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Surfactant modified poly (Acrylamide) hydrogels for ranitidine delivery

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ABSTRACT

Topical advances in drug delivery have been directed towards the design of number of drug delivery systems for treatment of various diseases. In the present invention, we describes the development of poly(acrylamide-co-surfactant) hydrogel for the incorporation of ranitidine drug for potential application in anti ulcer and treatment of other conventional diseases. For this purpose, poly(acrylamide-co-surfactant) hydrogels were prepared by polymerizing an aqueous solution of acrylamide (AM) in the presence of a reactive surfactant (Latemul PD 104) using ammonium persulfate /N,N,N,N-tetramethyl ethylenediamine (APS/TMEDA) as initiating system and N,N-methylenebisacrlyamide (MBA) as a cross-linker. The formation of hydrogels were confirmed by Fourier Transform infrared spectroscopy (FTIR) and scanning electron microscopic (SEM) studies. The variation in the hydrogel networks formation by changing the concentrations of synthetic parameters was verified with swelling property. The ranitidine drug release studies were observed with this surfactant modified hydrogel systems.

KEYWORDS

Hydrogels;
Surfactant;
Cross-linker;
Swelling kinetics;
Drug release.

INTRODUCTION

Pharmaceutical research has led to the development of novel drug delivery systems possessing several inherent advantages compared to conventional dosage formulations. This promoted to design novel experimental activities in the development of smart polymeric devices which are able to release drugs in a controlled manner under different sensitive environmental conditions. In this direction, particularly an intense research is going on concerning the development of surfactant modified hydrogels for controlled drug delivery. During the last decade, a number of studies were focused to understand the interaction between hydrogels and surfactants[1-4]. In general, hydrogels are three dimensional network polymeric materials containing a large number of hydrophilic groups capable of holding large amount of water in their three-dimensional networks. They swell many times by absorbing water and shrink on drying. By utilizing this inherent property, the hydrogels have been employed in wide variety of fields[5,6]. In addition to the conventional applications, the hydrogels are extended for immobilization of enzymes as well as for drug delivery systems[7-12].

For drug delivery applications, hydro-, micro- and nano-gels are constructed by introducing hydrophobic and hydrophilic repeating units in the gels for example, poly (N-isopropylacrylamide) gels, (PNIPAM gels). Such hydrogel systems have paid great attention for loading both hydrophilic and hydrophobic drugs and allows to control the release behavior by external stimuli, such as temperature, pH, ionic strength, electric and magnetic field, pressure, light intensity, solvent composition, and so on[13-15].

Recently various biodegradable polymeric nanoparticles and gel macromolecules have been developed and approved for cancer, ulcer, inflammatory and other conventional disease treatment[16-18].

Additionally, a few bottom-up approaches have been developed to obtain nano-ordered structures at the molecular level in materials, such as polymeric micelles, nanocapsules, physical nanogels, pluronic polymers, and core-shell polymers by self-assembly mechanisms in which hydrophobic and hydrophilic segments spontaneously associates to form nanostructures[18-22]. However, the effective function of these micelle systems as drug delivery carriers greatly depends on their stability, i.e., static structure of micelle. Considering the noble dynamic process of micellular molecules that determines the loading and release of drugs[19-23], it was noticed that the surfactant molecules can influence the hydrogel characteristics thereby promoting the drug releasing properties of the hydrogels. For example, the influence of a surfactant on the PNIPAM volume phase transition was actively studied[24-30]. Most of these studies were concerned with the interaction of surfactant molecules with modified PNIPAM linear chains. Generally, the surfactant molecules promotes both inter- and intramolecular solubility thereby increasing the phase transition temperature (T_c) with the increase of surfactant concentration. The interaction of the surfactant hydrophobic tails with the hydrophobic side groups or back bone of PNIPAM has been suggested to answer for these results. Khokhlov et al.[31] predicted that the interaction of a polyelectrolyte gel with an oppositely charged surfactant results in three effects. At lower concentration, the surfactant cannot form micelles inside the network and the gel behavior is similar to a solution of in low molecular-weight salts so as to shrink slightly. At higher concentration, the surfactant molecules inside the gel exceed the critical micelle concentration (CMC) so that the micelles are formed inside the network and the gel collapses because of decrease of the osmotic pressure exerted by the surfactant molecules. At still higher surfactant concentration, no additional micelles are formed inside the network and the network dimensions coincide with those of the neutral network.

