

SODIUM ALGINATE BASED INSITU GELLING SYSTEM OF FAMOTIDINE: PREPARATION AND IN-VIVO CHARACTERIZATIONS

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Abstract

The aim of the present study was to design and evaluate in situ gelling system for oral sustained release drug delivery of Famotidine, which was selected as a model drug due to its short biological half-life (2-3 hrs) and as an H₂ receptor antagonist to be released in stomach. On the basis of the preliminary trials, a 3² full factorial design was employed to study the effect of independent variables, concentration of pectin (X₁) and concentration of CaCl₂ (X₂) on dependent variables like viscosity, drug content, Q₅₀, Q₈₀ and similarity factor. Main effects and interaction terms of the formulation variables could be evaluate quantitatively by a mathematical model. It was found that both the pectin and concentration of CaCl₂ had significant impact on viscosity, drug content, Q₅₀, Q₈₀ and similarity factor (f₂) of the system. In-vitro release study revealed that drug released from the insitu gel followed non-fickian diffusion. In vivo study for the selected batch of sodium alginate was carried out by pylorus legation method in rats, which showed gel formation in gastric juice and reduction in ulcer index. Stability study was also carried out for three months, which showed no major changes from their initial state.

Keywords: Famotidine, pectin, situ gel formation, mucoadhesion.

Introduction

In situ gel forming drug delivery systems are in principle capable of releasing drug molecule in a sustained manner affording relatively constant plasma profiles. These hydrogels are liquid at room temperature but undergo gelation when in contact with body fluids or change in pH. These have a characteristic property of temperature dependent, pH dependent and cation induced gelation. Compared to conventional controlled release formulations, in situ forming drug delivery systems possess potential advantages like simple manufacturing processes and ease of administration.^{1,2}

Intimate contact of a delivery system at the absorbing site maximizes not only drug absorption, but also influences the rate of drug absorption. These in situ gel preparations can be easily formulated in bulk and these formulations give homogeneity of drug distribution when compared to other conventional suspensions. These in situ gels also have good mucoadhesion property, which helps in coating of the ulcer lining once the sol comes in contact with the gastric pH.³

Famotidine, an antiulcer agent was chosen as a drug which is an H₂ receptor antagonist, which is 8 times more potent than ranitidine, and 20 times more potent

than cimetidine. Famotidine is rapidly and incompletely absorbed from gastrointestinal tract with the bioavailability of about 43 % having an elimination half life ($t_{1/2}$) of 3 hours. Some patients with reflux oesophagitis who are being treated with proton pump inhibitor may continue to produce acid in the night (nocturnal acid breakthrough) and could be benefited by taking a sustained release formulation of H₂ receptor antagonist.⁴

It is also reported that oral treatment of gastric disorders with an H₂-antagonist like ranitidine or famotidine used in combination with antacids promotes local delivery of these drugs, also increases stomach wall receptor site bioavailability and increases the efficacy of drugs to reduced acid secretion.⁵ Several approaches are currently used to prolong gastric retention time. Among them the principle of bioadhesive preparations offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release.⁶ Thus in the present study an attempt was made to prepare a formulation of famotidine as in situ gel forming drug delivery system for oral delivery by using mucoadhesive polymer of sodium alginate.⁷

MATERIALS AND METHODS

Materials

Famotidine was a gift sample from Shehat Pharma. Ltd. Himmatnagar, Gujarat, India. Pectin, Sodium citrate, Calcium chloride, Sodium hydroxide (S. D. Fine Chemicals, Mumbai, India) were obtained from commercial sources. All other reagents and chemicals used were of analytical reagent grade.

Preparation insitu gelling system of famotidine

The different concentration of sodium alginate solutions was prepared in ultra pure water containing sodium citrate at 60°C. Calcium chloride was added to the solution after cooling at below 40°C with stirring. Famotidine (40 mg) was dissolved separately in 0.1N HCL solution and then added slowly to the above sodium alginate solution while stirring on a magnetic stirrer to get the homogeneous dispersion of the drug. 0.1 N NaOH was added to the above solution to neutralize the hydrochloric acid while stirring. The above formulations were sonicated in a bath sonicator for 15 minutes & then checked the viscosity of the solutions and then add the prepared solutions in pH 1.2 buffer, to see the gel formation and checked its physical appearance and took the dissolutions of the prepared gels.⁸ Figure 1 and 2 show the sodium alginate solution and the gel formation of sodium alginate solution in pH 1.2 buffer.

Physical appearance and pH

All the prepared sodium alginate based insitu solutions of famotidine were checked for their clarity and the pH of the solutions. After administered of the prepared solutions in pH 1.2 buffer, the time required for gel formation and consistency of gel formed was checked visually. The pH was also measured in each of the solution of sodium alginate based insitu solutions of famotidine, using a calibrated digital pH meter at 25°C. The measurements of pH of each data were in triplicate and the average values of preliminary trial of sodium alginate are shown in Table 1.

Determination of viscosity

The viscosity of the prepared solutions were determined using a Brookfield digital viscometer (Model no LVDV 2P230) with spindle number 1. The sample temperature was controlled at 25±1°C before the each measurements. The viscosity of the solutions (drug free) prepared in water was determined at ambient condition using 2 ml aliquot of the sample.

