C

Sample code	Swelling (%)
Cs 1	282
Cs 2	235
Cs 3	5580
Cs 4	742
Cs 5	4199
Cs 6	120
Cs 7	4787
Cs 8	3511
Cs 9	1299

3.3. Effect of percentage of drug loading on the releasing rate of the drug

The effect of drug loading percentage on the drug-releasing rate is shown in Table 4. In most of the investigated system it was observed that the releasing rate was increased with increasing the drug loading percentage. In all our system, the effect of drug loading percentage has a minimal effect on the releasing rate except in the presence of PHPMA, where the drug release reached maximum value of releasing the drug. Both particle size and the loading percentage can be varied to control the rate of releasing of the drug. In case of higher percentage of loading the drug particles on the surface of the matrix touch each other, and a large cluster of drug

Table 2
Effect of radiation dose and composition on gelation (%) at 25 °C and pH 7

Sample code	Radiation dose (kGy)	Gelation (%)
Cs 1	10	99.5
	15	98
	20	99
Cs 2	10	99
	15	99
	20	100
Cs 3	10	100
	15	92
	20	92
Cs 4	10	96
	15	99
	20	99
Cs 5	10	91
	15	100
	20	91
Cs 6	10	100
	15	100
	20	100
Cs 7	20	42
Cs 8	20	77
Cs 9	20	96

Table 4
Effect of percentage of drug loading on releasing rate at different time and pH 9

Sample code	Radiation dose (kGy)	Loading (%)	% of drug release at pH 9			
			1 h	2 h	24 h	48 h
Cs 1	10	66	18	21	51	78
	15	74	20	23	50	73
	20	50	41	51	78	99
Cs 2	10	76	39	55	61	72
	15	59	20	22	45	85
	20	70	23	24	60	83
Cs 3	10	87	24.6	36.5	54	75
	15	96	32	54	63	70
	20	97	43	50	60	72
C s 4	10	79	31	22	29	65
	15	81	32	35	42	69
	20	83	39	21	43	69
Cs 5	10	90	26	40	60	88
	15	80	38	50	63	88
	20	82	35	59	63	82
Cs 6	10	23	39	71	79	100
	15	23	55	73	81	100
	20	82	55	60	89	100
Cs 7	20	89	42	53	61	80
Cs 8	20	88	35	48	63	76
Cs 9	20	91	25	41	58	69

particles was extended from the surface deep into the matrix. These clusters result in a connected pore space upon dissolution of the drug molecules from the polymeric beads. Therefore, the entire drug molecules from the cluster were released leading to an increase in the percentage of drug release (Langer et al., 1984). This was observed in our system.

3.4. Effect of pH on the releasing rate of the drug

The effect of pH on the drug-releasing rate from the polymeric hydrogels was shown in Figs. 1 and 2. These figures show that when the pH of the medium changed from 2 to 9 the releasing rate enhanced drastically. From the graph it seems that the increase in the releasing rate on changing the pH was affected by the percentage of drug loading and crosslinking employed in the percentage of hydrogels. The increase in the releasing rate in hydrogel sample Cs 6 may be due to hydrolysis of ester linkage, which was connected between the hydrogel networks, leading to an opening of channels that allows the drug molecules present in the inner core of the hydrogels to elute freely to the surroundings.

When we compared the effect of pH on the type of hydrogels used PAAc, PVA and PHPMA grafted hydrogels the rate of drug release was enhanced markedly upon changing pH (from 2 to 9). This may be due to the fact that these types of hydrogels swell more easily in alkaline medium as result of sodium salt formation of acrylic acid than it does in neutral medium. This type of difference in their swelling behaviour was found to be responsible for difference shown on the rate of drug release towards changing the pH of the medium. This sort of pH-sensitive hydrogels were presented in literature (Chiu, Wu, & Lin, 2001).

