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# Development of novel hydrogels by functionalization of sterculia gum for use in anti-ulcer drug delivery

Baljit Singh *, Nisha Sharma

*Department of chemistry, Himachal Pradesh University, Shimla, HP 171005, India*

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ABSTRACT

In view of the pharmacological importance of sterculia gum and drug delivery devices based on hydrogels, the present study is an attempt to synthesize sterculia gum and poly(AAm) based hydrogels by using *N*,*N*′-MBAAm as crosslinker and ammonium persulfate as initiator. The polymeric networks were characterized by SEMs, FTIR and swelling studies. The release dynamics of model anti-ulcer drug (ranitidine hydrochloride) from the hydrogels has been studied for the evaluation of the release mechanism and diffusion coefficients. The values of the diffusion exponent '*n*' (0.43, 0.44 and 0.62) and gel characteristic constant '*k*' ($8.669 \times 10^{-2}$, $8.016 \times 10^{-2}$ and $2.964 \times 10^{-2}$) have been obtained, respectively, in distilled water, pH 2.2 buffer and pH 7.4 buffer. The release of drug from the hydrogels occurred through Fickian diffusion mechanism in distilled water and in pH 2.2 buffer, and through non-Fickian diffusion mechanism in pH 7.4 buffers.



## 1. Introduction

Natural gums are promising biodegradable, nontoxic, freely available and less expensive polymeric materials for use in drug delivery systems (Bhardwaj, Kanwar, Lal, & Gupta, 2000). However, these materials have certain drawbacks, like uncontrolled rate of hydration, thickening, drop in viscosity on storage, microbial contamination and require functionalization/modification to overcome these problems (Durso, 1980). 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 practices to modify and to improve the functional properties of polysaccharides and forms the three-dimensional polymeric networks (hydrogels), those swell quickly by imbibing a large amount of water (Mostafa & Morsy, 2004). Hydrogels based on polysaccharides have attracted the considerable attention for use in drug delivery (Cascone et al., 2001; Chen, Jo, & Park, 1995). Amount and type of polysaccharide backbone, monomer and crosslinker concentration affect the swelling ratio of the hydrogels (Mundargi, Patil, Agnihotri, & Aminabhavi, 2007; Mundargi, Patil, & Aminabhavi, 2007; Zhang, Wang, Lu, Yang, & Yan, 2005). Lower crosslinker concentration results in the formation of very loosely crosslinked networks which increase the swelling and decrease the gel strength (Das, Wadhwa, & Srivastava, 2006; Korsmeyer & Peppas, 1981; Zohuriaan-Mehr, Motazedi, Kabiri, & Ershad-Langroudi, 2005). The releasing medium such as simulated gastric fluid and simulated intestinal fluid affects the release pattern of the drugs from the formulations (Ji, Xu, & Wu, 2007). Chaurasia and coworkers (Chaurasia et al., 2006) have studied the in vitro release of methotrexate loaded crosslinked guar gum microspheres in phosphate-buffered saline, gastrointestinal fluid of different pH, and rat cecal content. Significant increase in drug release has been observed in medium containing rat cecal content (Das et al., 2006).

The use of natural gums such as xanthan gum (Verhoeven, Vervaet, & Remon, 2006), guar gum (George & Abraham, 2007), gum arabic (Chang, Leung, Lin, & Hsu, 2006), gellan gum (Agnihotri, Jawalkar, & Aminabhavi, 2006; Coviello, Alhaique, Dorigo, Matricardi, & Grassi, 2007) in drug delivery have been reported in the literature. Gum arabic has been investigated as sustained-release of drugs in tablets formulations and the release profile has further increased by coating the tablet with polyvinyl acetate and ethylene vinyl acetate (Baveja, Ranga Rao, & Arora, 1988). Due to gelling property of gum arabic, rate of release has been decreased as the amount of gum arabic in the pellets increased (Ray, Batra, Bhowmick, & Behra, 1994). The formulations coated with guar gum degraded in dissolution medium containing rat cecal contents and have affected the release dynamics (Krishnaiah, Muzib, Rao, Bhaskar, & Satyanarayana, 2003). Guar gum alone has not efficiently controlled the release dynamics of the drug release. Preparations

* Corresponding author. Tel.: +91 1772830944; fax: +91 1772633014.
*E-mail address:* baljitsinghhpu@yahoo.com (B. Singh).

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of enteric coated matrix tablets with gums containing polymeric matrix formed by the grafting of methacrylic acid on to gums have showed enhanced release rates in the simulated colonic fluids because of the microbial degradation or polymer solubilization phenomena (Mundargi, Patil, & Agnihotri, et al., 2007; Mundargi, Patil, & Aminabhavi, 2007). The sterculia gum has been used to control the release of varying proportions of two model drugs, caffeine and diclofenac sodium, which have different solubility in aqueous medium (Munday & Cox, 2000).

Sterculia gum, is a medicinally important naturally occurring polysaccharide, composed of galacturonic acid, beta-D-galactose, glucuronic acid, L-rhamnose, and other residues (Weiping, 2000). It exudes from the tree *Sterculia urens*, belongs to the family 'Sterculiaceae' and is commonly known as karaya or sterculia etc. (Leung, 1980). Sterculia gum has unique features such as high swelling and water retention capacity, high viscosity, inherent nature of anti-microbial activity and abundant availability (Gauthami & Bhat, 1992). It has been used in the treatment of diarrhea (Huttel, 1983), ulcers (Love-Mignogna & Wind, 1978; May, 1982; Zide & Bevin, 1980), irritable bowel syndrome (Capron, Zeitoun, & Julien, 1981), chronic colonic diseases (Guerre & Neuman, 1979; Hunold, 1979) reducing cholesterol and improving glucose metabolism without adversely affecting most mineral balances (Behall, 1990; Behall, Scholfield, Lee, Powell, & Mores, 1987). Sterculia gum is an effective bulk laxative as the gum particles absorb water about 100 times of their original volume. In absorbing water the coarse particles swell enormously, forming a discontinuous type of mucilage that is very effective as a laxative (Meier, Seiler, & Stahelin, 1990; Verbeken, Dierckx, & Dewettinck, 2003). The swelling profile of sterculia gum has been used to produce denture adhesive and a bulk laxative (Park & Munday, 2004). In adhesive property, it has reduced 97 percent adhesion of *Streptococcus salivarius* to dentures in vivo (Wilson & Harvey, 1989) and has improved the adhesion in ileostomy and colostomy appliances (Kanamori et al., 2007).