In-vitro drug release study

The drug release study was carried out using USP XXVI basket apparatus (Electrolab, TDT-06T, Mumbai, India) at $37 \pm 0.5^\circ$ and at 100 rpm using 900 ml of pH 1.2 buffer as a dissolution medium (n=3) as per USP XXVI dissolution test prescribed IP.¹²

In situ gels equivalent to 40 mg of famotidine were used for the test. 10 ml of sample solution was withdrawn at predetermined time intervals, filtered through a 0.45 μ membrane filter, dilute suitably and analyzed UV spectrophotometrically at 265 nm. Same amount of fresh dissolution medium was replaced immediately after withdrawal of the test sample. Percent drug dissolved at different time intervals was calculated using the Beer Lambert's equation (Absorption = $0.0314x + 0.02$, $R^2 = 0.9996$). The results of F1 to F9 are shown in Figure 3.

Comparison of dissolution profiles^{9,10}

The similarity factor (f_2) given by SUPAC guidelines for modified release dosage form was used as a basis to compare dissolution profile. The dissolution profiles of products were compared using a similarity factor (f_2). This similarity factor is calculated by following formula,

$$f_2 = 50 \times \log \left\{ \left[1 + \frac{1}{n} \sum_{j=1}^N |R_j - T_j|^2 \right]^{-0.5} \times 100 \right\} \quad (1)$$

Where 'n' is the number of dissolution time and R_j and T_j are the reference (theoretical) and test dissolution values at time 't'. Two dissolution profiles are considered similar when the f_2 value is 50 to 100. The similarity factors (f_2) of all the batches F1-F9 of sodium alginate based formulations were determined with the help of theoretical release profile as reference by the above formula. The results of the similarity factors f_2 values for all the batches F1-F9 of sodium alginate based in situ gels famotidine are mentioned in Table 2.

Kinetics modeling of drug dissolution profiles

The dissolution profile of all the batches was fitted to Zero order, First order^{11,12}, Higuchi and krosmeier peppas model^{13,14} to ascertain the kinetic modeling of the drug release. The dissolution pattern of the drug release form all the formulations were also checked by the following equation in which data corresponding to $60\% \pm 5$ release were fitted using the equation proposed by krosmeier-peppas

$$Mt/M_\infty = kt^n \quad (2)$$

Where, Mt/M_∞ is the fraction of drug released at time t, k the kinetic constant and n is the release exponent that characterizes the mechanism of drug release. The correlation coefficient values of the zero-order, first order, higuchi kinetics and kromeyer peppas kinetics are shown in Table 3.

Measurement of water uptake by the gel

The water uptake by the gel can be determined using a thermogravimetric analyzer. But in this present study a simple method has been adopted to determine the water uptake by the gel. The in situ gel formed in 40 ml of gastric acid buffer (pH 1.2) was used for this study. From each formulation the gel portion from the buffer was separated and the excess buffer was blotted out with a tissue paper. The initial weight of the gel taken was weighed and to this gel 10 ml of distilled water was added and

after every 30 minutes of the interval water was decanted and the weight of the gel was recorded and the difference in the weight was calculated and reported.³ The result of the water uptake study for sodium alginate based gel is depicted in Figure 4.

Stability study

Prepared sodium alginate based insitu gel of famotidine was stored in a glass containers (well stoppered) for three months and the stability of the aqueous solutions of the sodium alginate based insitu gels of famotidine was monitored up to 3 months at room temperature ($25\pm 1^\circ\text{C}$) and normal humidity conditions.^{15,16,17} Periodically (initial, 1 and 3 months interval) samples were removed and characterized by pH, viscosity and drug content. The results of the stability study for the selected batch (F5) of sodium alginate based insitu formulation is given in Table 4.

In-vivo study

In the selected formulation (F5) of sodium alginate based insitu gel of famotidine 'pyrolus legation method in rats' was used for in vivo study and also checked whether the gel was formed in collected gastric juice from the rats.

Pyrolus legation method in rats: The wistar rats weighing between 150-250 gms, were divided into 3 groups, in which each group contain 2 rats.

- *Group-1:* Served as control
- *Group-2:* Served as control plus immediate tretment
- *Group-3:* Served as treated (insitu famotidine gel)

The rats were fasted for 24-h then anaesthetized with ether and a portion of the abdomen was opened by a small midline incision under the xiphoid process. The pylorus portion of the stomach was lifted and legated. During this process, care was taken to avoid the traction to the pylorus or damage to its blood supply. The stomach was closed by interrupted sutures.¹⁸

Group-1 After 5 hours the animal was sacrificed and the stomachs was removed, cut along the greater curvature and subjected to measurement of ulcer index and collect the gastric secretion for in vitro gel formation.

Group-2, In immediate tretment group, sodium alginate based insitu gel of famotidine is administer orally after 5 hours of legation, after 20 min the animal was sacrificed and the stomachs was removed, cut along the greater curvature observed whether gel is form or not and subjected to measurement of ulcer index.