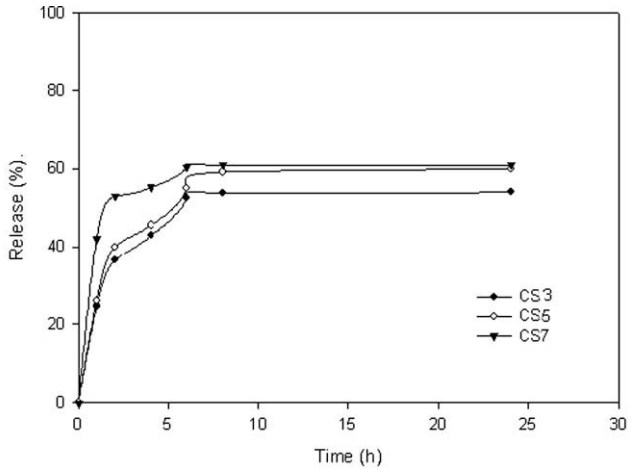


Fig. 1. Relationship between time (h) and the release (%) of Oxttetracycline for the hydrogel of different composition in pH 9 media at 25 °C.

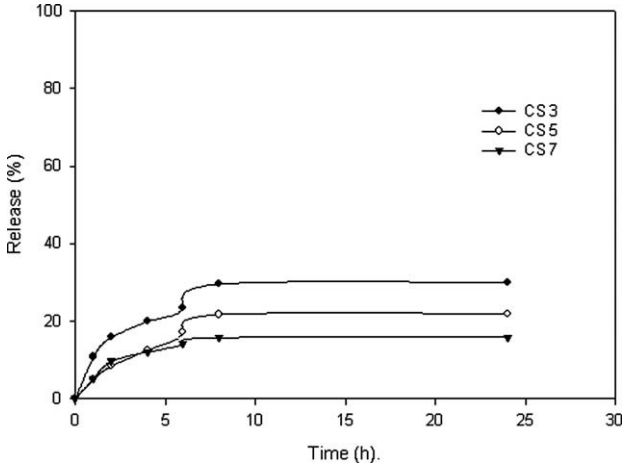


Fig. 2. Relationship between time (h) and the release (%) of Oxttetracycline for the hydrogel of different composition in pH 2 media at 25 °C.

We have observed that only a very small quantity of drug was released in the acidic pH. This fact could be useful for the sustained oral delivery benefiting from the pH difference between the stomach and intestine, as it has described for other type of drug delivery system (Davaran, Hanace, & Khosravi, 1999). This may be attributed to hydrogen bond formed between –COOH of PAAc and –OH of PVA which retard drug release in acidic medium.

3.5. Effect of radiation dose on the releasing rate of the drug

The effect of radiation dose on the releasing rate of the drug is shown in Table 4. This show that in most of the cases an increase in the crosslinking at high radiation dose leads to an increase in the rate of the drug release, where the surface of the polymeric hydrogels becomes soft and smooth and the surface show a lot of pores in it which may be due to heterogeneity (or small cavities) in the polymeric network proceed by crosslinking in the formation of polymeric hydrogels. This type of inner cavities in the hydrogels will be more pronounced with increasing crosslinking (Scranton, Mikos, Scranton, & Peppas, 1990). This was observed in case of Cs 1, Cs 2 and Cs 4, whereas, in case of Cs 3 and Cs 5 loosely crosslinked networks swell more readily in the testing medium and the releasing rate of the solute was faster (Peppas & Lustig, 1984).

3.6. Effect of monomer (AAc, PVA, HPMA) on the releasing rate of the drug

The effect of hydrogel compositions on the releasing rate of the drug was shown in Table 4. This show that the release of *Oxttetracycline* increased on the acrylic acid as radiation dose decreased. Too large monomer content and radiation dose to a dense and tight polymeric network, resulting in the decrease of flexibility and hydration ability of the hydrogel. Therefore, the release of *Oxttetracycline* by diffusion could be hindered by the decrease of the pore size distributed in the gel fraction, which is the path of loading or release of the drug (Shem & Nho, 2003). Cs 4 show the same behaviour with respect to PVA, the blending of PVA–AAc with chitosan appears to be important in controlling the release of *Oxttetracycline* over an extend period of time.