In view of the pharmacological importance of sterculia gum and drug delivery devices based on hydrogels, sterculia gum, if suitably tailored to prepare the hydrogels, can act as the potential candidate for the novel drug delivery systems. Modification of the sterculia gum to develop the hydrogels is not much reported in the literature and the potential of sterculia gum to develop the drug delivery systems has not been explored. Therefore, the present study is an attempt, to synthesize sterculia gum and poly(AAm) based hydrogels by using *N*,*N*′-MBAAm as crosslinker and ammonium persulfate (APS) as initiator. The polymeric networks thus formed were named as sterculia-*cl*-poly(AAm) hydrogels thereafter, and have been characterized by FTIR and swelling studies. Swelling kinetics of the hydrogels has been studied as function of monomer concentration, initiator concentration, amount of sterculia and crosslinker concentration. Effect of pH and [NaCl] on swelling kinetics has also been studied. The release dynamics of model drug ranitidine hydrochloride from hydrogels has been studied for the evaluation of the release mechanism and diffusion coefficients.

## 2. Experimental

### 2.1. Materials and methods

Acrylamide (AAm) was obtained from Merck-Schuchardt, Germany. Ammonium persulphate (APS) was obtained from Qualigens Fine Chemicals Mumbai-India and *N*,*N*′-methylenebisacrylamide (*N*,*N*′-MBAAm) was obtained from Sisco Research Laboratory Pvt. Ltd. Mumbai, India. Ranitidine hydrochloride was obtained from the Scott-Edil Pharmacia Ltd. Himachal Pradesh, India. Sterculia gum was obtained from herbal medical store.

### 2.2. Synthesis of sterculia-cl-poly (AAm) polymers

Reaction was carried out with 1 g of sterculia gum, definite concentration of APS, definite concentration of monomer and crosslinker in 10 mL distilled water taken in test tube at 65 °C temperature for 2 h. The polymers thus formed were stirred for two hours in distilled water and for two hours in ethanol to remove the soluble fractions in the polymers and were than dried in oven at 40 °C. These polymers were named as [sterculia-*cl*-poly(AAm)]. The optimum reaction parameters were evaluated for the synthesis of sterculia-*cl*-poly(AAm) by varying [AAm] (from 0.281 to 1.407 mol/L), [APS] (from 4.386 to 21.930 mMol/L), amount of sterculia from 0.2 to 1.0 g and [*N*,*N*′-MBAAm] (from 6.486 to 32.432 mMol/L). These reaction parameters were evaluated on the basis of the swelling of the hydrogels after 24 h in distilled water, and shape and structural integrity maintained by the hydrogels during swelling. The optimum reaction conditions for the synthesis of sterculia-*cl*-poly(AAm) were obtained as [AAm] = 1.125 mol/L, [APS] = 13.158 mMol/L, sterculia gum = 0.8 g and [*N*,*N*′-MBAAm] = 6.486 mMol/L. Further sterculia-*cl*-poly(-AAm) hydrogels were synthesized at the optimum reaction conditions and were used to study the swelling kinetics hydrogels and release dynamics of drug from the hydrogels in different pH buffer.

### 2.3. Characterization

Sterculia gum and sterculia-*cl*-poly(AAm) polymers were characterized by the Scanning Electron Micrography (SEM), Fourier Transform Infrared Spectroscopy (FTIR) and swelling studies. To investigate and compare the surface morphology of sterculia gum and sterculia-*cl*-poly(AAm), SEMs were taken on ZEISS EVO 50 Microscope. FTIR spectra of sterculia and sterculia-*cl*-poly(AAm) polymers were recorded in KBr pellets on Nicolet 5700FTIR (THERMO).

Swelling of the polymeric networks was carried out in triplicate by gravimetric method. Known weight of polymers were taken and immersed in excess of distilled water 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 amount of water uptake by the polymers after definite time intervals. Swelling behavior of the polymer networks was studied as function of monomers concentration, initiator concentration, amount of sterculia and crosslinker concentration. Effect of pH and [NaCl] on swelling kinetics was also studied.

### 2.4. Release dynamics of the model drug

#### 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) at $\lambda_{max}$ 313 nm and calibration graph was constructed. The concentration of the drug (ranitidine hydrochloride) in the sample solution was read from the graph as the concentration corresponding to the absorbance of the solution. Three calibration graphs were made in distilled water, pH 2.2 buffer and pH 7.4 buffer to determine the amount of drug release from the drug-loaded polymeric matrix in these medium.

#### 2.4.2. Drug loading to the 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 (Singh, 2007).

*2.4.3. Drug release from polymer matrix*

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 drug released was measured spectrophotometrically in distilled water, pH 2.2 buffer and pH 7.4 buffer after every 30 min in each case (Singh, 2007).

*2.4.4. Preparation of buffer solution*

Buffer solution of pH 2.2 was prepared by taking 50 mL of 0.2 M KCl and 7.8 ml of 0.2 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 (Pharmacopoeia of India, 1985).

*2.5. Mechanism and mathematical modeling of drug release from polymer matrix*

Based on the relative rate of diffusion of water into polymer matrix and rate of polymer chain relaxation, swelling of the polymers and the drug release profiles from the swelling polymers have been classified into three types of diffusion mechanisms (Alfrey, Gurnee, & Lloyd, 1966; Peppas & Korsmeyer, 1987) These mechanisms are Case I or Simple Fickian Diffusion, Case II Diffusion and Non-Fickian or Anomalous Diffusion (Ritger & Peppas, 1987a; Ritger & Peppas, 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 constants. 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. Ritger and Peppas have showed that the above power law expression could be used for the evaluation of drug release from swellable systems. In this case, $M_t/M_\infty$ replace $M_s$ in above equation to give Eq. (2). For cylindrical shaped hydrogels, the initial diffusion coefficients ($D_i$), average diffusion coefficient $D_A$ and late diffusion coefficients have been calculated from the Eqs. (3)–(5), respectively.

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

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

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

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

where $M_t/M_\infty$ 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 $M_\infty$ is drug released at time '$t$' and at equilibrium, respectively, $D$ is the initial diffusion coefficient and '$\ell$' is the thickness of the sample. $t^{1/2}$ is the time required for 50% release of drug (Ritger & Peppas, 1987a; Ritger & Peppas, 1987b). The values of diffusion coefficients have been evaluated for the swelling of the polymer and for the release of the drug from the polymer and results are presented in Tables 1 and 2.

