Original Research Article

Formulation and evaluation of mixed matrix gastro-retentive drug delivery for famotidine

Dasharath M Patel, Mehul J Patel, Ankit N Patel, Chhagan N Patel

Department of Pharmaceutics and Pharm Technology, Shri Sarvajanik Pharmacy College, Mehsana, Gujarat, India

Abstract

Introduction: Present investigation describes an influence of ratio of Gelucire 43/01(hydrophobic) to hydroxypropyl methylcellulose K4M (HPMC K4M) (hydrophilic) and different fillers on release of famotidine from gastro-retentive tablets using 3^2 full factorial design. Ratio of Gelucire 43/01 to HPMC K4M (X_1) and the type of filler (X_2) were selected as independent variables while buoyancy lag time (BLT), drug release at 1h (Q_1), 6h (Q_6), and the 12h (Q_{12}) were selected as dependent variables. **Materials and Methods:** Gastro-retentive tablets of famotidine were prepared by a solvent free melt granulation technique using Gelucire 43/01 as a hydrophobic meltable binder. HPMC K4M and sodium bicarbonate were used as matrixing agent and gas-generating agent, respectively. Prepared tablets were evaluated for *in vitro* dissolution, *in vitro* buoyancy, friability, hardness, drug content and weight variation. Dissolution data were fitted to various models to ascertain kinetics of drug release. The data were analyzed using regression analysis and analysis of variance. **Results:** All formulations (F_1-F_9) showed floating within 3min and had total floating time of more than 12h. It was observed that a type of filler and the ratio of Gelucire 43/01 to HPMC K4M had significant influence on buoyancy lag time (P = 0.037) and Q_6 (P = 0.011), respectively without significant influence on Q_1 and Q_{12}. **Conclusion:** Formulation F_5 was selected as an optimum formulation as it showed more similarity in dissolution profile with theoretical profile (Similarity factor, f_2 = 83.01). The dissolution of batch F_5 can be described by zero order kinetics (r^2 = 0.9914) with anomalous (non-Fickian) diffusion as a release mechanism (n = 0.559). The difference observed in *in vitro* release profile after temperature sensitivity study at 40°C for 1 month was insignificant.

Key words: Buoyancy lag time, full factorial design, Gelucire 43/01, melt granulation

INTRODUCTION

Frequency of drug administration in a conventional dosage form depends upon the elimination half-life of drug ($t_{1/2}$).[1] Controlled release dosage form reduces a frequency of drug administration and the fluctuations in plasma drug concentration. A gastro-retentive drug delivery system that can be retained in the stomach is useful for controlled release and for site specific drug absorption. There are number of approaches used to prolong gastric retention time, such as floating drug delivery system, swelling and expanding system, polymeric bioadhesive systems, modified shape systems, high density system and raft formation.[2-4]

Famotidine is histamine receptor (H_2) antagonist used in a treatment of zollinger ellision syndrome, gastro esophageal reflux disease and peptic ulcer in the dose ranging from 10 to 80 mg.[5] Half life of a drug is about 2.5−3.5 h and the oral bioavailability is 45 ± 14% indicating its promising candidature for sustained release formulation.[6] Oral treatment of gastric disorders with H_2 receptor antagonist such as famotidine or ranitidine in combination with antacids promotes local delivery of these drugs to the receptor of parietal cell wall. Local delivery also increases a bioavailability and the efficacy of drug to reduce acid secretion.[7]

Hydrophilic matrices are widely used and accepted for sustained release but a drug release from such matrices is time dependent with very less possibility of zero order drug release.[8] Initially, a drug present at surface of the matrix is released quickly, yielding a burst effect, then with time, as the diffusion path length increases the release rate is progressively reduced. Several authors have described various approaches to limit the burst effect from monolithic matrix systems in order to obtain zero order drug release.[9-13] Conte and co-workers designed a multilayered hydrophilic matrix system (GeomatrixR) to obtain zero order

Address for correspondence:
Dr. Dasharath M. Patel,
Department of Pharmaceutics and Pharm Technology, Shri Sarvajanik Pharmacy College, Near- Arvind Baug, Mehsana- 384 001, Gujarat, India. E-mail: drdmpatel1971@gmail.com