Since PVA is water soluble and hence, it is readily miscible with chitosan and PAAc which is more hydrophilic but the hydrogel with high content of PVA show longer drug release rates than other formulations which, can be attributed to the dependence of the drug release upon the nature of the polymer matrix as well as pH of the media (Rao, Naidu, Subha, Sairam, & Aminabhavi, 2006).

Table 4 shows that the drug-releasing rate of PAAc, PVA onto chitosan was high than that of PHPMA. This was due to the increase of hydrophobic nature of PHPMA as a result the swelling rate decrease due to the increase in the hydrophobicity of the hydrogel (Katime, Novoa, & Zuluaga, 2001).

The hydrogel samples Cs 3, Cs 5 and Cs 7 were chosen to study the effect of drug loading and drug diffusion as well as the effect of temperature on the released rate, because these blends have shown a moderate release rates and better swelling than the other formulations.

To observe the diffusion of water into polymeric matrix (Cs 3, Cs 5 and Cs 7) at different pH values dry hydrogels were placed in bidistilled water and allowed to equilibrate for 24 h. The initial swelling data were fitted to the exponential heuristic equation (Franson and Peppas (1983), Peppas & Franson, 1983).

$$F\ (\%) = \frac{M_t}{M_\infty} = kt^n$$

Here F is the fractional uptake, M_t/M_∞ where M_t is the amount of water absorbed at time t, M_∞ is the maximum amount absorbed, k is a constant incorporating characteristic of macromolecular network system and the penetrate, n is the diffusional exponent, which is indicative of the transport mechanism.

For Fickian kinetics in which the rate of penetrate diffusion is rate limiting, $n = 0.5$, whereas values of r between 0.5 and 1 indicate the contribution of non-Fickian process such as polymer relaxation. The plots of $\ln F$ versus $\ln t$ for hydrogel samples (Cs 3, Cs 5 and Cs 7) were illustrated in Fig. 3. The swelling exponent was calculated using previous equation and represented in Table 4. It can be clearly seen from the table that the values of the diffusion exponent range between 0.4 and 0.5 at pH 9, between 0.2 and 0.3 at pH 7 and between 0.13 and 0.2 at pH 3. The diffusion of water into pure hydrogel sample Cs 3 is Fickian type. On the other hand the content of gelatin, PVA and PAAc mainly influences the diffusion behaviour because of the ionic interaction between gelatin and chitosan (see Table 5).

3.7. Temperature dependent drug release behaviour

The model drug release behaviour hydrogel samples (Cs 3, Cs 5 and Cs 7) is shown in Figs. 4–6. When the drug-loaded polymer become into contact with buffer solution, the loaded drug at the surface of the disc gets released with an increase in temperature, the trapped drug inside the matrix diffuse out of the device due to the increased chain relaxation. An increase in temperature from 25 to 43 °C shows a higher and faster drug release. This may be due to extensive swelling chain reaction.

The removal of unreacted monomers during the boiling and washing steps was confirmed by the no visualization, in the last washing solutions, of their UV characteristic absorption band around 204–250 nm. This indicates that no reactive center remain in the discs and ensure a good chemical compatibility and lack of cellular toxicity (Turkish & Galin, 1980).

3.8. Characterization of model hydrogel

Fig. 7 shows scanning electron images of the dry hydrogel samples Cs 3 (7a) and hydrogel after loading with Oxttetracycline (7b). From fig. 7a it can be seen that for dry hydrogel there is smooth structure and no pores or cracks on the surface which confirms the miscibility of the prepared hydrogel. However, it should be, when the hydrogel is loaded with Oxttetracycline for 12 h as shown in Fig. 7b the hydrogel present a highly porous film structure. The formation of an open structure on its surface in Fig. 7b could be attributed to electrostatic bonds between $-COO^-$ groups from PAAc and protonated amino group from chitosan, which allow the drug to be diffused into the network of the polymer and aggregate on its surface.

