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Formation of sterculia polysaccharide networks by gamma rays induced graft copolymerization for biomedical applications

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ABSTRACT

In the present study radiation induced graft-copolymerization of sterculia gum–PVA has been carried out to develop the hydrogels meant for drug delivery formulations. The polymers have been characterized with scanning electron micrography (SEM), energy dispersion X-ray analysis (EDAX), Fourier transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA) and swelling studies. The swelling of hydrogel and release of drug from the hydrogels have been carried out in solution of different pH to determine the swelling and drug release mechanism. The sterculia-*cl*-poly(VA) hydrogels were synthesized by varying the total radiation dose from 8.42 kGy to 50.54 kGy during polymerization reaction. The values of diffusion exponent '*n*' indicate that the swelling and release of drug from the hydrogels followed non-Fickian diffusion mechanism. In this mechanism, the rate of drug diffusion from the polymer matrix and rate of polymer chain relaxation are comparable.

1. Introduction

Sterculia gum is a natural gum exudate of *Sterculia urens* tree belongs to the family *Sterculiaceae* (Khan & Abourashed, 2009). It is a complex branched and partially acetylated polysaccharide which has very high molecular mass. It consists of glucuronic acid, galacturonic acid, galactose and rhamnose structural units (Cert, Irinei, & Muller, 1990). It is used in food and pharmaceutical applications. While no side effects of sterculia gum have been reported till date but its intake without adequate fluid is harmful. Intestinal obstruction may result in the patients taking bulk laxatives without excessive fluid. Sterculia gum has unique physicochemical properties such as high swelling, high viscosity and poor solubility. It is a highly hydrophilic polysaccharide, but least soluble of the exudates polymers. It does not form a true solution but its particles swell to 60–100 times (by volume). Its viscosity ranges from about 120 to 400 cps (0.5% dispersions) to about 10,000 cps (3% dispersions). Aging or high temperature or high humidity storage is harmful to its stability. 1% solution of sterculia gum has pH 4.6 and addition of small amounts of alkali change its pH to 7 or 8 but buffering action of the gum will gradually reduce the pH again to the acidic range (Murali Mohan Babu, Prasad, & Murthy, 2002a; Murali Mohan Babu et al., 2002b; Nussinovitch, 1997).

It is 'Generally Recognized as Safe' in the USA (Anderson, 1989). When taken at moderate levels, it has been reported as non-toxic, non-allergenic non-teratogenic and non-mutagenic. It has been reported as therapeutic and drug delivery agent (Singh & Sharma, 2009; Singh & Vashishtha, 2008). Sterculia gum due to its hydrophilic nature has been used to control the release of drugs from the formulations. It has been used as excipient for the drug formulations (Murali Mohan Babu, Prasad, et al., 2002a; Murali Mohan Babu et al., 2002b; Park & Munday, 2004). Generally, polysaccharide gums are promising biodegradable, nontoxic, freely available and less expensive polymeric materials which have been used to develop various drug delivery devices (Sriamornsak & Kennedy, 2010). However, these materials have certain drawbacks, like uncontrolled rate of hydration, thickening, drop in viscosity on storage, microbial contamination and required functionalization/modification to overcome these problems. The modification of polysaccharides to develop the hydrogels is a powerful tool, to control the interaction of the polymer with drugs, to enhance the load capability and to tailor the release profile of the drug (Nishimura et al., 1993). Grafting and crosslinking of vinyl monomers are the common techniques to modify and to improve the functional properties of polysaccharides and to make them advanced materials for use in drug delivery applications (Biswal et al., 2007).

Radiation method of crosslinking produces pure, sterile and residue-free hydrogels and no catalysts or additives are needed to initiate the reaction. It is relatively simple and the degree of crosslinking, which strongly determines the extent of swelling of hydrogels, can be controlled easily by varying the radiation dose. Therefore, this method is found to be very useful in preparing hydrogels for medical applications, where even a small contamination is undesirable. A series of hydrogels comprised of crosslinked

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networks of synthetic/natural polysaccharides have been prepared using gamma radiolysis of aqueous solutions of the polymers. The primary effect of high-energy photons on organic compounds is the ejection of an electron from a molecule, thus giving rise to a positively charged ion-radical. The ejected electron is highly energetic and loses its energy by interaction with the electrons of other molecules. In doing so it gives rise to many thousands of secondary ionizations and excitations so that the influence of the initial ionization on the ensuing chemical change is negligible (Francis & Varshney, 2005; Hill, Whittaker, & Zainuddin, 2011; Park & Nho, 2003; Tomic, Micic, Filipovic, & Suljovrujic, 2007a, 2007b).

The feed reaction contents influence the swelling characteristics and the releasing behavior of hydrogels (Tomic et al., 2007a, 2007b). The physical properties such as gelation, water absorptivity, and gel strength have been greatly improved when additives have been added during polymerization. The incorporation of polysaccharides increased the equilibrium degree of swelling of the hydrogels from 320 to 800 g/g (Francis, Kumar, & Varshney, 2004) and activated carbon has improved the elasticity and flexibility (Qiu et al., 2007). Zhai et al. (2004) have prepared a series of blended transparent and elastic hydrogels composed of pH and temperature responsive monomers by γ-irradiation. Park, Nho, and Kim (2004) have observed that pH responsive copolymer hydrogels have not shown any noticeable change in swelling at lower pH range. However they showed an abrupt increase in swelling at higher pH range due to the ionization of carboxyl groups. This pH-responsive swelling behavior has been applied for site specific drug delivery.

