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FORMULATION AND OPTIMIZATION OF MOUTH DISSOLVING TABLETS OF FAMOTIDINE USING LYOPHILIZATION TECHNIQUE

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ABSTRACT

Gastric acid secretion and duodenal ulcers are the common problems among the people. Although there are many oral dosage forms available but problem comes with the geriatric, pediatric, bed ridden, mentally ill patients suffering from dysphagia (difficulty in swallowing).Purpose of the present study was to develop mouth dissolving tablet of Famotidine which can be proved useful for patients and provide optimal patient compliance. Solid dispersion of Famotidine was prepared using PEG6000 as a polymer using lyophilization technique. Among the five ratios (1:1,1:3, 1:5, 1:7,1:9) SD2 i.e. 1:3 showed better results. Pre-compressional and post–compressional studies were performed which comes within prescribed limit .XRD and FTIR studies were done to check drug polymer interaction.3^2 full factorial design was used for optimization. Camphor and crospovidone were used as independent variables and disintegration, percentage friability were used as dependent variables for optimizing the results. Results of multiple linear regression showed that for obtaining rapidly disintegrating tablet with minimum friability optimum concentration of camphor and increased percentage of crospovidone is used. Contour plot, response surface plots were presented. Tablets were subjected to vacuum drying for sublimation of camphor to make them porous.

KEYWORDS: Famotidine, PEG6000, Solid dispersion, Lyophilization technique,Mouth dissolving tablet, Optimization.

INTRODUCTION

Although various novel and advanced drug delivery system have been introduced for therapeutic use, the popularity of oral dosage form have not been eclipsed.[1] Tablets are most accepted oral dosage form because of accurate dosing, convenience of administration, stability compared with oral liquids. But the patient groups such as bed ridden ,disabled, uncooperative and nauseated patients suffering from motion sickness may find difficulty in swallowing tablets and capsules which leads to patient non-compliance.[2] To improve the quality of life and treatment compliance of such patients, mouth dissolving tablets is the better alternative.

Famotidine is H_2 receptor antagonist[3] which promotes healing of duodenal ulcers. Half life of Famotidine is 2.5-4 hrs and its elimination through metabolic and renal route therefore it is important to reduce the dose of drug for patients with kidney and renal failure.[4] This model drug was selected due to its low solubility and bioavailability. The purpose of this study was to increase solubility by solid dispersion using lyophilization method and to formulate and optimize mouth dissolving tablet of Famotidine with low dose of drug.

MATERIALS AND METHODS

Materials

Famotidine was obtained as gift sample from Ind Swift Pvt .Ltd., Dera Bassi,India. PEG6000, camphor, microcrystaline cellulose, magnesium stearate, talc, lactose were obtained from Loba chem. Pvt. Ltd,(Mumbai,India) and Crospovidone ,TBA(tertiary butyl alcohol)obtained from signet Pvt. Ltd.,India.

Methods

Preparation of solid dispersions by Lyophilization technique

Five ratios of solid dispersions were prepared 1:1,1:3,1:5,1:7,1:9 using PEG 6000 as a polymer.TBA (tertiary butyl alcohol) was used as co-solvent to solubilise hydrophobic drug (famotidine).[5,6] 10 mg Famotidine was dissolved in 20 ml TBA and different ratios were mixed with 5ml of water .Both solutions were mixed and frozen at -20ºC in deep freezer for 1hr.Solutions were taken in RBF and frozen for 2hrs followed with condenser temperature of -78.5ºC.After complete freezing was achieved RBF were subjected to lyophilization for 4hrs.Dried powder was achieved in RBF in the end.[7]

Fig 1: Materials being lyophilized in lyophilizer

PRE COMPRESSIONAL PARAMETERS

Determination of solubility

Pure Famotidine and solid dispersions equivalent to 20 mg of Famotidine was added to 10 ml of phosphate buffer pH 6.8 in 25 ml volumetric flasks. The volumetric flasks was capped properly and shaken at 37 ± 2 ˚C in a temperature controlled water bath (Shaking water bath) for 48 h. Resultant samples containing undissolved solid dispersions suspended in the volumetric flasks was filtered through Whatman filter paper no. 41, suitably diluted with phosphate buffer pH 6.8 and analyzed by UV spectrophotometer at 268 nm.

Dissolution studies

The dissolution study of Famotidine was determined using USP XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 as a dissolution medium, at 37 ± 0.5 ˚C and 75 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus in order to keep total volume constant. at time interval of 5,10,15,20,25,30 minutes. The samples were filtered through a Whatman filter paper(41). Experiment was performed in triplicate and absorbance of these solutions was measured at 268.0 nm using a Shimadzu-1700 UV- Visible spectrophotometer.

Fourier Transform Infrared Spectroscopy (FTIR): FTIR spectra of pure drug, polymer PEG6000 and solid dispersion was recorded using IR spectrophotometer Bruker (alpha E). It revealed the interaction between drug and polymer used. The scanning range was 4000 -400 cm^{-1}.

XRD studies

Powder X-ray diffraction (XRD) pattern of pure drug, PEG6000 and solid dispersion were recorded using X-ray diffractrometer. Scanned range was 5-50º,CuKα as monochromatic radiation, voltage 45 KV , current 40 mA at ambient temperature.

PREPARATION OF TABLETS

Mouth dissolving tablets were prepared by direct compression method using sublimation technique. SD2 (1:3) was selected as best formulation to compress into tablets. Camphor was used as sublimating agent and crospovidone as superdisintegrant.In the end tablets were subjected to vacuum drying at 50ºC.[8]

EXPERIMENTAL DESIGN OF FAMOTIDINE MOUTH DISSOLVING TABLET

A 3^2 Full factorial design (FFD) was chosen for the current formulation optimization study. In a full factorial design, all the factors are studied in all the possible combinations, as it is considered to be most efficient in estimating the influence of individual variables (main effects) and their interactions, using minimum experimentation.

Concentration of two formulation variables camphor and crospovidone were selected as independent factors whereas disintegration time (DT),and percentage friability (%F) were measured as responses. Based on initial trials, levels of crospovidone and camphor were selected. Nine formulations were prepared according to 3^2 factorial design and evaluated. The responses were analyzed for ANOVA using Design Expert version 9.0.4. A mathematical equation was generated for each response parameter. The mathematical models were tested for significance. Response surface plots were generated for each response to study the behaviour of the system.

To evaluate responses statistical model, $Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1X_1 + b_{22}X_2X_2$, incorporating interactive and polynomial terms was used . where Y is the dependent variable, b_0 is the arithmetic mean response of the nine runs and b_1 is the estimated coefficient for the factor X_1. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The term (X_1X_2) indicates the interaction between two factors. The polynomial terms (X_1X_1 and X_2X_2) are tells us about nonlinearity.