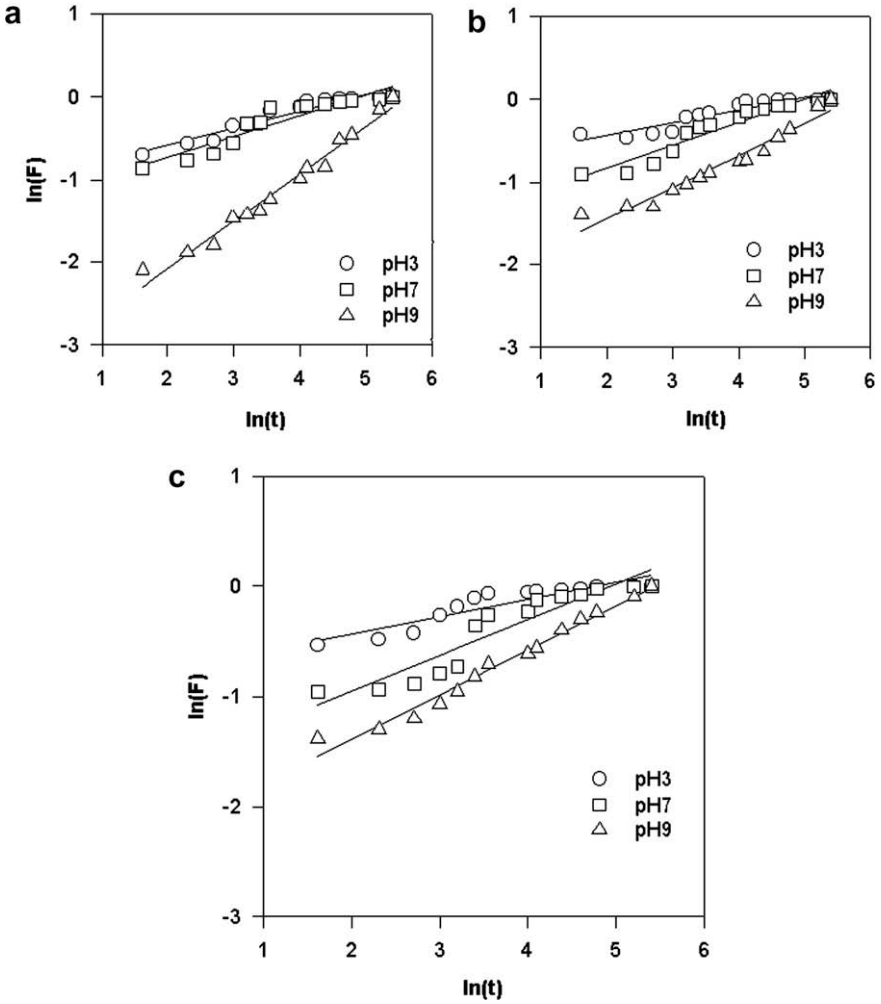


Fig. 3. The plots of $\ln F$ versus $\ln t$ of CS 3 (a), Cs 5 (b) and CS 7 (c) at different pH values at 25 °C.

Table 5
Parameters of diffusion of water into hydrogel at different monomer compositions at pH 3, 7, 9

Sample code	*n*	pH
Cs 3	0.2	3
	0.25	7
	0.58	9
Cs 6	0.15	3
	0.28	7
	0.39	9
Cs 9	0.16	3
	0.32	7
	0.40	9

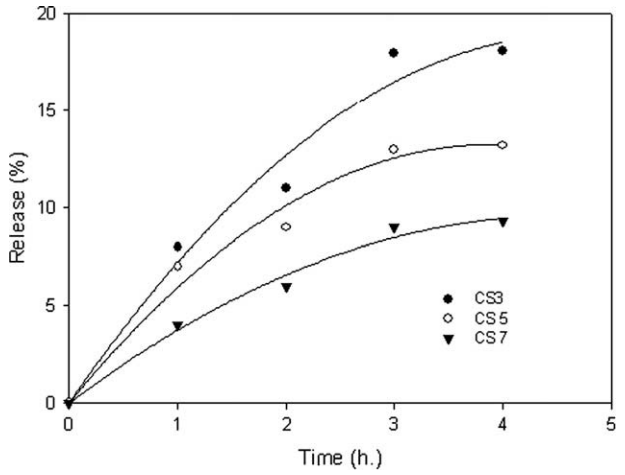


Fig. 4. Relationship between time (h) and the release (%) of Oxttetracycline for the hydrogel of different composition at 25 °C at pH 7.