## 3. Results and discussion

*3.1. Characterization*

The morphology of sterculia and sterculia-*cl*-poly(AAm) was examined by SEMs and is presented in the Fig. 1a and b, respec-

**Table 1**
Results of diffusion exponent '$n$', gel characteristic constant '$k$' and various diffusion coefficients for the swelling kinetics of sterculia-*cl*-poly(AAm) hydrogels in different medium at 37 °C

| S. No. | Parameter | Diffusion exponent '$n$' | Gel characteristic constant '$k$' $\times 10^2$ | Diffusion coefficients ($Cm^2\ min^{-1}$) | | |
|---|---|---|---|---|---|---|
| | | | | Initial $D_i \times 10^4$ | Average $D_A \times 10^4$ | Late time $D_L \times 10^4$ |
| *Effect of [AAm]* | | | | | | |
| 1 | 0.281 M/L | 0.50 | 3.357 | 1.994 | 3.864 | 0.340 |
| 2 | 0.563 M/L | 0.50 | 3.412 | 2.047 | 3.992 | 0.348 |
| 3 | 0.844 M/L | 0.50 | 3.483 | 3.533 | 7.671 | 0.620 |
| 4 | 1.125 M/L | 0.50 | 3.504 | 8.014 | 15.263 | 1.369 |
| 5 | 1.407 M/L | 0.47 | 3.793 | 8.837 | 17.069 | 1.445 |
| *Effect of [APS]* | | | | | | |
| 1 | 4.386 mM/L | 0.50 | 3.504 | 8.014 | 15.263 | 1.369 |
| 2 | 8.772 mM/L | 0.56 | 2.014 | 9.378 | 18.077 | 1.563 |
| 3 | 13.158 mM/L | 0.57 | 2.042 | 10.857 | 19.746 | 1.757 |
| 4 | 17.544 mM/L | 0.56 | 2.075 | 8.444 | 15.850 | 1.395 |
| 5 | 21.930 mM/L | 0.54 | 2.845 | 10.289 | 17.555 | 1.662 |
| *Effect of amount of sterculia* | | | | | | |
| 1 | 0.2 g | 0.53 | 2.198 | 4.635 | 10.555 | 0.853 |
| 2 | 0.4 g | 0.52 | 2.773 | 8.385 | 16.895 | 1.454 |
| 3 | 0.6 g | 0.50 | 3.342 | 7.900 | 16.657 | 1.398 |
| 4 | 0.8 g | 0.50 | 3.516 | 9.318 | 20.588 | 1.693 |
| 5 | 1.0 g | 0.57 | 2.042 | 10.857 | 19.746 | 1.757 |
| *Effect of [N,N′-MBAAm]* | | | | | | |
| 1 | 6.486 mM/L | 0.50 | 3.516 | 9.318 | 20.588 | 1.693 |
| 2 | 12.973 mM/L | 0.56 | 2.173 | 13.404 | 25.087 | 2.211 |
| 3 | 19.459 mM/L | 0.53 | 2.655 | 12.926 | 24.629 | 2.168 |
| 4 | 25.945 mM/L | 0.53 | 2.410 | 10.555 | 22.159 | 1.852 |
| 5 | 32.432 mM/L | 0.60 | 2.061 | 16.707 | 25.771 | 2.545 |
| *Effect of pH* | | | | | | |
| 1 | Distilled water | 0.50 | 3.516 | 9.318 | 20.588 | 1.693 |
| 2 | pH 2.2 buffer | 0.50 | 2.624 | 8.456 | 19.494 | 1.571 |
| 3 | pH 7.4 buffer | 0.50 | 2.904 | 8.736 | 20.323 | 1.618 |
| *Effect of salt* | | | | | | |
| 1 | Distilled water | 0.50 | 3.516 | 9.318 | 20.588 | 1.693 |
| 2 | 0.9% NaCl | 0.50 | 2.754 | 8.903 | 20.211 | 1.637 |

**Table 2**
Results of diffusion exponent '*n*', gel characteristic constant '*k*' and various diffusion coefficients for the release of ranitidine hydrochloride from drug-loaded sterculia-*cl*-poly(AAm) hydrogels in different medium at 37 °C

| S. No. | Drug releasing medium | Diffusion exponent '*n*' | Gel characteristic constant '*k*' × $10_2$ | Diffusion coefficients ($Cm^{-2}$ $Min^{-1}$) | | |
|---|---|---|---|---|---|---|
| | | | | Initial $D_i \times 10^4$ | Average $D_A \times 10^4$ | Late time $D_L \times 10^4$ |
| 1 | Distilled water | 0.43 | 8.669 | 25.857 | 5.585 | 6.627 |
| 2 | pH 2.2 buffer | 0.44 | 8.016 | 30.691 | 5.760 | 7.576 |
| 3 | pH 7.4 buffer | 0.62 | 2.964 | 47.499 | 4.520 | 8.646 |

tively. It is observed from the SEMs that sterculia has smooth and homogeneous morphology whereas modified sterculia has structural heterogeneity.

FTIR spectra of sterculia and sterculia-*cl*-poly(AAm) were recorded to study the modification of the sterculia and are presented in Fig. 2a and b, respectively. The broad absorption bands at 3427.5 $cm^{-1}$ was observed due to —OH stretching which indicated association in the polymeric networks. Absorption bands due to C═O stretching of amide has been observed at 1670.1 $cm^{-1}$ in sterculia-*cl*-poly(AAm) apart from the usual peaks in sterculia gum.

### 3.2. Swelling kinetics of sterculia-cl-poly(AAm) hydrogels

Swelling parameters are the most important factor for hydrogel characterization, because a fundamental relationship exists between the swelling of a polymer and the nature of the swelling medium. In order to evaluate the optimum reaction parameters for the synthesis of sterculia-*cl*-poly(AAm) hydrogels, swelling of the hydrogels and structural integrity maintained by the hydrogels after 24 h swelling were taken as the criteria. Swelling of the polymers was studied as a function of [AAm], [APS], amount of sterculia, [*N*,*N*′-MBAAm] in the polymer matrix and as a function of pH and [NaCl] of the swelling medium.