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drug delivery by coating one or both sides of the matrix tablet with HPMC based barrier.[14-16] Krogel and Bodmeier invented a system composed of hydrophilic matrix tablet placed in impermeable polypropylene cylinder, reducing drug release to the open ends of the cylinder.[17] Colombo *et al.* described a modulation of drug release by physically restricting matrix swelling through partial coating of the matrix with impermeable cellulose acetate propionate film.[18] Danckwerts developed a core-in-cup tablet consisting of inert cup of ethylcellulose and carnauba wax into which drug-containing matrix layer was compressed, thus leading to matrix with only one side in contact with the surrounding medium.[19] Although these devices are able to reduce drug release, they have in common that their production process is complicated and time-consuming. Hydrophobic polymers are most suitable matrix formers to limit the burst effect from monolithic matrix system containing hydrophilic polymers.[20]

So the purpose of this research was to prepare a mixed matrix gastroretentive tablet of famotidine using Gelucire 43/01 and hydroxylpropyl methylcellulose K4M (HPMC K4M). A 3^2 full factorial design was employed to investigate effect of two independent variables , i.e. a ratio of Gelucire 43/01 to hydroxypropyl methylcellulose (HPMC K4M) and the type of filler (lactose, dicalcium phosphate, microcrystalline cellulose) on the dependent variables, i.e. buoyancy lag time (BLT), Q_1, Q_6 and Q_{12} (% drug release after 1, 6, 12 hr, respectively).

MATERIALS AND METHODS

Materials

Famotidine was received as a gift sample from Mann Pharmaceuticals Ltd, Mehsana, India. Hydroxypropyl methylcellulose K4M (HPMC K4M) was obtained from Yarrow Chem. Products, Mumbai, India. Gelucire 43/01 was obtained from Gattefosse, France. Sodium bicarbonate and magnesium stearate were obtained from Shakti Chemicals, Mehsana, India. Lactose and talc were obtained from Chemdyes Corporation, Ahmedabad, India. All other materials and chemicals used were of either pharmaceutical or analytical grade.

Methods

Preparation of famotidine floating tablets by melt granulation

Gelucire 43/01 was melted in a large petridish at 50°C and the required quantity of famotidine was added to melted mass. Previously prepared geometric mixture of HPMC K4M and sodium bicarbonate was added to famotidine - Gelucire 43/01 mixture and stirred well to mix. This mass was removed from a hot plate and subjected to scrapping until it attained room temperature. The coherent mass was passed through 22 mesh and the resulting granules were resifted using 44 meshes to separate fines. The granules were collected and mixed with talc (2%) and magnesium stearate (1%). The lubricated blend was compressed using round tooling on Rimek-I rotary tablet machine (Karnavati Engineering, Kadi, India). Compression pressure was adjusted to obtain tablets with hardness in a range of 2−3 kg/cm^2.

In vitro buoyancy studies

The *in vitro* buoyancy of the tablets was studied at 37 ± 0.5°C in 100 ml of simulated gastric fluid (SGF) at pH 1.2 without pepsin (USP). The duration of tablet floatation was observed visually.[21]

In vitro dissolution study

The *in vitro* dissolution study of famotidine tablets was performed using USP apparatus (model TDT-08T, Electrolab, Mumbai, India) fitted with paddle (50 rpm) at 37 ± 0.5°C using SGF (pH 1.2; 900 mL) as a dissolution medium. At predetermined time intervals, 10-mL samples were withdrawn, filtered through a 0.45μm membrane filter, diluted and assayed at 265 nm using Shimadzu UV 1800 double-beam spectrophotometer (Shimadzu, Kyoto, Japan). Cumulative percentage drug release was calculated using an equation obtained from calibration curve.

Preliminary screening

Preliminary screening was performed to optimize amount of sodium bicarbonate and total amount of polymer in a formulation. Tablets were prepared by melt granulation method using 40% of total concentration of polymers (Gelucire 43/01 and HPMC K4M in ratio of 3:5) and varying amount of sodium bicarbonate (5%, 10%, 15%) as shown in Table 1. Prepared tablets were tested for *in vitro* buoyancy studies and intactness. Tablets were prepared using 10% of sodium bicarbonate and varying amount (30%, 40%, 50%) of polymer (Gelucire 43/01 and HPMC K4M in ratio of 3:5) as shown in Table 2. Tablets prepared with varying amount of polymer were tested for *in vitro* buoyancy studies, intactness and *in vitro* drug release.

