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ORIGINAL RESEARCH ARTICLE

Formulation Development and Evaluation of Controlled Release Tablets of Famotidine

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ABSTRACT

The objective of present work to formulate controlled release tablets of Famotidine using different concentrations of polymer (xanthum gum) and diluets (MCC, Lactose) in order to prolong the drug release and to increase the GI transit time, for localization of drug action. Controlled release tablets [six tablet formulations (200 mg each): L1, L2, L3 and M1, M2, M3] of famotidine were prepared by wet granulation method. The granules were evaluated for angle of repose, bulk density, tapped density, hausners ratio and compressibility index and were found to be 25.42±0.35, 0.612±0.003 g/cm^3, 0.694±0.005 g/cm^3, 1.14±0.016 and 12.95±1.23 respectively for optimized formulation (M3). The tablets were subjected to uniformity of weight, drug content, thickness, hardness and friability and were found to be 200.14±1.45 mg, 99.25±0.45 (%), 1.92±0.03 mm, 6.54±0.04 kg/cm^2 and 0.24±0.16 (%) respectively for optimized formulation (M3). Cumulative percent drug release of optimized formulation (M3) after 10 hours were found to be 84.86 %. In-vitro release studies revealed that famotidine formulation with high proportion of lactose was able to sustain the drug release for 10 hours. Fitting the in-vitro drug release data to kinetic analysis, all the formulations followed the mechanism of both diffusion and erosion. All the formulations were stored at 45^{0}C±2^{0}C, 75 ± 5% RH and subjected to stability studies up to 45 days. Drug content and cumulative percent drug release after storing formulation for 45 days of optimized formulation (M3) were found to be 99.55±1.41 and 84.7 (after 10 hours) respectively. It showed that all the formulations are physically and chemically stable. Formulation M3 appears suitable for the further pharmacodynamic and pharmacokinetic studies to evaluate clinical safety of this formulation in suitable animal and human models.

Key words: Controlled release, famotidine, hydrophilic polymer, wet granulation, optimized formulation, cumulative percent drug release and peptic ulcer.

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance, and cost-effective manufacturing process. Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:

1. Drugs with short half-life requires frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
3. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the C_{SS} values fall or rise beyond the therapeutic range.
4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs [1].

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Controlled drug delivery systems are conveniently divided into four categories:

1. Delayed release 2. Sustained release 3. Site-specific targeting 4. Receptor targeting

MATERIALS AND METHODS

Materilas: Famotididne was received as a gift sample from IPCA Laboratories, Indore. Xanthan gum and PVP were obtained from Boba Chemical Pvt. Ltd., Mumbai. Lactose and microcrystalline cellulose were obtained from Suvchem Labs., Mumbai. Talc was obtained from Molychem, Mumbai. Magnesium stearate was obtained from Oxford Labs, Mumbai. Isopropyl alcohol was obtained from Merk Chem., Mumbai. All ingredients, reagents and solvents were of analytical grade.

Methods: The ingredient were weighted accurately and mixed thoroughly. Granulation was done with a solution of PVP K-30 in sufficient isopropyl alcohol. The wet mass was passed through sieve no. 20 for the preparation of granules. The granules were dried in conventional hot air oven at 40^0C at 2 hr. The dried granules were sized through 22 mesh sieve. Lubricated with magnesium stearate and purified talc and then compressed on a tablet punching machine.

PRELIMINARY STUDIES:

Before preparation and characterization of pharmaceutical dosage form containing therapeutic moiety, preformulation studies must be done to characterize the physiochemical property of the drug that could affect the development of efficacious dosage form [2].

Test for Identification

Physical appearance: Physical appearance analysis of pure drug was carried out by visual inspection.

Melting point: The melting point was determined by the capillary method using melting point apparatus (Jyoti Scientific Industries, Gwalior).

***FT-IR spectroscopy*:** The FT-IR spectra for pure drug (famotidine) was obtained by powder diffuse reflectance on a FT-IR spectrophotometer in the wave number region of 4000-400 cm^{-1}.

Determination of absorption maxima (λ_{max}) in 0.1N HCl: The UV absorption maxima was determined by scanning 10 µg/ml solution of famotidine in 0.1 N HCl. The solution was scanned in the range of 200–400 nm in the UV/Visible spectrophotometer (Shimadzu 1800).

Preparation of standard curve in 0.1N HCl: 10 mg accurately weighed famotidine was dissolved in the 10 ml 0.1N HCl (1000µg/ml). From this stock solution different dilutions were prepared in the concentration range of 10, 20, 30, 40 and 50µg/ml in 10 ml volumetric flask and absorbance were taken at 265 nm.

