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Research Article

FORMULATION AND IN-VITRO EVALUATION OF GASTRORETENTIVE MUCOADHESIVE FILM OF FAMOTIDINE

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ABSTRACT

The present work is based on the formulation and *In-vitro* evaluation of a gastroretentive mucoadhesvie based drug delivery system containing Famotidine for controlled release. It consists of a drug loaded polymeric film folded into a hard gelatin capsule. After administration film unfolds and its swelling and bioadhesion to the gastric mucosa. Famotidine, a histamine H_2 receptor antagonist used for gastroesophageal reflux disease (GERD), duodenal ulcer and gastric ulcer. Famotidine absorbed only in the initial part of gastro intestinal tract (GIT) and has less bioavailability. Thus by retaining the drug in the gastric region improves its bioavailability. Films were prepared by solvent-casting method using HPMC K4M, Eudragit RLPO and Carbopol 971P NF as polymers and PEG 400 as the plasticizer. The prepared film were evaluated for various parameters such as film thickness, folding endurance, uniformity of weight, surface pH, determination of drug content, moisture content, swelling index, *In-vitro* mucoadhesive study retention time, *In-vitro* unfolding behavior and *In-vitro* drug release studies and drug release kinetics. Differential scanning calorimetry revealed there were no polymorphic changes in drug as well as polymers during the formulation of polymeric film. Optimized formulation showed 99.02 % drug release at the end of 12 hrs and it follows the Korsmeyer-peppas kinetics model of drug release which involves the non- Fikion diffusion mechanism.

Keywords: Gastroretentive mucoadhesive film, Solvent casting method, Famotidine.

INTRODUCTION

Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutics advantages , such as ease of dosing administration, patient compliance and flexibility in formulation. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have limited bioavailability because of short residence time thus drug release in stomach is often short. This problem can be overcome by prolonging the residence time of drug in the stomach. The most important approach for achieving a prolonged release of drug in GIT is to control the gastric residence time (GRT) by preventing its elimination from the GIT. Dosage forms with an increased gastric residence time (GRT) are known as gastroretentive dosage forms (GRDF), this will provide new and important therapeutics options. To extend the residence time of dosage form in stomach, a number of strategies have been developed, including (a) reducing density to promote floating in gastric content (b) increasing the density to promote retention in the lower part of stomach (c) introducing mucoadhesive properties and (d) producing a formulation that swell or unfold in the stomach to hinder its escape through the pyloric sphincter.

An alternative strategy is to combine mucoadhesion with the ability to expand by unfolding and swelling. Gastroretentive mucoadhesive drug delivery system prolong

the drug release rate from formulation in stomach and upper part of small intestine until all the drug released for desired period of time. The aim of present work was to develop innovative gastroretentive mucoadhesive formulation based on drug loaded polymeric film folded in hard gelatin capsule. After ingestion the capsule dissolves and releases the film which then unfolds in stomach and swells to a larger dimension resulting in its increased retention. Based on this hypothesis, the gasrroretentive mucoadhesive film was designed in such way that they should be retained in the stomach for a prolonged period of time, thus maximizing the exposure of the drug to its absorption site.

Famotidine, 3-[({2-[(diaminomethylidene) amino]-1, 3-thiazol-4-yl} methyl) sulfanyl]-N'-sulfamoylpropanimidamide) is a histamine H_2 receptor antagonist. It has been used in treatment of gastroesophageal reflux disease (GERD), duodenal ulcer and gastric ulcer. Fomotidine may be given orally in a dose of 20-40 mg daily. The half life of Famotidine is about 2-3 hrs and has only 40-45 % absolute bioavailability after oral administration due to incomplete absorption. On this basis, a controlled release formulation of Famotidine is very desirable.

The present work was undertaken to formulate gastroretentive mucoadhesive film of Faomtidine for gastric retention has been developed using solvent casting method and evaluated to provide a prolonged drug release and improve bioavailability and therefore efficacy by retaining it in the stomach for a longer period.

MATERIALS AND METHODS

Materials

Famotidine and HPMC K4M were obtained as a gift sample from IPCA Laboratories, Mumbai. Eudragit RLPO was obtained as gift sample from Evonik Pharma, Ind, Mumbai. Carbapol 971 P NF and PEG 400 were obtained from Modern Science Apparatus Pvt. Ltd. Nashik.

Method

Pre-formulation study

UV spectroscopy

The drug was scanned in UV Spectrophotometer to detect the λmax and to drawn the calibration curve of the drug in 0.1 N HCl as a solvent. The drug was used in concentration ranges of 5-25 ppm. The spectra and calibration curve of the drug is as shown in Figure 1and 2.

Differential scanning calorimetry (DSC)

Thermogram of Famotidine was obtained using differential scanning calorimetry. Sample was kept in aluminium pan, sealed and heated at constant rate of 10°C/min over temperature range of 10 to 200°C. By purging nitrogen with flow rate of 10 mL/min inert atmosphere was maintained.

FT-IR spectrum

The drug was subjected to FT-IR studies (Shimadzu; 8400S) for the purpose of characterization. FT-IR technique is one the most powerful technique of chemical identification. Drug was mixed with potassium bromide in 1:99 proportions and spectrum was obtained in range of 400-4000 cm^{-1}. Potassium bromide was used as a blank while running spectrum.

Compatibility studies

Differential scanning calorimetry

Thermogram of physical mixture i.e. drug with polymers was obtained using differential scanning calorimeter. Sample was kept in aluminium pan, sealed and heated at constant rate of 10°C/min over temperature range of 10 to 200°C. By purging nitrogen with flow rate of 10 mL/min inert atmosphere was maintained.