From the above studies, it is confirmed that the surfactant molecules are in a position to influence the hydrogel characteristics, so that they may improve the drug loading and release characteristics of drugs. In view of this, our interest is to design modified poly (acrylamide) based hydrogels with a new surfactant for better drug delivery system. The study includes optimizing the various reaction parameters to obtain higher swelling characteristics to the hydrogels as well as to evaluate their drug delivery application, using a model drug (ranitidine).

EXPERIMENTAL

Materials

Acrylamide (AM), ammonium persulfate (APS) and N, N^1-methylenebisacryl amide (MBA) were supplied by S.D.Fine Chemicals Ltd (Mumbai, India). The surfactant (Latemul PD-104) was a kind gift from Ryuuhei Yoshikawa, Polymer Materials & Additives Chemical Company, Kao Corporation (Tokyo, Japan) (http://www.kao.co.jp/e/). N,N,N^1,N^1-tetramethylethylenediamine (TMEDA) was purchased from Aldrich Chemical Company Inc. (Milwaukee, WI, USA). All the chemicals were used as received. Double distilled water was used for all the hydrogels preparation as well as for the swelling studies.

Monomer, cross-linker, and initiator solutions

Monomer (AM) (1 g/2 ml distilled water), cross-linker (MBA) (1 g/100 ml distilled water), initiator (APS) (5 g/100 ml distilled water) and activator (TMEDA) (1 g/100 ml distilled water) solutions were prepared for the synthesis of hydrogels.

(a) Preparation of surfactant modified poly(acrylamiade) hydrogels

The surfactant modified poly (acrylamide) hydrogels were prepared at room temperature by redox co-po-

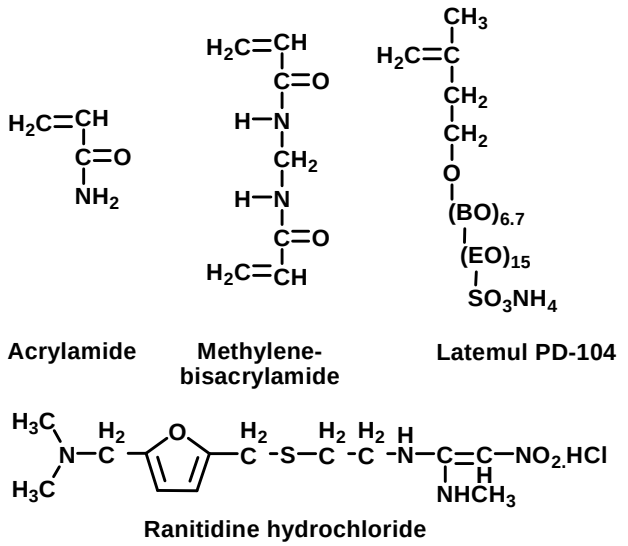


Figure 1 : Chemical structures of monomer, surfactant, cross-linker and drug molecules used to prepare hydrogels and drug loaded hydrogels

lymerization using AM as monomer, latemul PD-104 as reactive surfactant co-monomer, in the presence of a cross-linker (MBA) and an APS/TMEDA as redox initiating system. In typical series of reactions, 1 g of AM, different amounts of surfactant (0.1-1.0 g) were dissolved in 2 ml of distilled water in 100 ml beaker. To this solution, 1 ml of MBA (1 g/100 ml), 1 ml of APS (5 g/100 ml) and 1 ml of TMEDA (1 g/100 ml) solutions were added sequentially to the reaction mixture by stirring at 100 rpm on a magnetic stir plate. The polymerization was initiated instantaneously and the hydrogels were formed within 30 min. However, to get complete hard networks throughout the hydrogels the reactions were continued for about 8 hr. The hydrogels were purified by placing them in 1 liter beaker containing 500 ml DI water (re-filled fresh water for every 8 hr for a week) to extract the un-reacted monomer, the cross-linker, the surfactant, the initiator and the activator from the hydrogels. Finally, the hydrogels were dried and cut into small pieces for further studies.

In a similar fashion, the polymerization reactions were carried out by varying the reaction parameters such as concentration of MBA, APS and TMEDA. TABLE 1 provides the detailed information of various components used to synthesize the hydrogels and the hydrogel codes. Figure 1 provides the chemical structures of the monomer, surfactant, cross-linker and the drug.