The appropriate strength of the hydrogel is required which are used in controlled drug delivery system in the biological medium. Otherwise the immediate degradation of matrix will occur and it will release the drug immediately and will perform like conventional drug delivery system. The polyvinyl alcohol (PVA) can provide sufficient strength to the polymer matrix for its use in drug delivery system (Pal, Banthia, & Majumdar, 2008). PVA is a water-soluble, non-toxic and non-carcinogenic polymer. These properties make it excellent candidate for use in biomaterials (Tanigami, Yano, Yamaura, & Matsuzawa, 1995). At the same time, the design of new materials based on blends of biological and synthetic polymers producing new processable polymeric materials that hopefully possess both good mechanical properties and biocompatibility. Therefore the present study is an attempt to prepare the sterculia gum–polyvinyl alcohol hydrogels by radiation crosslinking method. The optimum reaction conditions have been determined for the synthesis of hydrogels by radiation method (by varying the content of sterculia gum, PVA and total radiation dose). The polymers have been characterized with SEMs, EDAX, FTIR, TGA and swelling studies. The swelling of hydrogel has been carried out in solution of different pH. This article also discusses the in vitro release dynamics of antimicrobial model drug (tetracycline hydrochloride) from the dug loaded hydrogels in distilled water, pH 2.2 buffer and pH 7.4 buffer to determine the drug release mechanism.

2. Experimental

2.1. Materials and methods

Polyvinyl alcohol (PVA) of molecular weight 125,000 [S.D. Fine Chemical Ltd. Mumbai, India], sodium hydroxide (NaOH), sodium chloride (NaCl), sodium bicarbonate ($NaHCO_3$) [S.D. Fine Chemical Ltd. Mumbai, India], sodium dihydrogenphosphate (NaH_2PO_4), potassium chloride (KCl) [Merck Specialities Pvt. Ltd. Mumbai, India] were used as received. Tetracycline hydrochloride was obtained from Nicholas Piramal India Ltd. Gujarat, India. Sterculia gum was obtained from herbal medical store.

2.2. Synthesis of sterculia-cl-PVA hydrogels by radiation method

Solution of definite concentration of sterculia gum and PVA was prepared in a beaker and stirred for half an hour to get a homogeneous mixture. The reaction mixture was irradiated with gamma rays for definite time in ^{60}Co gamma chamber. The crosslinked-polymer formed after 3 h was stirred in 1:1 of distilled water:ethanol solution for half an hour to remove the soluble fraction left in polymer matrix and was named as sterculia-*cl*-poly(VA) hydrogel/polymer. Then it was dried in an oven at 40 °C. The optimum reaction parameters were evaluated for synthesis of sterculia-*cl*-poly(VA) hydrogels by varying reaction parameters such as contents of sterculia gum, PVA and total radiation dose, on the basis of swelling of the hydrogel and surface consistency maintained by hydrogel after 24 h swelling. In order to determine the optimum reaction parameters the contents of sterculia gum was varied from 0.025 g to 0.125 g, PVA was varied from 0.050 g to 0.250 g, total radiation dose was varied from 8.42 kGy to 50.54 kGy and water content was varied from 9 ml to 15 ml during the synthesis of hydrogels. The optimum sterculia gum, PVA, total radiation dose and amount of solvent were obtained as 0.125 g, 0.250 g, 8.42 kGy and 13 ml, respectively.

2.3. Characterization

Sterculia gum, PVA and crosslinked polymers/hydrogels prepared by radiation method were characterized by scanning electron micrography (SEM), energy dispersion X-ray analysis (EDAX), Fourier transform infrared spectroscopy (FTIR) and thermogravimetric analysis (TGA). SEMs and EDAX were taken on QUANTA 200 FEG model (Netherlands). FTIR spectra of polymers were recorded in KBr pellets on Nicolet 5700FTIR THERMO (USA). TGA were recorded on Perkin Elmer (Pyris Diamond) thermal analyzer DTA-DTG-TG in air (200 ml/min) at heating rate of 10 °C/min.

2.4. Swelling studies

Swelling studies of polymers were carried out by gravimetric method (Singh, 2007). Known weight of polymers were 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 gave the gain in weight at different time intervals.

2.5. Release dynamics of model drugs from the drug loaded hydrogels

The release profile of drug from the drug loaded polymer matrix was determined in distilled water, pH 2.2 buffer and pH 7.4 buffer. All the studies were carried out in triplicate. Preparation of buffer solutions, calibration curves of tetracycline HCl, drug loading and drug release are discussed in brief.

Buffer solution of pH 2.2 and 7.4 were prepared as per the procedure reported in pharmacopoeia of India (Pharmacopoeia of India, 1985). The amount of drug released from the polymer device in different releasing medium was measured from the calibration curves made in distilled water, pH 2.2 buffer and pH 7.4 buffer. The absorbance of samples solution was measured on the UV Visible Spectrophotometer (Cary 100 Bio, Varian). The constant loading of tetracycline HCl into the polymer matrix was carried out by swelling equilibrium method. The hydrogels were allowed to swell in 20 ml drug solution of known concentration for 24 h at 37 °C and then were dried to obtain the drug release device. In vitro release studies of the drug were carried out by placing dried and drug loaded samples in definite volume of releasing medium (20 ml) at 37 °C temperature. The amount of drug released in distilled water, pH 2.2 buffer and pH 7.4 buffer after every 30 min was measured from the standard curve.

2.6. Mechanism of swelling and drug release

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 drug loaded polymers have been classified into three types of diffusion mechanisms. These mechanisms are Case I or Simple Fickian Diffusion, Case II Diffusion and Non-Fickian or Anomalous Diffusion (Peppas & Korsmeyer, 1987; Ritger & Peppas, 1987a,1987b).

In the case of water uptake, the weight gain (M_S) is described by the Eq. (1)

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

where k and n are constant. For Fickian diffusion the value of the 'n' is ≤ 0.5, while for Case II diffusion the value is ≥ 1.0. The value of 'n' is between 0.5 and1.0 which indicates a mixture of Fickian and Case II diffusion and 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_∞ replaces (M_s) in Eq. (1) and it gives Eq. (2). For cylindrical shaped hydrogels, the initial diffusion coefficients (D_i), average diffusion coefficient (D_A) and late diffusion coefficients (D_L) have been calculated from the Eqs. (3)–(5), respectively.

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

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

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

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

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_∞ indicates the amount of drug released at time 't' and at equilibrium, respectively, 'l' is the thickness of the sample and $t^{1/2}$ is the time required for 50% of the total drug release.