FTIR spectrum

The physical mixture i.e. drug with polymers was subjected to FT-IR studies (Shimadzu; 8400S) for the purpose of to check any possible drug polymers interaction. IR technique is one the most powerful technique of chemical identification. Drug was mixed with potassium bromide in 1:99 proportions and spectrum was obtained in range of 400-4000 cm^{-1}. Potassium bromide was used as a blank while running spectrum.

Preparation of gastroretentive mucoadhesive films

The mucoadhesive films were prepared by solvent casting technique. The polymer solution was prepared by overnight soaking of HPMC K4M, Carbapol 971 P NF in water to obtain clear and bubble free solution and Eudragit RLPO was dissolved in isopropanol: water (3:1). HPMC K4M, Carbapol 971 P NF and Eudragit RLPO were mixed followed by continuous stirring to which PEG 400 was added as plasticizer. Famotidine solution mixed in polymeric solution with vigorous stirring to give clear viscous transparent solution. The resulting solution was poured in glass petriplate and allowed to firmly set for 30 min at room temperature. This plate was then dried in oven at 50 ^{o}C. Once the film is

completely dried it cut into size 4 cm x 1 cm rectangles and used to fill hard gelatin size 0 capsules by zigzag folding is as shown in Figure 7.

Formula design

From the literature survey studies the concentration of HPMC K4M and Eudragit RLPO was selected. Based on concentration 2 factors will be evaluated, each at 3 levels, & experimental trials will be performed at 9 possible combinations. The amount of HPMC K4M(X1) and Eudragit RLPO(X2) were selected as independent variables. The composition of formula is as shown in Table 1.

Evaluation of gastroretentive mucoadhesive films

Thickness

Three films of each formulation were taken and the film thickness was measured by using micrometer screw gauge at different strategic locations (3 locations). Mean thickness of each was calculated.

Folding endurance

Three films of each formulation of 4 cm × 1 cm were cut by using sharp blade. Folding endurance was determined by repeatedly folding a small strip of film at the same place till it break. The number of times, the film could be folded at the same place without breaking gives the value of folding endurance. The mean value of three readings was calculated.

Uniformity of weight

Three films of every formulation were selected randomly and individual weight of each 4 cm×1 cm film was noted on digital balance. The average weight was calculated.

Drug content

Accurately size 4 cm×1 cm of the films were taken and dissolved in 100 mL of 0.1 N HCl solutions in 100 mL volumetric flask then whole solution was sonicated. After sonication and subsequent filtration, suitable dilutions were made with 0.1 N HCl solutions. The prepared solutions were analyzed by using UV spectrophotometer.

Moisture content

The prepared films weighed individually and kept in a desiccators containing calcium chloride at room temperature for 24 hrs. The films were weighed again after a specified interval until they showed a constant weight. The percent moisture content was calculated by using following formula.

% Moisture content = [Initial weight – Final weight / Final weight] x 100

Surface pH

The film to be tested was placed in a test tube and was moistened with 1.0 mL of distilled water and kept for 30 seconds. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation.

Swelling index

Swelling of films was examined for triplicate in 0.1N HCl. After recording the initial weight of a film (W1), it was immersed in medium of temperature 37 ± 1^{0}C for 360 min and weighed again (W2).

Swelling index (%) = (W2-W1)/W1 x 100.

***In-vitro* mucoadhesive study**

Fresh goat gastric mucosa was obtained from a local slaughter house, placed in saline solution, and used within 2 hrs of slaughter. The mucosal membrane was cleaned and separated by removing the underlying fat and loose tissues. Bioadhesive strength of the film was measured on a balance torsion type. The left arm of the balance was replaced by a small plastic cap vertically suspended through a thread. The goat gastric mucosa was cut into pieces and washed with 0.1N HCl. A piece of gastric mucosa was tied to the open mouth of a small glass beaker which was placed and tightly fitted in the center of large glass beaker. The 0.1N HCl (37 ± 2 $^\circ$ C) was filled in to the glass beaker in such a way that it makes contact with gastric mucosal surface. The film was stuck to the lower side of flat surface plastic cap with cyanoacrylate glue. The balance was balanced with weight on the right hand scale. A weight was removed from the right hand side scale, which lowered the pan along with the film over the mucosa. The balance was kept in this position for 5 min contact time, and then slowly the weights were increased on the right hand side scale till the film separated from the mucosal surface**.**

Mucoadhesive strength was measured as force of adhesion in Newton's by using formula-

Force of adhesion (N) = Mucoadhesive strength / 1000 X 9.81

Retention time

The film was applied to freshly prepared goat stomach mucosa fixed to a glass slide with cyanoacrylate glue and suspended from a disintegrating apparatus. The slide was

suspended in a beaker filled with 900 mL 0.1 N HCl and moved vertically in and out of the medium by switching on the motor. The experiment was continued until the film detached or eroded from the mucosa.

***In-vitro* unfolding behavior**

The capsules were taken for *In-vitro* unfolding behavior study in 900mL 0.1N HCl at 37 ± 0.5ºC using the dissolution USPXXIII Apparatus1 basket (Electrolab) at 50 rpm. Baskets were removed after 5, 15,30,60,90,120,240,480 and 720 min and the films were examined for their unfolding behavior.