Optimization of variables using full factorial design

A 3^2 randomized full factorial design was used in present study. In this design 2 factors were evaluated, each at 3 levels, and experimental trials were performed for all 9 possible combinations. Ratio of Gelucire 43/01 to HPMC K4M (X_1) and type of filler

Table 1: Formulation of famotidine floating tablets using different amount of sodium bicarbonate

Name of ingredient	Quantity in mg/tablet		
	CO1	CO2	CO3
Famotidine	40	40	40
Gelucire 43/01	30	30	30
HPMC K4M	50	50	50
Sodium bicarbonate	10	20	30
Lactose	70	60	50
Talc	4	4	4
Magnesium stearate	2	2	2
Buoyancy lag time	>5min	58 sec	30 sec
Total buoyancy time	>24hr	>24hr	<10hr
Intactness	Intact	Intact	Broken

HPMC indicates hydroxypropyl methylcellulose; the average weight of tablet is 206 mg

(lactose, microcrystalline cellulose, dicalcium phosphate) (X_2) were chosen as independent variables while BLT, percentage drug release in 1 h (Q_1), 6 h (Q_6), and 12 h (Q_{12}) were taken as dependent variables. The formulation layout for the factorial design batches (F_1-F_9) is shown in Table 3. Prepared formulations were evaluated for assay, friability and hardness in addition to *in vitro* buoyancy and release study. Results of this evaluation are shown in Table 4.

Kinetic modeling of dissolution data

Dissolution profile of all batches were fitted to various models such as zero order, first order, Higuchi,[22] Hixon Crowell,[23] Korsemeyer, and Peppas[24] to ascertain kinetics of drug release. The method described by Korsemeyer and Peppas was used to describe mechanism of drug release.

Table 2: Formulation of famotidine floating tablets using different amount of polymers

Name of ingredient	Quantity in mg/tab		
	PO1	PO2	PO3
Famotidine	40	40	40
Gelucire 43/01	22.5	30	35
HPMC K4M	37.5	50	65
Sodium bicarbonate	20	20	20
Lactose	80	60	40
Talc	4	4	4
Magnesium stearate	2	2	2
Buoyancy lag time	52 sec	58 sec	70 sec
Total buoyancy time	>24 hr	>24 hr	>24 hr
Intactness	Intact	Intact	Intact

HPMC indicates hydroxypropyl methylcellulose; the average weight of tablet is 206 mg.

Comparison of dissolution profiles for selection of optimum batch

The similarity factor (f_2) given by SUPAC guidelines for modified release dosage forms was used to compare dissolution profiles. The dissolution profiles are considered to be similar when f_2 is between 50 and 100. The dissolution profile of products were compared using f_2, which is calculated from following formula,

$$f_2 = 50 \times \log\left\{\left[1 + \left(\frac{1}{n}\right)\sum_{t=1}^{n} w_t (R_t - T_t)^2\right]^{-0.5} \times 100\right\}$$

Where, n is the dissolution time and R_t and T_t are the reference (here it is theoretical dissolution profile of famotidine) and test dissolution value at time t.[25]

Fourier transform infrared spectroscopy

Fourier transform infrared (FTIR) spectra of famotidine, HPMC K4M, Gelucire 43/01 and a physical mixture of these ingredients were recorded using KBr mixing method on FTIR instrument available at central instrument laboratory of the institute (FTIR-1700, Shimadzu, Kyoto, Japan).

Table 3: Formulation and evaluation of batches in 3^2 full factorial design

Batch code	Variable levels in coded form		BLT(s)	Q_1	Q_6	Q_{12}
	X_1	X_2				
F1	-1	-1	68	25.37	72.23	101.04
F2	-1	0	71	16.02	52.6	93.22
F3	-1	1	117	16.39	64.2	90.59
F4	0	-1	84	10.76	59.37	90.28
F5	0	0	62	23.77	63.02	92.56
F6	0	1	134	14.78	67.88	101.44
F7	1	-1	106	16.46	99.16	100.00
F8	1	0	63	27.05	97.99	100.00
F9	1	1	178	64.37	95.88	100.00

Coded values	Actual values	
	X_1	X_2
-1	10%: 30%	Lactose
0	20%: 20%	MCC
1	30%: 10%	DCP

All batches contained 40 milligrams of Famotidine, 20mg sodium bicarbonate, 4mg talc, 2mg magnesium stearate X1 indicates the ratio of Gelucire 43/01(%): HPMC K4M(%); X2, type of filler. MCC and DCP indicate microcrystalline cellulose and dicalcium phosphate respectively. Q1, Q6, and Q12 indicate percentage drug released after 1, 6 and 12 hours, respectively. BLT indicates Buoyancy lag time.

