Original Research Article

RAFT FORMING BUOYANT PH DEPENDENT THIXOTROPIC GELLING SYSTEMS INCORPORATED WITH GELUCIRE 43/01 AS A POTENTIAL STOMACH SPECIFIC DRUG DELIVERY SYSTEM FOR FAMOTIDINE

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ABSTRACT

Famotidine (FMT) is known as a histamine blocker (H_2) that inhibits stomach acid production and it is commonly used in the treatment of peptic ulcer disease and gastric-esophageal reflux disease. It has a short half life (2.5-3.5 hours), low bioavailability (40-45%). It has excellent solubility in acidic pH just reverse in alkaline pH. Therefore an attempt has been made to develop raft buoyant gastro-retentive sustains release delivery system with *in situ* gelling property which is based on thixotropy behavior. Twelve formulations (Excluding two controlled formulations i.e. F and F*) were designed to contain 40 mg of FMT using Chitosan; CH (cationic polymer), Sodium Alginate; SA (anionic polymer), Gelucire 43/01; G 43/01 (lipid phase) as retardant and adhesive polymers.

Emulgel was prepared and evaluated for their physicochemical properties like buoyancy and lag time, cumulative % drug release, drug release kinetics and drug excipient interaction studies by thermal studies and functional group characterization. All formulations showed that with the increase in concentration of the polymer, the gel strength increased, but the % drug release decreased F8>F12>F11>F6>F5>F10>F7>F9>F3>F4>F1>F2>F*>F. Formulations F9, F10, and F12 were found to be optimum. They followed the non-ficikian mechanism of drug release.

Keywords: Famotidine, *in situ* gel, buoyant gastro-retentive, Chitosan, Sodium alginate, Gelucire 43/01

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INTRODUCTION

Use of oil and waxes in the buoyant drug delivery systems is not new. These ingredients are low in density are used to impart buoyancy as well as release retardants. However, these systems also suffer from disadvantages associated with lipid materials such as rancidity; too slow drug release, varied chemical composition, etc [1, 2]. Use of tailor made lipid materials having a known chemical composition may solve these shortcomings. Gelucires are representative of one such class. These are polyethylene glycol glycerides composed of mono-, di- and triglycerides and mono- and diesters of polyethylene glycol (PEG). Depending on the chemical composition, Gelucires are used for different purposes. The wide varieties of Gelucires are characterized by a wide range of melting points from about 33^0C to about 64^0C and most commonly from about 35^0C to about 55^0 C, and by a variety of HLB values of from about 1 to about 14, most commonly from about 7 to about 14. Low HLB Gelucire can be used to reduce the dissolution rate of drugs, whereas, High HLB Gelucire can be used for faster release of drugs [3, 4, 5].

Besides this *in-situ* gelling system includes a number of advantages in terms of biocompatibility and biodegradability, these systems are too fragile and do not have mechanical strength to hold the entrapped drug [6]. Combining these hydrophilic polymers with lipid materials has been utilized in the past to overcome the hurdle of fast release of drug from the matrices [7]. Upon the literature survey, it was found that there is a lack of studies reporting a combination of lipids with hydrophilic polymers to develop liquid *in-situ* gelling system [8].

In the work undertaken, an attempt has been made to develop *in situ* gelling emulgels using Gelucire 43/01 as lipid phase and low viscosity Sodium Alginate/Chitosan solution in deionized water as an aqueous phase of an emulsion. Nature of Gelucire is attributed to the long hydrocarbon chain and the alcohol moieties that make these bases suitable as a lipid carrier for both hydrophilic and lipophilic drugs [9].

For formulation of buoyant formulations, polymers belonging to two groups i.e. Cationic (Chitosan), anionic (Sodium alginate) was selected. The *in situ* Emulgel were prepared in the presence of Chitosan by incorporating Gelucire 43/01 and same with the Sodium Alginate separately. It is also formulated in combination with Chitosan and Sodium Alginate in Gelucire 43/01. It is believed that incorporating both these cationic and anionic polymers there is formation of Polyelectrolyte Complex (PEC), which retard/sustained the drug. In this primarily a polymer solution was prepared with water. Then remaining ingredients and active constituent (drug) were mixed in polymeric solution. Polymeric gel formulations respond to chemical or physical signals, including pH, metabolite, ionic factor or temperature. The polymers will select for this purpose includes Alginates, Chitosan alone or in varied proportion according to the need [10, 11].

The present work was aimed to develop buoyant oral *in situ* Emulgel system of Famotidine which would float and release the drug at a controlled rate during its residence in the stomach, which provides the required acidic environment for its complete absorption thereby increasing its bioavailability.

Famotidine is a drug of choice and it is a histamine H_2 receptor blocker, which inhibits acid production in the stomach and commonly used to treat peptic ulcer and GERD. Famotidine was selected as model drug because of its bioavailability problem (40-45 %) and less biological half life (2.5-3.5 hours). Thus the major aim of the study is to develop a GRDDS sustained release *in-situ* gel of Famotidine to enhance the bioavailability of drugs which is retained in the upper part of the stomach and used for the treatment of GI tract infection. The pH of the stomach in the fasting state is 1.5-2.0 and in the fed state it is 2 -6. A large volume of water administered with an oral dosage form resists the pH of the stomach contains from 6 - 9, and stomach does not have time to produce sufficient acid to dissolve the drug before the liquid is emptied. In addition the meal also brings pH difference, according to the type of meal consumed; hence in general the basic drug has a better chance of dissolving in the fed state than the fasting state [12].

The drug Famotidine shows the pH dependent solubility and exhibits good solubility in acidic media, whereas it is nearly insoluble in alkaline media. Therefore, for an orally ingested dosage form of Famotidine the acidic environment of stomach favors complete absorption. However the gastric emptying interferes with this. Therefore buoyant *in situ* Emulgel system would overcome this problem by increasing the gastric residence time, thereby reducing drug wastage and enhancing bioavailability.

EXPERIMENTAL

Materials and Equipments

Famotidine was purchased from Yarrow Chem; India, Sodium alginate was purchased from CDH (Central Drug house, India). Gelucire 43/01 (Waxy Solid, Melting Point 43^0C, HLB Value 01) gift sample from

Gattefosse SAS., St. Priest., Cedex., France. Acetonitrile, Methanol (HPLC Grade), HPLC Water was procured from Rankem India.

For method validation, HPLC used is of the Water Breeze 2 system, Water Spherisorb ® analytical column used which have the dimension of 5 µm, 4.6*250mm. All the chemicals and reagents used were of analytical grade.

Development of validated HPLC method for estimation of Famotidine

HPLC method was chosen for estimation of Famotidine. In this linearity, recovery studies, ruggedness and intermediate precision and method validation were determined**.** The HPLC used is of Water Breeze 2 computing intergrator software.

Preparation of Mobile phase

300ml: 200ml: 500ml: 2ml ratio of Methanol: Acetonitrile: HPLC water: phosphoric acid was taken into 1 liter volumetric flask and volume made up to 1000 ml with distilled water and adjusts the pH to 5.0 by phosphoric acid or 1N sodium hydroxide and filtered it through 0.45 micron membrane filter by vacuum filtration unit. These solvents are further sonicated for 30 minutes on ultrasonicator to remove the gases which are formed during the preparation of solvents.

Preparation of solution system for in situ Emulgel using Gelucire 43/01

HPLC water heated at 50^0C and polymer was added into it and mixed properly than lowering down the temperature to 30^0C drug was added and mixed it properly than calcium carbonate and Gelucire 43/01 was added and mixed properly then cooled at room temperature. These prepared liquids stored in an ambered colored glass container, away from heat and light. Buoyant *in situ* emulgels were formulated as per the formulation given in table1. Each formulation containing 40 mg drug. 14 batches of formulation were obtained and subjected to evaluation.