***In -vitro* drug release study**

The in vitro drug release study of gastroretentive mucoadhesive film in capsule was carried out in the dissolution USPXXIII Apparatus I basket (Electrolab) 900 mL 0.1 N HCl was used as a dissolution medium. Temperature was maintained at 37±0.5°C and basket was rotated at the speed of 50 rpm. Drug release was monitored for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 hrs. 5 mL of samples was withdrawn at each time intervals and sink condition was maintained by replacing an equal amount of fresh dissolution medium. Samples were filtered and analyzed by UV spectrophotometer at 265.8 nm.

Dissolution kinetics

The dissolution profile of formulations was subjected to various models such as Zero order kinetics, First order kinetics, Higuchi, Korsemeyer-Peppas and Hixson-Crowell to assess the kinetics of drug release from prepared gastroretentive mucoadhesive film of Famotidine.

Differential scanning calorimetry (DSC)

Thermogram of mucoadhesive film formulation batch F8 was obtained using differential scanning calorimeter. Film sample were kept in aluminium pan, sealed and heated at constant rate of 10°C/min over temperature range of 10 to 200°C. By purging nitrogen with flow rate of 10 mL/min inert atmosphere was maintained.

RESULTS AND DISCUSSION

For pre-formulation study

UV Spectroscopy

The λmax of Famotidine obtained at 265.8 nm and the calibration curve was constructed using concentration range 1-25 ppm, equation was found to be y = 0.027 X + 0.035 and the regression coefficient R^2 =0.995.Spectra and calibration curve shown Figure1 and 2.

Differential scanning calorimetry (DSC)

As reflected by DSC thermogram shown in Figure 3, sharp endothermic peak was observed at 160.65 ºC corresponding to melting point of drug in crystalline form; reflecting purity of Famotidine .

FT-IR spectroscopy

FT-IR spectrum of procured Famotidine was shown in Figure 4 and spectral interpretation was done. The characteristics IR absorption peaks of Famotidine at 3348.54 cm^{-1} (N-H asymmetric, sulphonamide), 3240.52 cm^{-1}(N-H symmetric, sulphonamide), 1288.49cm^{-1} (C=N stretching) 1145.75 (O=S=O stretching), 906.57cm^{-1} (S-N stretching) were there in drug sample spectrum; which confirmed the purity of Famotidine.

Compatibility Studies

To check out any possible interaction between drug and polymers used, compatibility study using DSC and FT-IR was carried out. DSC results reflected similar thermal behaviour of physical mixture as that of pure drug. A sharp endothermic peak noted at 163.45 °C in case of Famotidine, indicative of its melting point shown in Figure 5. FT-IR spectroscopic study results discovered no any new peak appearance or disappearance of existing peaks, discarding any chemical interaction probability amongst drug and polymers used. The characteristic peaks at 3340.82 cm^{-1} (N-H asymmetric, sulphonamide), 3240.52 cm^{-1}(N-H symmetric, sulphonamide), 1276.92 cm^{-1} (C=N stretching) 1161.19 (O=S=O stretching), and 902.72 cm^{-1} (S-N stretching) were recognized in all peaks shown in Figure 6. All characteristic peaks of Famotidine were in physical mixture spectrum. Thus, FT-IR spectroscopy results showed Famotidine was compatible with selected polymers and possess good stability.

For gastroretentive mucoadhesive film formulation

Thickness

The average thickness of all films is given in Table 2. The average thickness of all the mucoadhesive films ranged from 0.26 ± 0.0471 to 0.51 ± 0.0623 mm. The thickness values were uniform for films within the respective formulation batch.

Folding endurance

The number of folding required to break or crack a film was taken as the folding endurance. The average folding endurance of mucoadhesive films ranged from 224.6± 2.867 to 295.6 ± 1.699 times. The folding endurance

was found to be increased with an increasing concentration of HPMC-K4M and presence of PEG 400. All films showed good value of folding endurance in Table 2. Indicate no breakage of film during its use.

Uniformity of weight

The average weight of all films is given in Table 2. Uniformity of weight values (mg) of different films were found to be in the range of 122 ± 0.0026 to 201 ± 0.0017 mg. The weight uniformity weight values were uniform for films within the respective group of formulation type. There was proportional gain in weight of films with that of increase in the quantity of polymers.

Surface pH

Surface pH of film was determined to check whether the film causes irritation to the mucosa. The pH of all films was found to be in the range of that normal pH 6.10 ± 0.021 to 7.21 ± 0.046 given in Table 2. Hence no mucosal irritation was expected from these prepared films. As an acidic or alkaline pH may cause irritation, it was determined to keep the surface pH as close to neutral as possible.

Drug content

The percentage drug content was determined by UV spectroscopy method using the standard calibration curve and it was determined for three films of each formulation in the range of 93.82 ± 2.24 to 99.07 ± 0.419 % shown in Table 2. As the drug content values of the respective group of formulation did not show any significant difference that means the drug was uniformly dispersed in the films, provided accurate dose to patient.

Moisture content

The moisture content was found to be in the range of 1.17 ± 0.028 to 3.46 ± 0.041 % given in Table 3. It was found that there is negligible amount of moisture present in films.

Swelling index

The swelling property of polymer is important for its mucoadhesion and its drug release pattern. The swelling indexes of all films were found to be in the range of 83.16 ± 0.623 to 145.57 ± 0.421 % given in Table 3. The swelling index was directly proportional to the amount of hydrophilic polymer HPMC K4M and hydrophobic polymer Eudragit RLPO. The batch F8 showed high swelling index due to high content of HPMC K4M and Eudragit RLPO. Whereas batch F2 showed lowest swelling index due to lower content of HPMC K4M and Eudragit RLPO.