3. Result and discussion

3.1. Characterization

3.1.1. SEM and EDAX analysis

SEMs of sterculia gum, PVA and sterculia-*cl*-poly(VA) polymers prepared by radiation method are presented in Fig. 1a–c, respectively. SEMs of sterculia gum have been studied at magnification of 1000× which revealed the assembled particle while in case of PVA the large globules with pressed structure observed. The SEMs of sterculia-*cl*-poly(VA) polymers show a sheet like structure with pressed surface and polymer networks indicate the change in morphology of the material. It is observed from the SEMs that sterculia gum has smooth and homogeneous morphology whereas modified sterculia gum has structural heterogeneity. The change in surface morphology of the modified sterculia gum is clear in the SEMs and some crosslinked networks have been observed. Similar porous structure has been reported in the literature by Lanthong, Nuisin, and Kiatkamjornwong (2006). These workers have observed that the starch granules have an irregular shape with smooth surface while the graft copolymers have coarse porous structure and broad network. Semi-porous structures with thick struts between pores are region of water permeation and interaction sites of external stimuli with the hydrophilic groups of the graft copolymers. The EDAX spectrum of sterculia gum, PVA and sterculia-*cl*-poly(VA) hydrogels were taken and quantitative elemental composition was recorded.

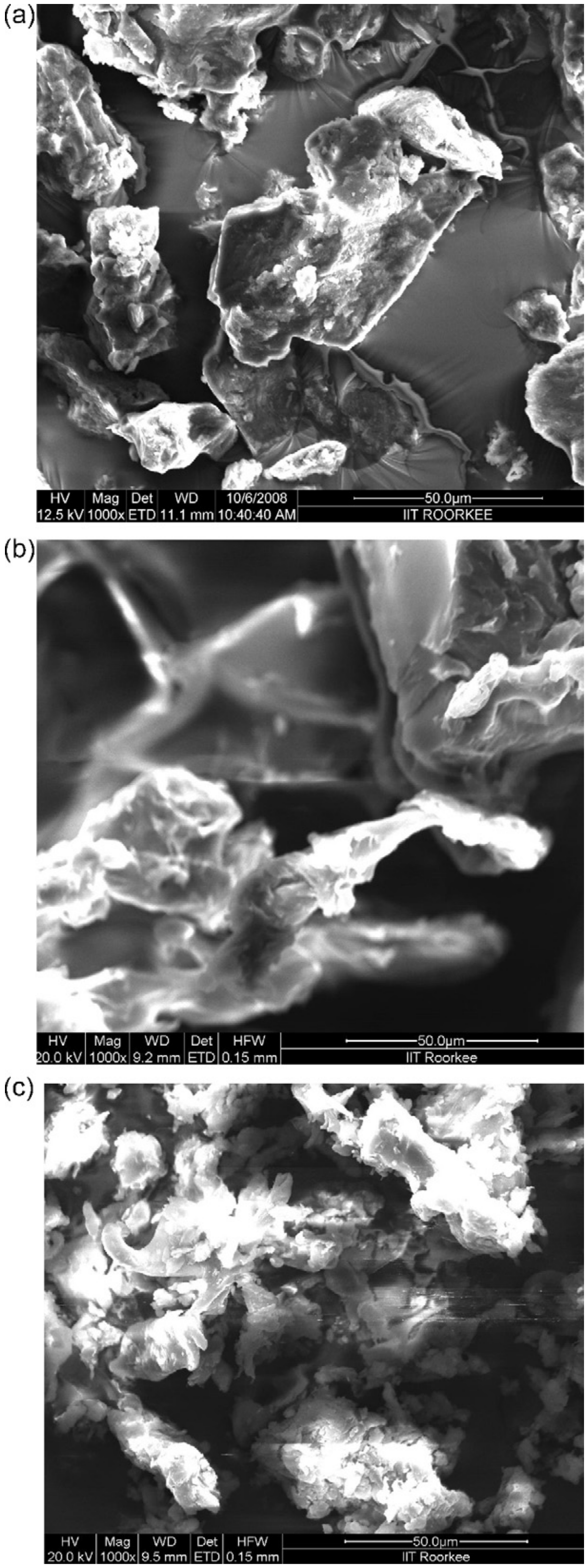

Fig. 1. Scanning electron micrographs (1000×) of (a) sterculia gum, (b) PVA and (c) sterculia-*cl*-poly(VA) hydrogels prepared by radiation method.

3.1.2. Fourier transform infrared spectroscopy (FTIR)

The FTIR spectra of sterculia gum, PVA, sterculia-*cl*-poly(VA) polymers synthesized by radiation method are presented in Fig. 2a–c, respectively. In case of sterculia gum the absorption band at 3441.6 cm^{-1} has been observed due to –OH stretching along with some complex bands in the region of 1200–1040 cm^{-1} due to C–O and C–O–C stretching vibrations which are the characteristic of the natural polysaccharides. An absorption band at 2934.9 cm^{-1} is attributed to C–H stretching modes of CH_2 group, and at 1741.3 and 1619.7 cm^{-1} are due to stretching vibration of C=O groups of free carboxylic acid and methylated ester of the galactouronic acid of the gum (Sutar, Mishra, Pal, & Banthia, 2008). The pyranose ring absorption band of sterculia gum is clearly observed in the range of 1172–1076 cm^{-1} (i.e. 1153.2 cm^{-1}) (Akgun, Ekici, Mutlu, Besirli, & Hazer, 2007). Band at 1429.4 cm^{-1} is arising from ($-COO^-$) and C–C stretching of $-CH_2$ scissoring and 1256.4 cm^{-1} due to ($-CH_3CO$) group in the polysaccharide backbone. The absorption peak at 1379.2 cm^{-1} reflects the C–H bending vibration modes of the methylene groups and O–H bending vibration of sterculia gum (Nayak, Biswal, Karmakar, & Singh, 2002). In literature typical absorption bands at around 3300 cm^{-1}, between 1675–1610 cm^{-1} and 1730–1240 cm^{-1} have been assigned, respectively to the hydroxyl, uronic acid and acetyl groups present in the sterculia gum (Cert et al., 1990). In case of PVA, a broad band at 3430.9 cm^{-1} due to the O–H stretching vibrations, a band at 1264 cm^{-1} due to the O–H bending vibration and at 2854 cm^{-1} is attributed to the stretching vibration of $-CH_2$. The band at 1461.1 cm^{-1} is due to C–H bending vibration has been observed (Mansur, Sadahira, Souza, & Mansur, 2008). In case of sterculia-*cl*-poly(VA) polymer radiation crosslinked, a broad band with less intensity compared to both sterculia gum and PVA matrices at 3428.1 cm^{-1} is due to –OH stretching vibrations and the intense bands, which appeared at 2923.3 and 2854.3 cm^{-1} are due to the aliphatic $-CH_2$ stretching vibrations. The bands at 1717.4 and 1628.2 cm^{-1} are due to the presence of carboxyl groups in sterculia gum. Absorption band at 1457.8 cm^{-1} is due to $-CH_2$ bending vibrations and band appearing at 2363.8 cm^{-1} confirms the cross-linking in polymer matrix.