Determination of absorption maxima in Phosphate Buffer saline pH 7.4: The UV absorption maxima was determined by scanning 10µg/ml solution of famotidine in phosphate buffer 7.4 pH in range of 200-400 nm by UV/visible spectrophotometer (Shimadzu 1800).

Preparation of standard curve in phosphate buffer saline pH 7.4: 10 mg accurately weighed famotidine was dissolved in the 10 ml PBS pH 7.4 (1000µg/ml). From this stock solution different dilutions were prepared in the concentration range of 10, 20, 30, 40 and 50µg/ml in 10 ml volumetric flask and absorbance were taken at 265 nm.

Solubility Studies: Drug (5mg) was suspended successively in 5 ml of different solvents at room temperature in a tightly closed 10 ml volumetric flask and shaken for about 5-10 min.

Drug and excipients interaction studies: Drug-excipients interactions were determined by infrared absorption spectroscopy, the spectrum of the pure drug and polymer was compared and interaction was studied. The FT-IR sperctra for pure drug was obtained by powder diffuse reflectance on a FT-IR Spectrophotometer in the wave number region of 4000-400 cm^{-1}.

FORMULATION TABLE OF TABLETS [3]:

Table No.1: Composition of Controlled Release Tablets of Famotidine

S. No	Ingredients (in mg)	L1	L2	L2	M1	M2	M3
1	Famotidine	40	40	40	40	40	40
2	Xanthan gum	20	30	40	20	30	40
3	Lactose	127	117	107	-	-	-
4	Microcrystalline cellulose	-	-	-	127	117	107
5	PVP K-30	3	3	3	3	3	3
6	Talc	6	6	6	6	6	6
7	Magnesium stearate	4	4	4	4	4	4
8	Isopropyl alcohol	qs	qs	qs	qs	qs	qs
Total weight of tablets (in mg)		200	200	200	200	200	200

PRECOMPRESSION EVALUATIONS:

Characterization of Powder Blend:

Angle of repose (θ):

The frictional forces in loose powder or granules can be measurement by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

$$\tan\theta = h/r$$

$$\theta = \tan^{-1}(h/r)$$

Where, the θ is the angle of repose, h = height (in cm) and r = radius (in cm)

Table No. 2: Relationship between Angle of Repose (θ) and Flow Properties

S. No	Angle of repose	Flow properties
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Very poor

Loose bulk density and tapped bulk density:

Both loose bulk density (LBD) and tapped density (TBD) were determined. Accurately weighted fixed amount of sample taken in a 25 ml measuring cylinder of Borosil. Measured the sample volume before and after the tapping.

$$LBD\ (loose\ Bulk\ Density) = \frac{Mass\ of\ Powder}{Bulk\ Volume\ of\ Packing}$$

$$TAB\ (tapped\ bulk\ density) = \frac{Mass\ of\ Powder}{Tapped\ Volume\ of\ Packing}$$

Hausner's ratio:

A flow property of powder mixure was determined by Hausner's ratio calculated by following formula:

$$H = \frac{\rho_T}{\rho_B}$$

Where; ρ_B is the freely settled bulk density of the powder,

ρ_T is the tapped bulk density of the powder

H is Hausner ratio

A Hausner ratio greater than 1.25 is considered of poor flow ability.

Percentage Compressibility:

Percentage compressibility of powder mixture was determined by carr's compressibility index calculate by following formula.

Carr's Index%=TBD-LBD/TBD×100

Table 3: Grading of powders for their flow properties according to Carr's Index

S. No	Carr's index	Flow properties
1	5-15	Excellent
2	12-16	Good
3	18-21	Fair to passable
4	23-25	Poor
5	33-38	Very poor
6	>40	Very very poor

FORMULATION OF CONTROLLED RELEASE TABLETS:

The ingredient were weighted accurately and mixed thoroughly. Granulation was done with a solution of PVP K-30 in sufficient isopropyl alcohol. The wet mass was passed through sieve no. 20 for the preparation of granules. The granules were dried in conventional hot air oven at 40^0C at 2 hr. The dried granules were sized through 22 mesh sieve. Lubricated with magnesium stearate and purified talc and then compressed on a tablet punching machine.

Post compression evaluations:

Hardness: The hardness of the tablet was determined using a Monsanto Hardness tester. It is expressed in kg / cm^2.

Friability: The friability of the tablet was determined using Roche friabilator. It is expressed percentage (%).10 tablets were initially weighed ($W_{initial}$) and transferred into the friabilator. The friabilator was operated at 25 rpm for 4 mins. The tablets were weighed again (W_{final}). The % friability was then calculated by:-

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} X100$$

Thickness: The thickness of all the tablets was measured by Vernier caliper. It is expressed mm.