***In-vitro* mucoadhesive study**

Mucoadhesive strength was found to be directly proportional to the concentration of HPMC K4M and presence of optimum amount of Carbaopol 971 P NF polymer. This may be due to the formation of strong gel which penetrates deeply into the molecules of mucin and show strong bioadhesion. Thus formulations F2 which contain lowest amount of HPMC K4M showed lowest bioadhesion while F8 containing highest amount of HPMC K4M.Result is as shown in Table 3.

Retention time

Retention time was found to be varied from 8 to 12 hrs given in Table 3. As the content of HPMC K4M increased, the residence time of film increased and also depend on presence of Carbapol 971 P NF. The F2 formulation showed lowest residence time while F8 showed the highest residence time; this may be due to high content of hydrophilic polymer HPMC K4M which leads to increased swelling of formulation and mucoadhesive bond formation due to presence of Carbapol 971 P NF for longer time.

***In-vitro* unfolding behavior**

The film was folded in Zigzag manner and was filled in capsules they gave a good unfolding action within 10-90 min shown in Table 3 and Figure 8. Once the capsule was completely dissolved in gastric media they are ready to attach to the gastric mucosa.

***In-vitro* drug release study**

From dissolution data, it was found that the drug release from the film varied with respect to the proportion of polymers. With increase in polymer concentration the viscosity of the gel layer increases as well as the diffusion path length of the drug increases this causes the less drug release at the higher level of the HPMC K4M and vice versa. The formulation F4, F8 and F9 shows good drug release. Increased amounts of HPMC K4M retard the drug release up to some extent but presence of Eudragit RLPO might be extend drug release up to 12 hrs. Figure 9 shows graphical presentation of comparative dissolution profile of all batches.

Dissolution kinetics

The in-vitro drug release data was best fit to Korsemeyer-peppas release model for most of the formulations because of higher R^2 value and interpretation of release exponent values (N) enlightens in understanding the release mechanism from the delivery system. This is shown in Table 4.The release exponent values

thus obtained were ranged from 0.574 to 0.879.Thus the all formulations exhibited anomalous (non-Fickian transport) diffusion mechanism i.e. rate of solvent penetration and drug release are in the same range.

Differential scanning calorimetry (DSC)

DSC thermogram of the film of optimized batch F8 is shown in Figure 10. Results showed that the sharp endothermic peak was observed of the drug at 161.89 ^{0}C .Thus, there was not a significant shift in peak endothermic of formulation as that obtained from individual drug sample, it can be concluded that there was no interaction occurred between the polymers and drug Famotidine in the film formulation.