Characterization of hydrogels

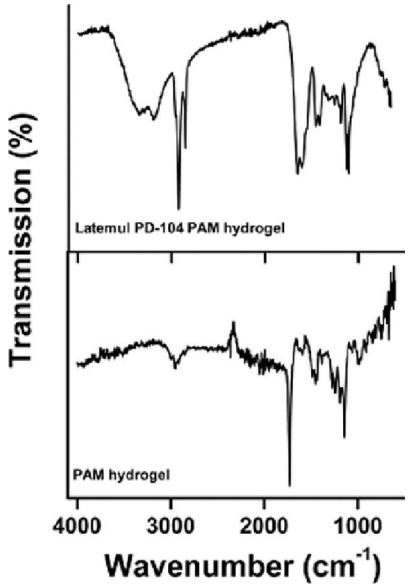


Figure 2 : FTIR spectrum of PAM hydrogel and surfactant modified poly(acrylamide) hydrogel (PAM-PM3)

(1) Fourier transform infrared spectroscopic analysis

FTIR spectrophotometer was used to determine the hydrogel formation, surfactant incorporation in hydrogel networks. To record the FTIR spectra of these hydrogels, the hydrogel samples (crushed powder) were completely dried in an oven (Baheti Enterprises, Hyderabad, India) at 60°C for 6 hr and were grinded with KBr to make pellets. The FTIR spectra were recorded between 600 to 4000 cm^{-1} on a Bruker IFS 66V FTIR spectrometer (Ettlingen, Germany) with scanning speed of 2 cm^{-1} per second. The average of 62 scans was presented as FTIR spectra.

(2) Scanning electron microscopic studies

To know the surface phenomenon and the morphological changes in hydrogels with surfactant modification, the hydrogel samples were coated with a thin layer of palladium gold alloy. These samples were observed under JEOL JSM 840A scanning electron microscope (Tokyo, Japan).

(3) Swelling studies

The conventional gravimetric method was employed to calculate the swelling ratio (S) of hydrogels[32]. Typically, about 20–30 mg of hydrogel was placed in 100 ml distilled water/swelling medium. The weight of swollen hydrogel was determined at different time intervals

and the swelling experiment was continued to a constant weight. The excess water was removed superficially by filter paper and then weighed accurately. By using the swelling experimental weights of hydrogels, the swelling ratios of hydrogels were calculated using the following equation.

$$\text{Swelling (S)} = [(W_s - W_d) / (W_d)]$$

where W_d and W_s denotes the weight of dry gel and swollen gel, respectively.

(4) Drug loading

Ranitidine hydrochloride is a (RH) (gift sample from Aurobindo Pharma Limited, Hyderabad, India), a hydrophilic drug (anti-ulcer) used to treat ulcers and gastroesophageal reflux disease (GERD)[33]. This drug was used as a model drug to load into the hydrogels. To load the drug, RH (10 mg/25 ml phosphate buffer solution PBS, pH 7.4) solution was employed.

The loading of RH into hydrogels was conducted by swelling equilibrium method. Typically, 50 mg of hydrogel sample was allowed to swell in ranitidine solution (10 mg/25 ml phosphate buffer solution, PBS, pH 7.4) for 24 hr. Then, the hydrogel was taken out from the drug solution and washed with 20 ml of water (3 times) to remove the excess of drug present on the surface of the hydrogel. Finally, the hydrogel was dried at room temperature for 48 h to obtain the release device. Drug encapsulation efficiency was calculated by using the remaining amount of drug solution after hydrogel loading was done. After removing the hydrogel from the drug solution, the remaining drug solution was analyzed by using Elico SL164 UV Spectrophotometer (The Science House, Hyderabad, India) at λ_{max} 315 nm. The encapsulation efficiency was calculated by using the following equation.

$$\text{\% Encapsulation efficiency} = \left(\frac{\text{\% Drug loading}}{\text{\% Theoretical loading}}\right) \times 100$$

(5) *In vitro* drug release

The *in vitro* drug release from drug loaded hydrogel formulations was investigated in PBS. These hydrogels were suspended in 5 ml PBS and transferred into dialysis tube (8 kD MWCO, 12 mm flat width, Spectrum Lab, Houston, TX). The sample within the dialysis bag was taken in a conical flask containing 50 ml of PBS as the dissolution medium on rotary shaker (REMI Instruments Limited, Vasai, India) at 100 rpm at 37°C. The amount of drug released from the hydrogels to the medium was determined by withdrawing 1 ml aliquots of the sample at selected specific time intervals. The volume withdrawn was immediately replaced with an equal volume of pre-warmed PBS solution at 37°C. The drug released samples were analyzed by using Elico SL164UV spectrophotometer (The Science House, Hyderabad, India) at λ_{max} 315 nm.