Table 1: Optimized formulations composition of *in-situ* Emulgel

Formulation code	Famotidine (mg)	Sodium alginate (mg)	Gelucire 43/01 (mg)	$CaCO_3$ (mg)	Chitosan (mg)
F	40	100	**-**	100	**-**
F1	40	100	40	100	-
F2	40	120	30	100	-
F3	40	140	20	100	-
F4	40	160	10	100	-
F5	40	140	25	100	-
F6	40	140	30	100	-
F7	40	140	35	100	-
F8	40	140	40	100	-
F*	40	100	-	100	150
F9	40	100	40	100	150
F10	40	120	30	100	150
F11	40	140	20	100	150
F12	40	160	10	100	150

Total volume of each formulation was 10 ml.

Thermal characterization by Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) was performed by EXSTAR TG/DTA 6300. DSC was employed to find out the characteristic peaks (exothermic and endothermic) and exact melting point of drug, excipient and drug excipient samples used in the present investigation. The DSC analysis was carried out over melting point at a rate of 5°C/ min., in presence of inert nitrogen (N_2) using duplicate samples of 5 mg in crimped aluminum pans.

Functional group characterization of drug, excipient and drug excipient composition by using Fourier Transform Infrared spectroscopy (FTIR) studies

Fourier Transform Infrared spectroscopy **(**FTIR) was performed by BX2, Perkin Elmer, Norwalk, USA. The FTIR analysis of the samples was carried out for qualitative compound identification and to ascertain that there is any drug excipient interaction occurs or not and secondly to confirm the presence of functional group in the compound and its comparison to official compendium. The method involved is of direct compression technique by using potassium bromide (KBr). The KBr pellet of approximately 1 mm diameter of the drug was prepared grinding 3-5 mg of sample with 100-150 mg of KBr in pressure compression machine. The sample pellet was mounted in FTIR compartment and taken scan at wavelength 4000cm^{-1} – 400cm^{-1}.

In vitro buoyancy and lag time studies

In vitro buoyancy studies was carried out in 0.1 M HCl L^{-1} having volume of 900 ml, temperature 37 ^{0}C. This study will help in determining how much time our formulation will remain buoyant in the stomach, which is a prerequisite parameter for achieving gastro-retention. Lag time studies refers that how much time it will take coming upward to the surface of media from the bottom. All the readings were recorded in triplicate.

In vitro gelation studies

In vitro gelation studies was carried out in 0.1 M HCl L^{-1} (pH 1.2) having a volume of 900 ml, temperature 37 ^{0}C. 20 ml of the prepared Emulgel solution was incorporated into the 0.1 M HCl L^{-1} (pH 1.2) and time was recorded for the conversion of sol to gel by changing the pH of the media. All the readings were recorded in triplicate.

Viscosity measurement of *in situ* gel

The viscosity of sols prepared in water was determined at 37 ± 1 °C with Brookfield cone and plate viscometer with cone angle 0.8^0 (DV +Pro; Brookfield) using spindle cp 40. A typical run comprised changing of the angular velocity from 0.5 to 100 rpm at a controlled speed. After 6 seconds at 0.5 rpm, the velocity was increased to 100 rpm with a similar wait at each speed. The average of two readings was used to calculate the viscosity. Evaluations were conducted in triplicate.

A surface Topographical study by Scanning Electron Microscopy (SEM)

Shape and surface signature of *in situ* Emulgel was carried out at 100x and at 500x (top surface and transverse section), to study the structural arrangement of the gel. This will also help in the study of effect of ageing on its storage, what surface structural changes take place.

In vitro drug release studies from prepared in situ gel

In-vitro drug release studies were carried out using USP XXVII dissolution apparatus type II at 50 rpm **[12]**. The dissolution medium consisted of 900 ml of 0.1 M HCl L^{-1} (pH 1.2), maintained at 37±0.5^{0}C. The dissolution samples were collected at every 1 hour interval and replaced with an equal volume of 0.1 M HCl

L^{-1} (pH 1.2) to maintain the volume constant. The sample solution was diluted sufficiently and analyzed at 264 nm using a UV spectrophotometer. The study was performed in triplicate.

Curve fitting analysis

In order to explain the drug release from the formulation, various equations are used like Zero order, First order, Higuchi role model and Korsmeyer- Peppas equation [13, 14]. The results of *in vitro* release profiles obtained for all the formulations were fitted into four models of data treatment as follows [15] **:**

1. A cumulative percent drug released versus time (Zero order kinetic model).
2. Log cumulative percent drug remaining versus time (First order kinetic model).
3. Cumulative percent drug released versus square root of time (Higuchi role model).
4. Log cumulative percent drug released versus log time (Korsmeyer-Peppas equation).

The results of *in-vitro* dissolution studies of *in-situ* Emulgel were fitted with various kinetics models, like zero order, first order, Higuchi's model, but these models failed to explain the drug release mechanism due to swelling (upon hydration) along with the gradual erosion of the gel. Therefore, the dissolution data were also fitted to well-known Korsmeyer and Peppas semi-empirical model to ascertain the mechanism of drug release.

$$\log (Mt/M\infty) = \log k + n \log t$$

Where, $M\infty$ is the amount of drug release after infinite time; k is the release rate constant which considers structural and geometric characteristics of the *in situ* gel; and n is the diffusional exponent; indicative of the mechanism of drug release.

Statistical analysis

All the data were analyzed by Students t test and one way ANOVA to determine statistical differences between the results. A probability value $p < 0.05$ was considered statistically significant. Statistical analysis of obtaining the data was done by using Graphpad Instat® software.

RESULTS AND DISCUSSION

Validation of HPLC method

UV spectrum of FMT was measured in 0.1 mol L^{-1} HCl and buffer ratio Methanol: Acetronitrile: Water: Phosphoric acid (300: 200: 500: 2ml). In solvents the wavelength was found to be 264 nm and was reproducible. FMT shows the linear range of (1-50 µg/ml) and the coefficient (r^2) was found to be 0.9979 (y = 63360x + 115300). The retention time (RT) was 2.416 min. The recovery studies were performed at 50 %, 100 % and 150 % levels and the % RSD (Relative Standard Deviation) should not be more than 2% as mentioned by ICH guidelines and it was found to be 0.835 within the specified range [16].

Ruggedness and Intermediate precision % RSD was found to be 0.719 and it also conferred the limitation within the mentioned by ICH guidelines. Method precession, % RSD also found to be 0.767 and it expresses that the method is precise. The results obtained from the validation parameters meet the requirements. It explains and suggests that it follows the Beer's Lamberts law [16]**.**