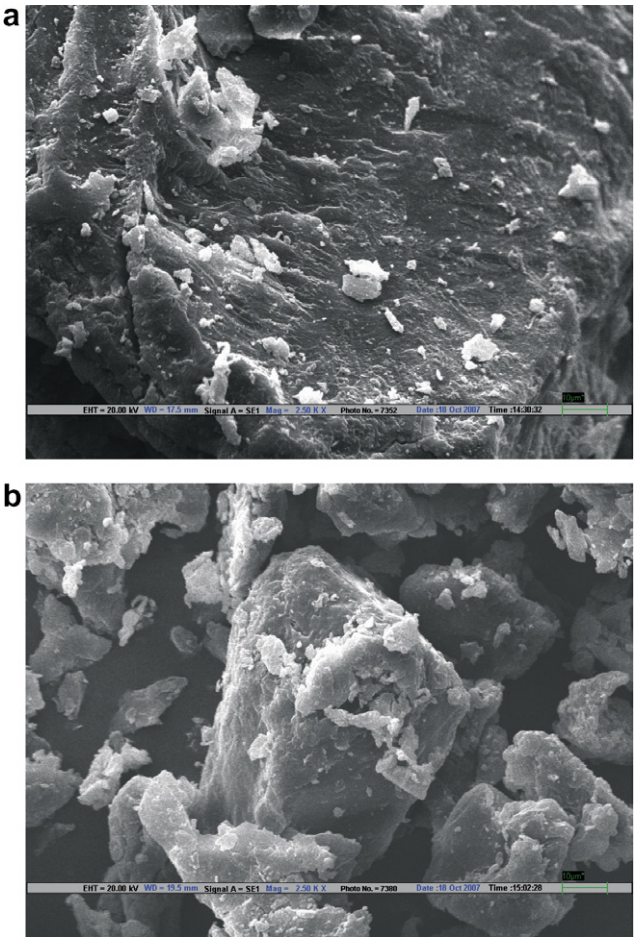


**Fig. 1.** (Singh and Sharma) Scanning electron micrograph of (a) sterculia gum (b) sterculia-*cl*-poly(AAm).

#### 3.2.1. Swelling as a function of monomer concentration

Effect of monomer concentration, used during the synthesis of hydrogels, on the swelling of the crosslinked polymers was studied as a function of [AAm] and results are presented in the Fig. 3.1. It has been observed from figure that swelling of polymer decreases with increase in monomer concentration in the polymer matrix. After 24 h, maximum (16.04 ± 2.05 g) water uptake has occurred by per gram of the polymer prepared with 0.281 mol/L of [AAm] but structural integrity has not been maintained by the hydrogels after 24 h swelling. Therefore, in the present case optimum concentration for the further synthesis of polymers was taken as 1.125 mol/L. At this concentration maximum water uptake (12.20 ± 1.46 g) has occurred after 24 h swelling and hydrogels have maintained its cylindrical shape. The values of diffusion exponent '*n*' and gel characteristic constant '*k*' have been evaluated from the slope and the intercept of the plot ln $M_t/M_\infty$ versus ln *t* and the results are presented in the Table 1. It is clear from the values of the '*n*' that the Fickian diffusion mechanism has occurred for the hydrogels prepared with different monomer concentration. The values of diffusion coefficients are presented in the Table 1.

#### 3.2.2. Swelling as a function of initiator

At the optimum monomer concentration, to observe the effect of initiator concentration on the network formation, the hydrogels were prepared with different initiator concentration. The [APS] was varied from 4.386 to 21.930 mMol/L and effect of this variation on the swelling of sterculia-*cl*-poly(AAm) hydrogels is presented in Fig. 3.2. Swelling of the polymer matrix decreases as the concentration of initiator increased during the synthesis of polymeric networks. This may be due to the reason that higher concentration of the initiator has started the formation of number of polymer chains which has decreased the chain length and affected the network formation. The maximum (13.25 ± 0.52 g) water uptake has occurred for the hydrogels prepared with 13.158 mMol/L of [APS]. It is clear from the values of the diffusion exponent that diffusion of water molecule from the polymer matrix occurred through non-Fickian type diffusion mechanism. The values of the initial and average diffusion coefficients have been obtained higher than the late diffusion coefficients which indicate that in the starting the rate of swelling of polymer matrix was higher than the latter stages of swelling.

#### 3.2.3. Swelling as a function of amount of sterculia gum

In order to study the effect of amount of sterculia gum on the structure of the polymer, the hydrogels were prepared with different gum contents and their swelling was taken in distilled water at 37 °C. Polymers were synthesized by varying the of sterculia gum from 0.2 to 1.0 g and results are presented in Fig. 3.3. The swelling of the polymers increases with the increase in sterculia contents in the composition of polymer matrix. This is probably due to the reason that higher degree of gum hydration has occurred in the hydrogels prepared with higher gum contents, which has increased the