Tabe 1: Preliminary trial batches of Famotidine mouth dissolving tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
SD3 (Dose=10mg)	40	40	40	40	40	40	40	40	40
Camphor	2.5	5	7.5	-	-	-	-	-	7.5
Crospovidone	-	-	-	2.5	5	7.5	-	-	7.5
Mannitol	40.5	38	35.5	40.5	38	35.5	43	43	28
Talc	2	2	2	2	2	2	2	2	2
Lactose	2	2	2	2	2	2	2	2	2
Mag.Stearate	3	3	3	3	3	3	3	3	3
MCC	10	10	10	10	10	10	10	10	10
Total	100	100	100	100	100	100	100	100	100

Table 2: Experimental plan of 3^2 factorial design

BATCH CODE	Variable Levels in Coded Form		D.T.	Friability
	X_1(camphor)	X_2(crospovidone)	Y_1(sec)	Y_2 (%)
F-1	-1	-1	62	0.96
F-2	-1	0	52	0.85
F-3	-1	+1	40	0.78
F-4	0	-1	62	0.98
F-5	0	0	48	0.95
F-6	0	+1	37	0.80
F-7	+1	-1	35	0.98
F-8	+1	0	24	0.92
F-9	+1	+1	20	0.82

Coded Values	Actual Values	
	X_1 (camphor)	X_2 (crospovidone)
-1	2.5	2.5
0	5	5
+1	7.5	7.5

EVALUATION OF PREPARED TABLETS

General appearance

This includes tablets size, shape, colour, presence or absence of an odour,, surface texture, physical flaws, consistency and legibility of any identifying marking.

Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance and also in counting by suing filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer (Mityato, Japan).

Uniformity of weight

As per IP, twenty tablets were taken and weighed individually and collectively using digital balance. The average weight of one tablet was calculated. The weight variation test would be satisfactory method of determining the drug content uniformity.

Table 3: Weight variation limits for tablets as per IP

Average of Tablets (mg)	Maximum % difference allowed
80 or less	10
80-250	7.5
More than 250	5

Tablet hardness

It can be defined as the force required per unit area to break the tablet.. Hardness of the tablets was determined by using Pfizer tester.

Friability

Friability of the tablets was determined using Roche friabilator.. The friability (%F) is determined by the formula.

$$\%F = (1 - \frac{W}{W_0}) \times 100$$

Where, W_0 is initial weight of the tablets before the test and W is the weight of the tablets after test.

Disintegration test

Modified method: Disintegration of mouth dissolving tablets is achieved in the mouth owing to the action of saliva, No tablet disintegration test was found in USP and IP to simulate *in vivo* conditions. A modified method was used to determine disintegration time of the tablets.

A cylindrical vessel was used in which 10-meshscreen was placed in such way that only 2 ml of disintegrating or dissolution medium would be placed below the sieve. To determine disintegration time, 6 ml of phosphate buffer (pH 6.8), was placed inside the vessel in such way that 2 ml of the media was below the sieve and 4 ml above the sieve. Tablet was placed on the sieve and the whole assembly was then placed on a shaker. The time at which all the particles pass through the sieve was taken as a disintegration time of the tablet. Six tablets were chosen randomly from the composite samples and the average value was determined.[9] Similar test was performed by taking 4ml of saliva

Wetting time

The method was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petri dish (ID = 65 cm) containing 10 ml of phosphate buffer (pH 6.8), A tablet was put on the paper, and the time for the complete wetting was measured. Three trials for each batch were performed and the standard deviation was also determined.[10]

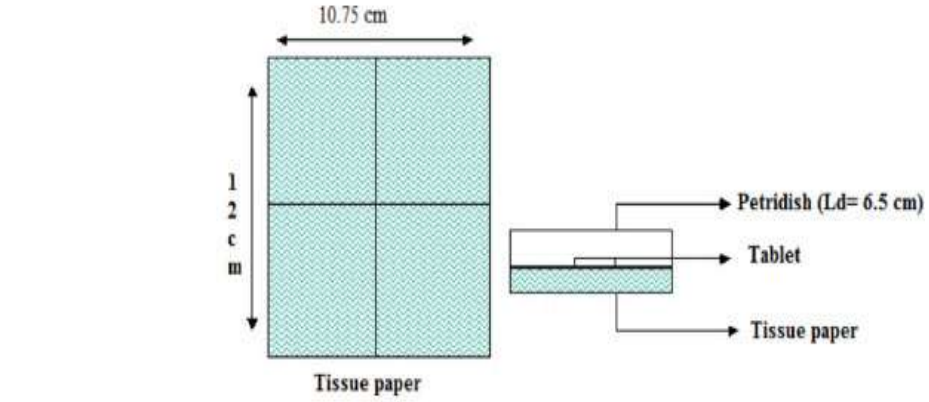

Fig2: Wetting time determination of mouth dissolving tablet

***In- vitro* dissolution study**

Dissolution study was carried out manually as no pharmacopoeia detail is mentioned regarding dissolution of mouth dissolving tablets. 25 ml beaker was placed on mechanical stirrer containing 6 ml phosphate buffer (pH 6.8) as dissolution medium maintained at 37 ± 0.5 ^{O}C. The medium was stirred as 75 rpm. Aliquots 1 ml dissolution medium were withdrawn at 5,10,15, 20 25, 30 min time intervals and same amount was replaced with thedissolution medium. The collected samples were analysed after filtration at 268 nm using UV spectrophotometer against the blank. Drug release studies were carried out in triplicate and cumulative percentage drug release was calculated.

STABILITY STUDIES[11-13]

Temperature dependent stability studies

The optimized mouth dissolving tablets of Famotidine were packed in wide mouth air tight glass container and stored at (40 ± 2 ˚C and 75 ± 5 % RH) for a period of 3 months.

The tablets were withdrawn after a period of 15 days and analyzed for physical characterization and drug content spectrophotometrically at 268 nm Among several methods investigated Moorie and Flanner method for dissolution profile comparison, *f2* is the simplest method .

$$f_2 = 50 \cdot \log \{[1+1/n\sum_{t=1}^{n}(R_t - T_t)^2]^{-0.5} \cdot 100$$

Where R_t and T_t are the cumulative percentage dissolved at each of the selected n time points of the reference and test product respectively.

When the two profiles are identical, *f2*=100. An average difference of 10% at all measured time point's results in a *f2* value of 50. FDA has set a public standard of *f2* value between 50 - 100 indicate similarity between two dissolution profiles.

RESULTS AND DISCUSSIONS

Solubility study: Five ratios were prepared and SD2 formulations shows greater solubility than others and was selected for preparation of tablets. Solubility of pure drug and solid dispersion is shown in figure 3 and table 4.