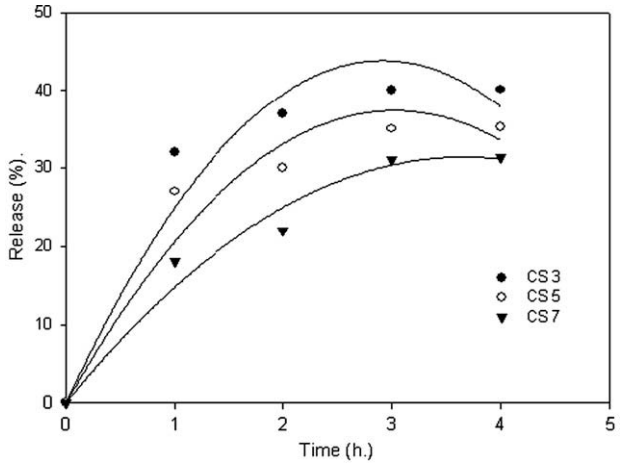


Fig. 5. Relationship between time (h) and the release (%) of Oxttetracycline for the hydrogel of different composition at 35 °C at pH 7.

3.9. FTIR spectroscopy

FTIR studies were carried out to confirm grafting of PVA and PAAc onto chitosan. Fig. 8 shows the FTIR spectra of chitosan (8a), PAAc (8b), PVA (8c) and the prepared hydrogel (8d).

The spectrum of plain chitosan powder (8a) has shown two peaks around 894 and 1153 cm^{-1} corresponding to saccharine structure (Yoshioka, Hirano, Shioya, & Kako, 1990), the absorption peaks observed at 1653 and 1322 cm^{-1} are, respectively, characteristics of chitin and chitosan moieties. The observed sharp peaks at

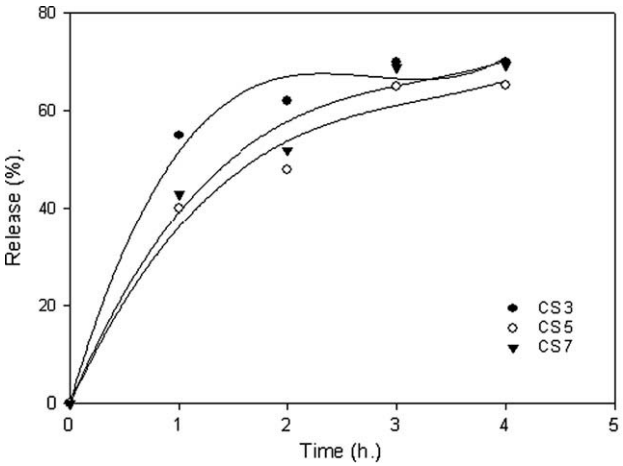


Fig. 6. Relationship between time (h) and the release (%) of Oxttetracycline for the hydrogel of different composition at 43 °C at pH 7.