Weight variation: 20 tablets were selected randomly from the lot and weighed individually to check for weight variation. IP limit for weight variation in case of tablets less than 250 mg is 5.0%.

Drug content: The drug content in each formulation was determined by triturating 20 tablets and powder equivalent to average weight was added in 100 ml of phosphate buffer saline pH 7.4. Followed by stirring for 30 min. Dilute suitably and the absorbance of resultant solution was measured spectrophotometrically at 265 nm using phosphate buffer saline pH 7.4 as a blank.

In-vitro drug release studies:

The release rate of famotidine from controlled release tablets was determined using USP dissolution testing apparatus 2 (paddle method). The dissolution test performed using 900 ml of phosphate buffer saline pH 7.4 at 37±0.5^0C and 50 rpm. A sample (5ml) of the solution was withdrawn from the dissolution apparatus hourly and the sample was replaced with fresh dissolution medium. The sample were filtered through a 0.45 µ membrane filter and dilute to a suitable conc. with phosphate buffer saline pH 7.4. Absorbance of these solutions was measured at 265 nm using UV/Visible spectrophotometer. The percentage drug release was plotted against time to determine the release profile [4, 5].

In-vitro assessment of dissolution data:

In order to assess the mechanism and kinetics of drug release, in-vitro dissolution drug release data was analyzed by five different kinetics models.

Zero-order release equation describes systems where drug release is independent of its concentration.

$$Q_t = k_0\ t$$

First-order equation describes systems where drug release rate depends on its concentration.

$$\log Q_t = \log Q_0 - k_1 t$$

Higuchi's model describes drug release from insoluble matrix by diffusion.

$$Q_t = k_H t^{1/2}$$

Hixson-Crowell equation.

$$Q_0^{1/3} - Q_t^{1/3} = k_H C_t$$

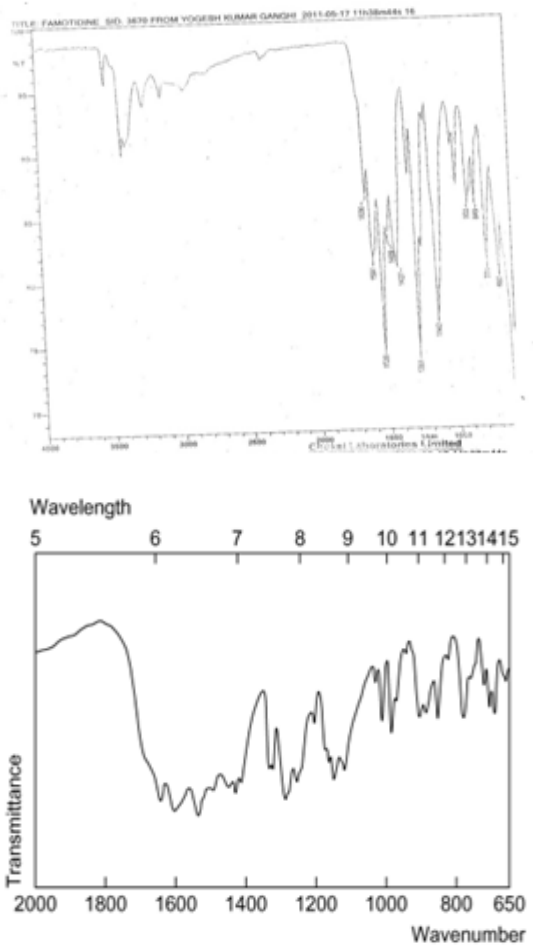
Korsmeyer-Peppas equation

$$M_t/M_\infty = k_{kp} t^n$$

Where; Q_t is the amount of drug released at time t. Q_0 is the initial amount of the drug in the formulation, k_0, k_1, k_H , k_{kp} , is the release rate constant for zero-order, first order, Higuchi, Hixson-Crowell and Korsmeyer-Peppas model respectively.

In Korsmeyer-Peppas equation M_t is the amount of drug released at time t, M_∞ is the amount of drug released at time ∞, n *is* the diffusional coefficient indicating release mechanism. When n approximates to 0.5 a Fickian/diffusion controlled release is implied, where 0.5<n<1.0 non Fickian and n is 1 for zero order (case II transport).When n value is greater than 1.0 it indicates super case II transport.

Figure 1: FT-IR Spectra of drug Famotidine Sample and Standard [8]



STABILITY STUDY:

The optimized formulation was subjected to stability at 45±2°C with 75±5% RH for 45 days and evaluated for their physical appearance and drug content at specified intervals of time.

RESULTS AND DISCUSSION

Preformulation studies for the selected drug Famotidine include test for identification (examination of physical appearance, melting point determination, and IR spectroscopy) and solubility studies.