Table 4: Results of factorial design batches (F_1-F_9)

Parameter	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Buoyancy lag time (sec)	68	71	117	84	62	134	106	63	178
Assay (%)	103.5	100.4	100.7	102.1	97.62	101.08	104.2	99.74	102.6
Friability (%)	0.148	0.020	0.289	0.91	0.90	0.570	0.572	0.430	0.862
Hardness (Kg/cm^2)	2	2.75	2.25	2	2.75	2	1.5	1.75	1.5
Similarity factor (f_2)	59.57	61.12	68.90	54.59	83.01	58.60	38.31	29.41	32.24

Temperature sensitivity study

To determine change in *in vitro* release profile and buoyancy behavior on storage, a temperature sensitivity study of the optimal batch was performed at 40°C in humidity jar with 75% relative humidity (RH). Samples were withdrawn at 1 month interval and evaluated for any change in *in vitro* drug release pattern and buoyancy behavior.

RESULTS AND DISCUSSION

Results of preliminary screening

Gelucire 43/01 was selected as a hydrophobic meltable material to impart sufficient integrity to the tablets. HPMC K4M (hydrophilic) was selected as a matrixing agent considering its widespread applicability and excellent gelling activity in sustained release formulations. Sodium bicarbonate generates CO_2 gas in a presence of hydrochloric acid present in dissolution medium. Generated gas is trapped and protected within a gel formed by hydration of HPMC K4M, thereby decreasing the density of tablet. As a density of tablet fall below 1 (density of water), the tablet becomes buoyant. Three batches (CO1, CO2, CO3) as shown in Table 1, were prepared using same amount of polymer Gelucire 43/01 and HPMC K4M while different amount of sodium bicarbonate (5%, 10%, 15%). From the evaluation results [Table 1] it was observed that as the amount of sodium bicarbonate increased from 5% to 15%, BLT was decreased. At higher amount of sodium bicarbonate, a tablet remained intact only for 10h and lost the matrix integrity. Batch containing 10% sodium bicarbonate remained buoyant and intact for 24h. Hence 10% of sodium bicarbonate was considered to be optimum. Three batches (PO1, PO2, PO3) as shown in Table 2, were prepared using 10%of sodium bicarbonate and different amount of polymer (30%, 40%, 50%). Formulations PO1, PO2, and PO3 were subjected to *in vitro* dissolution study. All formulations exhibited buoyancy lag time of less than 100 sec. Tablets of batch PO2 retained integrity throughout a study and released the drug in controlled manner (100.8 CPR in 11 h as shown in Figure 1. Tablets of batch PO1 did not maintain integrity) and released more than 90% of a drug in 6 h. Tablets of batch PO3 released only 80.2% drug in 12 h, which may be due to higher amount of polymer. Hence it was decided to keep total polymer concentration at 40% for acceptable formulation in further study.

Full factorial design

A statistical model incorporating interactive and poly nominal terms was used to evaluate the responses.

$$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2$$

Where Y is the dependent variable, b_0 is the arithmetic mean response of the 9 runs, and b_1 is the estimated coefficient for the factor Xi. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high values. The interaction terms (X_1X_2) show how the response changes when two factors are simultaneously changed. The polynomial terms (X_1^2 and X_2^2) are included to investigate nonlinearity. Dissolution profile for 9 batches showed a wide variation (i.e., initial 1 h release ranging from 14.78 % to 64.37 % and drug released after 12 h ranging from 90.28 % to 101.44%) [Figure 2]. Dissolution data indicated that drug release is strongly dependent on the selected independent variables. The coefficients for fitted equations (full and reduced) relating the responses, BLT, Q_1, $Q_6$and Q_{12} to the transformed factors are shown in Table 3. These polynomial equations can be used to draw conclusion after considering a magnitude of coefficient and the mathematical sign it carries (i.e., negative or positive). Table 5 shows the results of analysis of variance (ANOVA), which was performed to identify insignificant factors. The data were analyzed using Microsoft Excel.