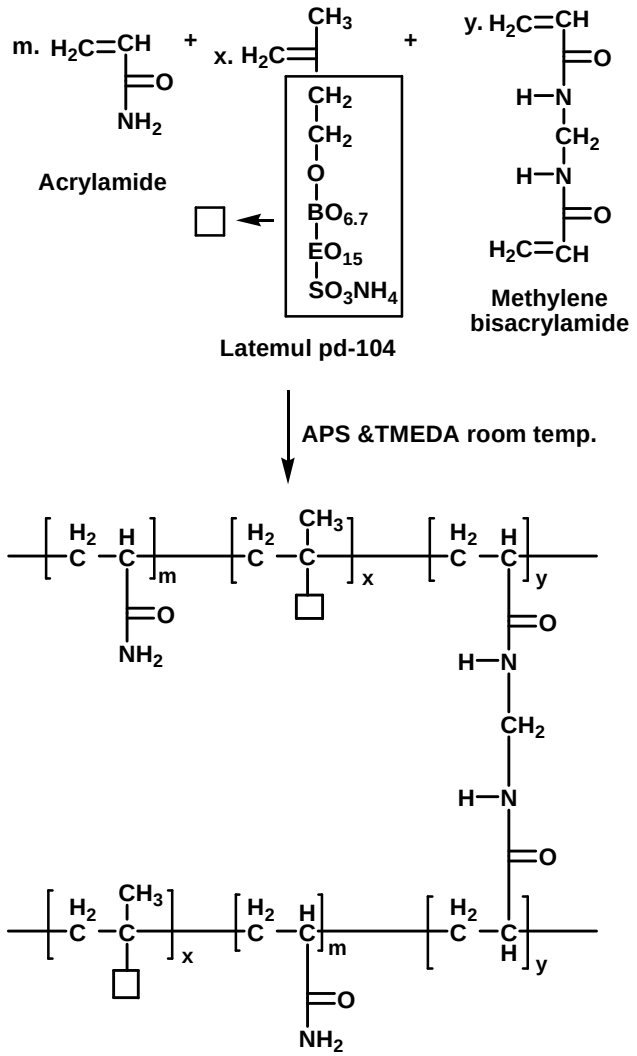
RESULTS AND DISCUSSION

The surfactant modified poly(acrylamide) hydrogels were prepared by solution redox copolymerization technique as described in the experimental section. Latemul PD-104 surfactant contains both hydrophilic (PEO) and hydrophobic (PBO) groups, which helps and affects the encapsulation of drugs as well as the drug release pattern from the hydrogel networks. This surfactant helps to load hydrophilic and hydrophobic drugs into hydrogels. The surfactant molecule contains a reactive double bond that involves in the polymerization and forms a co-polymer with acrylamide throughout the hydrogel networks. Since, surfactant units are linked together with acrylamide repeating units in the main cross-linked networks, it cannot escape from the hydrogel. The schematic representation of the reaction between acrylamide, surfactant and the cross-linker is represented in Scheme 1.

Preparation of hydrogels

Poly (acrylamide) (PAM) and Latemul PD-104 modified PAM hydrogels (PAM-PS1 to PAM-PS8; PAM-PM1 to PAM-PM7; PAM-PA1 to PAM-PA6; and PAM-PT1 to PAM-PT6) were prepared by redox-initiated free-radical cross-linking polymerization of aqueous mixtures of 1 mg of AM with different amounts of surfactant (Latemul PD-104), cross-linker (MBA), initiator (APS) and activator (TMEDA) for 30 min (TABLE 1). Most of the hydrogels were formed rapidly by the free radical cross-linking copolymerization within 30 min cure time following conventional redox initiating mechanism[30-32]. Such initiation is an efficient technique to produce hydrogels with low soluble contents.