Tests for Identifications:

Physical appearance: Famotidine was found to be a white to off white crystalline powder and it is similar to the appearance in specified [6].

Melting point: Famotidine was found to be melting at 163°C which is similar to specified in reference book [7].

FT-IR-spectra: The characteristic peaks were determined by FT-IR spectra, which identified the purity of drug.

Solubility Studies: A definite quantity (5 mg) of drug was dissolved in 5 ml of each investigated solvent at room temperature. The solubility was observed only by the visual inspection.

Table 4: Solubility studies of Famotidine

S. No	Solvents	Solubility
1	Distilled water	Slightly Soluble
2	Methanol	Slightly Soluble
3	Mineral acid	Soluble
4	Diamethyl Formamide and glacial acetic acid	Soluble

Determination of absorption maximum (λ_{max}) in 0.1 N HCl

For determination of absoption maxima, stock solution of 10 ug/ml was prepared. The solution was scanned in the range of 200-400 nm in the UV/Visible spectrophotometer. The λ_{max} was found to be 265 nm.

Preparation of standard curve in 0.1N HCl

10 mg accurately weighed famotidine was dissolved in the 10 ml 0.1N HCl. From this stock solution different dilutions were prepared in the concentration range of 10, 20, 30, 40, and 50 µg/ml in 10ml volumetric flask and absorbance was taken at 265 nm. Standard curve was prepared by the observations recorded in table**.** Correlation coefficientR^2=0.999.

Determination of absorption maxima in phosphate buffer solution pH 7.4:

For determination of absoption maxima, stock solution of 10 ug/ml was prepared. The solution was scanned in the range of 200-400 nm in the UV/Visible spectrophotometer. The λ_{max} was found to be 265 nm.

Preparation of standard curve in pH 7.4 phosphate buffer solution:

The standard curve of drug was prepared in PBS pH 7.4, in the concentration range of 10-50 µg/ml. A straight line with regression coefficient (R^2) = 0.999 was obtained, which indicates that drug follows Beer's law. Table 6.3 shows the absorbance values of famotidine.

Table No. 5: Standard curve of Famotidine in 0.1 N HCl at λ max (265 nm)

S. No	Concentration (µg/ml)	Absorbance
. 1	0	0.000
. 2	10	0.267
. 3	20	0.502
. 4	30	0.746
. 5	40	1.012
. 6	50	1.28

TableNo.6 Standard curve of Famotidine in PBS pH 7.4 at λ max (265 nm):

S. No	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.075
3	20	0.151
4	30	0.231
5	40	0.308
6	50	0.38

Fig 2: Standard curve of Famotidine in 0.1 N HCl at λ max (265 nm)

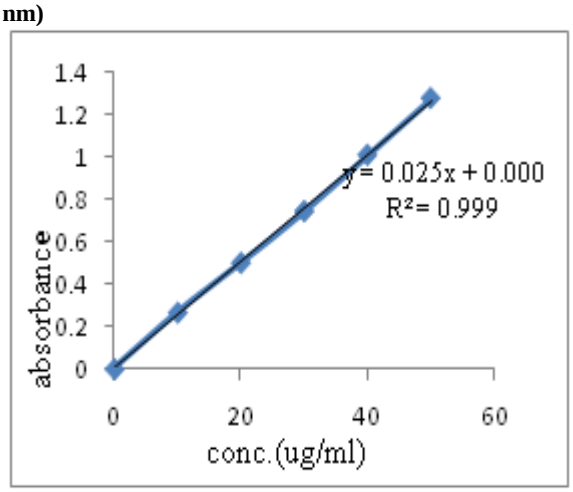


Fig 3: Standard curve of Famotidine in PBS pH 7.4 at λ max (265 nm):