R^2 value for BLT, Q_1, and Q6 are 0.9082, 0.8637, 0.9331, respectively indicating good correlation between dependent and independent variables. Low R^2 value for Q_{12} (0.485) indicates that drug release at 12h is less dependent on selected variables. Reduced models were developed for response variables by omitting the insignificant terms with $P > 0.05$. The terms with $P < 0.05$ were considered statistically significance and retained in the reduced model. The coefficients for full and reduced models for response variables are shown in Table 5. The coefficients of independent variables for Q_1 and Q_{12} were found - insignificance at $P > 0.05$ with out any contribution in prediction of Q_1 and Q_{12}.

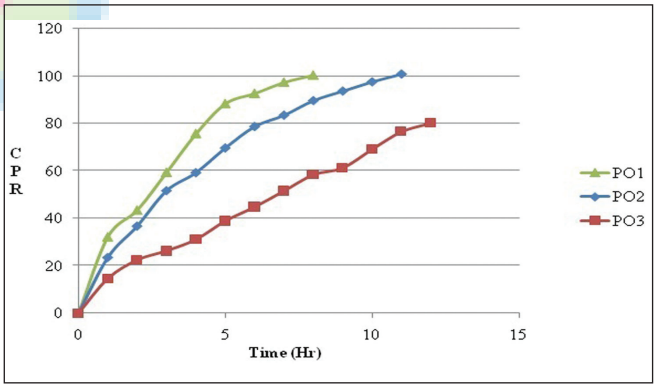

Figure 1: *In vitro* dissolution profile of batch PO1, PO2, and PO3

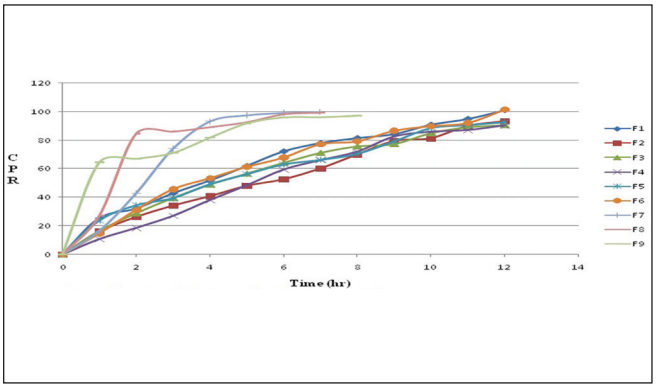

Figure 2: *In vitro* dissolution profile of formulation F1-F9

Full and reduced model for BLT

Significance levels of coefficients b_1, b_{12} and b_{11} were found to be $P = 0.153$, 0.597, and 0.639, respectively, hence they were omitted from a full model to generate the reduced model. Results of statistical analysis are shown in Table 5. Coefficients b_0, b_2, and b_{22} were found to be significant at $P < 0.05$; hence they were retained in a reduced model. Reduced model was tested in proportion to determine whether coefficients b_1, b_{12} and b_{11} contribute significance information in a prediction of BLT or not.[26] The results of model testing are shown in Table 6. The critical value of F for $\alpha = 0.05$ is equal to 9.28 (df = 3,3). Since a calculated value ($F_{cal} = 1.41$) is less than the critical value ($F_{cri} = 9.28$), it was concluded that coefficients b_1, b_{12}, and b_{11} did not contribute significantly in the prediction of BLT and could be omitted from full model to generate-reduced model.

Full and reduced model for Q_6

Significance levels of coefficients b_2, b_{12}, and b_{22} were found to be $P = 0.890$, 0.776, and 0.402, respectively, hence they were omitted from a full model to generate the reduced model. Results of statistical analysis are shown in Table 5. Coefficients b_0, b_1, and b_{11} were found to be significant at $P < 0.05$; hence they were retained in a reduced model. Reduced model was tested in proportion to determine whether coefficients b_2, b_{12}, and b_{22} contribute significance information in a prediction of Q_6 or not. The results of model testing are shown in Table 6. The critical value of F for $\alpha = 0.05$ is equal to 9.28 (df = 3,3). Since a calculated value ($F_{cal} = 0.355$) is less than the critical value ($F_{cri} = 9.28$), it was concluded that coefficients b_2, b_{12}, and b_{22} did not contribute significantly in a prediction of Q_6 and could be omitted from full model to generate-reduced model.