Group-3, while in treated group, the gel was administered orally 30 mins before starting the experiment in 24-h fasted rats and after 5 hours of surgery animal is sacrificed and observed for the effect of drug by counting the ulcer index.

Calculation for ulcer index

Each lesion of stomach was measured along its greatest length and breath. For circular lesion, diameter was measured and finally area was calculated. In case of petechiae, 5 of them were considered to be equivalent to 1 mm of ulcerated area. The ratio of total area of the stomach mucosa and that of ulcerated mucosa were calculated and then it was divided by 10 to obtain ulcer index.¹⁹

$$X = \frac{\text{Total area of stomach mucosa}}{\text{Total area of ulcerated mucosa}} \quad (3)$$

$$\text{Ulcer Index} = 10/X \quad (4)$$

The area of ulcerated portion is calculated as per the following formula:

Area of circular lesion = $\pi D^2/4$

Area of linear lesion = $L * B$

Area of stomach mucosa = $\pi D^2/8$

Where D = Diameter of the stomach mucosa

The results of in-vivo study of the selected formulations (F5) of the sodium alginate were presented in Figure 5 to 8. Figure 9 shows Pylorus ligation induced ulcer index for sodium alginate based insitu formulation of famotidine

RESULTS AND DISCUSSION

Preliminary trials

Preliminary studies were carried out to determine the pectin concentration necessary for drug delivery. Batches R1 to R12 (Table 1) were prepared to study the effect of polymer (pectin) concentration on the viscosity of the solutions, drug content, pH and the physical properties of the gel in pH 1.2 buffer. The concentration of pectin was varied from 0.5, 1, 1.5 and 2 %. In the batches R1 to R3 there was improper gellation which leads to rapid flow of the formulation and also the time required for gellation and drug content was also very lower then the other batches. In the batches R4 to R6 the gellation, the flow of the formulation, the time required for gellation and the drug content were slightly better then that of R1 to R3. While in the batches R7 to R12 all the characteristics of the gels are good than that of above batches but in the batches of R10 to R12 the viscosity of the solutions were very high because of the higher concentration of pectin which was difficult to pour the solution while it was not observed in batches R7 to R9. Thus we concluded that 1.5 % pectin was the optimum concentration. There was no significant effect of concentration of sodium citrate hence it was kept constant (0.25 % w/v) in all the batches. Here all the batches were prepared by using 0.075 % w/v concentration of CaCl_2 and 40 mg of drug. The pH of the solution was kept neutral.

Optimization by using 3^2 full factorial designs

On the basis of the preliminary trials in the present study a 3^2 full factorial design was employed to study the effect of independent variables, i.e. concentration of pectin (X_1) and the concentration of CaCl_2 (X_2) on dependent variables viscosity, drug content, Q_{50} , Q_{80} and similarity factor. A statistical model (equation 5) incorporating interactive and polynomial terms was utilized to evaluate the responses.

$$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2 \quad (5)$$

Where, Y is the dependent variables, b_0 is the arithmetic mean response of the nine runs, and b_1 is the estimated coefficient for the factor X_1 . The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The interaction terms (X_1X_2) show how the response changes when two factors are simultaneously changed. The polynomial terms (X_1^2 and X_2^2) are included to investigate non-linearity.²⁰ The results summarized in Table 2 clearly indicate that all the dependent variables are strongly dependent on the selected independent variables as they show a wide variation among the nine batches (F1 to S9). Fitted equations (full models) relating the responses i.e. viscosity, drug content, Q_{50} , Q_{80} and similarity factor to the transformed factor are shown in Table 5. The polynomial equation can be

used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries, i.e. positive or negative. The high values of correlation coefficient (Table 5) for the dependent variables indicate a good fit. The equation may be used to obtain estimate of the response because small error of variance was noticed in the replicates.

Factorial equation for viscosity

The viscosity is an important variable because it affects the gellation of the solutions, the flow of the formulation and time required for the gellation. The viscosity is dependent on the concentration of the polymer and concentration of the calcium chloride. The viscosity of the pectin solutions varied from 225 cp to 399 cp which was measured at 150 rpm (Table 2) and showed good correlation coefficient as 0.996 (Table 5). Results of the equation indicate that the effect of X_1 (concentration of pectin) is more significant than X_2 (concentration of CaCl_2). Moreover, volume of CaCl_2 had a negative effect on the viscosity, i.e. as the volume of cross-linking agent increase, the viscosity increases and has no significant effect on drug release.

Factorial equation for drug content

Data of drug content for all the batches (S1 to S9) are mentioned in Table 2. The drug content varied from 89.99% to 97.96% in batches S1 to S9 pectin based in situ formulations of Samotidine and showed good correlation coefficient as 0.989 (Table 5). Results of the equation indicated that both the concentration of the X_1 and X_2 were responsible for the drug content of the in situ formulations but the effect of X_1 (concentration of pectin) is more significant than X_2 (concentration of CaCl_2), the effect of the X_2 was very less so it was considered non significant compared to the concentration of X_1 .