Table 4: Solubility of pure drug and solid dispersion at 37± 2° C

Formulation number	Solubility(µg/ml)
Pure	32.56±0.001
SD1	144.44±0.006
SD2	266.12±0.006
SD3	164.51±0.008
SD4	188.23±0.003
SD5	194.42±0.002

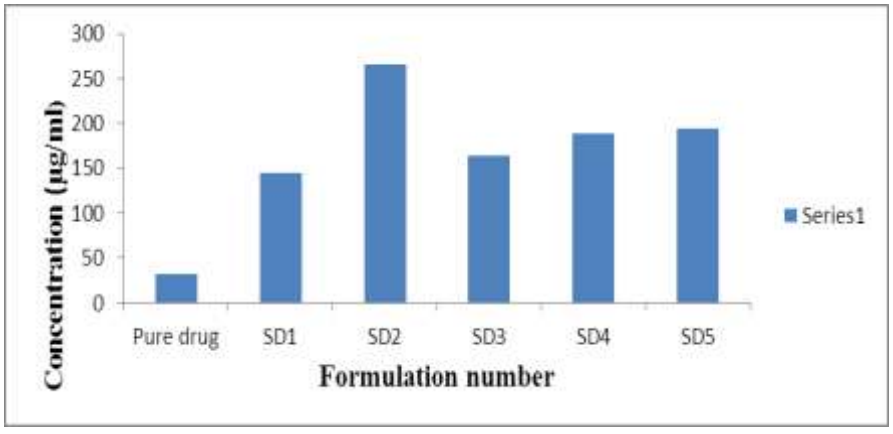

Fig3:Solubility of pure drug and solid dispersion at 37± 2° C

Dissolution studies

It is clear from the data that onset of dissolution of pure drug was very slow. There was hard need to enhance the dissolution which was found to be increased by adding PEG6000.It is clear from the graph that ratio 1:3 (SD2) shows fastest dissolution there was selected for further studies.

Table 5: Dissolution release profile of pure drug and from solid dispersion

Time (min.)	Pure drug	SD1	SD2	SD3	SD4	SD5
0	0	0	0	0	0	0
5	2.46±0.32	8.53±0.78	18.23±0.48	14.24±0.62	15.44±0.29	18.32±0.12
10	6.21±0.74	13.94±0.58	34.33±0.48	30.88±0.19	31.34±0.49	32.71±0.19
15	12.05±0.20	22.64±0.78	52.26±0.20	44.43±0.58	44.15±0.96	44.21±0.17
20	15.82±0.44	28.74±0.17	70.32±0.29	52.31±0.17	60.31±0.48	60.12±0.38
25	23.92±0.54	35.63±0.19	89.22±0.19	81.81±0.48	74.21±0.58	74.96±0.38
30	24.80±0.63	42.59±0.67	96.22±0.18	91.35±0.19	90.23±0.37	88.35±0.19

* Values represent the mean ±SD of three experiments

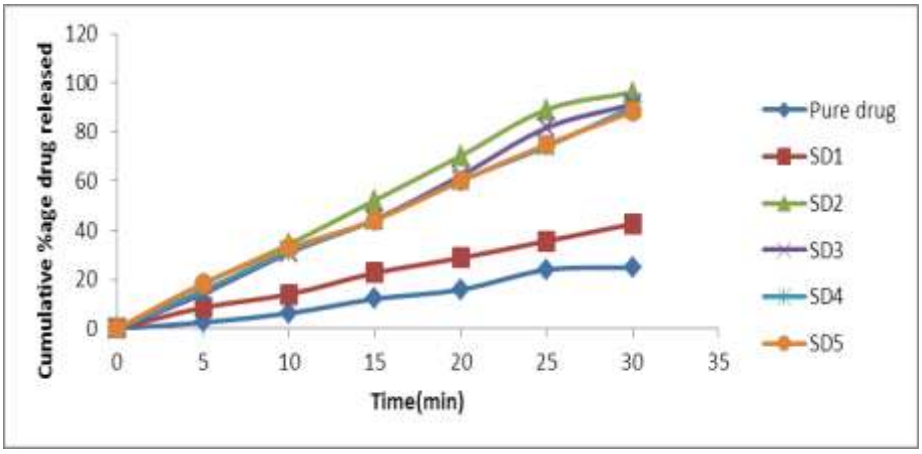

Figure 4: Percent release of pure drug and from solid dispersion

FTIR

FTIR spectra revealed about drug polymer interaction . Characteristics peaks observed in pure drug famotidine is shown in table 6. While FT-IR of PEG shows peaks at 2879.42 cm^{-1} corresponding to C-H stretch, at 1100.56 cm^{-1} corresponding to C-O(ether) stretch, at 3251.58 cm^{-1} corresponding to O-H stretching vibrations. FTIR spectra of solid dispersion shows all characteristic peaks of drug and PEG6000 which shows that there is no interaction between drug and polymer.

Table 6: FTIR peaks of pure drug Famotidine

Peak assignment	Famotidine(cm^{-1})
N-H stretching	3341.48
C-H (alkene) aromatic Stretching	3098.95
C-H (alkane) stretching	2898.47
(NH_2)in plane deformation bending	1528.34
Thiazole stretching	1280.13
O=S=O stretching	1137.90