Kinetic modeling of dissolution data

Kinetics of dissolution data were well fitted to zero order, Higuchi model, and Korsemeyer-Peppas model as evident from regression coefficients [Table 7]. In a case of -controlled

Table 5: Summary of results of regression analysis

For buoyancy lag time						
Response (BLT)	b_0	b_1	b_2	b_{12}	b_{11}	b_{22}
FM	60.56	15.17	28.50	5.75	7.17	49.17
RM	65.33	-	28.5	-	-	49.17
For Q_1						
Response (Q_1)	b_0	b_1	b_2	b_{12}	b_{11}	b_{22}
FM	14.83	8.35	7.15	14.22	11.17	2.41
RM	-	-	-	-	-	-
For Q_6						
Response (Q_6)	b_0	b_1	b_2	b_{12}	b_{11}	b_{22}
FM	59.23	17.33	-0.466	1.19	16.92	5.25
RM	63.42	17.33	-	-	16.92	-
For Q_{12}						
Response (Q_{12})	b_0	b_1	b_2	b_{12}	b_{11}	b_{22}
FM	93.45	2.53	0.118	2.62	2.71	1.97
RM	-	-	-	-	-	-

FM = Full model, RM = Reduced model, BLT= Buoyancy lag time

Table 6: Calculations for testing the model in portions

For buoyancy lag time						
	DF	SS	MS	F	R^2	
Regression						Fcalc.= 1.41
FM	5	11323.36	2264.67	5.94	0.9082	Ftable=9.28
RM	2	9708.22	4854.11	10.55	0.7787	DF(3,3)
Error						
FM	3	1143.52	381.17			
RM	6	2758.68	459.78			
For Q^6						
	DF	SS	MS	F	R^2	
Regression						Fcalc.=0.355
FM	5	2437.31	487.46	8.37	0.9331	Ftable=9.28
RM	2	2375.24	1187.62	30.10	0.9093	DF (3,3)
Error						
FM	3	174.70	58.23			
RM	6	236.77	39.46			

DF indicates degree of freedom; SS, sum of squares; MS, mean of squares; R2, regression coefficient; FM, Full model; RM, Reduced model

Table 7: Kinetic treatment of dissolution data

	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Zero order									
B	21.85	11.91	17.67	5.89	21.30	18.18	41.91	61.54	64.44
A	7.03	6.93	6.69	7.71	6.32	7.35	6.30	4.11	3.34
R^2	0.9879	0.9979	0.9796	0.9874	0.9914	0.9798	0.7812	0.6685	0.9030
First order									
B	1.44	1.28	1.34	1.14	1.43	1.36	1.55	1.74	1.82
A	0.053	0.063	0.059	0.049	0.050	0.062	0.050	0.029	0.017
R^2	0.9520	0.9563	0.9126	0.9324	0.9590	0.8887	0.7082	0.5981	0.8975
Higuchi									
B	-10.60	-19.22	-13.97	-29.53	-7.52	-16.52	6.49	37.29	48.06
A	32.29	31.47	31.08	35.35	28.89	34.11	31.77	21.22	15.88
R^2	0.9957	0.9938	0.9981	0.9934	0.9939	0.9980	0.8636	0.7580	0.9412
Hixon Crowell									
B	26.04	29.31	27.44	31.36	1.69	27.27	19.36	12.80	11.77
A	-2.343	-2.31	-2.23	-2.569	-0.145	-2.44	-2.10	-1.37	-1.11
R^2	-0.9876	-0.9978	-0.9795	-0.9874	-0.9742	-0.9797	-0.7813	-0.6684	-0.9030
Korsemeyer and Peppas									
B	-0.630	-0.801	-0.753	-0.978	-0.638	-0.756	-0.598	-0.362	-0.212
N	0.590	0.705	0.692	0.905	0.559	0.738	0.675	0.412	0.202
R^2	0.9938	0.9998	0.9955	0.9962	0.9960	0.9867	0.8954	0.7952	0.9523