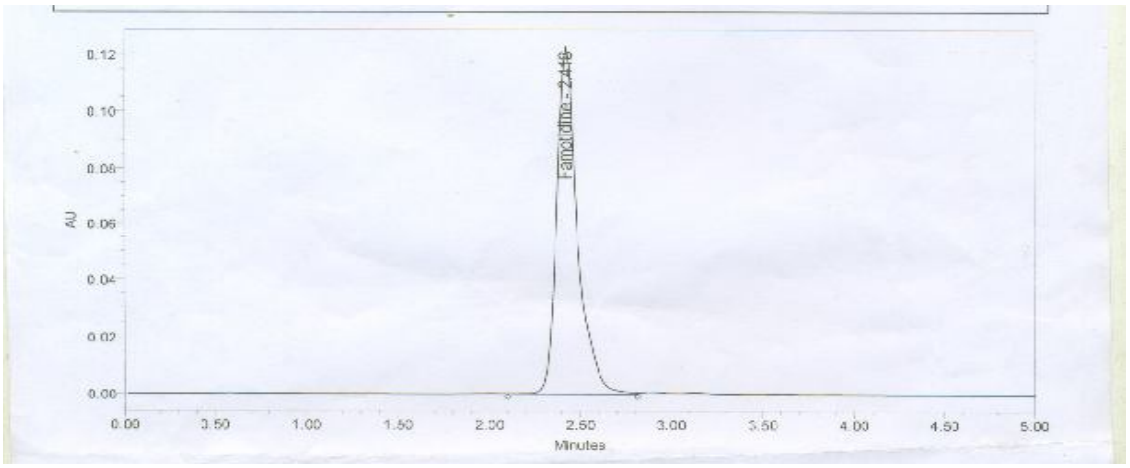

Figure 1: Chromatogram of Famotidine

Table 2: Optimized parameters for HPLC method validation of Famotidine

Parameters	Optimized condition
Chromatograph	Water Breeze 2
Column	C18
Mobile Phase	Methanol: Acetronitrile: Water: Phosphoric acid (300 : 200 : 500 : 2ml)
Dimension	4.6 x 75 mm
Flow rate	1ml/minute
Injection volume	20 µl
Detection wavelength	266 nm
Temperature	Ambient
Retention Time	2.416 minutes