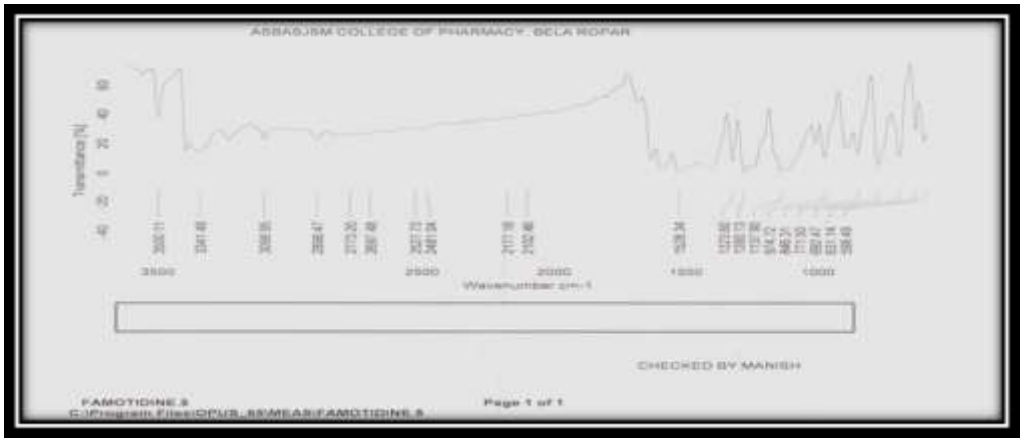

Figure 5 : FT-IR spectra of pure drug

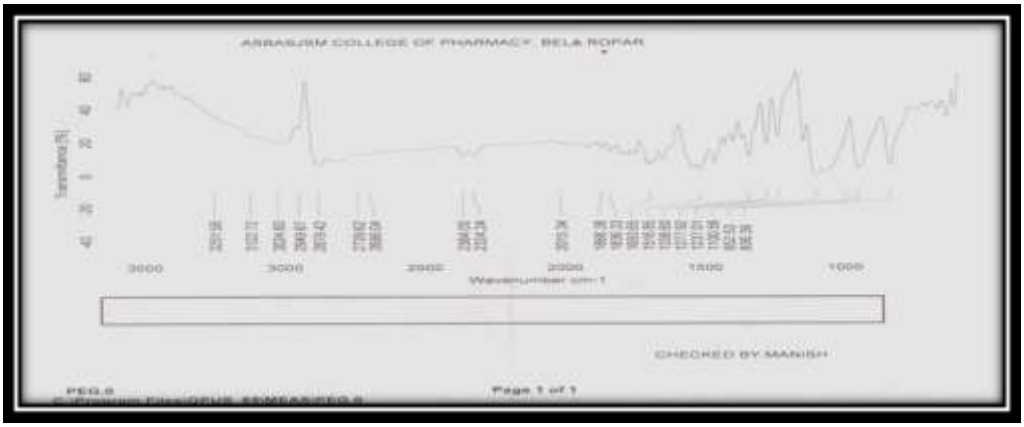

Fig 6: FT-IR Spectra of PEG 6000 (polymer)

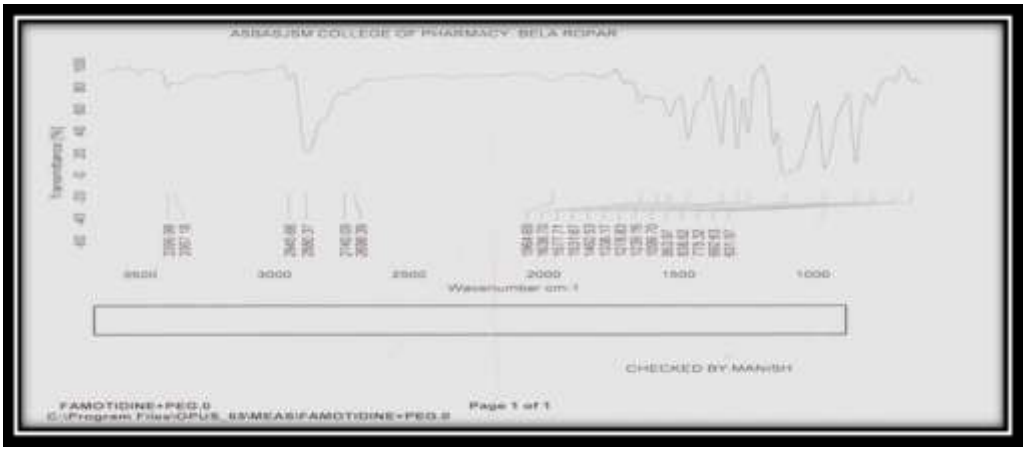

Figure 7: IR spectra of solid dispersion (SD2)

XRD Analysis

Pure Drug: XRD pattern of Famotidine showed several sharp high intensity peaks at diffraction angle 2θ of 15.0258^{o}, 17.8952^{o}, 19.6454^{o}, 20.3477^{o}, 22.7533^{o}, 24.8856^{o} which suggested Famotidine as crystalline in nature as shown in fig 8

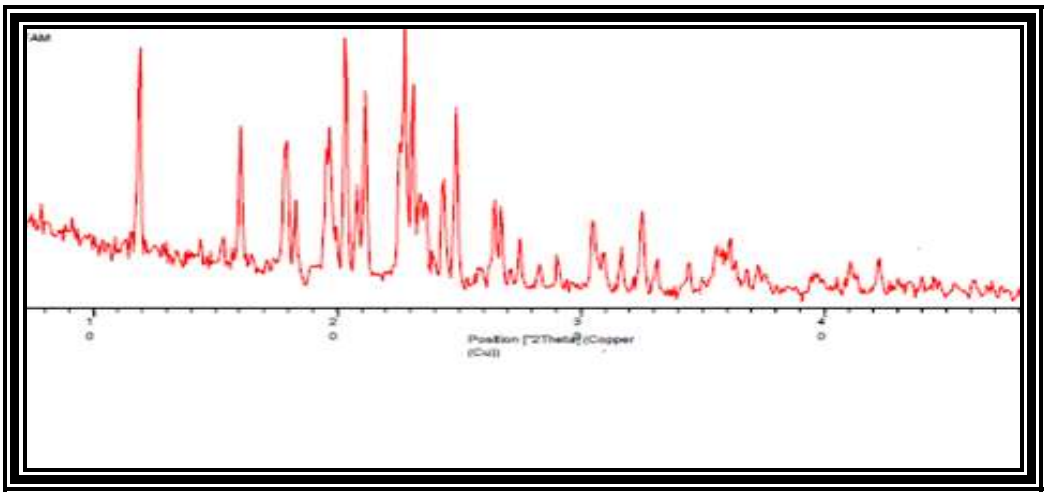

Figure 8: XRD Spectra of Famotidine

PEG 6000: XRD pattern of PEG 6000 showed two characteristic peaks of high intensity at diffraction angle 2θ of 19.2758º and 23.3711º respectively.

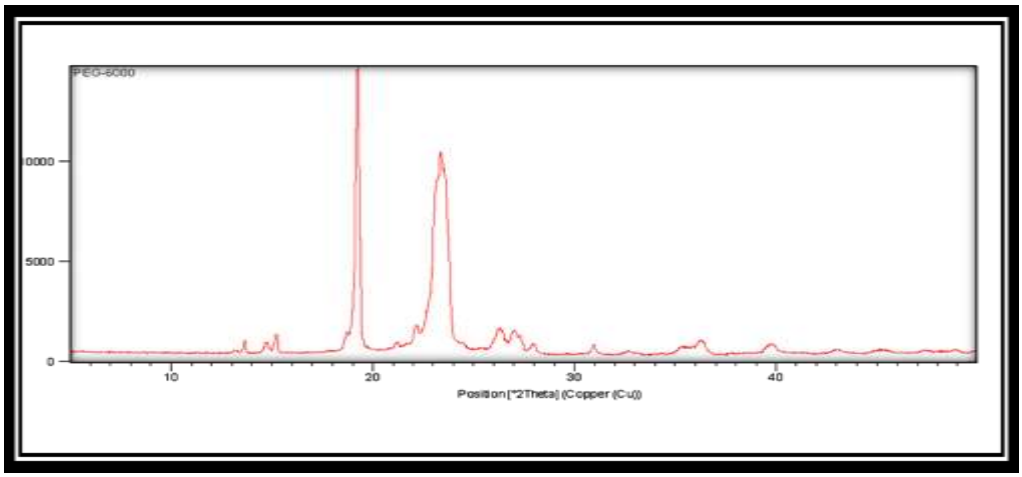

Figure 9: XRD Spectra of PEG6000

Solid dispersion: Solid dispersion shows peaks at 19.1582º, , 23.399º , 26.1743º .The XRD of solid dispersion exhibits peaks less than the sum of the number of peaks of Famotidine and PEG6000 in their pure form.