3.1.3. Thermogravimetric analysis (TGA, DTA and DTG)

The primary thermograms (TGA, DTA and DTG) of sterculia, PVA, sterculia-*cl*-poly(VA) polymers prepared by radiation method are shown in Fig. 3a–c, respectively. The decomposition temperature per 10% weight loss along with the initial decomposition temperature (IDT) and final decomposition temperature (FDT) for each sample was noted. In each case, weight loss due to entrapped moisture was ignored and IDT was taken as the temperature where the actual degradation of the polymers started.

In case of sterculia, initial 13.2% weight loss occurred between 23 and 100 °C temperatures. This shows that the sterculia has 13.2% bounded water. The IDT has been obtained at 254 °C and FDT has been occurred at 800 °C (residue left = 3.4%). In general, the decomposition of polysaccharides consists of four phases; each phase corresponds to the characteristic decomposition pattern of that polysaccharide. These include desorption of physically absorbed water, removal of structural water (dehydration reactions), depolymerization accompanied by the rupture of C–O and C–C bonds in the ring units resulting in the evolution of CO, CO_2 and H_2O and finally the formation of polynuclear aromatic and graphitic carbon structures (Parikha & Madamwar, 2006). In case of sterculia these decomposition processes occur between 23 and 800 °C temperature. Three stages decomposition mechanism has been observed from the primary thermograms of sterculia. These stages started at 254 °C (residue left = 81.5%), 401 °C (residue left = 33.8%) and 466 °C (residue left = 25.6%), respectively. It is also observed from this observation that about 50% of the polymer decomposition occurred during the first stage of decomposition. DTA curve of sterculia shows endothermic peak at 79 °C (−7.0 μV), due to endothermic release of water from polysaccharides. Additionally, presence of exothermic peaks for sterculia gum [481 °C (51 μV) and 289 °C (19 μV)] suggest exothermic decomposing of the polymers [DTA]. DTG analysis of sterculia was studied as a function of rate of weight loss (μg/min) vs temperature (°C). The temperature of maximum rate of weight loss (T_{max}) has been observed at 258 °C (964 μg/min) in case of sterculia gum.

In case of PVA, initial 10% weight loss occurred between 29 and 150 °C temperature. IDT and FDT have been obtained at 229 °C and 632 °C (residue left = 0.9%), respectively. Three stages decomposition mechanism has been observed for the decomposition of the PVA. The first stage started at 229 °C (residue left = 87%), second stage started at 368 °C (residue left = 57%) and third stage started at 482 °C (residue left = 36%), respectively. It is observed that 50% of the polymer decomposition occurred during the second stage of decomposition. Initial 7% weight loss has been occurred up to 100 °C temperature which shows that PVA has 7% bounded water. DTA curve of PVA has endothermic peak at 80 °C (−5.07 μV) due to endothermic release of water and exothermic peaks at 533 °C (23.31 μV) and 616 °C (23.75 μV) due to exothermic decomposition of the polymers.

In case of radiation crosslinked sterculia-*cl*-poly(VA) polymer, initial 4.5% weight loss occurred up to 100 °C temperature. IDT and FDT have been obtained at 241 °C and 517 °C (residue left = 1.8%), respectively. Three stages decomposition mechanism has been observed for the decomposition of the sterculia-*cl*-poly(VA) polymer. The first, second and third stage respectively started at 488 °C (residue left = 93%), 394 °C (residue left = 41%) and 474 °C (residue left = 19.3%). It is observed that 50% of the polymer decomposition occurred during the second stage of decomposition. DTA curve of sterculia-*cl*-poly(VA) polymer show endothermic peaks at 87.3 °C (−2.3 μV) due to endothermic release of bonded water from polymers. Additionally, presence of exothermic peaks for sterculia-*cl*-poly(VA) polymers at 488 °C (78.8 μV) suggest exothermic decomposing of the polymers. DTG analysis of sterculia-*cl*-poly(VA) show temperature of maximum rate of weight loss (T_{max}) at 291 °C having decomposition rate 647 μg/min.

3.2. Swelling studies

3.2.1. Swelling as a function of feed sterculia gum

Effect of feed sterculia gum on the network formation of sterculia-*cl*-poly(VA) hydrogels was studied by taking the swelling of hydrogels prepared by varying sterculia gum from 0.025 to 0.125 g. The results of swelling are presented in Fig. 4a. Swelling of the hydrogels increased with increase in feed sterculia content during polymerization. This may be due to increase in sterculia–PVA/crosslinker ratio and decrease in crosslinking density. On other hand increase in swelling can also explained probably on the basis of higher degree of gum hydration which has increased the number interactions with water and led to the higher swelling (Patel & Patel, 2007). The values of diffusion exponent '*n*' indicate that swelling occurred through non-Fickian diffusion mechanism. The values of the average diffusion coefficients have been observed higher than late time diffusion coefficients (Table 1).