Drug excipient interaction studies by using Differential Scanning Calorimetry

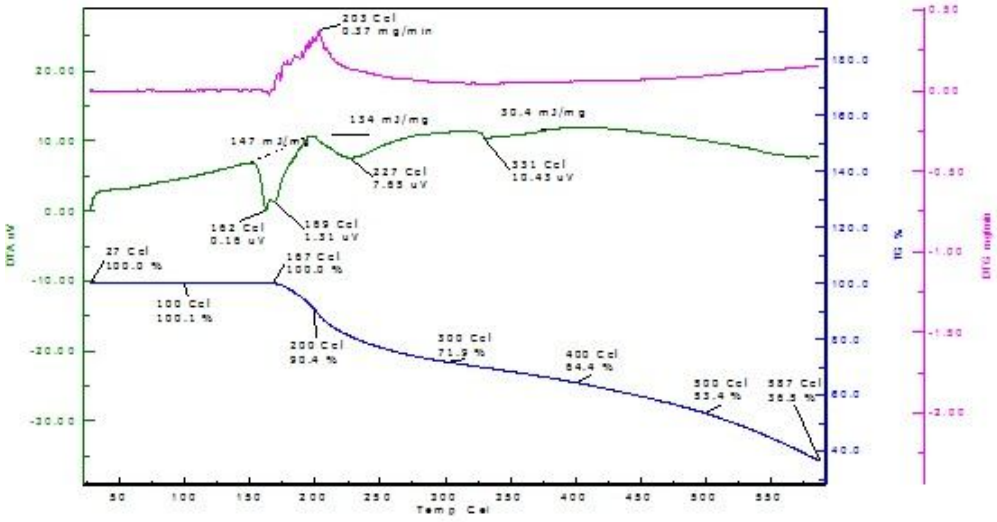

Figure 2: Thermogram of FMT

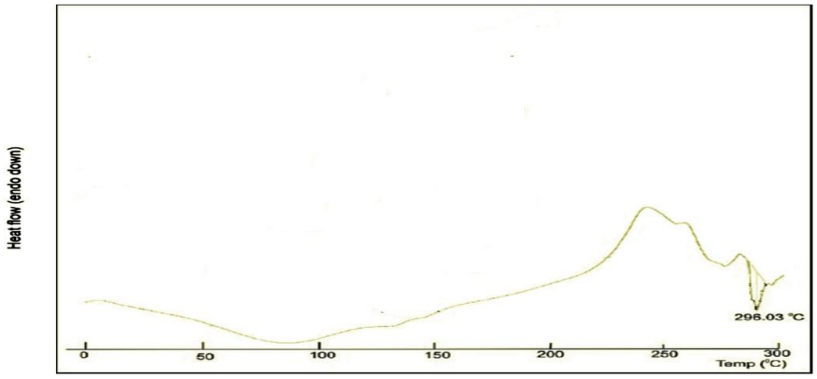

Figure 3: Thermogram of Sodium alginate

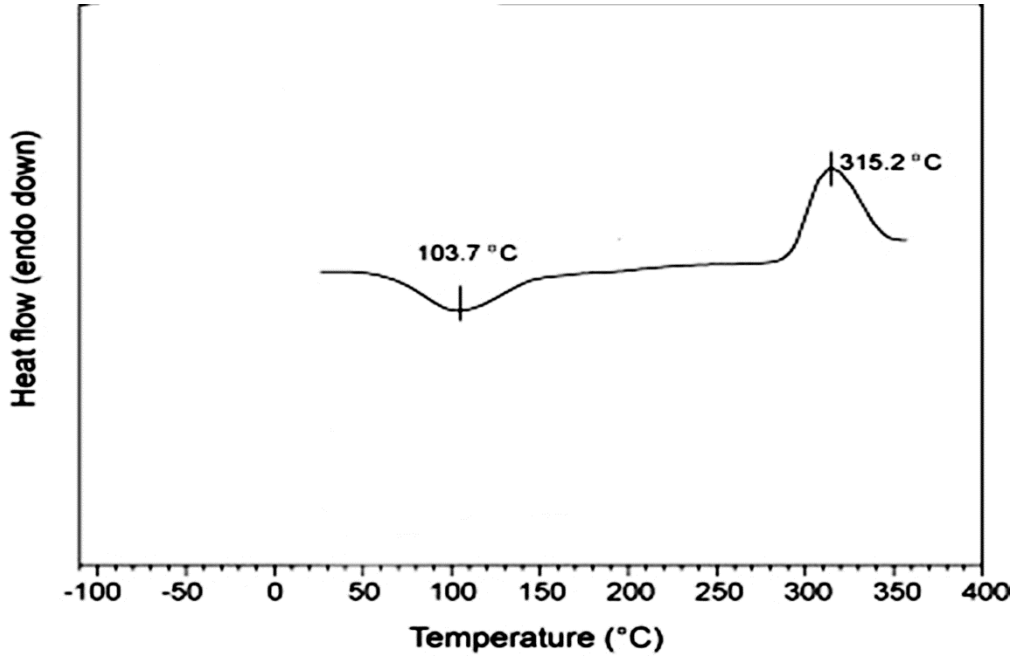

Figure 4: Thermogram of Chitosan

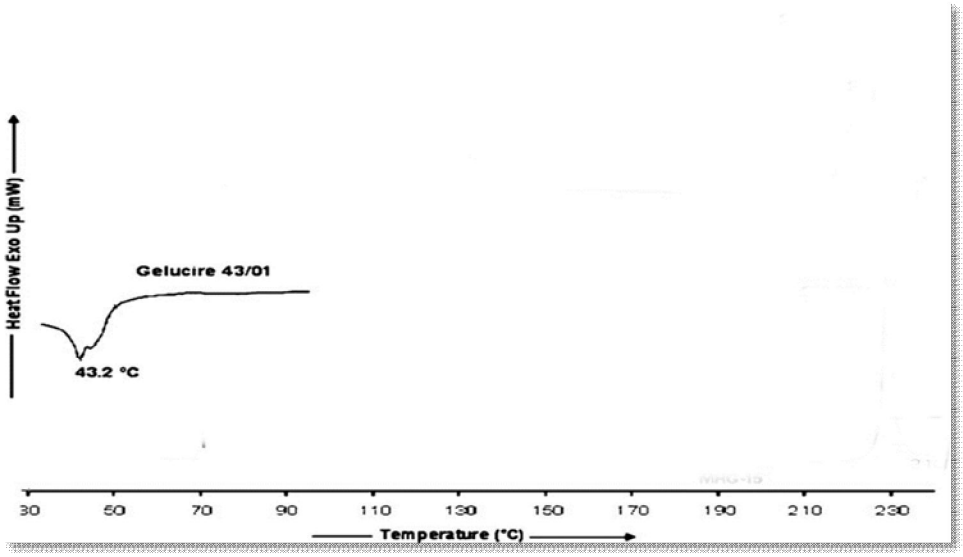

Figure 5: Thermogram of Gelucire 43/01

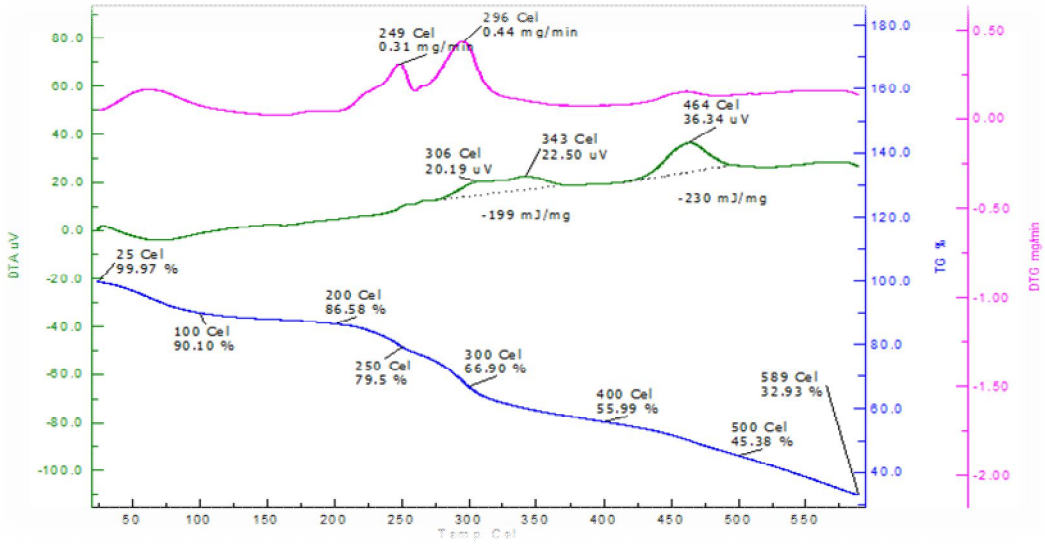

Figure 6: Thermogram of physical mixture of sodium alginate based formulation

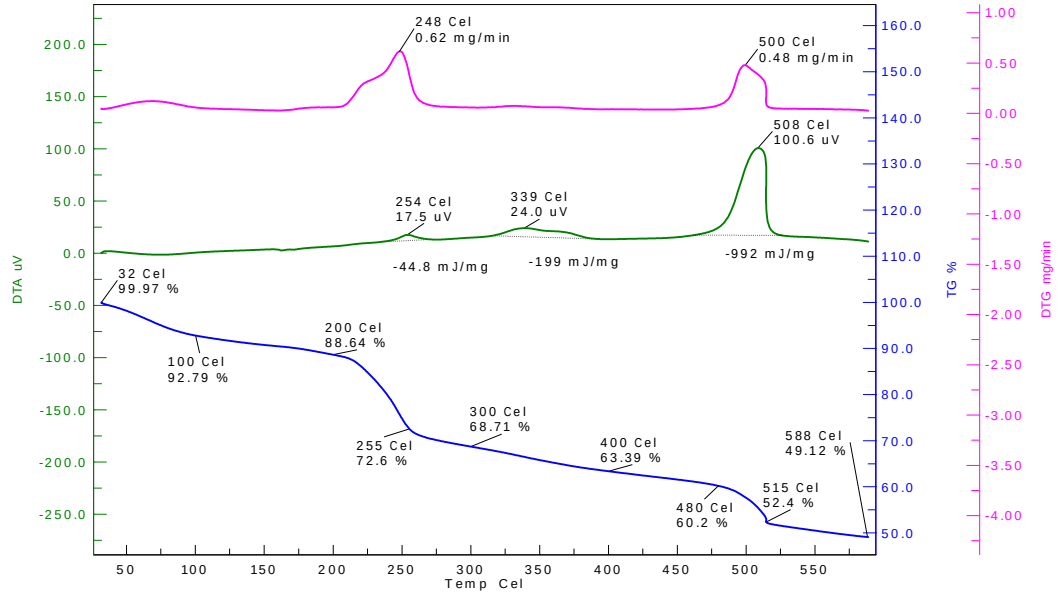

Figure 7: Thermogram of physical mixture of Chitosan based formulation

The DSC curve of Famotidine shows one sharp endothermic peak at 162ºC, which is reported in figure 2, this sharp curve indicates the melting of Famotidine at 162ºC and very narrow endothermic peak 331 ºC, which symbolizes the slow degradation of Famotidine. The DSC curve of Sodium Alginate (Fig. 3) produce one endothermic peak at 296.03 ºC, it represents melting of Sodium Alginate. DSC thermogram of Chitosan (Fig. 4) shows one endothermic and one exothermic peak at 103.7 ºC and 315.2 ºC respectively, the peak at 103.7 represents the glass transition temperature of Chitosan, the peak at 315.2 ºC represents the very slow degradation of Chitosan. The DSC thermogram of Gelucire 43/01 (Fig. 5) represents the very narrow endothermic peak at 43.2 ºC, which represents the melting of Gelucire 43/01.

Thermogram obtained of physical mixture of Sodium Alginate based formulation (F4). In this there was 10mg of Gelucire 43/01 with a drug used; the Famotidine seems to be mixed in Gelucire 43/01 and there

was no peak of the drug (Fig. 6). There are two narrow exothermic peaks at 254 ºC and 339 ºC, that revels the loss of water molecules from the polymer and at that place there is shifting of peak at 339 ºC of Sodium Alginate due to the slow melting of Gelucire 43/01 which forms little bit coating over the surface. Due to the slow transfer of heat over a surface, this increases the melting time of Sodium Alginate and this indicates that there is no drug and polymer interaction take place.

This physical mixture of Chitosan based formulation there are three exothermic peaks (Fig. 7) the two peaks at 316 ºC and at 343 ºC are broad exothermic peak and these two peaks indicates the melting of Chitosan and Sodium Alginate. There is a shifting of peak at lower temperature and higher temperature is due to the Gelucire 43/01 melting and it causes the shifting of the peaks. The peak at 464 ºC indicates the slow degradation of drug and polymer. There is an absence of drug peak because the small amount of drug is used which is mixed in the matrix of Gelucire 43/01 and the Famotidine peak was absent. It shows there is no interaction between drug and polymer.