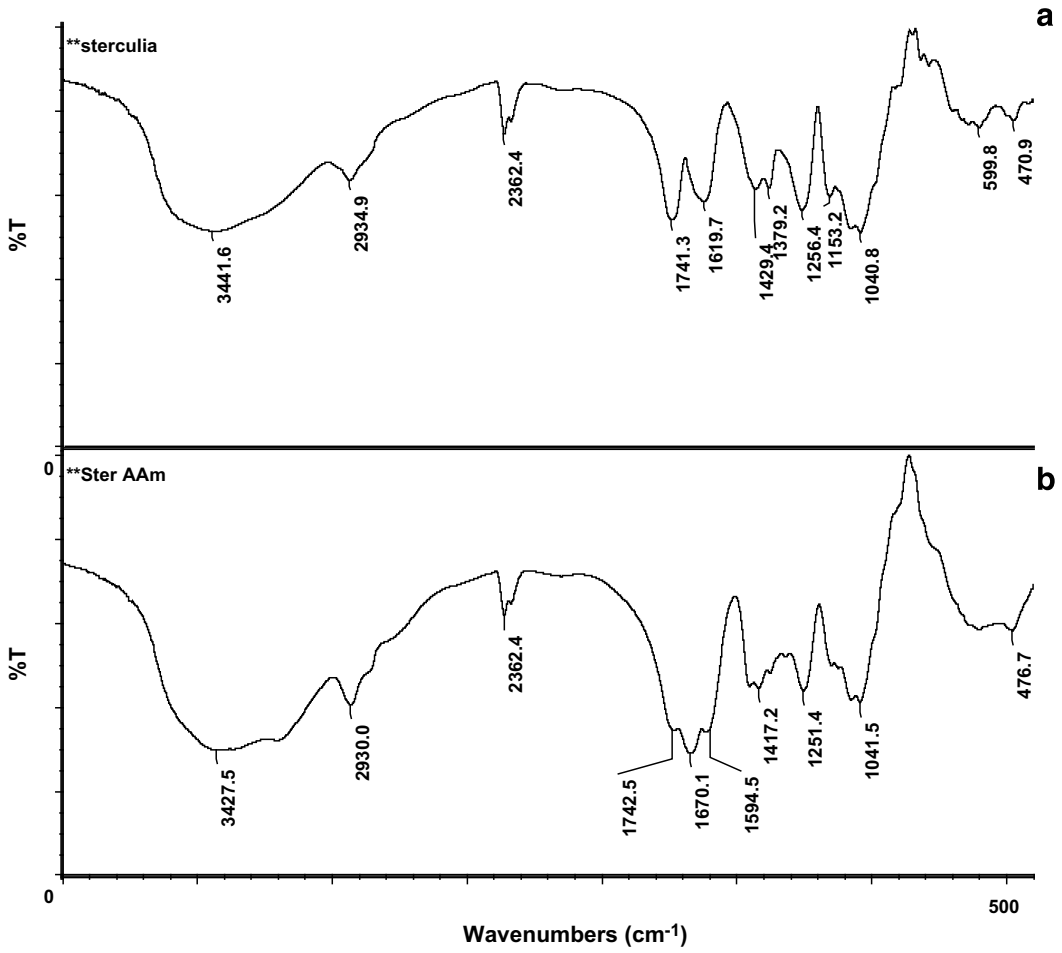


**Fig. 2.** (Singh and Sharma) FTIR spectra of (a) sterculia gum (b) sterculia-*cl*-poly(AAm).

number of intimate contacts between particle of gum and water, and led to high swelling (Patel & Patel, 2007). Maximum (12.62 ± 0.94 g) water uptake has occurred in the matrix prepared with 0.8 g of sterculia gum. The diffusion of water from the polymer matrix occurred through Fickian diffusion mechanism.

*3.2.4. Swelling as a function of [N,N′-MBAAm]*

At the optimum concentration of monomer, initiator and sterculia gum, the polymers were prepared with different crosslinker concentration. The polymer networks were prepared by varying the crosslinker concentration from 6.486 to 32.432 mMol/L. Swelling of the sterculia-*cl*-poly(AAm) was studied as a function of [*N*,*N*′-MBAAm] at 37 °C and the results are presented in the Fig. 3.4. It has been observed from the figure that swelling decreases with the increase in the concentration of crosslinker in the polymer matrix. This is due to the fact that with the increase in the concentration of crosslinker, crosslinking density increases which decreases the pore size in the crosslinked matrix and thereafter decreases the swelling in the polymer. Maximum amount of water uptake (12.62 ± 0.94) per gram of gel has occurred in case of polymer prepared with 6.486 mMol/L of [*N*,*N*′-MBAAm]. The values of diffusion exponent '*n*' is greater than 0.5, which indicate a non-Fickian type of diffusion mechanism occurred for the diffusion of water molecules in the polymer matrix prepared with different crosslinker concentration. The values of the diffusion coefficients for the swelling of the hydrogels prepared as a function of [*N*,*N*′-MBAAm] are presented in Table 1. It has been observed from the table that the values obtained for initial and average diffusion coefficient are higher than the late diffusion coefficient.

*3.2.5. Swelling as a function of pH and [NaCl] of the swelling medium*

At the optimum reaction conditions, polymers were synthesized and were used to study the effect of reaction medium on the swelling mechanism. The swelling of polymers in different

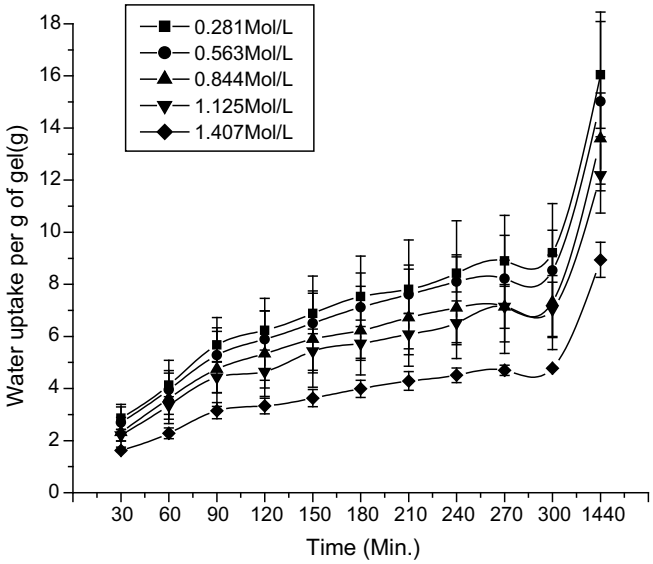


**Fig. 3.1.** (Singh and Sharma) Effect of [AAm] on swelling kinetics of sterculia-*cl*-poly(AAm) hydrogels in distilled water at 37 °C. {Sterculia gum = 1 g, [APS] = 4.386 mMol/L, [*N*,*N*′-MBAAm] = 6.486 mMol/L}.

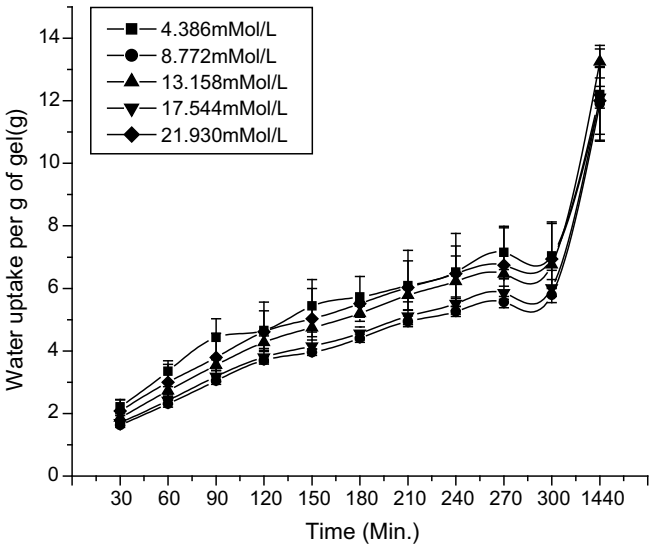


**Fig. 3.2.** (Singh and Sharma) Effect of [APS] on swelling kinetics of sterculia-*cl*-poly(AAm) hydrogels in distilled water at 37 °C.{Sterculia gum = 1 g, [AAm] = 1.125 Mol/L, [*N*,*N*′-MBAAm] = 6.486 mMol/L}.