FTIR spectra of hydrogels



Scheme 1 : Schematic illustration of hydrogel formation

FTIR spectroscopy was employed to find out the chemical repeating units present in hydrogels. Figure 2 depicts the FTIR spectrum of surfactant modified poly (AAm) hydrogel. A broad band is observed around 3184 cm^{-1} corresponding to hydrogen bonded N-H stretching of acrylamide/MBA repeating units. In addition, peaks are also observed at 1646 cm^{-1} and 1605 cm^{-1} corresponding to band I and band II of amide groups. The presence of peaks at 1115 cm^{-1} and 1093 cm^{-1} are assigned for -C-O-C- peaks of Latemul PD-104 surfactant molecule [poly(butylenes oxide) (PBO) and poly(ethylene oxide) (PEO) groups]. Typical peaks are also observed at 2918 cm^{-1} and 1449 cm^{-1} due to CH_2 stretching and CH_2 bending vibrations of the repeating units. Therefore, it is very clear from the FTIR analysis the incorporation of acrylamide (AM), surfactant (Latemul PD-104), and cross-linker (MBA) units throughout the hydrogel networks.

TABLE 1 : Composition of monomers, surfactant, cross-linker, and initiator/activators used to prepare hydrogels

Hydrogel code	Acrylamide (g)	Latemul PD-104 (g)	MBA (mM)	APS (mM)	TMEDA (mM)
Latemul PD-104 Variation					
PAM	1.0	NIL	0.648	2.18	0.86
PAM-PS1	1.0	0.1	0.648	2.18	0.86
PAM-PS2	1.0	0.2	0.648	2.18	0.86
PAM-PS3	1.0	0.3	0.648	2.18	0.86
PAM-PS4	1.0	0.4	0.648	2.18	0.86
PAM-PS5	1.0	0.5	0.648	2.18	0.86
PAM-PS6	1.0	0.6	0.648	2.18	0.86
PAM-PS7	1.0	0.8	0.648	2.18	0.86
PAM-PS8	1.0	1.0	0.648	2.18	0.86
MBA Variation					
PAM-M1	1.0	0.3	0.12	2.18	0.86
PAM-M2	1.0	0.3	0.259	2.18	0.86
PAM-M3	1.0	0.3	0.389	2.18	0.86
PAM-M4	1.0	0.3	0.518	2.18	0.86
PAM-M5	1.0	0.3	0.778	2.18	0.86
PAM-M6	1.0	0.3	0.908	2.18	0.86
PAM-M7	1.0	0.3	1.03	2.18	0.86
APS Variation					
PAM-PA1	1.0	0.3	0.648	1.09	0.86
PAM-PA2	1.0	0.3	0.648	1.53	0.86
PAM-PA3	1.0	0.3	0.648	1.75	0.86
PAM-PA4	1.0	0.3	0.648	2.63	0.86
PAM-PA5	1.0	0.3	0.648	3.06	0.86
PAM-PA6	1.0	0.3	0.648	3.5	0.86
TMEDA Variation					
PAM-PT1	1.0	0.3	0.648	2.18	0.43
PAM-PT1	1.0	0.3	0.648	2.18	0.6
PAM-PT1	1.0	0.3	0.648	2.18	0.688
PAM-PT1	1.0	0.3	0.648	2.18	1.03
PAM-PT1	1.0	0.3	0.648	2.18	1.2
PAM-PT1	1.0	0.3	0.648	2.18	1.37

SEM analysis of hydrogels

The representative SEM images of poly (acrylamide) (PAM) and surfactant modified poly(acrylamide) hydrogels are shown in figure 3. The SEM images (Figure 3 (b-d) demonstrates that the addition of surfactant molecules to the polymerization medium have changed their morphologies. A similar dominant morphological variation was observed by Mohan *et al.*[34] for poly(*N*-

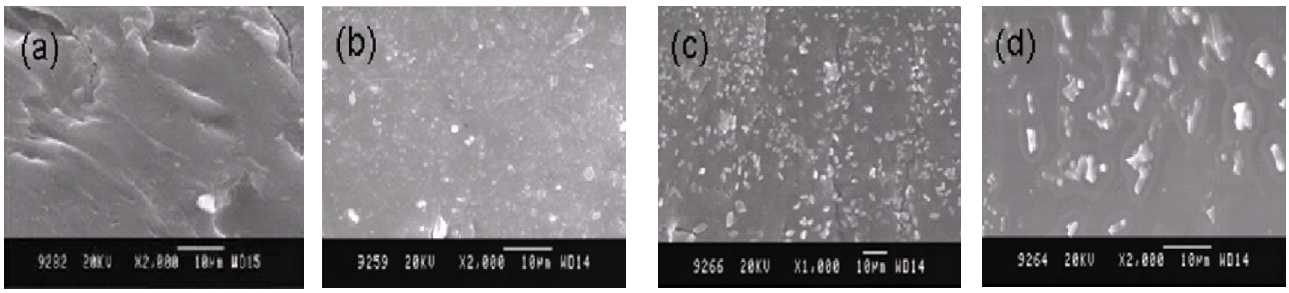


Figure 3 : Scanning electron microscope images of (a) PAM hydrogel, (b) PAM-PS (c) PAM-PS3 and (d) PAM-PS5 hydrogels