Functional group characterization of drug, excipient and drug excipient composition by using Fourier Transform Infrared spectroscopy (FTIR) studies

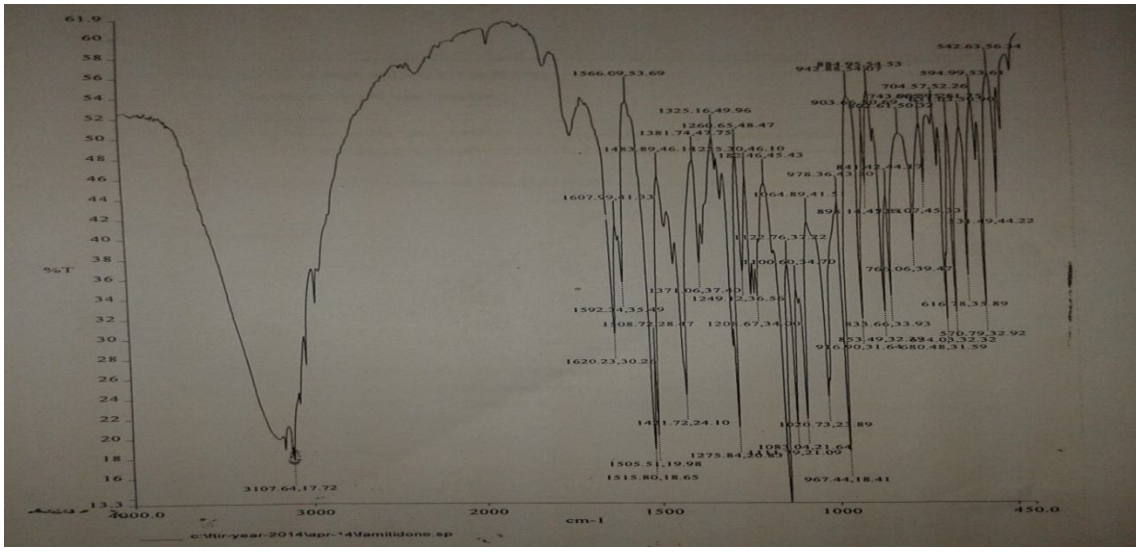

Figure 8: FTIR spectra of Famotidine

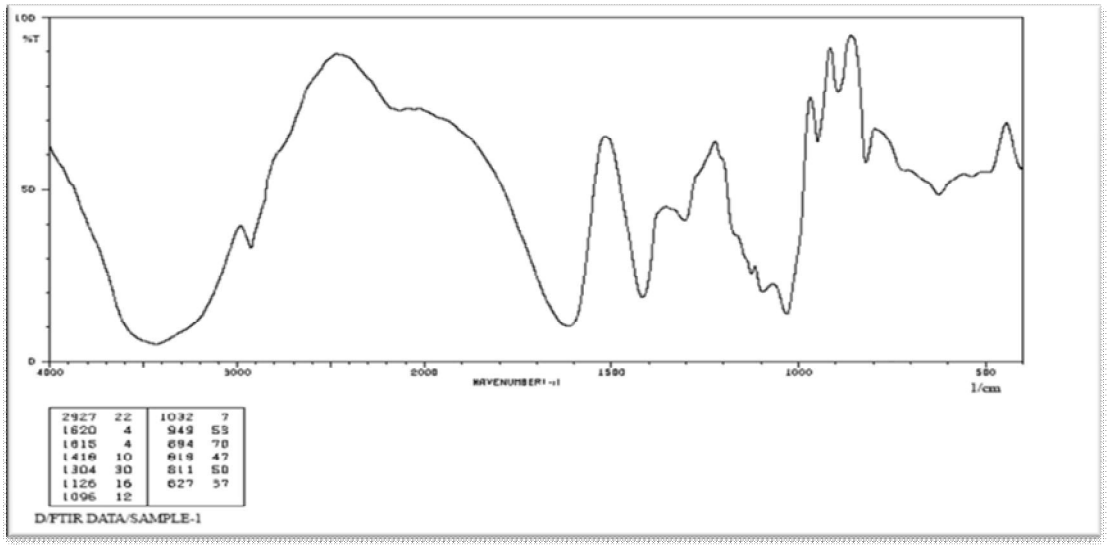

Figure 9: FTIR of Sodium Alginate

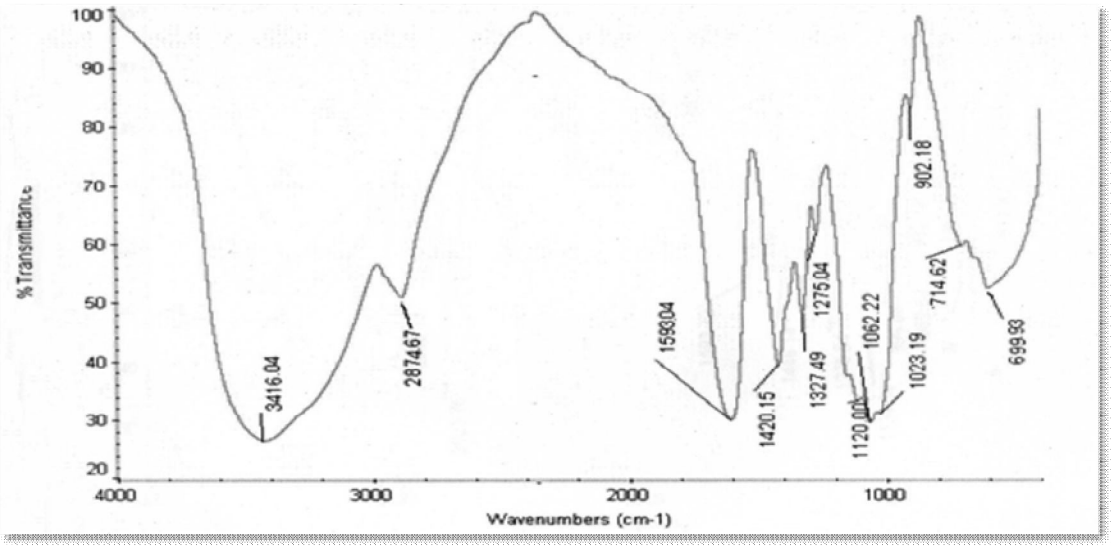

Figure 10: FTIR of Chitosan

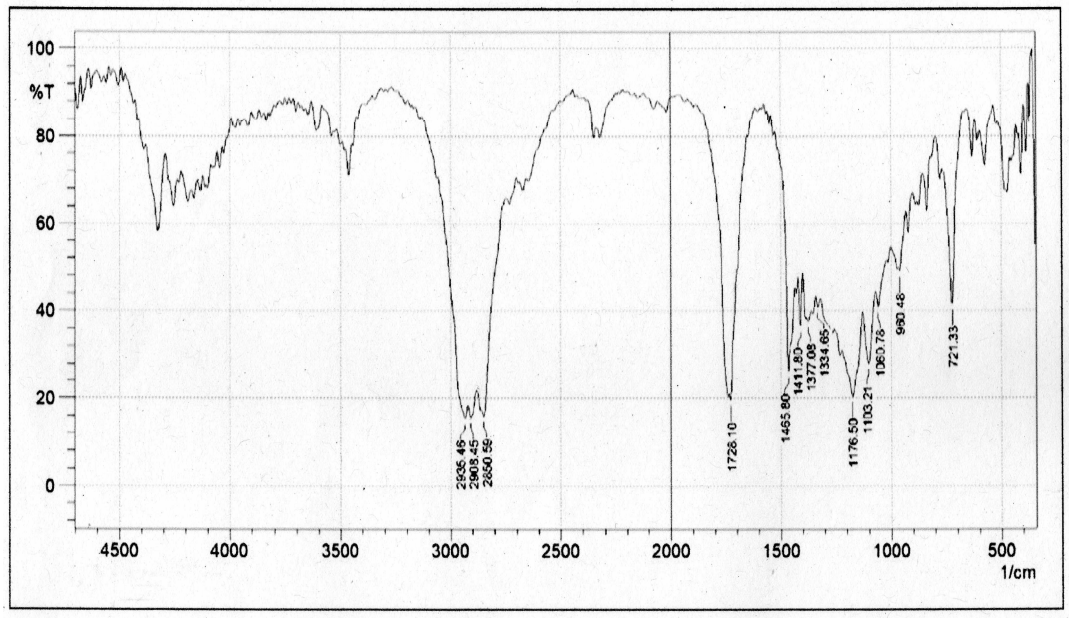

Figure 11: FTIR of Gelucire 43/01

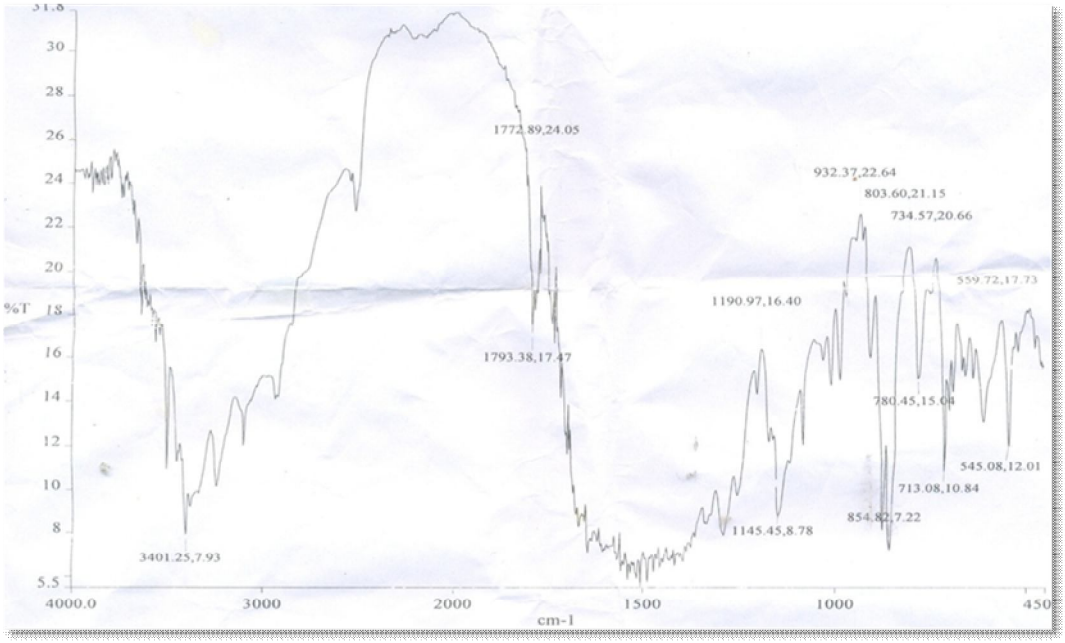

Figure12: FTIR spectra of physical mixture of sodium alginate based formulation

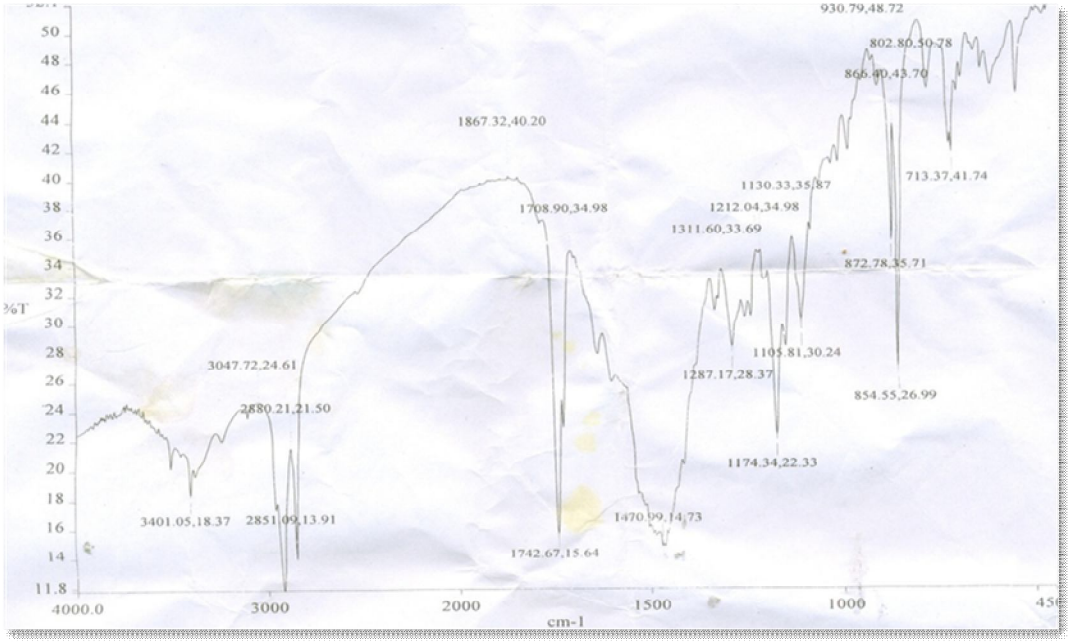

Figure 13: FTIR spectra of physical mixture of chitosan based formulation