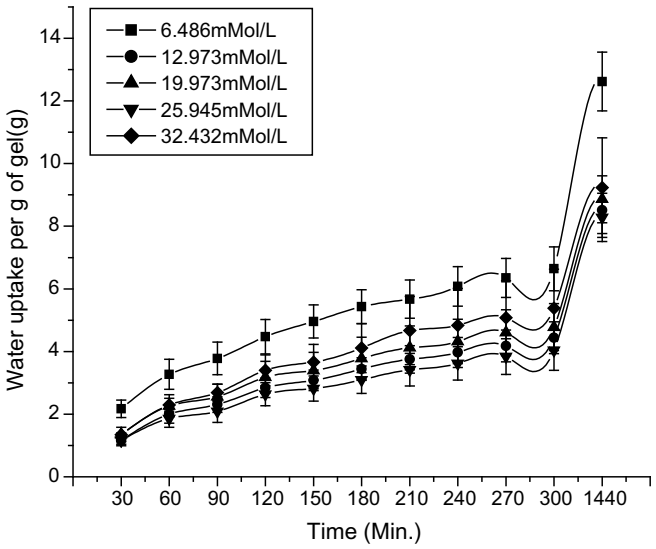


**Fig. 3.4.** (Singh and Sharma) Effect of [*N*,*N*′-MBAAm] on swelling kinetics of sterculia-*cl*-poly(AAm) hydrogels in distilled water at 37 °C. {Sterculia gum = 0.8 g, [APS] = 13.158 mMol/L, [AAm] = 1.125 Mol/L}.

pH and salt solution are presented in Figs. 3.5 and 3.6, respectively. When the effect of pH was studied the swelling was carried out in distilled water, pH 2.2 buffer, and pH 7.4 buffer for 24 h at 37 °C. It has been observed from the figure that swelling increases with increase in pH of the swelling medium and maximum (12.62 ± 0.94 g), (8.69 ± 0.54 g) and (10.05 ± 1.27 g) water uptake per gram of gel has occurred in distilled water, pH 2.2 buffer, pH 7.4 buffer, respectively. At lower pH, the —$CONH_2$ groups do not ionize and keep the network at its collapse state. At high pH solution, these groups get partially ionize, and the charged —COO— groups repel each other and cause more swelling of the polymer. To study the effect of salt concentration, swelling of the hydrogels was carried out in 0.9% NaCl at 37 °C and amount of water uptake by per gram of gel in salt solution was observed less as compared to the distilled water. In distilled water and 0.9% [NaCl] per gram of the gel has taken maximum (12.62 ± 0.94 g) and (8.63 ± 1.08 g) water, respectively.

The values of the diffusion exponent '*n*' has been obtained 0.5 in all the three mediums i.e. in distilled water, pH 2.2 buffer, and pH 7.4 buffer. These values show that swelling of the hydrogels occurred through Fickian type mechanism all the three releasing mediums. The values of the gel characteristic constant are different in different swelling medium which indicate that the polymer matrix showing different behavior in these mediums. In salt solution, hydrogel shows Fickian diffusion mechanism. In Fickian type diffusion mechanism the rate of diffusion of water molecules into the polymer matrix is much less than that of rate of relaxation of polymeric chains. The values of the initial diffusion coefficient, average diffusion coefficient and late diffusion coefficients for the swelling of sterculia-*cl*-poly(AAm) are presented in Table 1. In each swelling medium values of the initial and average diffusion coefficient have been observed higher than the other coefficients. It means the ini-

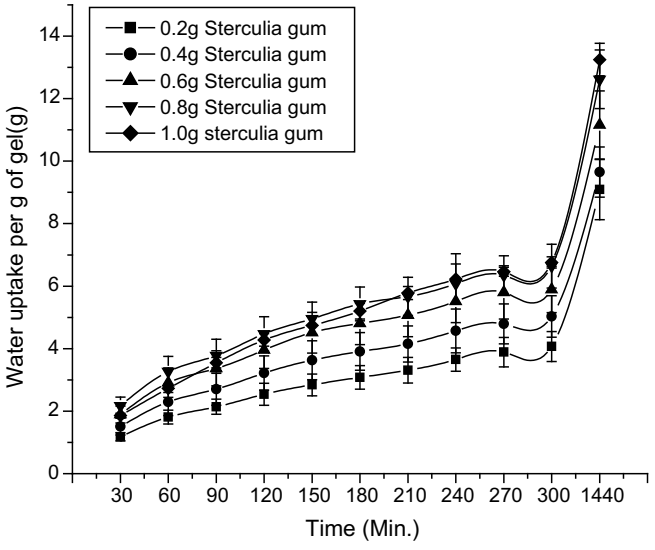


**Fig. 3.3.** (Singh and Sharma) Effect of amount of sterculia gum on swelling kinetics of sterculia-*cl*-poly(AAm) hydrogels in distilled water at 37 °C. {[AAm] = 1.125Mol/L [APS] = 13.158 mMol/L, *N*,*N*′-MBAAm] = 6.486 mMol/L}.