Factorial equation for Q_{50}

The amount of drug released in an important parameter for sustained release action of the in situ gel of famotidine. The amount of drug released at four hours from the in situ gel of famotidine varied from 38.56% to 99.02% (Table 2) and showed good correlation coefficient as 0.979 (Table 5). Results of the equation indicated that the effect of the concentration of pectin (X_1) was very less and in minus sign while the effect of the concentration of CaCl_2 (X_2) was also in minus sign but it was higher than X_1 so the concentration of the X_2 was very less effective as controlled release action of the gels than the concentration of the X_1 .

Factorial equation for Q_{80}

The amount of drug released at 8 hours is also important parameters for sustained action of the formulations. The Q_{80} for all the batches S1 to S9 varied from 74.70% to 99.02% (Table 2) and showed good correlation coefficient as 0.990 (Table 5). Results of the equation indicated that the effect of the concentration of pectin (X_1) was very less and in minus sign while the effect of the concentration of CaCl_2 (X_2) was also in minus sign but it was higher than X_1 so the concentration of the X_2 was very less effective as controlled release action of the gels than the concentration of the X_1 .

Factorial equation for similarity factor

The similarity factor (f_2) for all the batches S1 to S9 varied from 30.21 to 72.75 (Table 2) and showed good correlation coefficient as 0.951 (Table 5). Results of the equation indicated that the effect of X_2 (concentration of CaCl_2) was more significant

than X_1 (concentration of pectin) as a controlled release action of the gels. Moreover, the concentration of pectin increases the release rate decreases and give effect longer period of time. Means, we conclude that the concentration of pectin and concentration of CaCl_2 directly affects the similarity factor.

Release mechanism

The result of the regression from zero order, first order, Higuchi model and Krosmeier Peppas model (Table 3) showed that all the batches of pectin based in situ gels of famotidine F1-F9 followed Krosmeier Peppas model because good correlation coefficient obtained by this model and the batch F5 containing good correlation coefficient 0.9973.

Optimization of batch

The selection of the best batch depends on percentage viscosity, drug content, Q_{50} , Q_{80} and similarity factor. The viscosity of batch S5 is 314 cp which is easy for swallowing and good ability for gellation immediately after oral administration. Drug content for the batch S5 is 97.96% which is highest than other batches. Dissolution data and graph are recorded in Table 2 and Figure 3 respectively. In the batches F1 to F4 the rate of drug release are very high and in the batches S6 to S9 the rate of drug release are very slow while in batch S5 controlled release of drug at an appropriate time period is found. The amount of drug released for the batch S5 at four hours was 53.73 % which was similar to theoretical release profile and the 90.18 % drug release from the formulation within 8 hours means it is a prominent batch for sustained release formulation. The similarity factor of the batch S5 was 72.75 which was nearer to the hundred instead of other batches so, the batch S5 is selected for further study.

Formulation of the selected batch

The solution of this batch is shown in Figure 1 which showed the pH 7 and the solution was very clear containing the viscosity 314 cp which having the excellent ability for swallowing because the fluidity of the solution was maintained by addition of sufficient sodium citrate to the formulation to form a complex with all of the calcium ions present in the formulation and hence to effectively remove them from solution. After oral administration due to gastric condition pH (1.2) and temperature (37°C) the matrix type of gel is formed immediately after break down of the complex between CaCl_2 and sodium citrate, which is shown in Figure 2. Since 1.5 % solutions of pectin show lower viscosity they should not present difficulties in swallowing. Thus they can be used as delivery vehicle.²¹

Water uptake study

Release of the drug from a polymeric matrix depends on the amount of water associated with the system. The release of the drug may involve the penetration of water into the matrix and simultaneous release of the drug via diffusion or dissolution as governed by Fick's law. The water associated with the formulation at any point in time can be determined by TGA (Thermo gravimetric Analyzer) but in this present study a simple test was done for the selected batch F5 of pectin based in situ gel of famotidine, the graph of the water uptake study are recorded in Figure 4. The water uptake by the pectin based in situ gel of famotidine at 8 hours is 62.44 % and the graph indicates good correlation coefficient 0.9942, so linearly water uptake is takes place by the selected batch S5 which affect the drug release.³

Stability study

Short term stability study of pectin based insitu gel of famotidine was carried out for 3 months at normal room temperature and humidity condition. All the data are mentioned in the Table 4. Stability study revealed that no any major changes taken place throught the stability study for three months so we can say that pectin based insitu formulation having the good stability.

In-vivo study

The in-vivo study was carried out by pylorus legation method in rats and to see whether the gel is formed or not in the stomach of the rats and also checked the effect of the drug by counting the ulcer index. During the practical gastric juice was collected and checked for gel formation. In case of group 1 which is served as a control ulcer are produced (Figure 5). In case of group 2 which is served as a controlled and immediate treatment the gel is formed and the ulcers are also identified (Figure 6). While in group 3 which is served as a treated very less amount of the gel is seen after 5 hours of the treatment and ulcers are reduced (Figure 7). The gel formation takes place immediately after administered in the collected gastric juice of the rats (Figure 8). The ulcer index for group 1, 2 and 3 are plotted as a graph between the ulcer index and groups (Figure 9), so we can see that the gel formation takes place in the stomach of the rats and significant reduction in ulcers are also observed after the treatment of pectin based insitu gel of famotidine.