3.2.2. Swelling as a function of feed [PVA]

Effect of PVA contents on the structure of the hydrogels was determined by studying the swelling behavior of the hydrogels prepared by varying PVA from 0.050 to 0.250 g (Fig. 4b). Sterculia-*cl*-PVA hydrogels were not formed when the PVA was less than

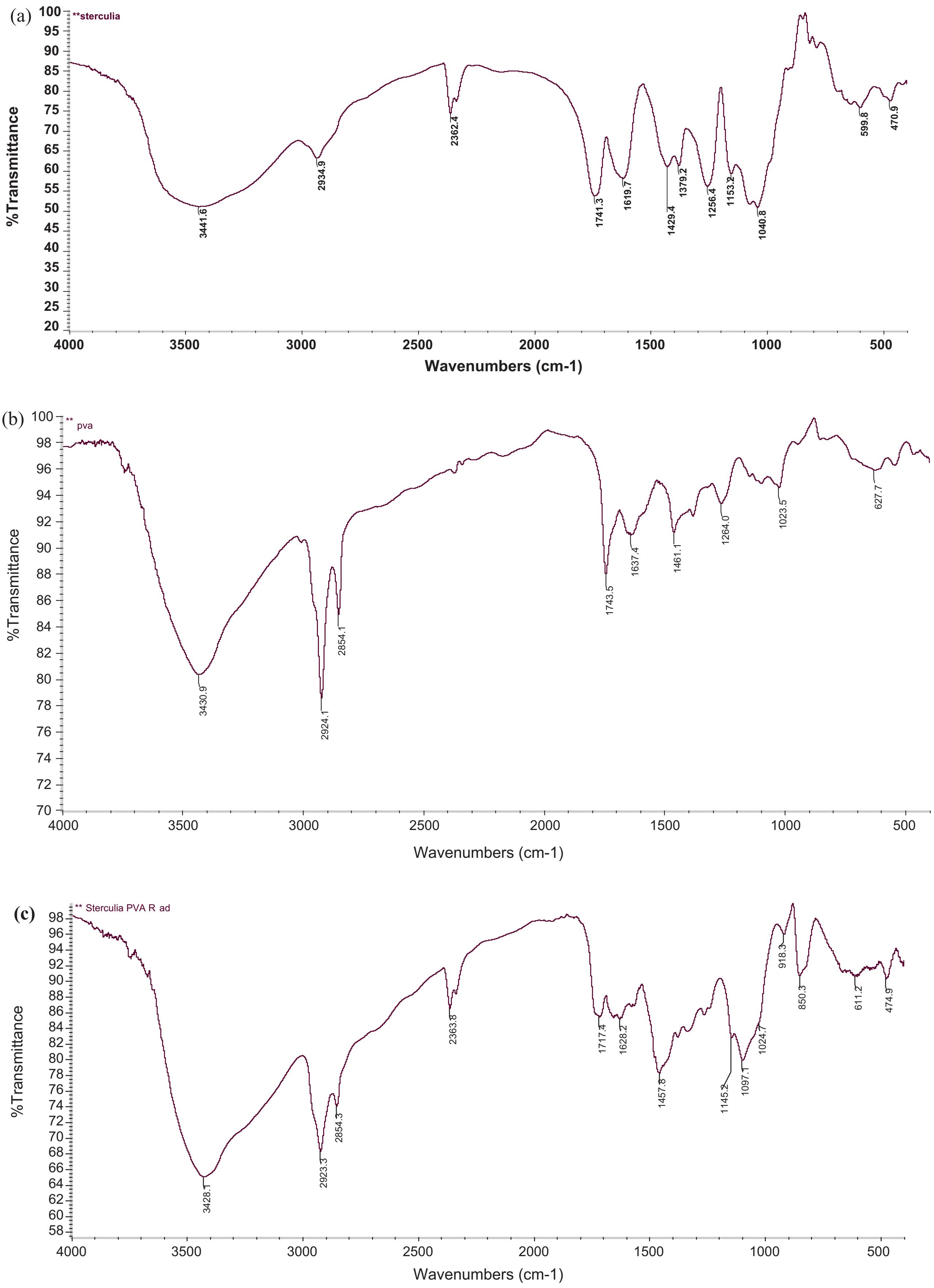

Fig. 2. FTIR spectrum of (a) sterculia gum (b) PVA and (c) sterculia-*cl*-poly(VA) hydrogels prepared by radiation method.