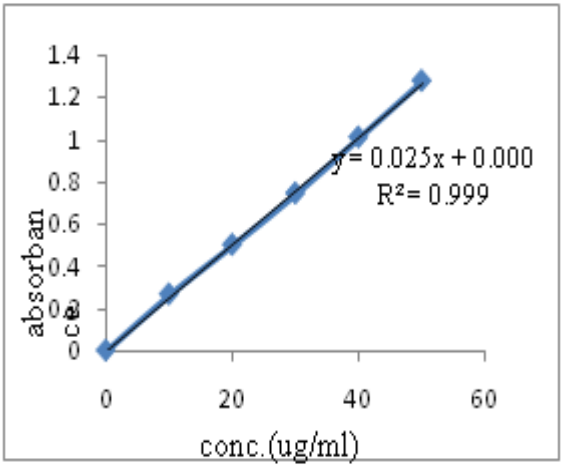


Fig 4: UV Spectrum of Famotidine in 0.1 N HCl

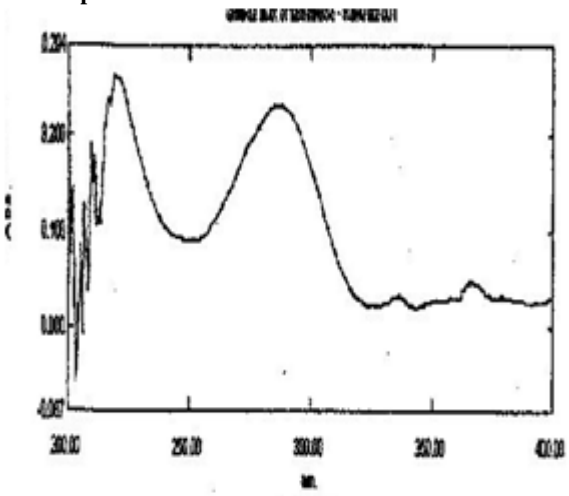
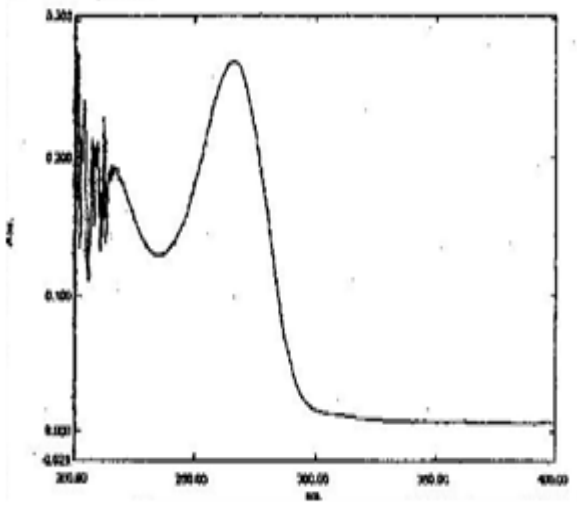


Fig 5: UV Spectrum of Famotidine in PBS pH 7.4



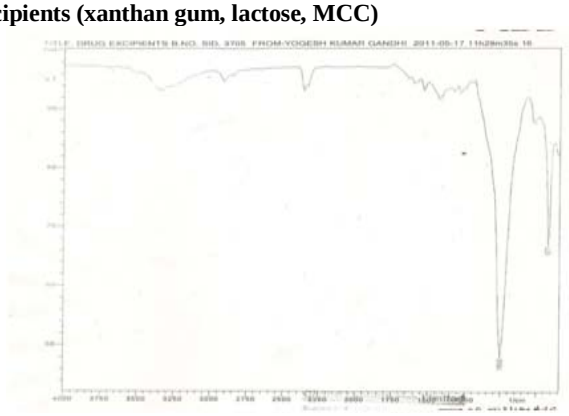
IR-Interpretation:

IR spectroscopy was used as a means of studying drug-excipient interaction. The IR spectrum of famotidine exhibits a peak at 3400.50 cm^{-1} due to the N-H stretching of sulfonamide group and peaks at 1286.55 cm^{-1} and 1147.03 cm^{-1} due to S-O stretching, confirms the structure of the drug.

In case of xanthan gum, a broad band was observed at 3473.6 cm^{-1} indicating the presence of poly hydroxyl groups in the IR spectrum. The C-H absorption frequency was noticed at 2924.2 cm^{-1} in confirmation of presence of alkyl moieties.

The IR spectrum of formulation shows a peak at 3401.40 cm^{-1} due to the N-H stretching of sulfonamide group and peaks at 1288.22 cm-1 and 1147.00 cm^{-1} due to S-O stretching, confirms the undisturbed structure of the drug in the formulation.

Fig 6: FT-IR spectra of famotidine and Physical mixture of Excipients (xanthan gum, lactose, MCC)



PRECOMPRESSION EVALUATION

Evaluation of granules

Angle of response (θ):

Table No. 7 shows the results obtained for angle of repose of all the formulations. The values were found to be in the range of 30^o to 40^o. All formulations showed the angle of repose within limit.

Bulk Density:

Both loose bulk density (LBD) and tapped density for all the formulations varied from 0.078 gm/cm^3 respectively (Table 7). The values obtained lies within the acceptable range and not large differences found between loose bulk density and tapped bulk density. This result helps in calculating the % compressibility of the powder.

Hausner's ratio:

Table 7 shows the results obtained for all the formulations. The values were found to be in the range of 1.14 to 1.12**.** All the formulations showed the hausner's ratio within 1.25.