CONCLUSION

The present investigation deals with the formulation, optimization and evaluation of pectin based insitu gel of famotidine. Pectin used as a polymer and CaCl_2 was used as a cross-linking agent. The insitu formulation exhibited well, viscosity, drug content and sustained drug release; this study reports that oral administration of aqueous solutions containing pectin results in formation of insitu gel, such formulations are homogenous liquid when administered orally and become gel at the contact site. The results of a 3^2 full factorial design revealed that the concentration of pectin and concentration of CaCl_2 significantly affected the dependent variables viscosity, Q_{50} , Q_{80} and similarity factor (f_2). The in-vivo study also demonstrated the excellent gel formation takes place in the stomach of the rat and significant anti-ulcer effect of the sustained release pectin based insitu gel of famotidine over long period of time. These insitu gels are, thus, suitable for oral sustained release of famotidine.

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Table 1: Results of preliminary trial batches for pectin based insitu gels of famotidine					
Batch No.	Conc. of pectin (%)	pH	Viscosity (cp)	Drug content (%)	Characteristic of insitu gels
R ₁	0.5	7.5	155	80.20	Gel is not form properly and less drug content
R ₂	0.5	7.5	154	83.32	
R ₃	0.5	7.6	150	84.45	
R ₄	1	7.2	228	89.98	Gel formation & drug content are slightly better
R ₅	1	7.3	227	91.76	
R ₆	1	7.4	225	90.89	
R ₇	1.5	7.1	314	96.98	Gel formation & good drug content
R ₈	1.5	7.0	317	97.98	
R ₉	1.5	7.0	315	98.25	
R ₁₀	2	6.7	398	94.56	Gel formation & good drug content
R ₁₁	2	6.6	398	95.11	
R ₁₂	2	6.5	399	93.12	

Note: All the batches were prepared using CaCl₂ 0.01%.

Table 2: 3² full factorial design layouts for pectin based insitu gels of famotidine							
Batch No.	Variables levels in coded form		Viscosity (cp)	Drug content (%)	% Drug release (Q ₅₀)	% Drug release (Q ₈₀)	Similarity factor (F ₂)
	X ₁	X ₂					
S1	-1	-1	225	89.99	99.02	99.02	30.21
S2	-1	0	238	91.70	98.00	98.00	31.38
S3	-1	+1	254	90.91	93.13	97.74	34.79
S4	0	-1	295	96.12	78.38	97.03	50.81
S5	0	0	314	97.96	53.73	90.18	72.75
S6	0	+1	345	95.69	50.52	85.03	61.99
S7	+1	-1	382	92.22	47.11	81.04	55.23
S8	+1	0	395	94.90	43.96	77.48	47.41
S9	+1	+1	399	93.85	38.56	74.70	42.42
Translation of coded levels in actual units							
Variables level			Low (-1)	Medium (0)	High (+1)		
Concentration of Pectin (X ₁)			1%	1.5%	2%		
Concentration of Calcium chloride (X ₂)			0.075%	0.1%	0.125%		
Note: All the batches contained the constant amount of drug as 40 mg, viscosity measured at 150 rpm and having the same pH 7.							

Table 3: Release kinetics for pectin based insitu gels of famotidine batches S1-S9				
Batch no.	Regression			
	Zero order kinetic	First order kinetic	Higuchi kinetic	Krosmeier peppas
S1	0.7061	0.4100	0.8277	0.9101
S2	0.7477	0.5000	0.8624	0.9300
S3	0.8111	0.5000	0.8992	0.9429
S4	0.8859	0.9170	0.9514	0.9754
S5	0.9933	0.8823	0.9886	0.9973
S6	0.9898	0.9679	0.9793	0.9925
S7	0.9899	0.9604	0.9820	0.9959
S8	0.9950	0.9655	0.9757	0.9906
S9	0.9960	0.9866	0.9617	0.9805

Time period for sampling	pH	Viscosity (cp)	Drug content (%)
Initial	6.99	314	97.95
After 1 month	7.01	316	97.90
After 2 month	7.1	317	97.88
After 3 month	7.15	320	97.80

Coefficient	B0	B1	B2	B11	B22	B12	Multiple R
Viscosity	317.33	76.5	16	-3	-2.5	1	0.996
Drug content (%)	97.73	1.39	0.35	-0.17	-4.3	-1.72	0.989
Q ₅₀ (%)	59.72	-26.75	-7.05	-0.66	8.7	2.22	0.979
Q ₈₀ (%)	90.38	-10.25	-3.27	-1.26	-2.7	0.54	0.990
Similarity factor (f2)	64.92	8.11	0.49	-4.34	-21.6	-4.60	0.951



Figure 1: Formulation of pectin based insitu solution of famotidine batch S5



Figure 2: Gel formation of pectin based insitu solution of famotidine in pH 1.2 buffer