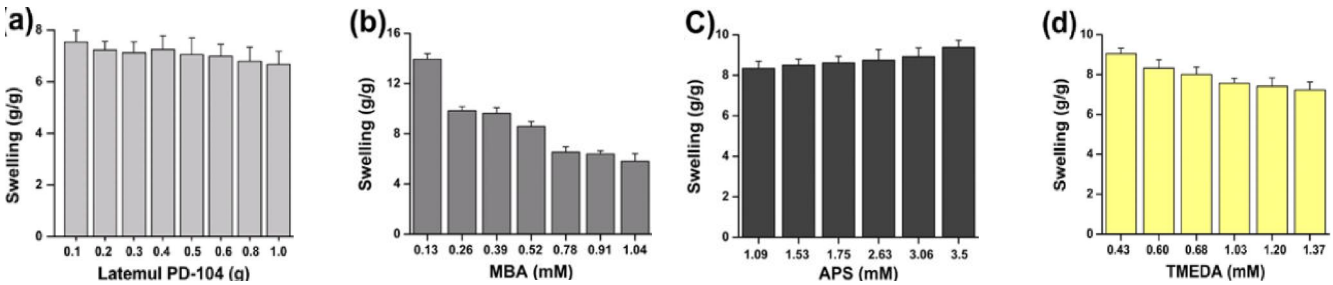


Figure 4 : Swelling behaviour of various hydrogel formulations (a) Latemul PD-104 variation (b) MBA variation, (c) APS variation, and (d) TMEDA variation

isopropylacrylamide) based hydrogel networks by altering the amount and type of surfactant in the polymerization media. In our study, PAM hydrogel showed a plain surface morphology throughout the gel (Figure 3a). By increase of the surfactant content (Latemul PD-104) in the polymerization media leads to change in the morphology due to incorporation of surfactant molecules in the hydrogels. In detail, with lower amount of surfactant (100 mg), the hydrogel (PAM-PS1) was formed containing few small clumps on the surface (Figure 3b); with further increase of surfactant content (300 mg), the gel (PAM-PS3) was formed by distributing the surfactant molecules uniformly throughout the hydrogel (Figure 3c); and with higher amount of surfactant molecules (500 mg), the hydrogel (PAM-PS5) was formed by aggregation of larger clusters throughout the hydrogel.

In this way, the cross-linked co-polymerization has resulted hydrogels forming rich domains of macroscopic networks of highly cross-linked interconnected surfactant chains and/or lightly cross-linked networked chains domains in other places. As per the present experimental data, 300 mg of surfactant is optimal to receive a perfect uniform distribution of surfactant molecules throughout the hydrogels and therefore this amount was fixed to prepare a number of combinations of hydrogel systems (TABLE 1).

Influence of reaction parameters on hydrogel characteristics

The synthesis of hydrogels by cross-linking co-polymerization technique involves use of number of components including different monomers, cross-linkers, and initiator/activator. In general, the concentration of components not only decides the reaction kinetics but also influence the overall characteristic of the hydrogel networks. Therefore, we have studied the variation of the components influence on the resulting hydrogels swelling characteristic which is the most important inherent property of hydrogel system.

Surfactant

The effect of surfactant content (0.1-1.0 g) in the feed mixture of the hydrogel on the swelling capacity was investigated (Figure 4a). The swelling capacity has decreased slightly with increase of surfactant amount from 0.1 g (S = 7.53 g/g) to 1.0 g (S = 6.67 g/g). In fact, there is no much change in their swelling capacity among all surfactant modified poly (acrylamide) hydrogels. The blank hydrogel (PAM hydrogel) has showed an absorbance of 7.24 g/g. Even less amounts of surfactant (<0.1 g) have similar swelling behavior.