This suggests that crystallinity of the drug and polymer is reduced in solid dispersion. Decrease in crystallinity of the drug and polymer contribute to enhancement of dissolution of drug.

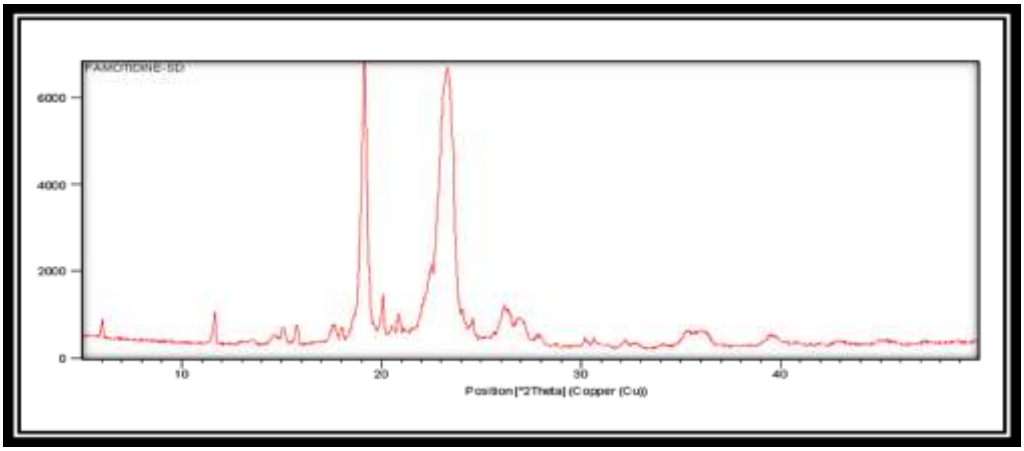

Figure 10: XRD Spectra of SD2

EVALUATION OF MOUTH DISSOLVING TABLETS OF FAMOTIDINE

Table 7: Characterization of blends (Pre-compression parameters)

Formulation codes	Bulk density (g/cc)	Tapped density(g/cc)	Hausner's ratio	Compressibili -ty index (%)	Angle of repose(°)
F1	0.590±0.010	0.672±0.006	1.171±0.001	12..107±0.075	37.59±0.907
F2	0.609±0.016	0.702±0.011	1.170±0.011	12.738±0.817	31.39±0.501
F3	0.668±0.031	0.757±0.025	1.179±0.016	11.599±1.270	28.33±0.608
F4	0.598±0.014	0.680±0.018	11.43±0.011	12.078±0.857	26.52±1.031
F5	0.668±0.031	0.754±0.010	1.230±0.013	11.362±0.993	28.77±0.996
F6	0.618±0.029	0.696±0.039	1.142±0.014	11.088±0.564	25.34±0.567
F7	0.598±0.007	0.782±0.006	1.149±0.007	13.648±0.014	32.04±1.004
F8	0.611±0.029	0.699±0.019	1.156v0.013	13.865±0.054	33.23±0.654
F9	0.567±0.034	0.640±0.023	1.165±0.012	11.523±0..865	21.65±0.524

*Values represent the mean ± SD of three experiments

Table 8: Characterization of mouth dissolving tablets (Post-compression parameters)

Formulation Codes	Average Weight(mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)
F1	92.30±1.54	3.123±0.089	3.246±0.086	0.94
F2	98.65±1.76	3.116±0.086	3.323±0.094	0.89
F3	92.1±1.98	3.250±0.083	3.156±0.095	0.85
F4	90.7±2.12	3.343±0.187	3.123±0.069	0.86
F5	95.1±1.98	3.340±0.091	3.054±0.058	0.84
F6	92.25±2.07	3.278±0.090	3.312±0.100	0.82
F7	93.55±1.54	3.281±0.06	3.234±0.08	0.98
F8	91.45±1.52	3.18±0.08	3.232±0.09	0.96
F9	92.0±1.88	3.214±0.09	3.356±0.08	0.80

*Values represent the mean ± SD of three experiments

Table 9: Characterization of mouth dissolving tablets

Formulation Codes	Disintegration Time(sec)		Wetting Time (sec)	Drug Content (%)
	Buffer (pH 6.8)	Saliva		
F1	55±0.47	53± 0.22	62±1.24	99.14±0.34
F2	52±1.25	51±0.42	58±1.20	99.17±0.40
F3	49±1.24	50±0.45	55±0.81	99.85±0.93
F4	52±0.82	45±0.32	60±0.82	99.14±0.62
F5	40±1.24	40±0.31	54±0.91	99.14±0.83
F6	37±1.52	38±0.25	52±1.22	99.56±0.47
F7	62±0.66	64±0.55	78±1.15	99.87±0.35
F8	70±0.82	62±0.45	72±1.44	99.56±0.65
F9	25±0.56	23±0.23	48±0.73	99.74±0.16

*Values represent the mean ± SD of three experiments

Table 10: *In vitro* release of Famotidine mouth dissolving tablets

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
5	34.12±0.19	38.11±0.49	42.32±0.35	38.69±0.42	46.61±0.58	50.27±0.62	30.12±0.18	32.44±0.19	52.13±0.55
10	43.97±0.39	48.32±0.59	52.61±0.52	45.92±0.44	52.33±0.70	57.53±0.46	36.32±0.44	40.34±0.24	58.34±0.55
15	56.60±0.49	57.92±0.68	60.39±0.69	57.63±0.68	59.60±0.72	64.77±0.44	40.64±0.16	49.32±0.33	62.34±0.66
20	66.03±0.49	68.03±0.29	72.99±0.49	68.02±0.78	75.67±0.59	75.47±0.37	45.14±0.54	54.55±0.45	72.45±0.34
25	74.59±0.58	78.72±0.34	80.42±0.78	76.63±0.83	80.02±0.59	84.03±0.57	52.45±0.34	60.34±0.46	81.56±0.76
30	82.85±0.37	84.32±0.79	88.02±0.53	84.46±0.47	88.22±0.48	91.38±0.65	60.76±0.32	68.34±0.45	92.66±0.445