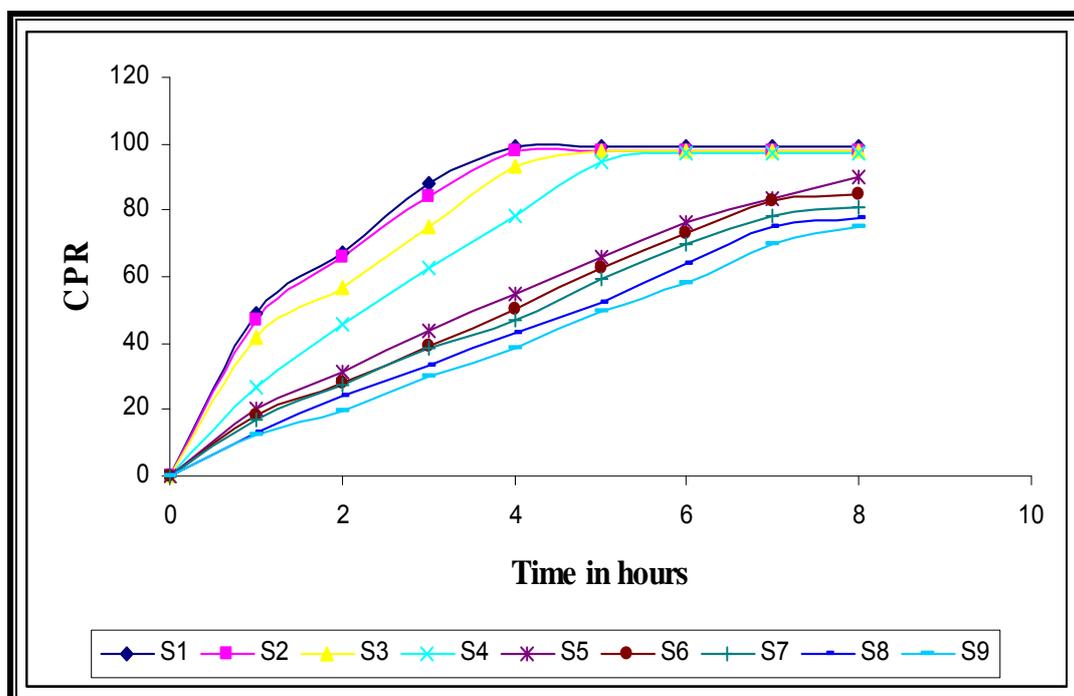


Figure 3: Cumulative % drug release for pectin based insitu gels of famotidine batches S1 to S9