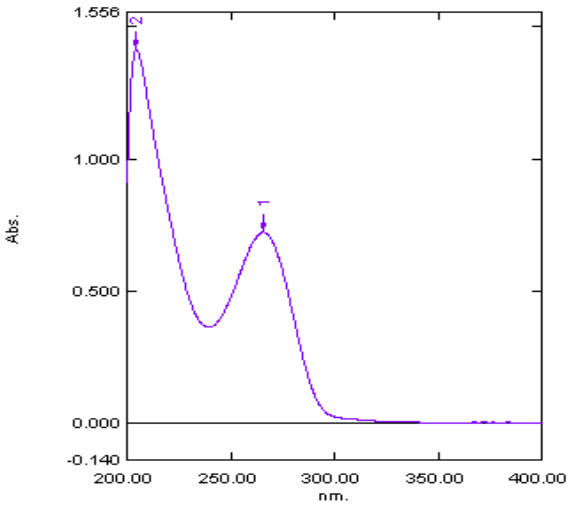

Fig. 1: UV spectra of Famotidine in 0.1 N HCl

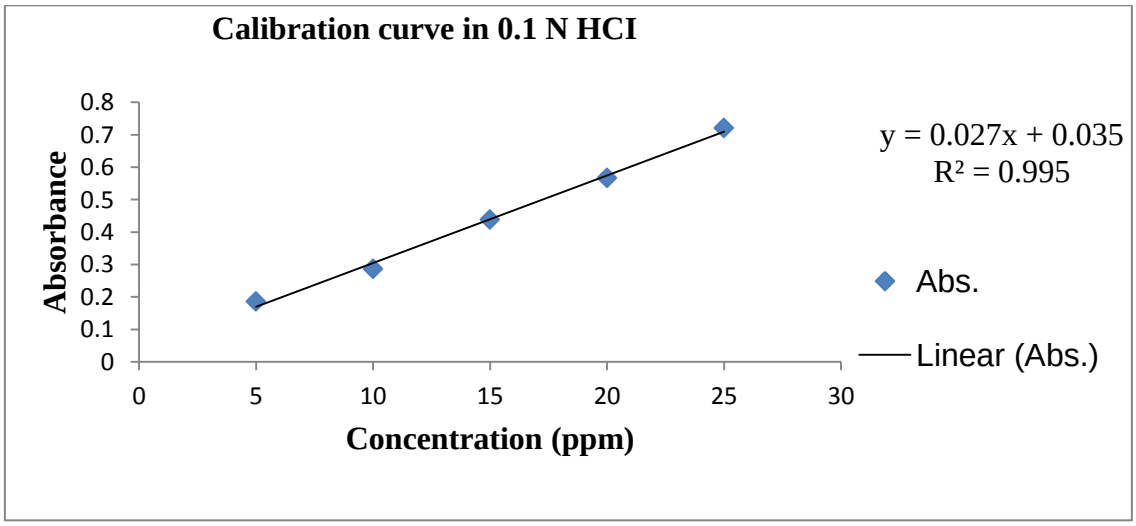

Fig. 2: Calibration curve of Famotidine in 0.1 N HCl

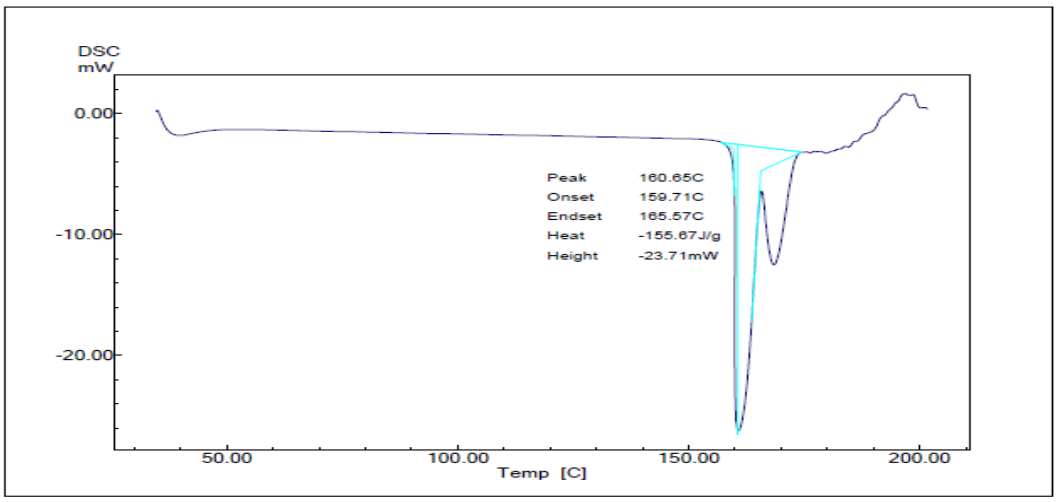

Fig. 3: DSC thermogram of Famotidine

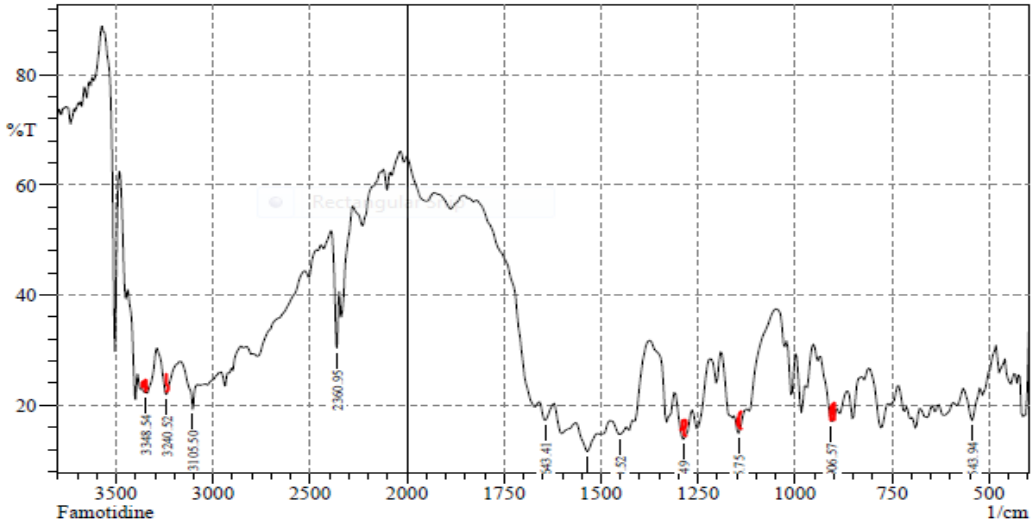

Fig. 4: FT-IR spectrum of Famotidine

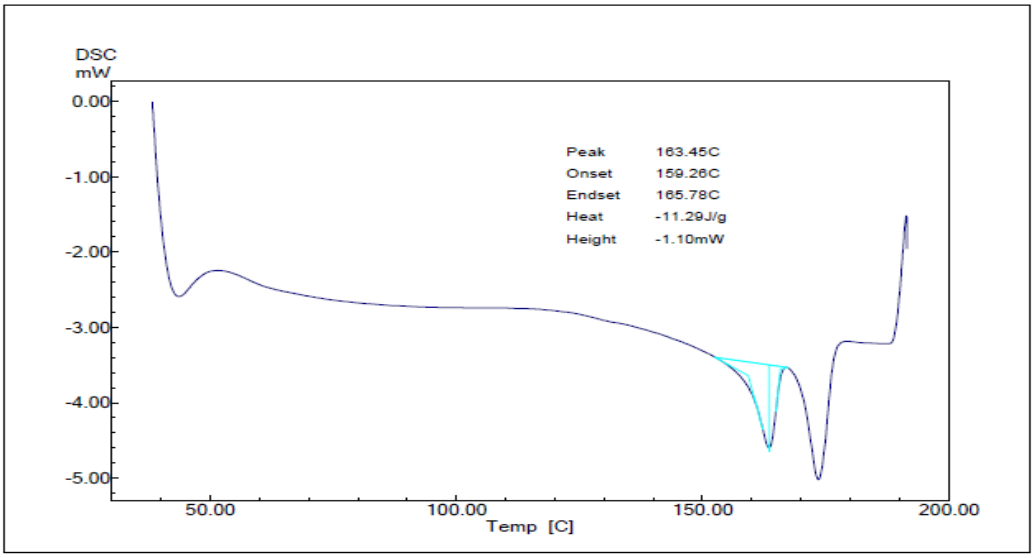

Fig. 5: DSC thermogram of physical mixture of Famotidine and excipients

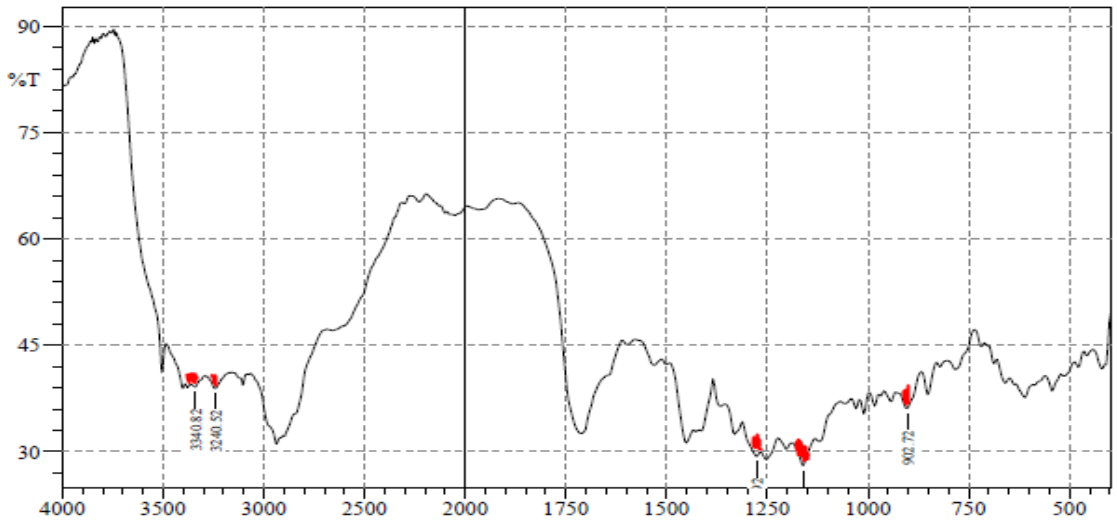

Fig. 6: FT-IR spectrum of physical mixture of Famotidine and excipients

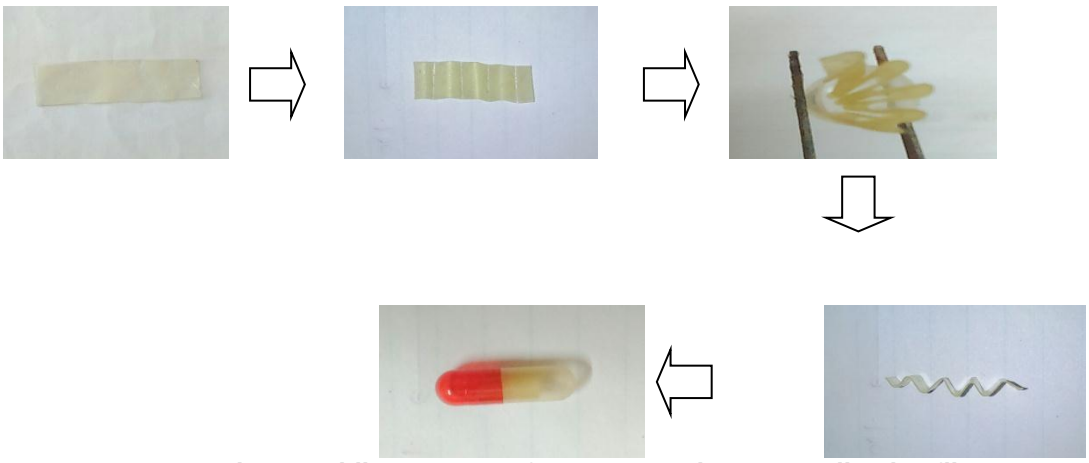

Fig. 7: Folding Pattern of gastroretentive mucoadhesive film

Table 1: Composition of gastroretentive mucoadhesive films

Ingredients	Batches and Quantity								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Famotidine (mg)	20	20	20	20	20	20	20	20	20
HPMC K4M (mg)	37	25	25	37	50	25	37	50	50