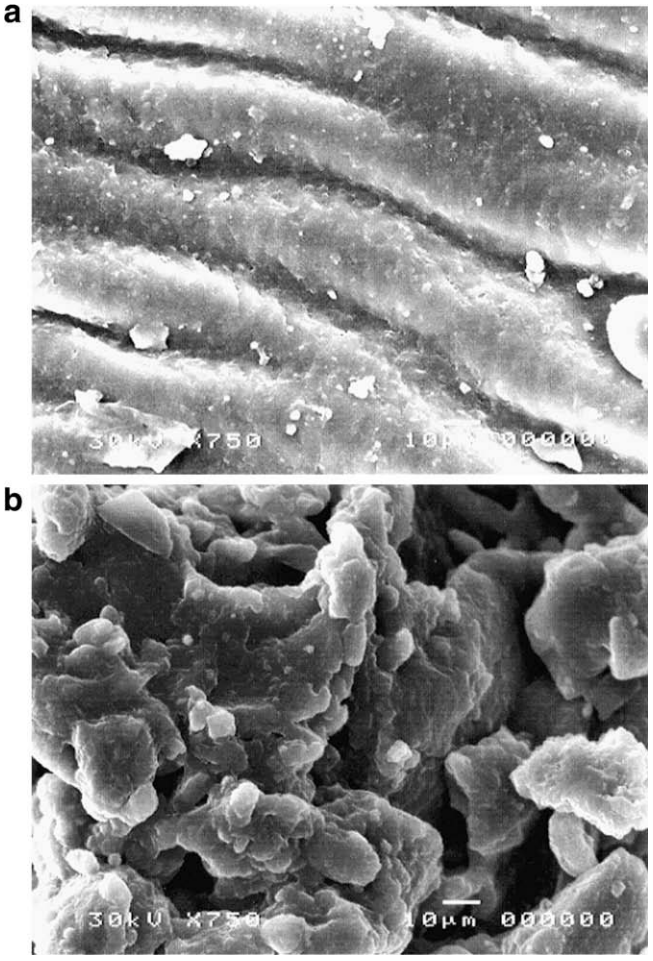


Fig. 7. SEM of (a) CS 5 and (b) after loading with Oxttetracycline.

1382 and 1413 cm^{-1} are assigned to CH_3 symmetrical deformation mode (Peng, Yao, Chen, & Goosen, 1994). A broad band appearing around 1073 cm^{-1} indicates the C–O stretching vibration of chitosan. Another broad band at 3450 cm^{-1} is due to the amine N–H symmetric vibration, which might be due to acetylation of chitosan.