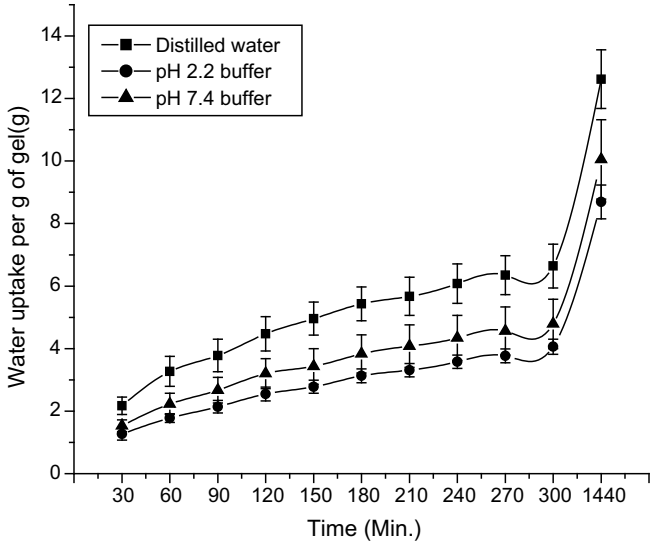


**Fig. 3.5.** (Singh and Sharma) Effect of pH on swelling kinetics of sterculia-*cl*-poly(AAm) hydrogels at 37 °C. {Sterculia gum = 0.8 g, [AAm] = 1.125 Mol/L, [APS] = 13.158 mMol/L, [*N*,*N*′-MBAAm] = 6.486 mMol/L}.

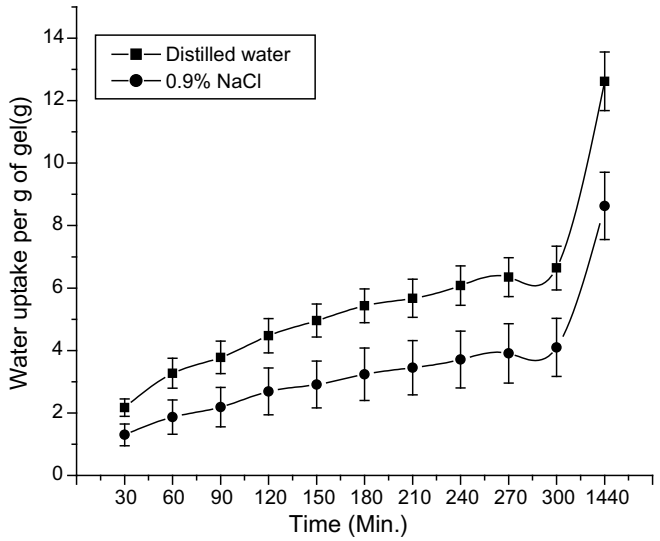


**Fig. 3.6.** (Singh and Sharma) Effect of [NaCl] on swelling kinetics of sterculia-*cl*-poly(AAm) hydrogels at 37 °C. {Sterculia gum = 0.8 g, [AAm] = 1.125 Mol/L, [APS] = 13.158 mMol/L, [*N*,*N*′-MBAAm] = 6.486 mMol/L}.

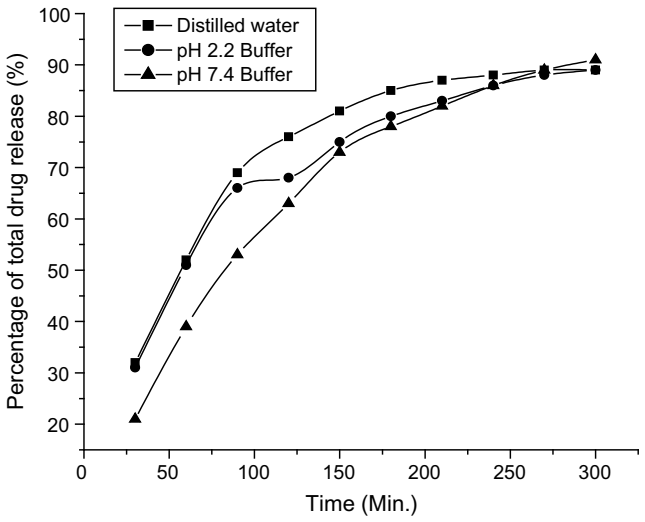


**Fig. 4.2.** (Singh and Sharma) Percentage of the total release of ranitidine hydrochloride from drug-loaded sterculia-*cl*-poly(AAm) hydrogels in different medium at 37 °C.

tial rate of diffusion of water molecule in the polymer matrix was higher than the late stages.

### 3.3. In vitro release dynamics of ranitidine hydrochloride

In vitro release profile of ranitidine hydrochloride from per gram of the drug-loaded hydrogel was studied in distilled water, pH 2.2 buffer and pH 7.4 buffer and results are presented in Fig. 4.1. It has been observed from the figure that the amount of drug released from per gram of the gel is higher in pH 2.2 solution as compared to the release of drug in solution of pH 7.4 and in distilled water. The trends obtained are not corresponding to the swelling pattern of the sterculia-*cl*-poly(AAm) hydrogels where the swelling has been observed higher in distilled water and pH 7.4 buffer. This may be due to the more solubility of ranitidine hydrochloride in pH 2.2 buffer. Fifty percent of the total release of the drug occurred in 47, 59 and 88 min in distilled water, pH 2.2 buffer and in pH 7.4 buffer, respectively (Fig. 4.2).

The diffusion exponent '*n*' and gel characteristic constant '*k*' has been obtained from the slope and intercept of the plot of ln $M_t/M_\infty$ versus ln *t*, for the release of ranitidine hydrochloride from the hydrogels (Fig. 4.3). The diffusion exponent '*n*' have 0.43, 0.44 and 0.62 values and gel characteristic constant '*k*' have $8.669 \times 10^{-2}$, $8.016 \times 10^{-2}$ and $2.964 \times 10^{-2}$ values in distilled water, pH 2.2 buffer and pH 7.4 buffer. It is clear from the values of the '*n*' that the release of drug from the drug-loaded hydrogels occurred through Fickian diffusion mechanism in distilled water and in pH 2.2 buffer and non-Fickian type of diffusion mechanism in pH 7.4 buffer. The values of the diffusion coefficients for the release of drug from the hydrogels in different pH buffer are obtained from the Figs. 4.4 and 4.5, and are presented in Table 2. The values obtained for initial diffusion coefficient are higher than the average and late diffusion coefficient. Higher values of the initial diffusion