Carr's index:

This percentage compressibility of powder mix was determined by carr's compressibility index. The percentage compressibility for all the six formulations lies within the range of 11.13 to 15.94**.** Formulations L1 and M1 are showing to excellent compressible index and formulation L2, L3, M2, M3 showing fair to passable.

Table 7: Evaluation of granules

Formulation Code	Angle of Repose(θ)	Loose Bulk Density	Tapped Bulk Density	Hausner's Ratio	Carr's Index
L1	34.28±0.65	0.614±0.004	0.695±0.007	1.14±0.017	14.29±1.65
L2	31.18±0.55	0.611±0.013	0.699±0.006	1.13±0.014	13.23±1.25
L3	28.64±0.42	0.610±0.008	0.696±0.005	1.13±0.008	12.65±1.52
M1	32.41±0.54	0.612±0.004	0.695±0.007	1.14±0.015	13.19±1.28
M2	30.55±0.50	0.609±0.008	0.696±0.005	1.12±0.012	13.83±1.69
M3	25.42±0.35	0.612±0.003	0.694±0.005	1.14±0.016	12.95±1.23

Each represents mean ± SD (n=3)

POST COMPRESSION EVALUATION

Evaluation of Tablets (Table. 8):

Shape and color of tablets:

Randomly picked tablets from each formulation batch examined under lens for shape and in presence of light for color. Tablets showed circular flat bottom and round shape in white color.

Weight variation test:

The percentage weight variation for all the formulation is tabulated in table. All the tablets passed weight variation test as the percentage weight variation was within the pharmacopoeial limits of 5%. It was found to be form 197 mg to 202 mg. The weight of all the tablets was found to be uniform.

Uniformity of thickness:

The thickness of tablets was measured by using vernier caliper by picking the tablets randomly. The mean values are shown in table. The values are almost uniform in all formulations. Thickness was found in range from 1.84 mm to 1.97 mm respectively.

Drug content uniformity:

The content uniformity was performed for all the six formulations and results are shown in table. five trials form each formulation were analysed spectrophotometrically. The drug content of the tablets was found between 97 to 99.7% of famotidine. The results indicated that all formulations the drug content was uniform.

Hardness test: Hardness was maintained to be within 5.36 kg/cm^2 to 6.58 kg/cm^2.

Friability test: Friability of tablets was found in the range from 0.19 % to 0.61 %.

Table 8: Evaluation of Tablet

S. No	Formulation code	Uniformity of weight (mg)	Drug content (%)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)
1	L1	198.35±1.25	98.96±0.40	1.92±0.05	5.47±0.11	0.29±0.13
2	L2	199.55±2.90	98.28±0.20	1.91±0.01	5.65±0.08	0.39±28
3	L3	198.25±1.38	98.49±0.41	1.9±0.06	6.45±0.17	0.20±0.10
4	M1	200.05±1.48	97.99±0.58	1.91±0.04	6.35±0.15	0.24±0.25
5	M2	199.85±2.46	98.12±0.65	1.89±0.05	6.15±0.20	0.49±0.12
6	M3	200.14±1.45	99.25±0.45	1.92±0.03	6.54±0.04	0.24±0.16

Each data represents mean ± SD (n=3)

In-vitro Dissolution studies:

All the six formulations were subjected for the *in vitro* dissolution studies using tablet dissolution tester USP apparatus I. The samples were taken at hourly intervals and analysed at 265 nm. *In-vitro* release of famotidine controlled release tablet of formulation L1, L2, L3 and M1, M2, M3 formulated with various percentage of lactose and MCC from the *in-vitro* dissolution data show in the (Table 9). It is clear that formulation L1 show rapid drug release.

Table 9: In-vitro release of famotidine controlled release tablet formulation

Time (hrs.)	Cummulative Percentage Drug Release					
	L1	L2	L3	M1	M2	M3
0	0	0	0	0	0	0
1	18	15.42857143	11.25	13.82142857	11.25	8.678571429
2	27.74285714	23.55	21.27678571	24.82678571	19.66964286	17.08392857
3	36.575	28.50178571	26.21607143	33.32142857	25.56428571	22
4	45.13392857	37.3375	34.71785714	41.8625	35.02678571	32.08571429
5	54.38214286	48.15	41.98035714	50.12857143	43.25535714	33.54821429
6	63.0375	55.80714286	48.31785714	59.725	51.52857143	44.66071429
7	73.34642857	66.07678571	60.15357143	68.40892857	60.16785714	55.19107143
8	81.78214286	75.11607143	71.08928571	76.81785714	68.21071429	66.42142857
9	89.94107143	85.16785714	80.79821429	83.34285714	79.83214286	72.56964286
10	99.42857143	95.27321429	91.84464286	94.40178571	90.23035714	84.85714286

In-vitro assessment of dissolution data:

Drug release mechanism and kinetics were determined by applying various kinetic equations to in-vitro dissolution data. Five different kinetics models were applied to analyze the in vitro data to find out the best fitting equation given in (Table 10)

Table 10: Kinetic values obtained from *in-vitro* release profile

Formulation	Zero order			First order			Higuchi's		Korsmeyer Peppa's		Hixson-Crowell's	
	Slope	Rate constant (K^0= -Slope)	Regration Coefficient (r)	Slope	Rate constant (K = - Slope* 2.303)	Regration Coefficient (r)	Slope	Regration Coefficient (r)	Slope	Regration Coefficient (r)	Slope	Regration Coefficient (r)
L1	9.44	-9.44	0.995	-0.159	0.366	0.693	32.13	0.953	0.281	0.479	-0.317	0.892
L2	9.124	-9.124	0.995	-0.108	0.248	0.83	30.5	0.921	0.513	0.461	-0.261	0.925
L3	8.803	-8.803	0.992	-0.091	0.209	0.848	29.14	0.9	0.585	0.486	-0.234	0.922
M1	9.037	-9.037	0.995	-0.104	0.239	0.871	30.63	0.947	0.638	0.666	-0.256	0.952
M2	8.698	-8.698	0.997	-0.086	0.198	0.874	28.89	0.911	0.686	0.642	-0.226	0.939
M3	8.243	-8.243	0.989	-0.072	0.165	0.892	27.08	0.884	0.74	0.638	-0.199	0.939