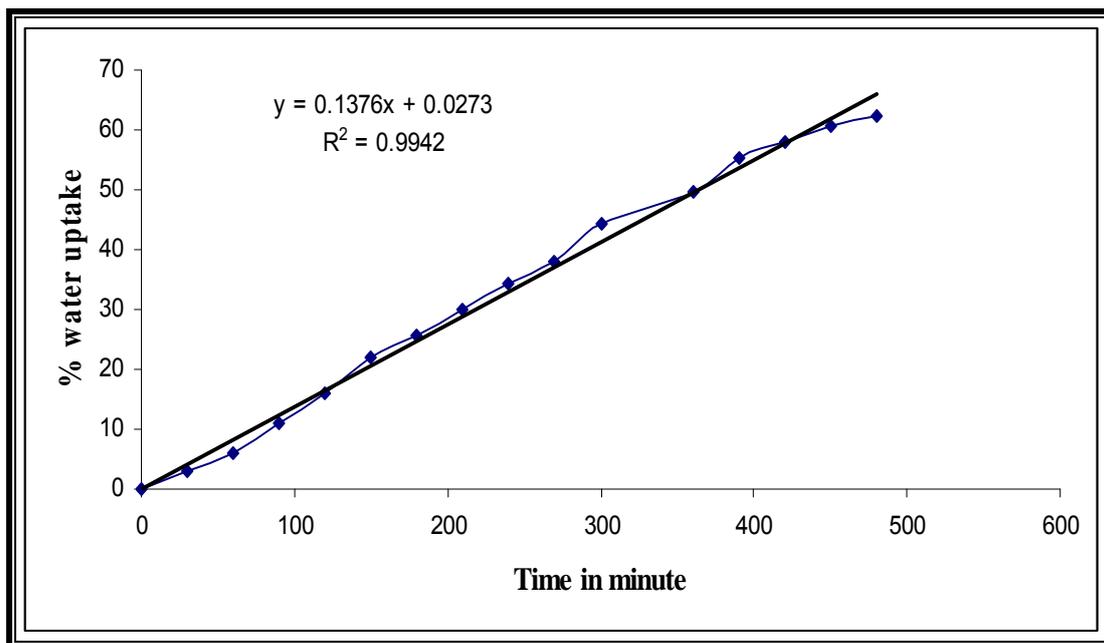


Figure 4: Water uptake study for pectin based insitu gel of famotidine batch S5

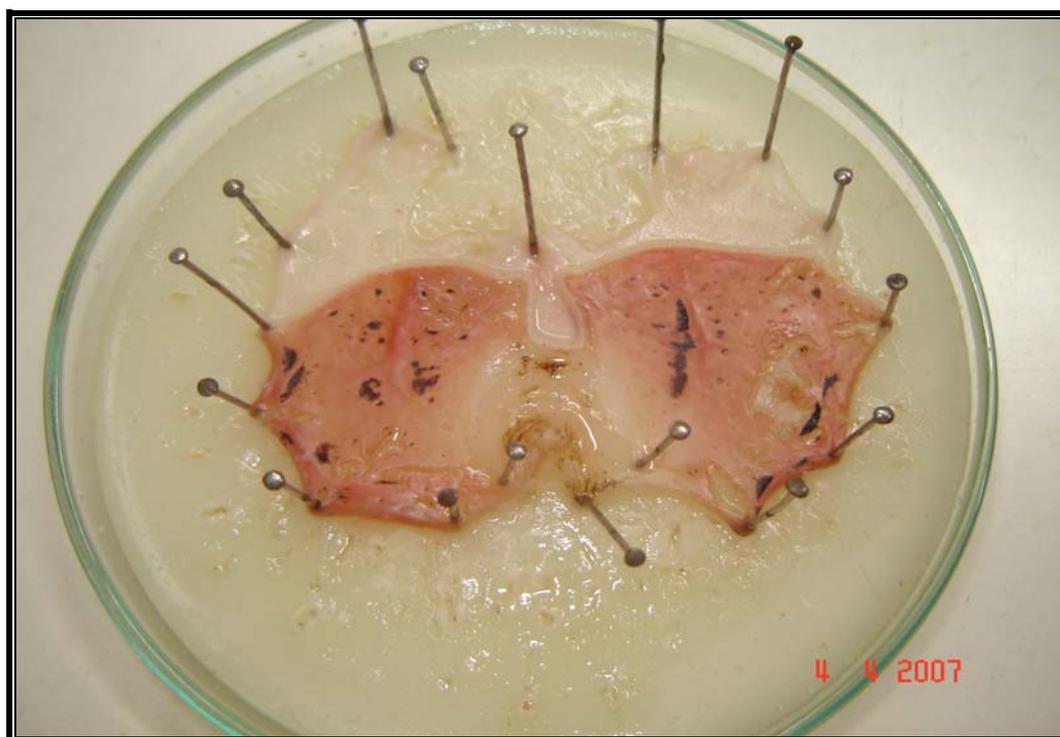


Figure 5: In-vivo study in rat- Group 1 served as a control

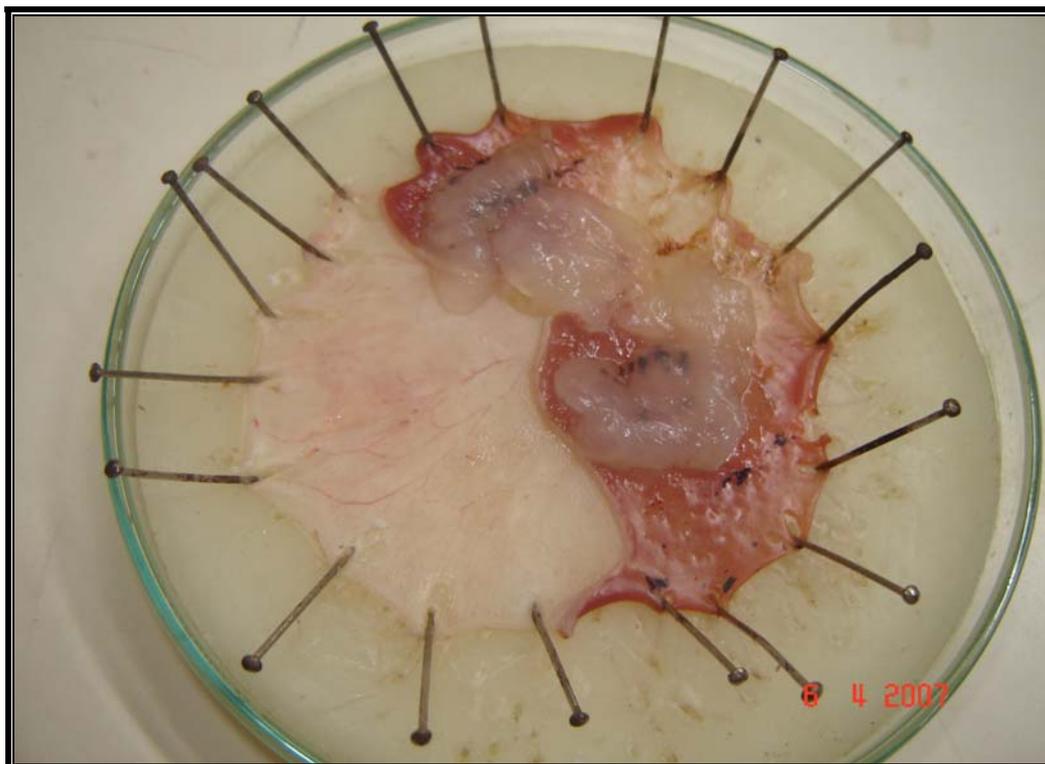


Figure 6: Group-2 served as control + immediate treatment by pectin based insitu solution of famotidine