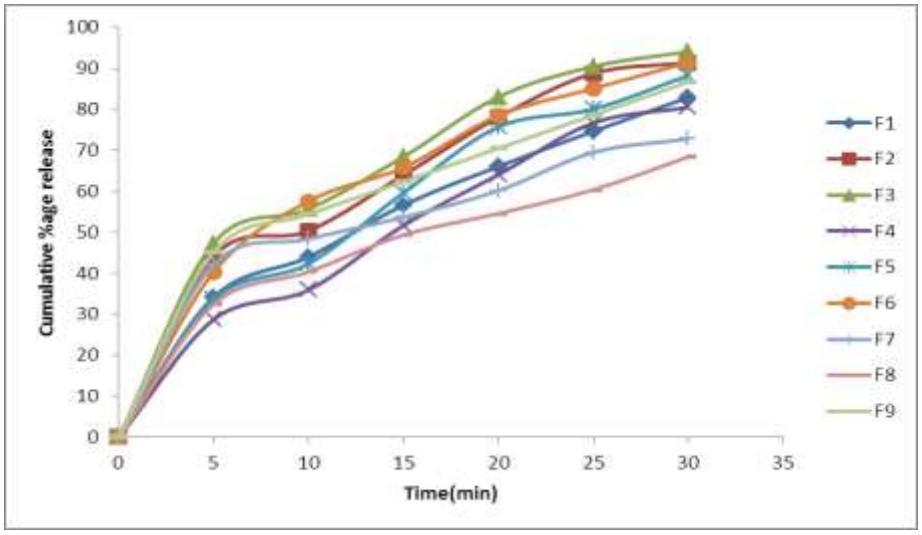

Fig 11:Cumulative %age drug release plot

OPTIMIZATION RESULTS

Preliminary experiments indicated that camphor(X1) and crospovidone(X2) are the effective variables for optimization stidies. Design expert version 9.0.4 software was selected for study.Full model having significant and non significant p values was selected in obtaining dependent variables.

Table 11: Optimization of mouth dissolving tablet

CONSTRAINTS			
NAME	**GOAL**	**Lower Limit**	**Upper Limit**
Camphor	Is in range	-1	+1
Crospovidone	Is in range	-1	+1
D.T. (sec)	Is target =41	20	62
Friability (%)	Is target =0.88	0.78	0.98

Table 12: Summary of results of regression analysis

Response	B_0	B_1	B_2	B_{12}	B_{11}	B_{22}
D.T.	48.11	-12.50	-10.33	1.75	-10.17	1.33
p value		0.0014	0.0024	0.2764	0.0121	0.5262
%Friability	0.92	0.022	-0.087	0.031	-0.025	-0.020
p value		0.1428	0.0042	0.7345	0.2798	0.3699

$D.T. = 48.11 - 12.50X_1 - 10.33X_2 + 1.75X_1X_2 - 10.17X_1X_1 + 1.33X_2X_2$ ...eqn (1)

$\%\ Friability = 0.92 + 0.022X_1 - 0.087X_2 + 0.031X_1X_2 - 0.025X_1X_1 - 0.020X_2X_2$…eqn(2)

Positive sign of the term indicates positive (additive) effect, while negative sign indicates negative (antagonistic) effect of the factor on the response.

Table 13: Results of analysis of variance

Response		df	Sum of square	Mean square	F	R^2
D.T.	Model	5	1800.69	360.14	51.79	0.9885
	Residual	3	20.86	6.95		
% Friability	Model	5	0.050	0.010	13.86	0.9585
	Residual	3	2.16	7.222		

Response Surface Plots

Response surface plots were generated for each response to study the effect of each factor and the behaviour of the system.

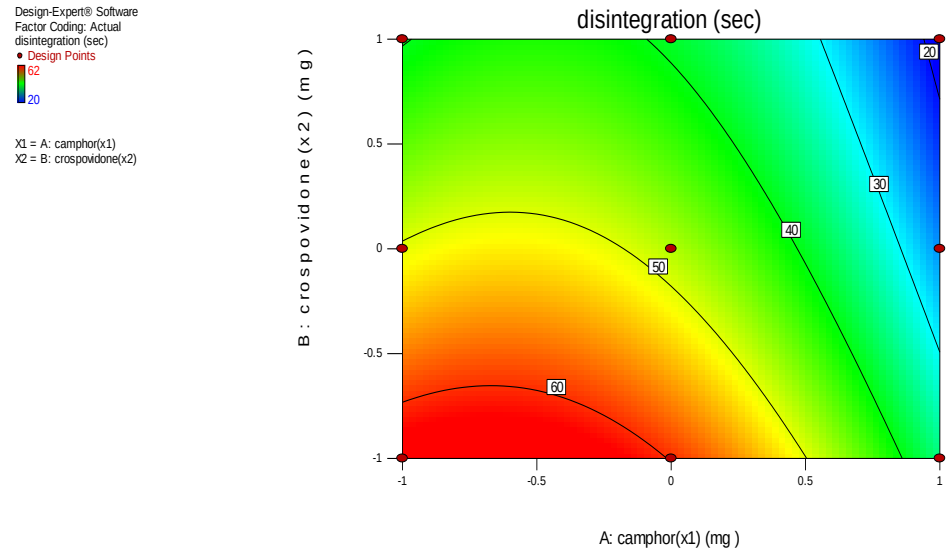

Figure 12: Contour plot for disintegration time

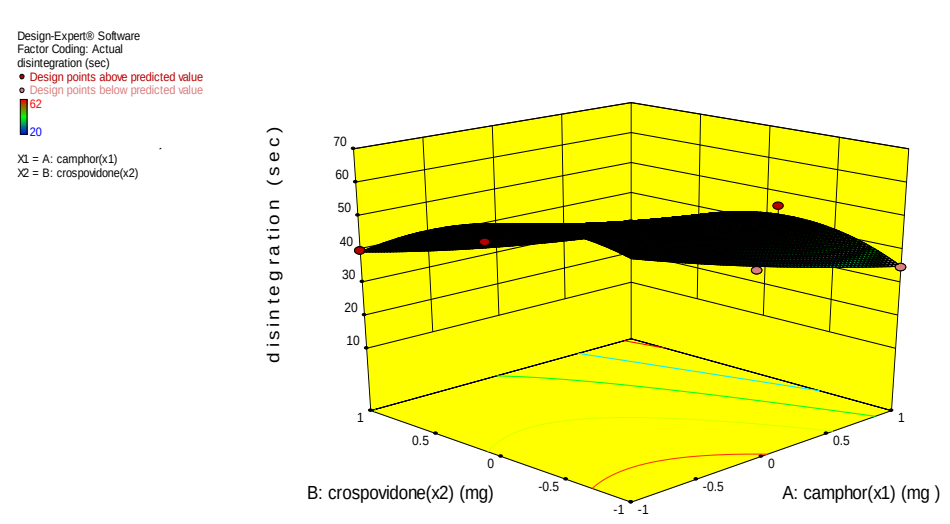

Figure 13: Response surface plot for disintegration time

It was observed that disintegration time was dependent on both factors. A linear decrease in the disintegration time was observed with an increase in the levels of both factors. Camphor and Crospovidone enhances faster disintegration.