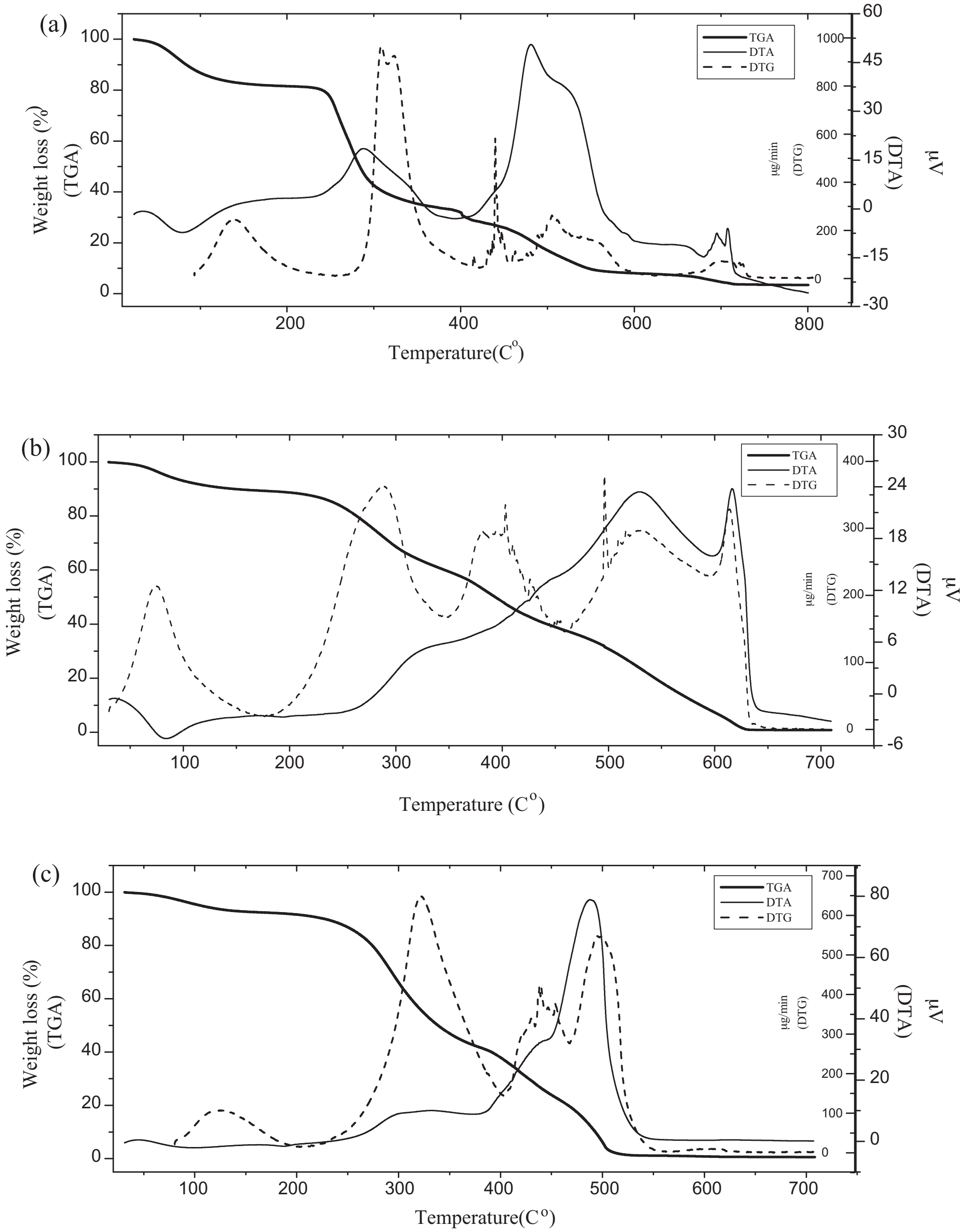

Fig. 3. Primary thermogram (TGA, DTA and DTG) of (a) sterculia gum (b) PVA and (c) sterculia-*cl*-poly(VA) hydrogels prepared by radiation method.

0.150 g in the reaction system. In radiation crosslinking gels, concentration of reactants i.e. polymer solution, monomer, nature of monomer and crosslinker, play an important role in formation of the polymer networks. In dilute solution, the long chain polymer molecules are in the form of coils, each having certain mobility. As the concentration increases, the mobility of coils decreases. At a critical concentration, known as gel point, the coils no longer move as units and can no longer interchange their places. After the gel point is reached, more and more of these loose groups become attached to network. The transition from a concentrated solution to a gel corresponds to the transition of a liquid to a solid. Swelling of the hydrogels decreased as the concentration of PVA increased from 0.150 g to 0.200 g and after that increase in PVA content in the reaction mixture has not exerted strong effect on the swelling of the hydrogels. Swelling of the hydrogels occurred through non-Fickian diffusion mechanism. The values of diffusion coefficients are shown in Table 1. The values of the average diffusion coefficients have been observed higher than late time diffusion coefficients (Table 1).

3.2.3. *Swelling as a function of feed water content*

Effect of water content on the networks of sterculia-*cl*-poly(VA) hydrogels was studied by varying water 9 ml to 13 ml during polymerization. Increase in water content not exerted any strong effect on swelling of hydrogel prepared by radiation method. This may be probably due the reason that dilution was very less. The values of diffusion exponent '*n*' indicate that swelling occurred through non-Fickian diffusion mechanism. The values of the average diffusion coefficients have been observed higher than late time diffusion coefficients (Table 1).

Table 1
Results of diffusion exponent ‘*n*’, gel characteristic constant ‘*k*’ and various diffusion coefficients for the swelling and drug release from sterculia-*cl*-poly(VA) hydrogels.

S. No.	Variation of different contents	Diffusion exponent ‘*n*’	Gel characteristic constant ‘*k*’ $\times 10^3$	Diffusion coefficients (cm^2/min)		
				Initial $D_i \times 10^3$	Average $D_A \times 10^3$	Late time $D_L \times 10^3$
Variation of sterculia contents (gram)						
1	0.025	0.82	8.47	2.25	8.59	2.25
2	0.050	0.59	25.88	0.99	7.50	0.98
3	0.075	0.60	25.36	1.26	9.36	1.23
4	0.100	0.64	21.10	1.57	10.72	1.51
5	0.125	0.59	24.81	0.92	8.29	0.88
Variation of PVA (gm)						
6	0.050	No product	–	–	–	–
7	0.100	No product	–	–	–	–
8	0.150	0.90	4.95	1.56	5.72	1.39
9	0.200	0.92	4.69	1.95	6.79	1.76
10	0.250	0.59	24.81	0.92	8.29	0.88
Variation of water (ml)						
11	10	0.73	8.81	1.45	6.82	0.64
12	11	0.74	8.22	0.63	5.97	0.55
13	12	0.52	29.70	0.75	8.85	0.79
14	13	0.59	24.81	0.92	8.29	0.88
15	14	0.77	9.13	1.08	7.28	0.86
16	15	0.84	5.30	1.14	8.41	0.91
Variation of total radiation dose(kGy)						
17	8.42	0.57	24.72	0.99	9.32	0.98
18	16.85	0.51	32.13	0.65	8.14	0.68
19	25.17	0.59	24.81	0.92	8.29	0.88
20	33.70	0.57	23.80	0.81	8.87	0.79
21	42.12	0.57	22.85	0.63	6.76	0.62
22	50.54	0.62	19.66	0.98	8.75	10.52
	Effect of pH on Swelling					
1	Distilled water	0.57	24.73	0.99	9.34	0.98
2	pH 2.2 buffer	0.72	13.65	1.77	10.42	1.68
3	pH 7.4 buffer	0.65	19.92	1.45	9.37	1.53
	Effect of pH on drug release					
1	Distilled water	0.80	7.41	1.28	9.15	1.02
2	pH 2.2 buffer	0.72	10.61	1.05	8.78	0.90
3	pH 7.4 buffer	0.68	15.46	1.15	8.81	1.01