Eudragit RLPO (mg)	75	50	100	100	50	75	50	100	75
Carbopol 971P NF (mg)	40	40	40	40	40	40	40	40	40
PEG 400 (mL)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1

Table 2: Results of evaluation parameters

Parameters / Batches	Thickness (mm)± SD	Folding endurance (times))± SD	Uniformity of weight (mg)± SD	pH ± SD	% Drug content ± SD
F1	0.31 ± 0.102	237± 1.632	162± 0.0024	6.45± 0.036	95.94±0.755
F 2	0.26 ± 0.0471	224.6± 2.867	122 ± 0.0026	6.79 ± 0.02	93.82±2.24
F 3	0.3 ± 0.0816	235.3± 2.867	172 ± 0.0024	7.02± 0.033	94.47±1.043
F 4	0.51 ± 0.0623	243± 1.632	185± 0.0029	6.37± 0.009	95.23±1.848
F 5	0.43 ± 0.1247	287.3± 1.247	151 ± 0.0024	7.21±0.0046	95.71±2.108
F 6	0.26 ± 0.1247	227.3± 2.054	153± 0.0032	6.10± 0.012	97.35 ±1.278
F 7	0.26 ± 0.0471	246± 2.943	137 ± 0.0024	6.65± 0.016	96.59 ±1.658
F 8	0.48 ± 0.0623	293.6± 0.943	201 ± 0.0017	6.63± 0.086	99.07 ±0.419
F 9	0.36 ± 0.1247	295.6± 1.699	176 ± 0.0020	6.99± 0.016	97.15± 1.811