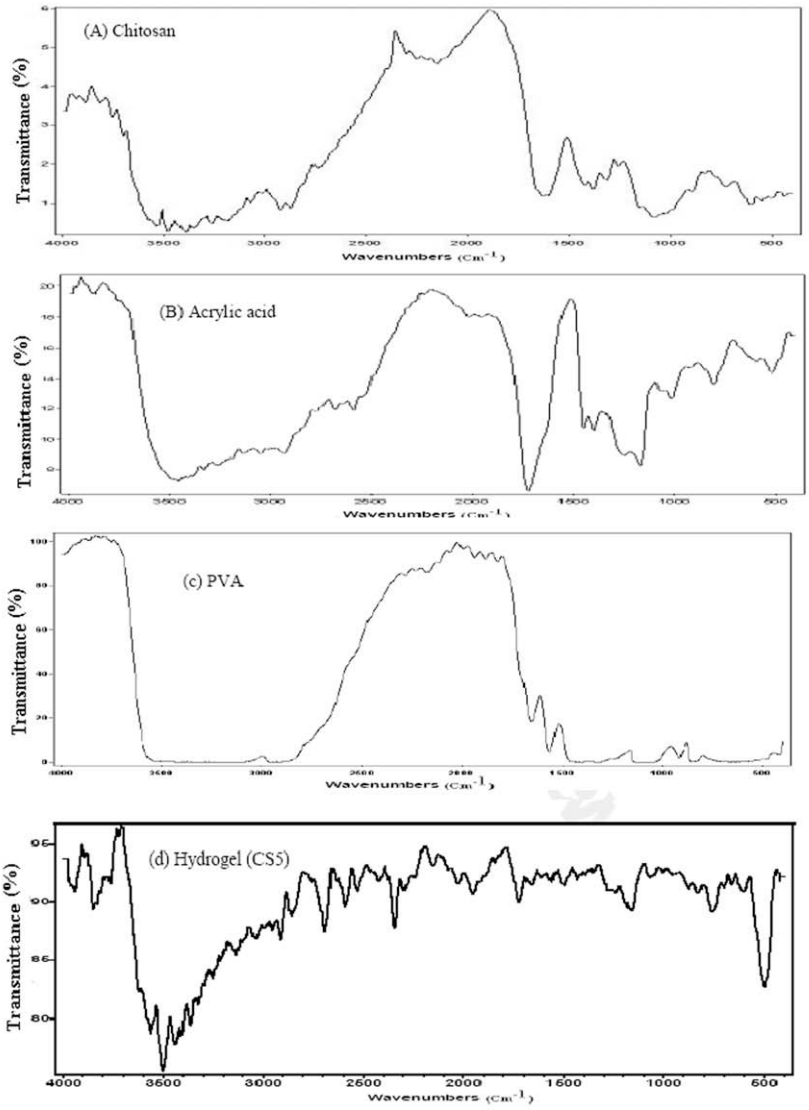


Fig. 8. FTIR spectra of (a) chitosan, (b) Poly acrylic acid, (c) PVA and (d) Cs 5 hydrogel.

In case of PAAc (8b) a broad band appearing at 3500 cm^{-1} corresponds to associate –OH stretching vibration. A relatively high intense peak at 1725 cm^{-1} corresponds to –COOH group.

FTIR spectrum of blends of chitosan with PVA and PAAc (8d) is different than that of chitosan because of the ionization of primary amino groups in the chitosan–PVA–PAAc complexes. The spectrum of chitosan–PVA–PAAc observed around 1550–1570 cm^{-1} is due to symmetric deformation of $-NH_3^+$, resulting from the ionization of primary amino group in the presence of carboxylic group of PAAc (Bellamy, 1980). On the other hand, the peak at 1409 cm^{-1} indicates the presence of carboxylic acid of the polymer. In the presence of amine group, carboxylic groups behave as dimmer and these peaks are observed at 1733 cm^{-1}. However, the presence of carboxylic dimmer was due to the formation of chitosan complex with carboxylic acid (Rao et al., 2006).

3.10. Thermal properties

The graft copolymers prepared in these studies were of natural/synthetic stimuli-responsive material. Thermal properties, in particular the melt temperature (T_m), of the graft copolymers are interesting in view of the structure–property relationship and for practical applications. The graft copolymers showed inflection points in the DSC profile suggesting the occurrence of structural phase transition. DSC measurements performed on chitosan–g–PVA–PAAc (Cs 5), PVA, PPAAc and chitosan are presented in Table 6. In the range of temperature scanned, only one endothermic change of the thermal heat capacity is observed that corresponds to the melt temperature (T_m). From the table, it is possible to determine the domain of temperature in which the melt transition occurs.

The value of T_m (taken at the mid-point of transition are 255, 257.1, 235 and 86.6 °C for Cs 5, PVA, PPAAc and chitosan, respectively. This evidence affirms the formation of chitosan–g–PVA–PAAc copolymer.

Table 6
T_m of Cs 5, PVA, PAAc and Chitosan

Polymer	Cs 5	PVA	PAAc	Chitosan
T_m (°C)	255	257.1	235	86.6

4. Conclusions

A new pH and temperature responsive hydrogel based on the chitosan grafted with PAAc, PVA, PHPMA and gelatin was developed for oral drug delivery. The preparation of these copolymeric hydrogels was carried out using the radical polymerization technique by gamma irradiation for the purposes of enhancing the drug release ability. The prepared hydrogels represented different swelling and gelation degree depending on the composition of chitosan, monomers and radiation dose. The equilibrium swelling measurement clearly showed the pH-responsive nature of these hydrogels.

The in vitro release of Oxttetracycline was established for different type of hydrogels. The hydrogel of lower content of PAAc and PVA and in absence of PHPMA show the highest degree of swelling and release rate of Oxttetracycline. Also the release behaviour of Oxttetracycline from the hydrogel was different according to pH of release medium, content of monomer and the radiation dose.

This investigation of grafted chitosan and gelatin based hydrogel indicated that the most preferable hydrogel for drug release is that of (PAAc/PVA)–g–chitosan prepared at lower radiation does which show also temperature responsive sensitivity as compared with other formulations. These hydrogels can lead to a successful application for localized drug delivery used for treating infections on the respiratory tracts, skin and gonorrhea.

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