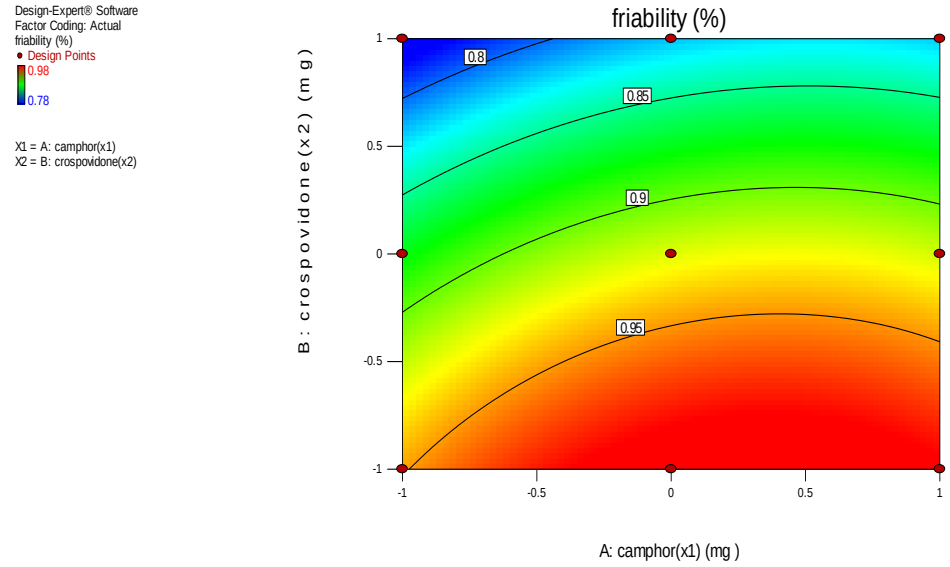

Figure 14: Contour plot for friability

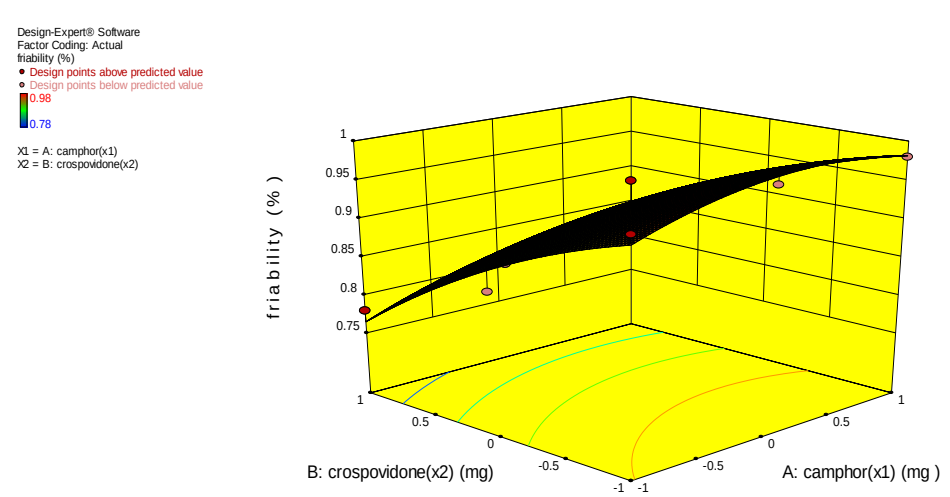

Figure 15: Response surface plot for friability

Response surface plots for percent friability clear that both the factors had influence on percent friability of the tablets. An increase in percentage friability observed with increasing concentration of camphor and linear decrease in percentage friability observed with increase in concentration of Crospovidone. Thus optimum values of friability were selected keeping in view this trend,

5.3 Optimum formulation

Using software Design Expert 9.0.4 , disintegration time, percentage friability were 41 sec,0.88% respectively and desirability was 1.

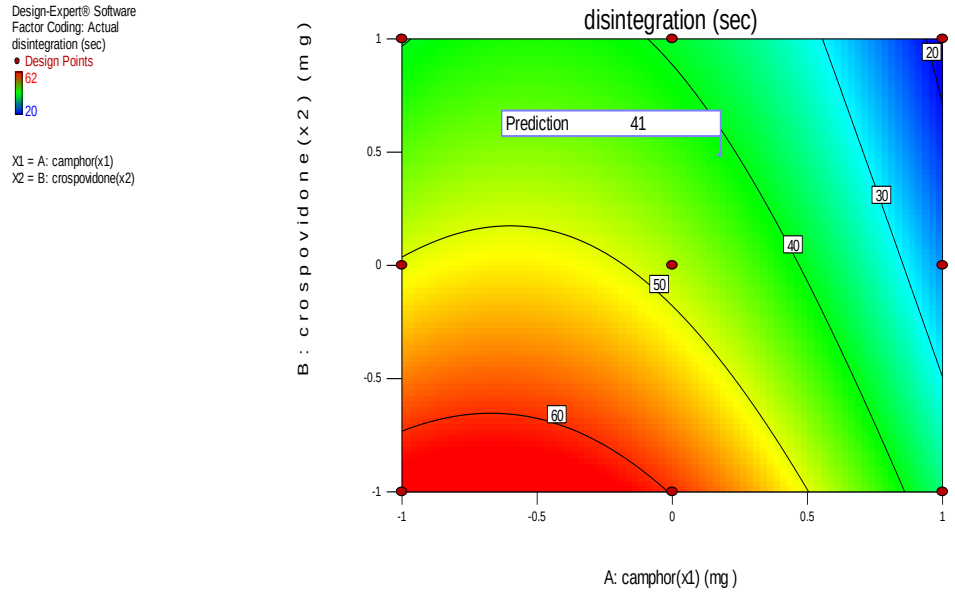

Fig 17:Response surface of optimized formulation (disintegration)

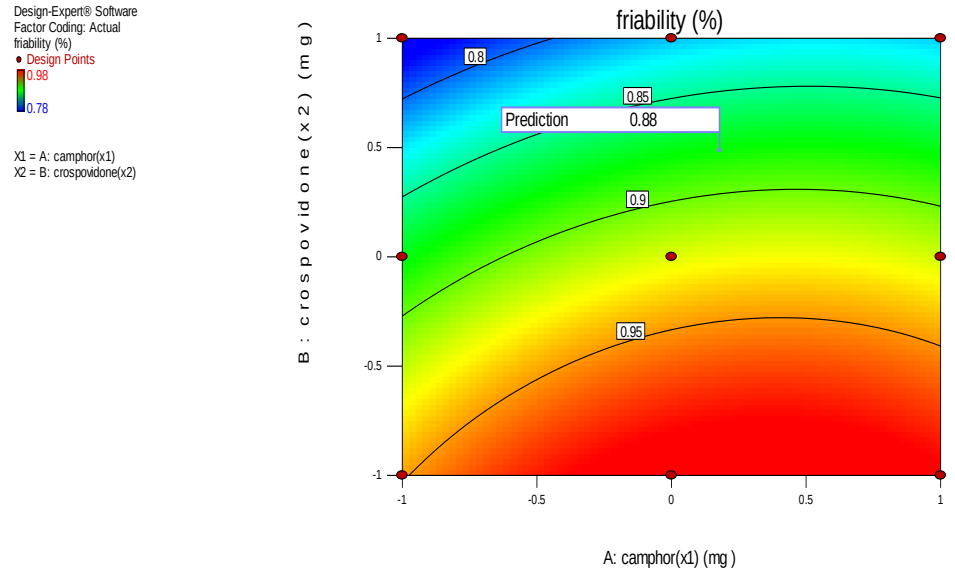

Fig 18:Response surface of optimized formulations (friability)