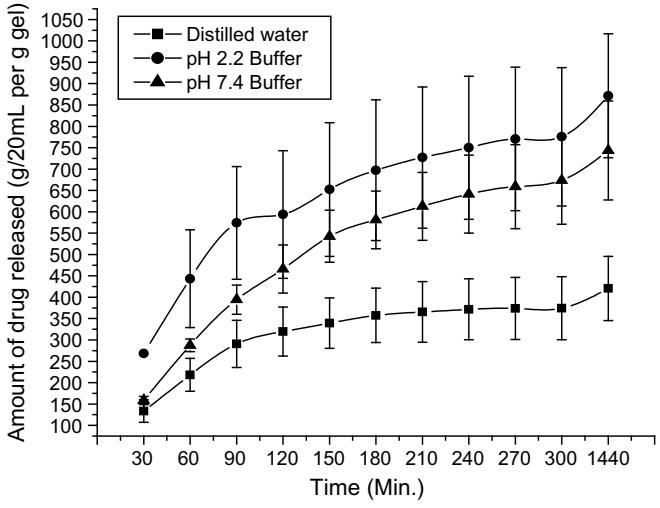


**Fig. 4.1.** (Singh and Sharma) Release profile of ranitidine hydrochloride from drug-loaded sterculia-*cl*-poly(AAm) hydrogels in different medium at 37 °C. {Sterculia gum = 0.8 g, [AAm] = 1.125 Mol/L, [APS] = 13.158 mMol/L, [*N*,*N*′-MBAAm] = 6.486 -mMol/L}.

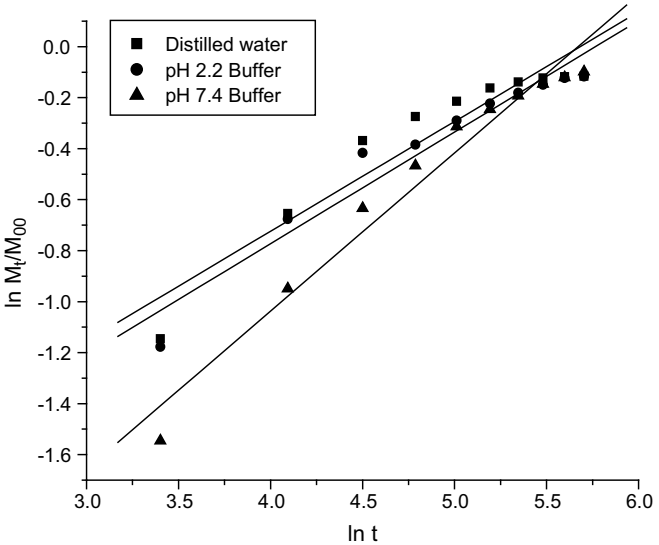


**Fig. 4.3.** (Singh and Sharma) Plot for the evaluation of diffusion exponent '*n*' and gel characteristic constant '*k*' for the drug release from sterculia-*cl*-poly(AAm) hydrogels in different medium at 37 °C.

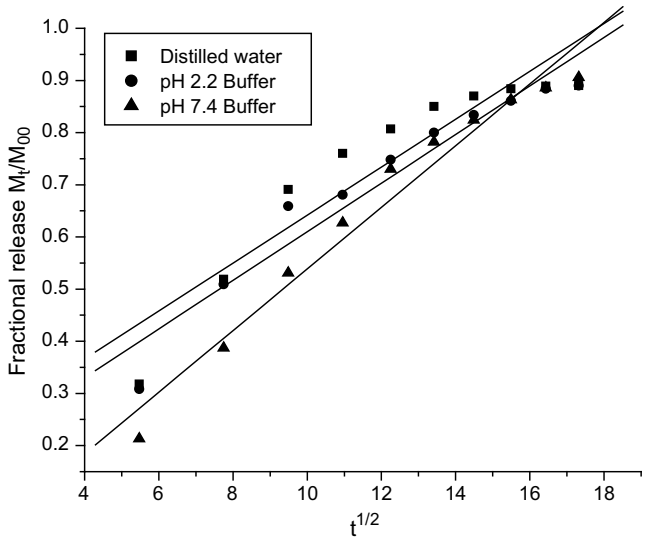


**Fig. 4.4.** (Singh and Sharma) Plot of $M_t/M_\infty$ versus $t$ for the evaluation of initial diffusion coefficient ($D_i$) for the drug release from sterculia-*cl*-poly(AAm) hydrogels in different medium at 37 °C.

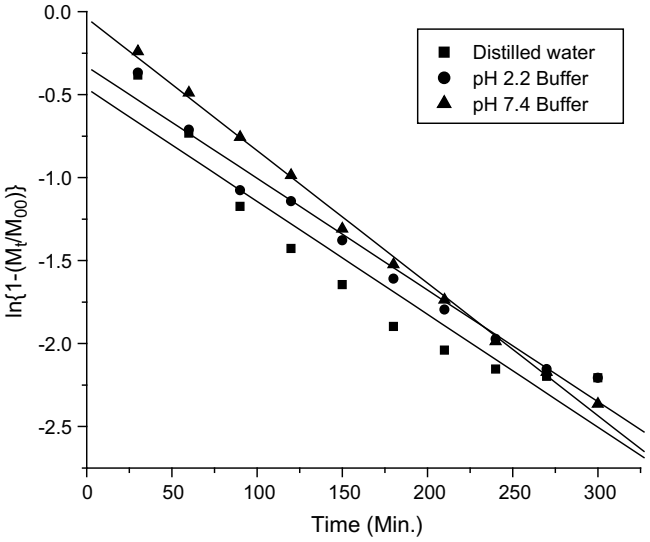


**Fig. 4.5.** (Singh and Sharma) Plot of $\ln\{1-(M_t/M_\infty)\}$ versus time for the evaluation of late diffusion coefficient ($D_L$) for the drug release from sterculia-*cl*-poly(AAm) hydrogels in different medium at 37 °C.

coefficient reflect that initially the rate of diffusion of drug from the polymer was higher than the rate of diffusion of drug from the later stages.

## 4. Conclusion

It is concluded from the foregone discussion that the composition of the hydrogels and pH of the swelling medium affects the swelling of the modified sterculia based hydrogels. During synthesis of polymer matrix the reaction parameters such as monomer concentration, initiator concentration, amount of sterculia gum and concentration of crosslinker have affected the pore size and network density which have been reflected in the swelling of the hydrogels. It is also concluded from the values of diffusion exponent '*n*' that swelling of the hydrogels and release of drug from the drug-loaded hydrogels occurred through Fickian type diffusion mechanism in distilled water and in pH 2.2 buffer. On the other hand, release of drug from polymer matrix in pH 7.4 buffer has occurred through non-Fickian type of diffusion mechanism. Further solubility of the drug also affects the release pattern.

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