3.2.4. *Swelling as a function of total radiation dose*

Radiation dose plays a very important role in controlling the pore size and network density of polymer matrix. In the present studies the sterculia-*cl*-poly(VA) hydrogels were synthesized by varying the total radiation dose from 8.42 kGy to 50.54 kGy during polymerization reaction and swelling of resultant hydrogels was measured. The results of swelling of polymers are presented in Fig. 4c. The results show that increase in total radiation dose decreases the swelling of hydrogel due to the increase in crosslinking density of hydrogel. Zhai, Yoshii, Kume, and Hashim (2002) have also observed the decrease in swelling of PVA/starch polymers with increase in radiation dose. Maziad (2004) has also observed the similar effect of irradiation dose on water uptake for the prepared polymeric hydrogels. It is found that with the change of irradiation dose from 5 to 50 kGy, the gel fraction of the hydrogel increased. Meanwhile, the water uptake increases at low doses to reach a maximum at 30 kGy; therafter it decreased. In addition, the production of high molecular weight hydrogel occurred and also the soluble fraction decreased by increasing the irradiation dose. This behavior may be caused by the increase of crosslinking density at higher irradiation dose. A compromise between the yield of the hydrogel and the water uptake percentage has also been considered during preparation of hydrogel under the effect of irradiation. Radiation-initiated reactions are responsible for grafting crosslinking and scission of the polymers. When the radiation from source interacts with a polymer material, the polymer material absorbs its energy and active species such as radicals are produced, thereby, initiating various chemical reactions. There are three fundamental processes that are the results of these reactions. The different responses to radiation for different polymers are intrinsically related to the chemical structures of the polymers. Crosslinking and degradation are two competing processes that always co-exist under radiation. The overall effect depends on which of the two is predominant at a certain time (Saum, Sanford, DiMaio, & Howard, 2001; Wang, Essener, & Zarnowski, 2002). In general, the formation of hydrogel networks occurs by crosslinking in the existing polymer chains. Crosslinking is the most important effect of polymer irradiation and control the various material applications. The increase in the amount of absorbed dose lessens the number of small chains. Thus, hydrogels exposed higher doses has higher crosslink density than hydrogel exposed lower doses. This means that a high amount adsorbed dose decrease the number average molar mass between crosslinks while a low amount of adsorbed dose increase the number average molar mass between crosslinks (Bhattacharya, 2000; Maziad, 2004; Mishra, Bajpai, Katare, & Bajpai, 2007; Nasef & Hegazy, 2004). The values of diffusion exponent ‘*n*’ indicate that the swelling followed non-Fickian diffusion mechanism. The values of diffusion coefficients are shown in Table 1. Swelling of the polymers occurred through non-Fickian diffusion mechanism. In this mechanism, the rate of solvent diffusion from the polymer matrix and rate of polymer chain relaxation are comparable. Further, values of the diffusion coefficients reflect that in the early stages the rate of swelling of drug from the polymer was higher than the latter stages. This is very good observation to develop the controlled and sustained drug delivery devices.

3.2.5. *Swelling as a function of pH*

Effect of nature of swelling medium on the swelling of hydrogels was studied by taking the swelling of the hydrogels prepared at the optimum conditions in the distilled water, pH 2.2 buffer,

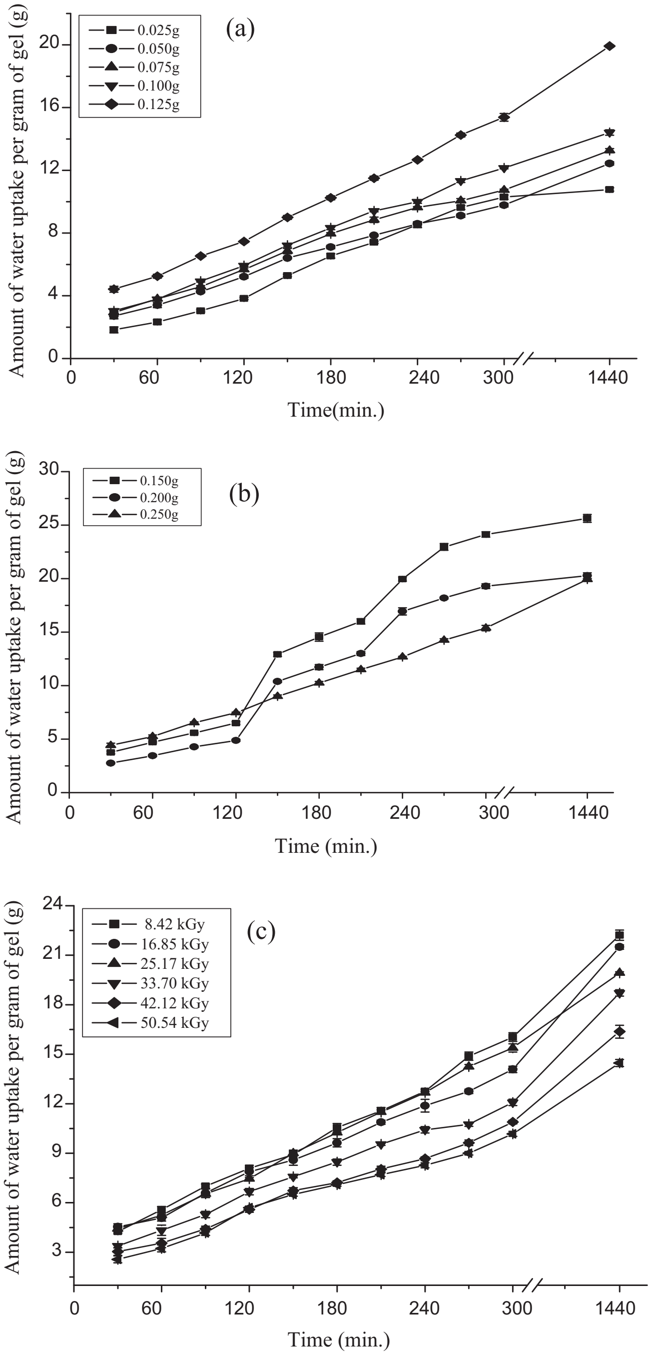

Fig. 4. Effect of (a) sterculia gum, (b) PVA and (c) total radiation dose on the swelling of sterculia-cl-poly(VA) hydrogels.