Cross-linker

The effect of cross-linker concentration (0.13 mM

to 1.03 mM) on the swelling characteristics of hydrogel systems was studied. Hydrogel synthesis parameters are fixed at AM (1 g), surfactant (0.3 g), APS (2.18 mM) and TMEDA (0.86mM) and varied the MBA concentration. The results are presented in Figure 4 (b). The swelling capacity of the hydrogels decreased drastically with increase of MBA concentration from 0.129 mM (13.93 g/g) to 1.03 mM (6.39 g/g). This is due to the fact that higher concentrations of cross-linker results in highly crosslinked network hydrogels which decreases the intermolecular spaces throughout the hydrogel networks, and thereby restricting the water penetration. Therefore, these highly cross-linked hydrogels exhibits lower swelling capacity.

Initiator/activator

In the case of hydrogels formed by variation of initiator, the hydrogels exhibited an improved swelling with increase of initiator (APS) concentration (Figure 4c). In detail, the hydrogels prepared with 0.109 mM APS results with swelling of 8.34 g/g. This swelling capacity improved continuously upto 9.38 g/g when 3.5 mM APS was used. This is due to the formation of larger amounts of free radicals during the reaction with an increase of APS concentration thereby resulting in less cross-linked gel network (lower density cross-linked networks), which ultimately increases the swelling behaviour. In contrast, an increase of TMEDA concentration (0.43 mM to 1.37 mM) in hydrogel synthesis leads to continuous fall in the swelling capacity of hydrogels (9.04 g/g to 7.22 g/g) (Figure 4d).

Encapsulation efficiency

Encapsulation efficiency of Ranitidine hydrochloride (RH) in surfactant modified poly (acrylamide) hydrogels are presented in TABLE 2. The loading is caused by interaction between hydrochloride portions of drug with SO_3NH_4 groups in addition to the amide groups of poly(acrylamide) chains. The % of encapsulation has clearly shown an increase pattern by the incorporation of surfactant molecules into the hydrogel networks (76±4.8%) compared to poly(acrylamide) hydrogel (65±3.2%). However, with increase of surfactant amount leads to decrease in encapsulation efficiency: PAM-PS1 (76±4.5%) > PAM-PS5 (71 ± 4.8) > PAM-PS8 (68±6.5%) > PAM (65±3.2%). A clear decrease in encapsulation efficiency was also observed in MBA cross-linked hydrogels. The reason is highly cross-linked networks restrict the penetration of drug molecules into the hydrogel networks. Therefore, overall encapsulation efficiency depends on the swelling behavior of hydrogels.

TABLE 2 : Ranitidine hydrochloride release kinetics parameters of different drug loaded hydrogel formulations

Formulation code	Encapsulation efficiency (EE)	k	n	Correlation coefficient r
PAM	65 ± 3.2	0.278	0.209	0.9294
PAM-PS1	76 ± 4.5	0.148	0.294	0.9221
PAM-PS5	71 ± 4.8	0.202	0.275	0.9674
PAM-PS8	68 ± 6.5	0.235	0.242	0.9285
PAM-PM1	65 ± 4.6	0.231	0.221	0.9682
PAM-PM4	63 ± 2.9	0.263	0.215	0.8877
PAM-PM6	59 ± 1.6	0.294	0.200	0.8898

***In vitro* drug release**

The release of rantidine hydrochloride (RH) from the hydrogels was investigated in PBS at 37°C. The drug release was determined at predetermined intervals upto 60 hr. The cumulative percentage release of RH is shown in figure 5 & 6. The drug release from hydrogels is a complex process which is due to diffusion process followed by degradation, and depends on molecular weight ratio of copolymer, protected layer stability, and drug physico-chemical properties. In our case, it is expected due to diffusion process via swelling/de-swelling approach. The initial release of RH from the formulations is considered due to quick release of deposited or weakly bounded drug molecules on the surface of hydrogels. This behavior is more in PAM hydrogels compared to surfactant modified hydrogels (Figure 5 & 6).

The drug release pattern is differing between each hydrogel formulation. For example, PAM-PS1 exhibited slower release compared to PAM and PAM-S5 and PAM-S8 (Figure 5). From this data, we can assume that PAM-S1 containing surfactant molecules holds drug molecules and releases slowly compared to other surfactant modified hydrogels, i.e., PAM-S5 and PAM-S8. Similarly, MBA cross-linker variation in the formulations also influences the drug release (Figure 6). Lower cross linker employed hydrogels having low cross linking networks allowed more drug molecules to