b = Slope, a = Intercept, R2 = Correlation coefficient, n = Diffusion exponent

or sustained release formulation, diffusion, swelling and erosion are the three most important rate controlling mechanisms. Formulation containing swelling polymers shows swelling as well as diffusion mechanism because a kinetic of swelling includes relaxation of polymer chains and imbibitions of water, causing the polymer to swell and changing it from glassy to rubbery state. Diffusion exponent n is an indicative of mechanism of drug release from the formulation. For a swellable cylindrical (tablet) drug delivery system, the n value of 0.45 is indicative of Fickian diffusion controlled drug release. Value of n between 0.5 and 0.85 signifies anomalous (non-Fickian) transport, n value of 0.85 indicates case II transport, and n value greater than 0.85 indicates super case II transport.[27,28] Value of diffusion exponent n for most factorial formulations is between 0.5 and 0.85 [Table 7] indicating non-Fickian drug release from the formulations.

Comparison of dissolution profiles for selection of optimum batch

Values of similarity factor (f_2) for batches F_1 to F_6 were greater than 50 compared with theoretical dissolution profile [Table 4] indicating good similarity in dissolution. Tablets of batch F_5 showed maximum value of f_2 (83.01), hence was selected as optimum batch. The tablets of batch F_5 were subjected to the temperature sensitivity study.

Fourier transform infrared spectroscopy

Drug excipients interactions play a vital role in the release of drug from formulation. Fourier transform infrared spectroscopy has been used to study physical and chemical interactions between a drug and the excipients used. The pure famotidine and its mixture with Gelucire 43/01 and HPMC K4M was mixed separately with IR grade KBr and were scanned over a range of 400-4500 cm^{-1} using FTIR instrument (FTIR-1700, Shimadzu, Kyoto, Japan). The drug exhibits peak due to primary amine and alkene group. It was observed that there were no changes in these main peaks in IR spectra of a mixture of drug and polymers [Figures 3-6]. The FTIR study revealed no physical or chemical interactions of famotidine with Gelucire 43/01 and HPMC K4M as evident from Figure 6.

Results of temperature sensitivity study

To determine any change in *in vitro* release profile on storage, a temperature sensitivity study of the optimal batch F_5 was performed at 40°C in humidity jar with 75% RH. Sample withdrawn after 1 month showed no significant change in *in vitro* buoyancy and *in vitro* drug release pattern.

CONCLUSION

From present investigation it was concluded that a combined matrix system containing hydrophobic and hydrophilic polymer minimized bust release of drug from tablet and achieved drug release by zero order kinetic, which is practically difficult with only hydrophilic matrix.

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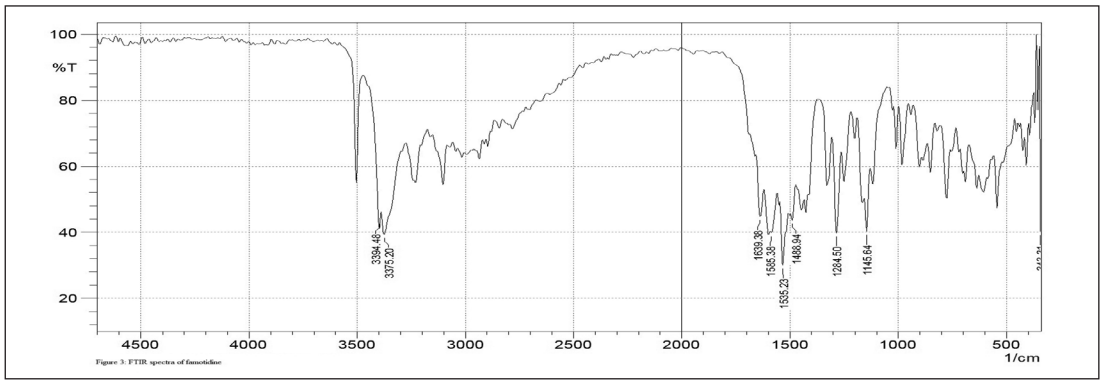