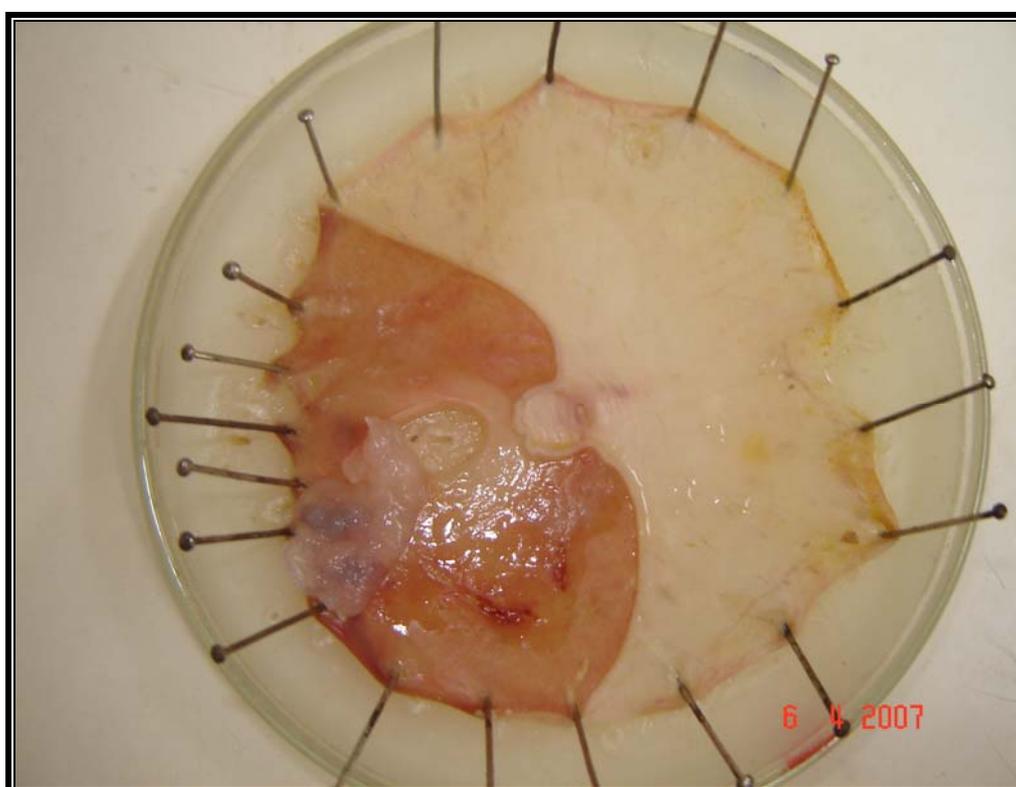


Figure 7: Group-3 served as treated + pectin based insitu solution of famotidine



Figure 8: Gel formation in gastric juice of rat for pectin based insitu formulation of famotidine

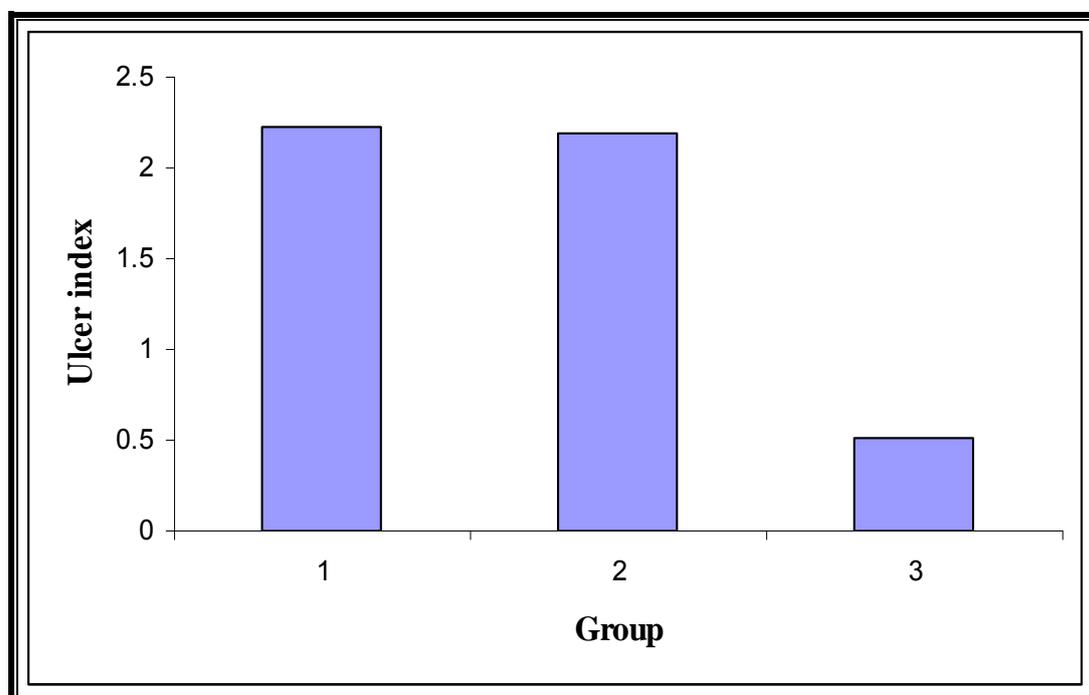


Figure 9: Pylorus ligation induced ulcer index for pectin based insitu formulation of famotidine