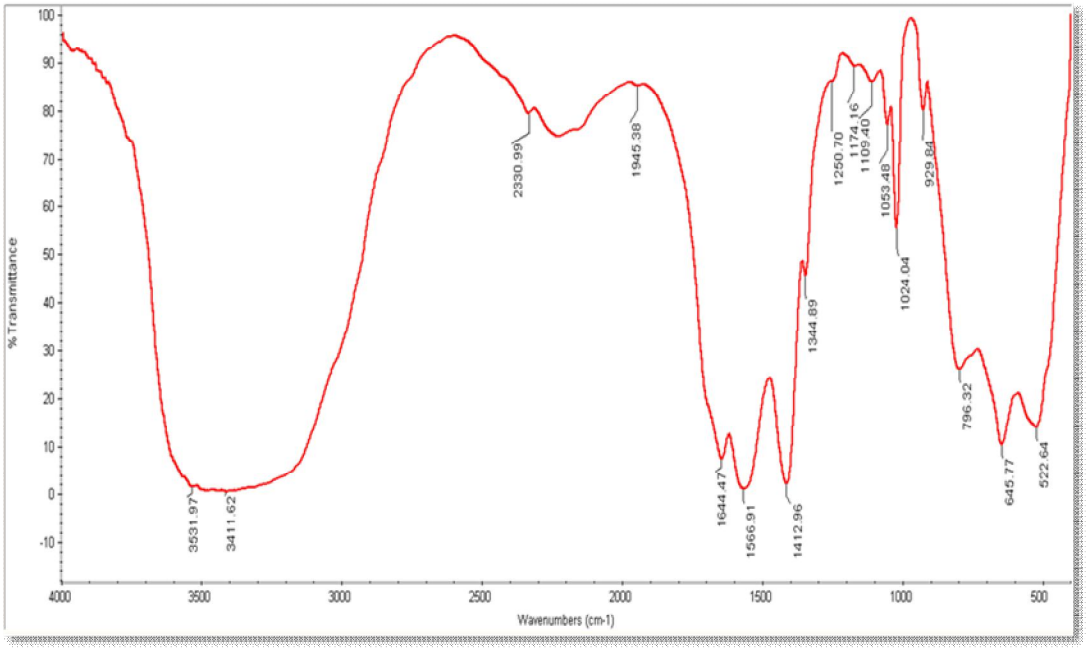

Figure 14: FTIR spectra of *in situ* gel of formulation

From all this it can be concluded that the major IR peaks involved like O-H stretching at 3401.25 cm^{-1}, N-H stretching at 3047.72 cm^{-1}, C-H (Alkane) stretching at 2880.21 cm^{-1} and 2851.09 cm^{-1}, C=O stretching at 1772.89 cm^{-1} and 1708.38 cm^{-1}, C-H stretching at 147.99 cm^{-1}. In the FTIR spectrum of physical mixture of

drug and excipients, all major peaks of drug and excipients are visible in the spectrum so it can be concluded that there is no possible interaction between drug and excipients takes place.