Figure 3: FTIR spectra of Famotidine

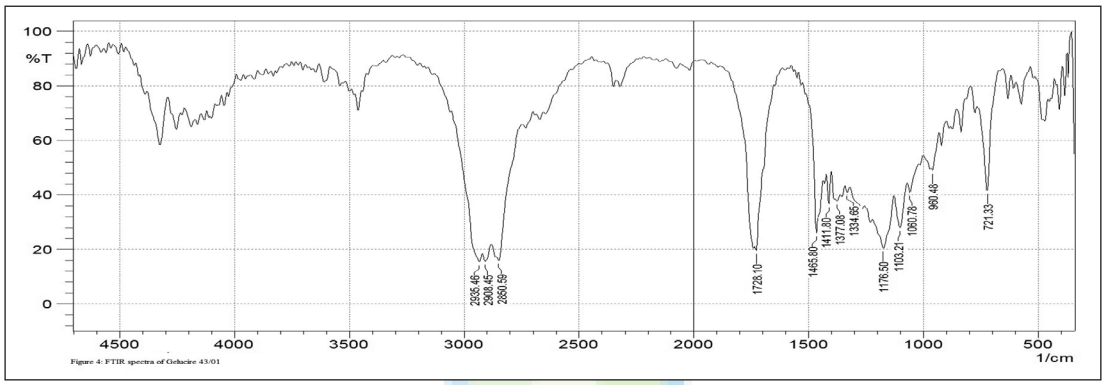

Figure 4: FTIR spectra of Gelucire 43/01

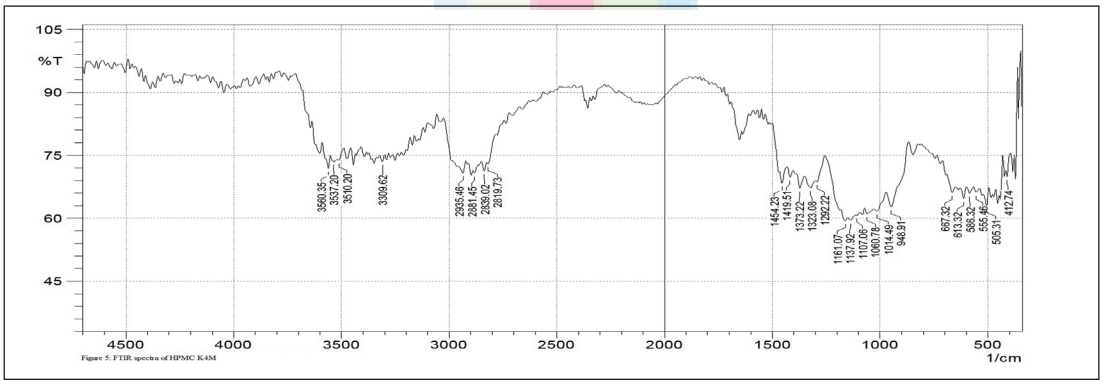

Figure 5: FTIR spectra of HPMC K4M

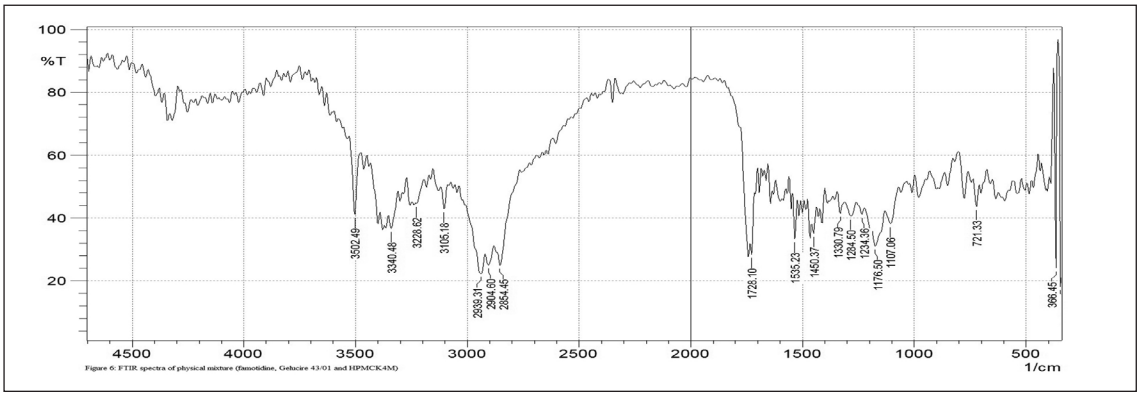

Figure 6: FTIR spectra of physical mixture (Famotidine, Gelucire 43/01 and HPMC K4M)

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