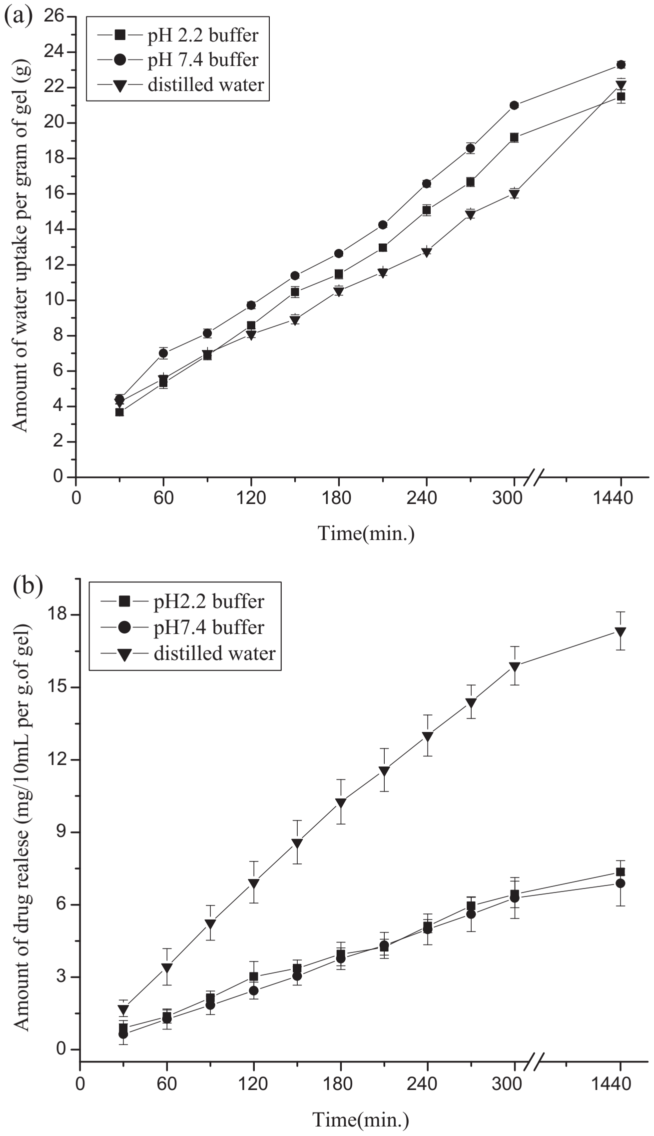

Fig. 5. Effect of pH on (a) swelling and (b) drug release from drug loaded sterculia-cl-poly (VA) hydrogels.

pH 7.4 buffers (Fig. 5a). Swelling of hydrogels has been observed more in pH 7.4 buffer as compared to other mediums. The values of diffusion exponent '*n*' indicate that swelling occurred through non-Fickian diffusion mechanism. The values of the average diffusion coefficients have been observed higher than late time diffusion coefficients (Table 1).

3.3. *Drug release studies*

The polymer used for the release dynamics of tetracycline HCl has been synthesized at optimum reaction condition. The release profile of the tetracycline HCl from the drug loaded polymer matrix in different release medium at 37 °C is presented in Fig. 5b. In the present studies, the effect of pH on the release pattern of tetracycline HCl has been studied by varying the pH of the release medium. Amount of drug released from the composite polymer matrix has been observed higher in distilled water than pH 2.2 buffer, pH 7.4 buffers. The values of diffusion exponent '*n*' and gel characteristic constant '*k*' for the release of drug from composite polymer matrix in different pH have been evaluated from the slope and intercept of the plot ln M_t/M_∞ versus ln t and results are presented in Table 1. The release of drug from the drug loaded hydrogels occurred through non-Fickian type of diffusion mechanism. In this mechanism the rate of diffusion of drug from the composite polymer matrix is comparable to rate of polymer chain relaxation. The values of initial and average diffusion coefficients (i.e. earlier stages diffusion coefficients) have been observed higher than the late diffusion coefficients. The release of drug from polymer matrix starts when the dried drug loaded sample is placed in the release medium, the solvent diffuses into the outermost surface of the hydrogel with which it is in immediate contact. Subsequently, the polymer chains relaxation start the release of the drug into the external medium. With time the gel swell more and more with simultaneous release of the drug. Finally, the release rate becomes extremely slow as the swelling of the device approaches the limiting value. This is very important observation to develop the controlled drug delivery system. It means after maintaining certain concentration, the release of drug has occurred in a controlled manner and hence these hydrogels can be used to deliver the drug controlled and sustained manner. The conventional drug delivery systems do not provide ideal pharmacokinetic profiles especially for the drugs, which display high toxicity and narrow therapeutic windows. For such drugs, the ideal pharmacokinetic profile will be one wherein the drug concentration reaches therapeutic levels without exceeding the maximum tolerable dose and maintain its concentration for extended period until the desired therapeutic effect is reached. In an ideal case scenario, such a profile can be achieved by use of the slow drug releasing device which releases the drug in controlled and sustained manner to maintain the therapeutic level. In our earlier study, the modification of sterculia gum polysaccharide has been carried out with 2-hydroxyethylmethacrylate (HEMA) and acrylic acid (AAc) by radiation-induced crosslinking polymerization to develop the hydrogels for biomedical applications. The release of anti-diarrhea model drug ornidazole from the hydrogels was also occurred through non-Fickian diffusion mechanism (Singh & Sharma, 2009; Singh & Vashishtha, 2008).

4. Conclusion

It is concluded from the foregone discussion that composition of hydrogels and network density is affected by the synthetic reaction parameters which is evident from the swelling studies. The increase in total radiation dose has increased the crosslinking/network density in the hydrogels and due to this water uptake decreased. Swelling of the polymers and release of drug from polymers occurred through non-Fickian diffusion mechanism. In this mechanism, the rate of drug diffusion from the polymer matrix and rate of polymer chain relaxation are comparable. Further, values of the diffusion coefficients reflect that in the early stages the rate of release of drug from the polymer was higher than the latter stages and release of drug has occurred in controlled manner and hence these hydrogels can be exploited for developing the controlled and sustained drug delivery systems.

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