Buoyancy, Lag Time Studies, Absolute viscosity and *In vitro* gelation studies

All the formulations show the excellent lag time and buoyant for the entire period of drug release. This is prerequisite parameters for gastro-retention. As the in situ gelling formulations when comes in contact with dissolution medium and $CaCO_3$ effervesces for production of CO_2 and releases Ca^{++} ions. Released Ca^{++} ions are than interacted with COO^- on the alginate network which causes formation of strong aggregation of pairs of helices at egg box junction (gelled network), where the released CO_2 entrapped in the gel network, and the gel rises to the surface of dissolution medium (*in vitro*) or in stomach fluid (*in vivo*). This type of low density structure had the consistency of soft, palpable swollen lipid-hydrocolloid matrix which remains buoyant on simulated gastric fluid (SGF), without disintegrating, the throughout period of the procedure. Even so the lag time of the buoyancy was observed. It was therefore able to fulfill its objective to producing sustaining action in the gastric environment where the drug is maximum absorbed due to its high solubility in acidic pH and would therefore be effective in the treatment of *peptic ulcer* [8].

The viscosity was found higher in all the formulations due to the increased amount of Gelucire and polymers, thus we can say that in all the formulations viscosity is directly proportional to the amount of lipid phase and amount of polymers, formulations F5, F10, F11 and F12 due to the concentration of lipid phase it forms a very viscous system leads to increase in viscosity. *In situ* gelling characters of formulations exhibits a thixotropic shear thinning system. The gelation study was conducted in simulated gastric fluid (SGF) pH 1.2. All the formulations showed immediate gelation when contacted with SGF (Fig. 15, a and b) showed photographs of selected gelled *in-situ* formulations. Almost all of the formulations were gelled within 25 Sec. as soon as they come in contact with SGF and gelling time was ranging from 10 to 25 Sec depending upon polymer, Gelucire and drug concentration.

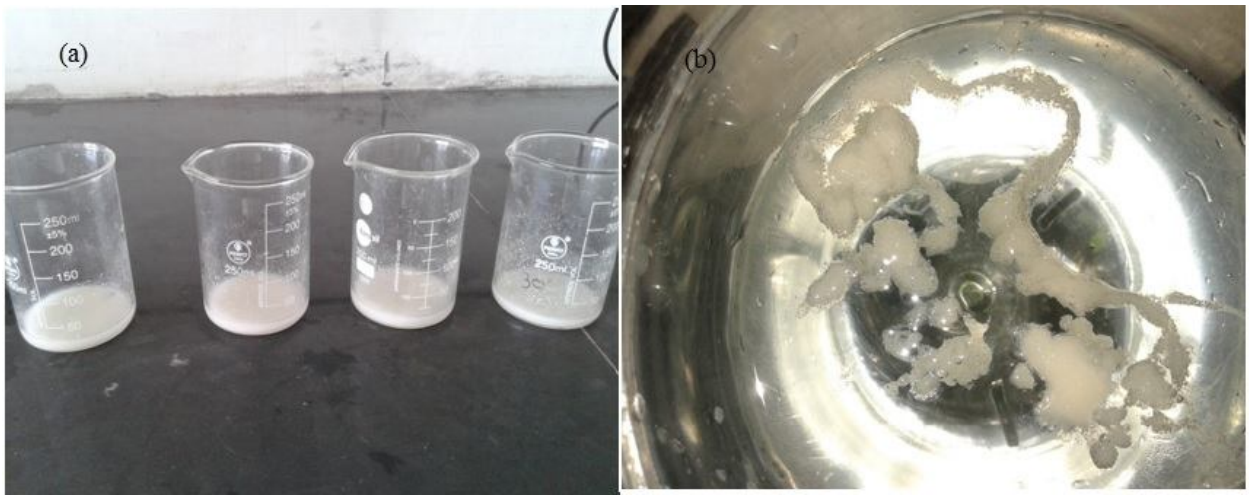

Figure 15: (a) Prepared emulsion gel at room temperature, (b) conversion of emulsion into the gel at 37 ± 0.5 ^{0}C in 0.1 M HCl L^{-1}

Table 3: Buoyancy, Lag Time Studies Absolute viscosity and *In vitro* gelation studies

Formulation code	Lag time (Sec) *	Buoyancy time (hour)	Absolute Viscosity (cps)* ± S.D	*In vitro* gelation time (Sec)*
F	10	6	122.11 ± 1.13	10
F*	10	6	112.33 ± 1.24	15
F1	12	6	152.33 ± 0.24	10
F2	11	6	174.21 ± 1.01	12
F3	14	6	158.22 ± 1.09	14
F4	13	6	197.31 ± 1.22	18
F5	14	6	256.11 ± 1.02	25
F6	12	6	198.54 ± 0.33	20
F7	11	6	189.37 ± 0.65	25
F8	14	6	179.22 ± 1.92	20
F9	11	6	159.54 ± 0.11	18
F10	13	6	199.04 ± 1.02	10
F11	14	6	269.94 ± 0.10	17
F12	12	6	199.34 0.90	23

*All the readings are taken in triplicate and mean values are calculated ± S.D (Standard Deviation)

Surface topography study by Scanning Electron Microscopy

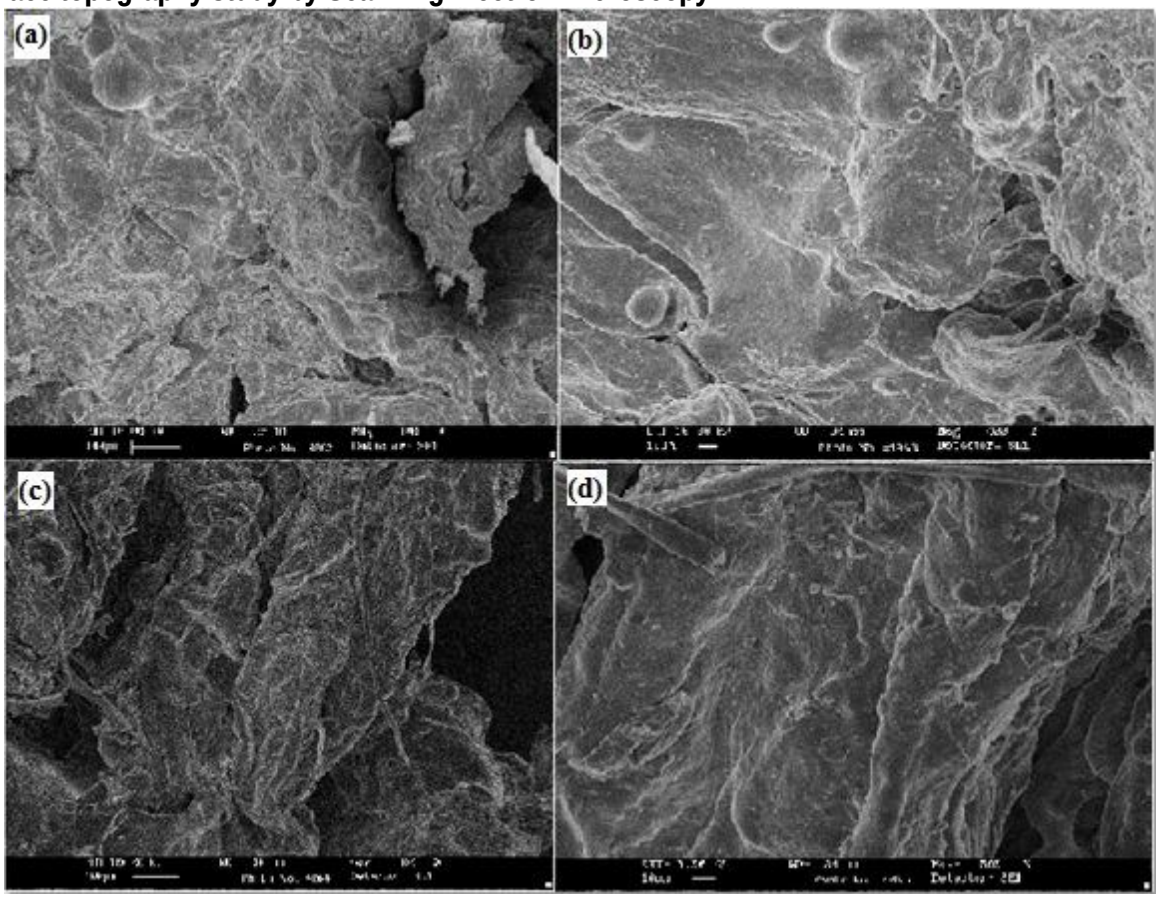

Figure 16: SEM image of *in situ* gel (a and b) at 100 X and 400X and Transverse section of gel (c and d) at 100 X and 400 X