Fig 7: Zero order release plots of formulations

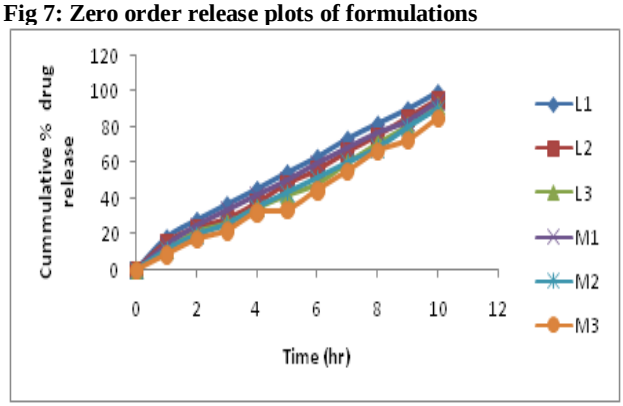


Fig 8: First order release plots of formulations

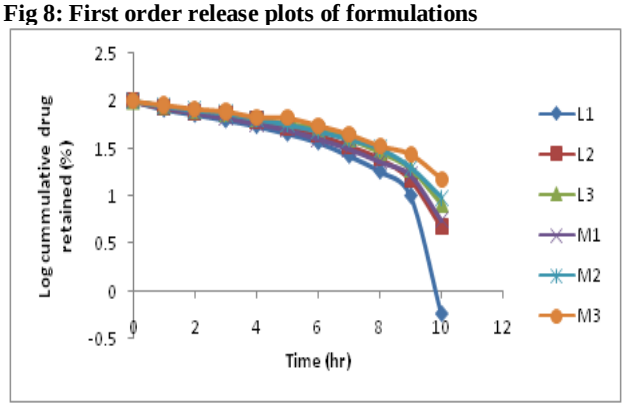


Fig 9: Higuchi Plots of formulations

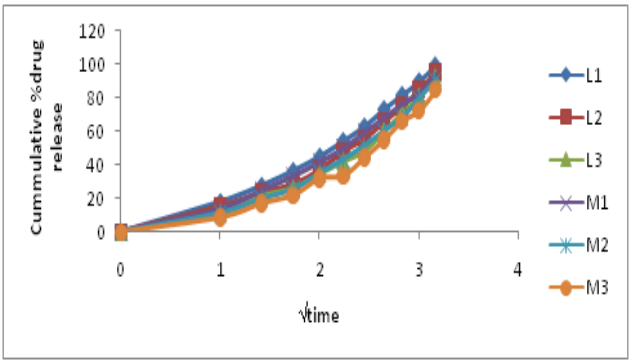


Fig 10: Korsmeyer peppa's plots of formulations

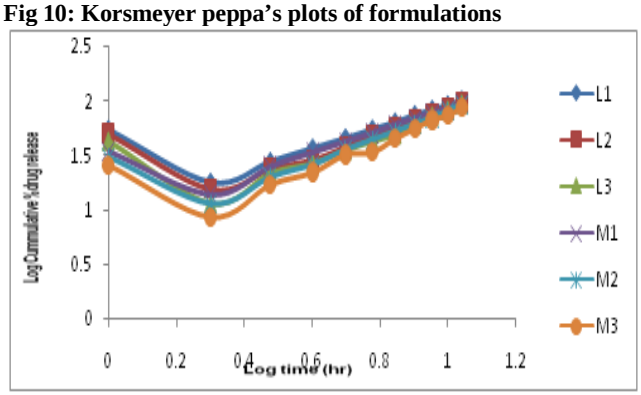
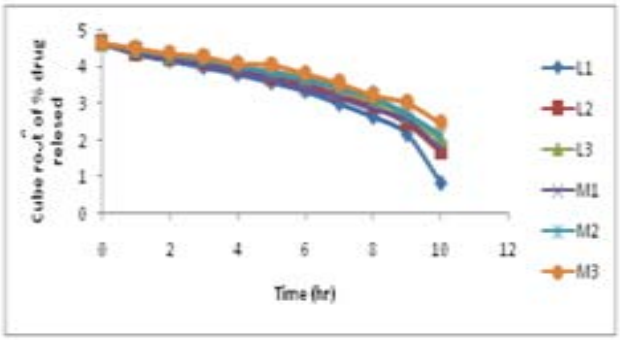


Fig 11: Hixson-Crowell's plots of formulation



STABILITY STUDIES

The optimized formulation was subjected to stability at 45±2°C with 75±5% RH for 45 days and evaluated for their physical appearance and drug content at specified intervals of time.

Table 11: **Stability study of M3 Famotidine controlled release tablet**

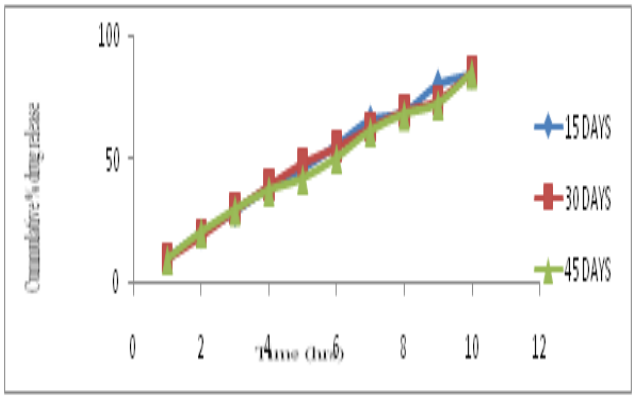
S. No	Stability duration	Appearance	Hardness (kg/cm^2)	Uniformity of weight (mg)	Friability (%)	Drug content (%)
1	Initial	White	6.15±0.13	197.55±1.90	0.20±0.19	99.35±1.50
2	After 15 days	White	6.05±0.09	197.55±2.90	0.20±0.15	99.55±2.90
3	After 30 days	White	5.75±0.05	198.55±1.35	0.24±0.23	98.25±1.25
4	After 45 days	White	5.45±0.15	199.55±1.27	0.27±0.15	99.55±1.41

Each representation mean ± SD (n=3

Table 12: *In-vitro* release of famotidine controlled release tablet of formulation M3

S. No	Time (hr)	Cummulative % drug release		
		15 days	30 days	45 days
1	1	9.3	9.9	9.3
2	2	19.9	19	20.3
3	3	28.7	29.4	29.4
4	4	38.5	39.2	37.2
5	5	46.1	48.4	41.9
6	6	55.7	54.8	50.2
7	7	66	62.8	61.1
8	8	69.2	69.5	67.9
9	9	80.5	73.8	72.1
10	10	84.5	85.4	84.7

Fig 12: In- vitro release profile of the formulation



CONCLUSION

A recent advance in novel drug delivery system aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is controlled drug delivery system.

- Controlled drug delivery system offers a simple and practical approah to achieve increase gastric resistance and to modify drug release profile essential for sustained drug action.
- Controlle release tablets of famotidine were developed by using natural polymer xanthan gum by wet granulation method. Lactose and MCC were used as diluents.
- All the prepared tablets were found to be good without chipping, caping and sticking.
- IR spectroscopic studies indicated that the drug is compatible with polymer and co-excipients.
- The drug –polymer ratio, different diluents were found to influence the release of drug.
- The *in-vitro* dissolution profile of all the prepared formulation of famotidine was found to extend the drug release over a period of 10 hrs.
- Optimized formulation of famitidine was found to be stable at 45^o ± 2^{0}C, 75 ± 5% RH for 45 days
- Finally, it may conclude that this controlled drug delivery system which offers the drug at controlled rate. The formulation of famotidine provides a better option for increasing the bio availability and reliability for peptic and duodenal ulcer.
- Formulation M3 appears suitable for the further pharmacodynamic and pharmacokinetic studies to evaluate clinical safety of this formulation in suitable animal and human models.

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