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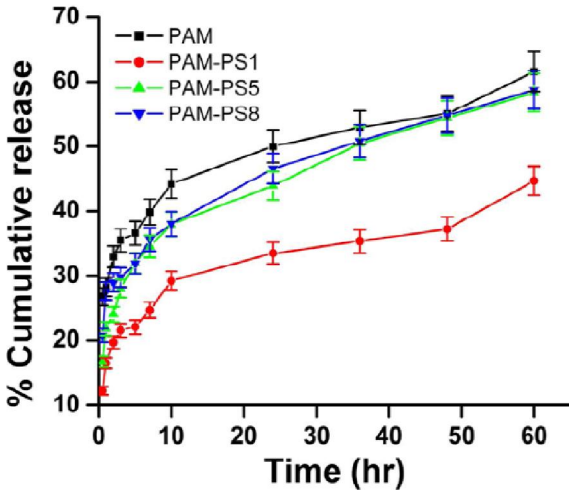

Figure 5 : Effect of variation of surfactant on drug release from different hydrogels

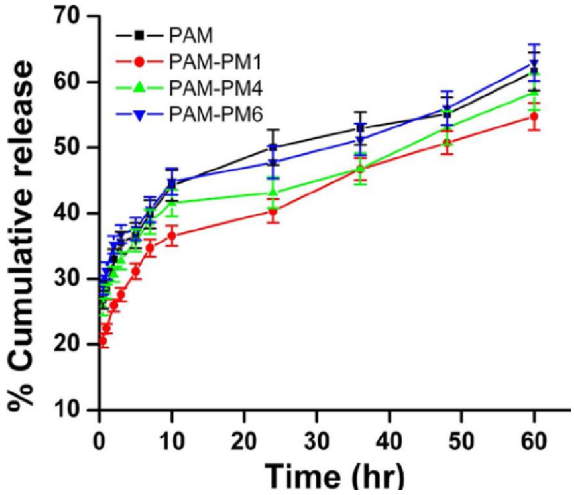

Figure 6 : Effect of variation of cross-linking agent on drug release from different hydrogels

link with surfactant molecules and causes lower amount of release with time (PAM-PM1). Whereas higher amount employed hydrogels contain dense networks which allow limited number of drug molecules to interact with amide or surfactant functional groups for effective linking and more molecules are just physically entrapped. These entrapped drug molecules were easily released from hydrogel networks which can be seen in the case of PAM-PM4 and PAM-PM6 similar to PAM hydrogel (Figure 6).

Drug release kinetics was analyzed by plotting the cumulative release data vs. time and fitting the data to exponential equation of the type [35] as given below.

$$\left(\frac{M_t}{M_\infty}\right) = kt^n$$

Here, M_t/M_8 represents the fractional drug release at time t, k is a constant characteristic of the drug-polymer system and n is an empirical parameter characterizing the release mechanism. Using the least square procedure, the values are estimated for n and k to all the seven formulations and these values are given in TABLE 2. If n = 0.5, the drug diffuses and releases out of the polymer matrix following a Fickian diffusion. If n = 1, completely non-Fickian or Case II release kinetics occurs. The intermediary values ranging between 0.5 and 1.0 are attributed to anomalous type diffusive transport mechanism[36].

The values of *k* and *n* have shown a dependence on the extent of cross-linking, % monomer content of the gel matrix. The values of *n* for the surfactant modified hydrogels by varying the amount of surfactant in the hydrogels, PAM-PS1, PAM-PS5 and PAM-PS8 ranged from 0.294 to 0.242. For the cross-linking variation the *n* values are ranged from 0.2246 to 0.2005 (TABLE 2).

From this study, formulation PAM-PS1 and PAM-PM1 has slower drug release characteristics compared to all other formulations including PAM hydrogel. Therefore, these hydrogel formulations may be useful for controlled and prolonged release applications. Since these hydrogels are made by a biocompatible poly (acrylamide) as a major component and therefore can be applied for drug delivery applications. However, to improve the biodegradability it requires employing a fully degradable cross-linker which enhances its degradation.

CONCLUSIONS

The present investigation involves the development of novel surfactant modified poly (acrylamide) hydrogel systems that can be employed for the delivery of hydrophilic drugs. A systematic evaluation was performed for different compositions of hydrogels through their swelling behavior. The morphological and chemical structures of systems were confirmed by using FTIR and SEM analysis. The drug release studies indicated that the drug can be released for a longer time with slow release. Therefore, this surfactant modified hydrogels can be used as drug delivery systems for ranitidine drug for the treatment of ulcer.

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