***** Mean± S.D., n=3

Table 3: Results of evaluation parameters

Parameters / Batches	Moisture content (%) ± SD	Swelling index (%) ± SD	*In-vitro* mucoadhesive study (N)±SD	Retention time (hrs)	*In-vitro* unfolding behavior (min)
F1	2.58±0.049	104.64 ±0.455	0.577±0.002	12	30
10	1.63±0.044	83.16 ±0.623	0.425±0.0032	8	10
F 3	1.17±0.028	91.25 ±0.891	0.436±0.0038	11	25
F 4	2.74±0.012	108.66±1.247	0.494±0.0033	12	90
F 5	3.36±0.044	107.86±0.659	0.587±0.0044	10	15
F 6	1.38±0.041	85.28±1.176	0.491±0.0078	8	15
F 7	2.28±0.024	96.35±0.954	0.59±0.0021	9	20
F 8	3.08±0.033	145.57±0.421	0.639±0.0043	12	90
F 9	3.46±0.041	133.52±1.058	0.618±0.0053	12	90

***** Mean± S.D., n=3

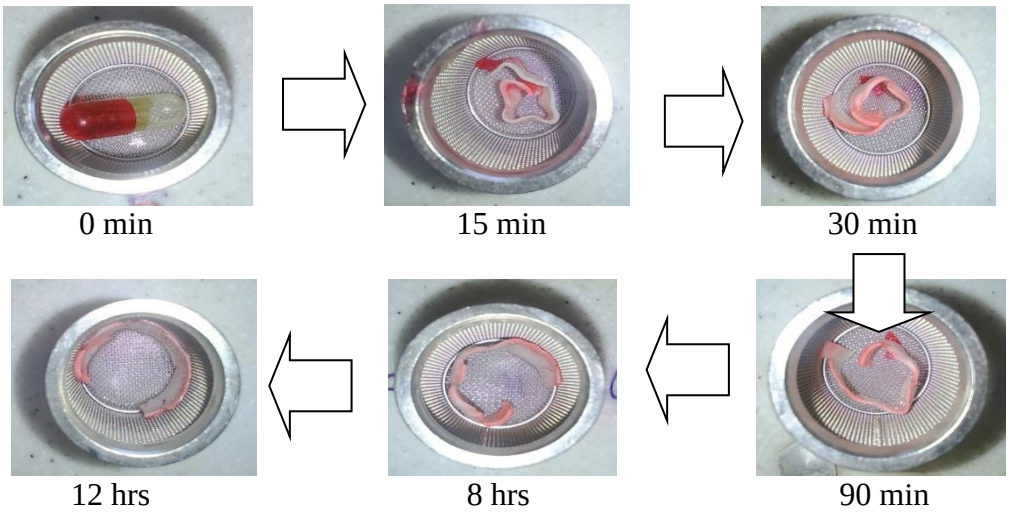

Fig. 8*: In-vitro* unfolding behaviour of film

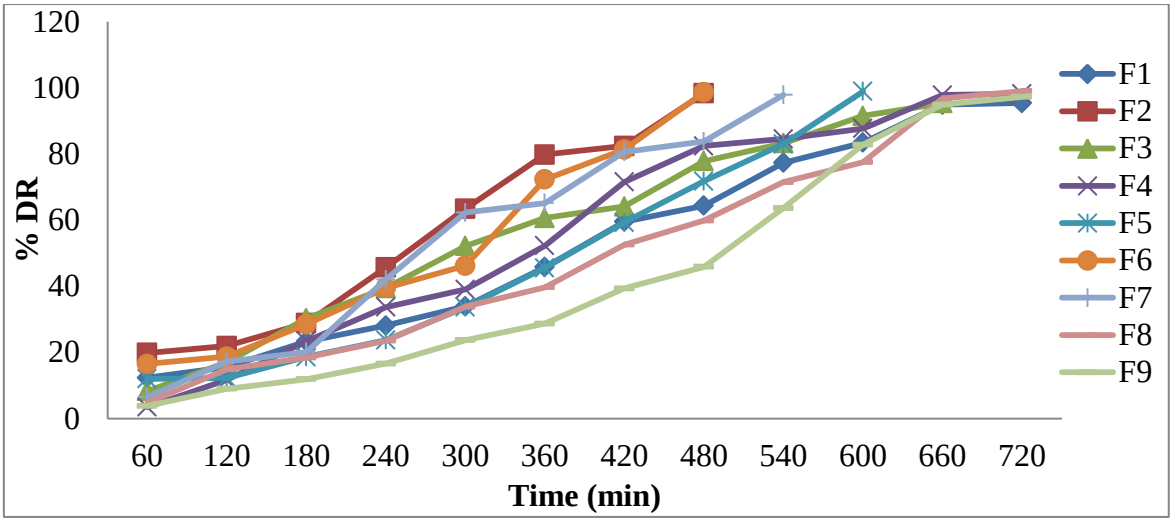

Fig. 9: Comparative *In- vitro* drug release profiles of gastroretentive mucoadhesive film of Famotidine