The SEM figure of gel represents the surface topography of gel. At 100X and 400X magnification the surface structure seems to be smooth due to the property of Gelucire 43/01 from which we can say that it makes a coating over an external surface and acts as a retardant for the drug. While at transverse section (T.S) of gel which is studied at 100X the polymer strands clearly seen. Inside the internal structure there is a smooth surface at 500X which also confirm that Gelucire 43/01 acts internally and forms inside coating and also acts as a retarding parameter for the release of the drug.

In vitro drug release studies

In vitro release of drug in different formulation is performed by the help of USP XXVII paddle type II dissolution apparatus (Electrolab TDT-08L). The formulation was gently placed in dissolution apparatus and suitable amount of the sample was withdrawn at regular interval and the drug released into 0.1 M HCl L^{-1} (pH1.2) was calculated by UV spectroscopy (Shimadzu UV 1800) at λ_{max} 264nm.

Figure 17: Cumulative % drug release in 0.1 M HCl L^{-1} of formulations F-F4

Figure 18: Cumulative % drug release in 0.1 M HCl L^{-1} of formulations F5-F8

Figure 19: Cumulative % drug release in 0.1 M HCl L^{-1} of formulations F9-F12

Drug release from the conventional *in situ* gelling formulation F & F* without incorporation of Gelucire 43/01 was too rapid and with around 40% of drug release and with around 65% in 4 hours respectively. The release of drug from gel was characterized by the initial phase of burst effect. In case of formulation F1-F8 the drug release was 13 hours ranges from approximate 78% drug release till the time of 13 hours. This is due to the there is the formation of free Ca^{++} ions which induce the gelation due to the dimeric association of G block resins of Sodium alginate in the same time lipid part (Nagarwal *et al.,* 2009) of the emulsion, Gelucire43/01 further increases the viscosity of formulation that gives rise to highly viscous thixotropic solutions with viscosity found to be depend on Gelucire 43/01. In addition to these in formulation F9-F12 when two different charges polymers are used there is a formation of Polyelectrolyte complex in the presence of Gelucire 43/01.Although this lipidic phase increases the viscosity which retards the release of drug approximate 14 hours.

Curve fitting analysis

On applying curve fitted analysis the drug release followed determination of the mechanism of the release was done by employing Zero order, First order, Korsmeyer Peppas, Higuchi equations. It was observed that formulation F1, F2, F3 and F9 follow Korsmeyer Peppas model and this suggest that the drug release is from polymer matrixes due to the amount of Gelucire 43/01 and the solid drug is dispersed in an insoluble matrix the release of rate of drug is related to the rate of diffusion of drug **[14]**. Formulation F5, F6 and F7 follows the Higuchi square root model which indicates that the release mechanism is to be based on diffusion. Formulation F4 follows First order kinetics and this argues that drug depends on concentration. Formulation F8, F10, F11 and F12 follows Zero order kinetics and this indicates that the drug release is not depend on drug concentration and not depend on polymer concentration. The n-value ranging from 0.14-0.84 that depending upon the formulation variables the Famotidine release follow Fickian mechanism (formulation F1,F2, F3, F4, F5 and F7) means the drug is transported from higher concentration to the lower concentration of the dissolution medium. Formulation F6, F8, F9, F10, and F12 followed non-fickian model and F11 follow super case II transport means the release of drug from the backbone of polymeric stand. Mostly the non-fickian model is seen in Polyelectrolyte Formulation.

Table 4: Curve fitting analysis data

Formulation code	R^2				N
	Zero order	First order	Higuchi model	Korsmeyer Peppas model	
F1	0.9021	0.8923	0.9379	0.9399	0.14
F2	0.8423	0.7842	0.9132	0.9383	0.28
F3	0.8705	0.9084	0.8298	0.8672	0.37
F4	0.8574	0.8881	0.8084	0.7963	0.30
F5	0.9269	0.8930	0.9318	0.8994	0.43
F6	0.9601	0.9277	0.9760	0.9706	0.44
F7	0.8780	0.8459	0.8980	0.8775	0.42
F8	0.9893	0.9653	0.9855	0.9743	0.47
F9	0.9887	0.9467	0.9881	0.9876	0.65
F10	0.9897	0.9618	0.9733	0.9724	0.70
F11	0.9948	0.9643	0.9715	0.9792	0.84
F12	0.9984	0.9771	0.9770	0.9851	0.68
F	0.9510	0.9075	0.9774	0.9810	0.46
F*	0.9622	0.9735	0.9382	0.9370	0.31

CONCLUSION

Attempts have been prepared to develop *in situ* Emulgel of Famotidine by involving polymers i.e. Chitosan (cationic), Sodium Alginate (anionic) alone or in varied proportion according to need in the presence of waxy material Gelucire 43/01 other than this, *in situ* gelling system includes some additional advantages in terms of biocompatibility and biodegradability, these systems are fragile in nature and these systems do not have any mechanical strength to hold entrapped drug present in it. Including these hydrophilic polymers with lipid materials has been employed in the previous time to overcome the hurdle of fast release of drug from the matrices. An attempt has been made in developing *in situ* gelling emulgels using Gelucire 43/01 as a lipid phase and Sodium Alginate with low viscosity, Chitosan solution in deionized water as an aqueous phase of an emulsion. Geluciers are glycerides and polyglycerides of fatty acids. Their ampiphilic nature of the long chain hydrocarbon and the moieties of alcohol that makes these bases suitable as a lipid carrier for both types of drugs i.e. hydrophilic and lipophilic drugs. *In situ* gelling system is one of the techniques to retain the gel in the gastric environment of the stomach so that the maximum amount of drug can be released thereby increasing the bioavailability. The extremely variable nature of gastric emptying time leads the unpredictable bioavailability and its times to achieve the maximum plasma levels. Incorporation of drug in the controlled release gastro retentive dosage form which remains in the gastric region for several times and would significantly prolong the gastric residence time and improve

bioavailability, reduced drug wastage and enhance solubility of the drugs which are less soluble in high pH. Famotidine is a drug with short half life and shows solubility in acidic pH. It is the most popular drug for *peptic ulcer* and it belongs to H_2 antihistaminic class. Although, broad extensive research is needed for to confer the formations of polyelectrolyte complex between Chitosan and Sodium alginate. However, we got some success on these polyelectrolyte formulations based on *in situ* gel as on initial phase.

ACKNOWLEDGEMENT

Authors are thankful to Sardar Bhagwan Singh PG Institute of Biomedical Sciences and Research, Balawala, Dehradun. Authors are also thankful to the Indian Institute of Technology, Roorkee (IIT - Roorkee), India and Wadia Institute of Himalyan Geology, Dehradun, India for characterization of samples in time**.**

CONFLICTS OF INTEREST

Authors declare no conflicts of interest.

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