Table 4: Dissolution kinetics

Batch	Zero	First	Highuchi	Hixson-crowell	Weibull	Korsemeyer-peppas	
	R^2	R^2	R^2	R^2	R^2	R^2	N
F1	0.985	0.887	0.943	0.941	0.647	0.963	0.868
F2	0.970	0.818	0.927	0.910	0.604	0.912	0.697
F3	0.988	0.937	0.991	0.981	0.735	0.979	0.764
F4	0.969	0.930	0.972	0.971	0.721	0.977	0.870
F5	0.961	0.716	0.886	0.839	0.481	0.908	0.695
F6	0.959	0.740	0.895	0.965	0.518	0.920	0.820
F7	0.974	0.863	0.962	0.944	0.741	0.977	0.758
F8	0.985	0.785	0.935	0.883	0.542	0.989	0.879
F9	0.944	0.774	0.865	0.847	0.516	0.976	0.889

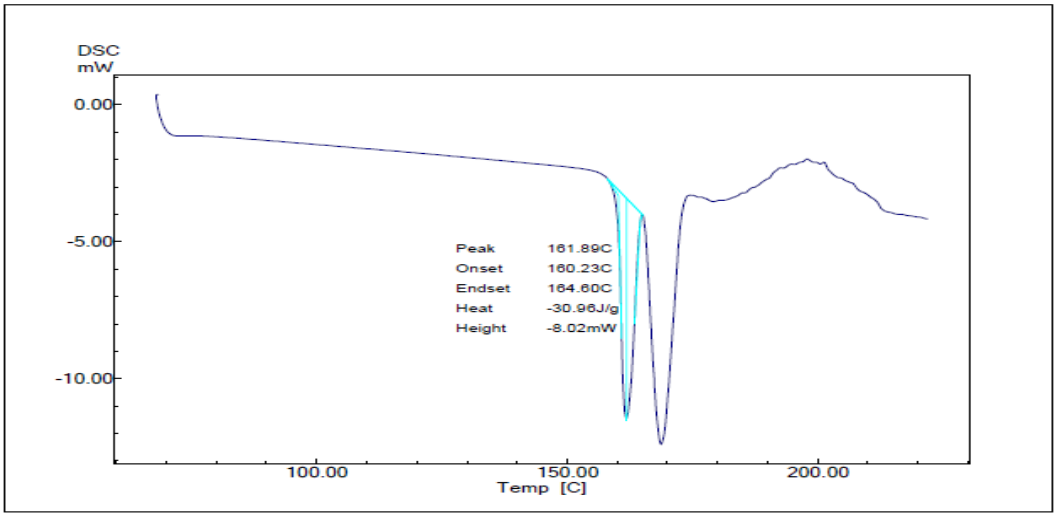

Fig. 10: DSC thermogram of gastroretentive mucoadhesive film of Faomotidine formulation batch F8

Table 5: Results of optimized batch F8

Sr. No.	Parameters	Results
1	Thickness(mm)±SD	0.48±0.0623
2	Folding endurance (times)±SD	293±0.943
3	Uniformity of weight± SD	201±0.001
4	pH± SD	6.63±0.086
5	Drug content± SD	99.07± 0.419
6	Moisture content(%)± SD	3.08± 0.033
7	Swelling index(%)± SD	145.57± 0.421
9	*In- vitro* mucoadhesive study (N) ± SD	0.639± 0.0043
8	Retention time(hrs)	12
10	*In- vitro* unfolding behavior (min)	90
11	*In-vitro* drug release study (%)	99.02 in 12 hrs
12	Dissolution kinetics	R^2 =0.989 and N=0.879 (non Fickian transport diffusion mechanism)
13	DSC	161.89 ^{0}C

CONCLUSION

Gastroretentive mucoadhesive film of Famotidine has been developed using solvent casting method to provide a control release action to treat gastroesophageal reflux diseases, duodenal ulcer and gastric ulcer. All films prepared were smooth and elegant in appearance and showed no visible cracks. Thus gastroretentive dosage form (GRDF) for controlled release of Famotidine has been developed and characterized for improved bioavailability. It consists of a drug loaded polymeric film, folded into a hard gelatin capsule. Compatibility study shows Famotidine was compatible with all selected polymers and possess good stability. Thickness and Folding endurance of optimized formulation was 0.48±0.6623 mm and 293±0.943 times; the folding endurance increased with an increase in HPMC K4M and presence of PEG400. Effect of HPMC K4M and PEG 400 on folding endurance was showed positive effect. Uniformity of weight, pH and drug content was obtained up to 201±0.0017 mg; 6.63±0.086 and 99.07±0.419 % respectively. Moisture content was 3.46 ± 0.041 % and swelling index was 145.57±0.421 %; the swelling index was directly proportional to the amount of hydrophilic polymer HPMC K4M and hydrophobic polymer Eudragit RLPO. Retention time 12 hrs and *In-vitro* mucoadhesive strength was 0.639±0.0043 N; it was mainly depend on HPMC K4M and presence of optimum amount of Carbaopol 971 P NF polymer. The complete unfolding action was obtained within 90 min and drug release was obtained up to 99.02 % in 12 hrs because increased amounts of HPMC K4M retard the drug release up to some extent but presence of Eudragit RLPO might be extend drug release with R^2 =0.989 and showing non-Fickian transport diffusion mechanism (0.45 > n <0.89 i.e 0.879). DSC of optimized batch F8 shows no any polymorphic changes in drug as well as polymers during the formulation of polymeric film. The optimized film formulation batch F8 showed satisfactory controlled release in the development of GRDF were safe and proper combination of polymers will yield a novel expandable GRDF with good dissolution, mucoadhesion of the film.

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