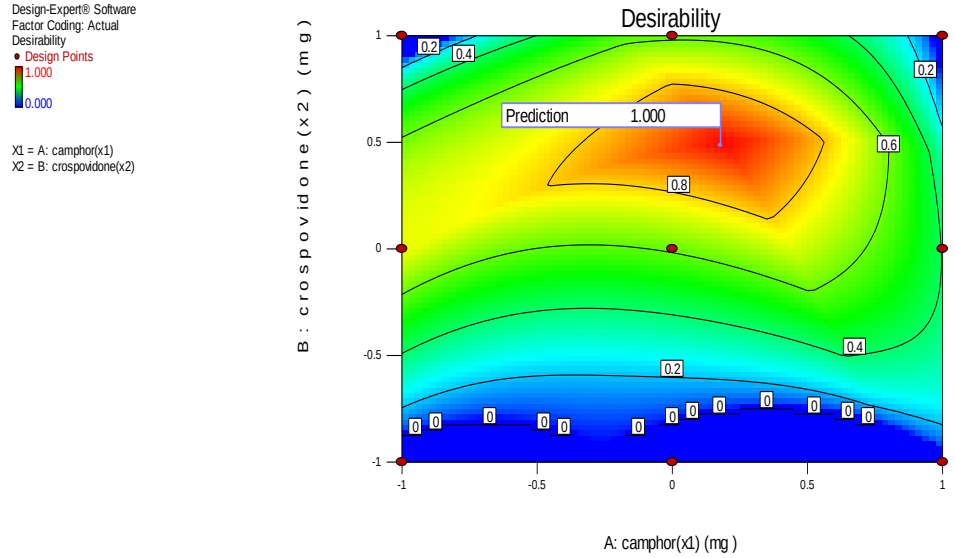

Fig 19:Response surface of optimized formulations (desirability)

Optimum formulation for mouth dissolving tablets of Famotidine

The optimized formulation was prepared with best concentration of camphor and crospovidone. The amount was suggested by the software design expert 9.0.4. The optimized tablets were prepared and characterized for their physiochemical properties.

Table 14: SOLUTION

Camphor X_1	crospovidone X_2	D.T. (sec)	Friability (%)	Desirability
0.179 (5.4mg)	0.486 (6.2 mg)	41	0.88	1.00

Table 15: Optimized Famotidine formulation

Ingredients	Quantity per tablet (mg)
Solid dispersion(1:3)	40
camphor	5.4
crospovidone	6.2
Avicel PH101	10
mannitol	31.4
Lactose	2
Talc	2.0
Magnesium Stearate	3.0

EVALUATION PARAMTERS OF OPTIMIZED BATCH

Table 16: Evaluation parameters

Parameters	Optimized Formulation
Avg. weight (mg)	102.38±0.99
Thickness (mm)	3.20±0.38
Hardness (kg/sq.cm)	3.33±0.094
Drug content (%)	99.94
Disintegration time(sec)	41.00±0.58
Friability(%)	0.88±0.78

In-vitro **drug release of optimized formulation and comparison with marketed tablets(Pepcid® oral disintegrating tablet**).

Table 17: Comparative release data with marketed formulation

Time (min)	% Drug cumulative Released of Optimized Formulation	% Drug cumulative Released of Marketed Formulation
5	43.41±0.52	18.05±0.59
10	51.72±0.68	25.82±0.19
15	67.32±0.20	31.23±0.51
20	76.24±0.59	36.74±0.20
25	85.92±0.90	39.92±0.11
30	96.21±0.30	41.22±0.52

Data expressed as mean ± S.D (n=3)

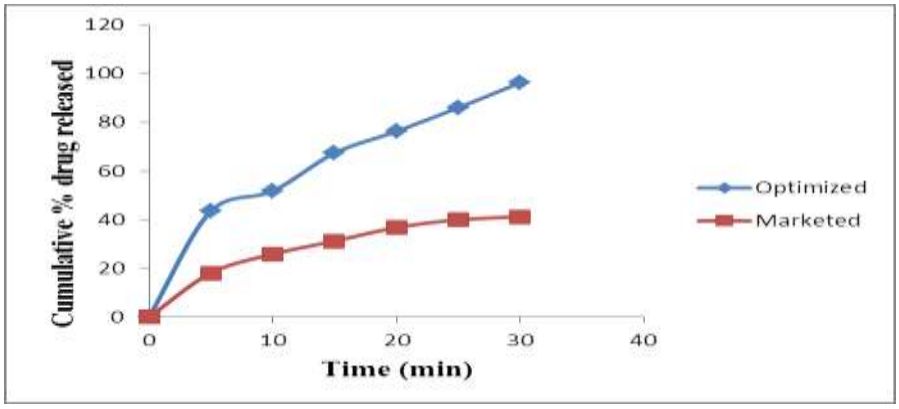

Figure 20: Percent drug release curve for optimized tablets and marketed tablets

STABILITY STUDIES

Table 17: Effect of storage conditions on optimized tablets

No. of days	Avg. weight (mg)	Hardness (kg/cm^2)	Friability (%)	Disintegration Time (sec)	Drug Content (%)
0	102.38±0.99	3.33±0.1	0.88±0.051	41±1.24	99.74±0.312
15	102.31±0.76	3.33±0.1	0.88±0.033	41±1.09	99.49±0.017
30	102.34±0.85	3.33±0.2	0.88±0.072	41±1.55	99.35±0.009
45	102.32±1.24	3.30±0.2	0.88±0.043	41±1.10	99.28±0.014

60	102.29±0.31	3.30±0.2	0.87±0.069	41±1.44	99.22±0.021
75	102.30±0.92	3.26±0.3	0.89±0.088	42±1.12	99.20±0.015
90	102.28±0.38	3.26±0.3	0.89±0.092	42±1.57	99.15±0.008

Data expressed as mean ± S.D

Table 18: Comparison of drug release data before and after storage

Time (min)	Percent Drug Released ± S.D.	
	Initial	After stability studies
5	43.41±0.52	41.93±0.70
10	51.72±0.68	49.55±0.70
15	67.32±0.20	65.39±1.03
20	76.24±0.59	75.49±0.52
25	85.92±0.90	84.98±0.52
30	96.21±0.3	94.32±0.62

Data expressed as mean ± S.D (n=3)

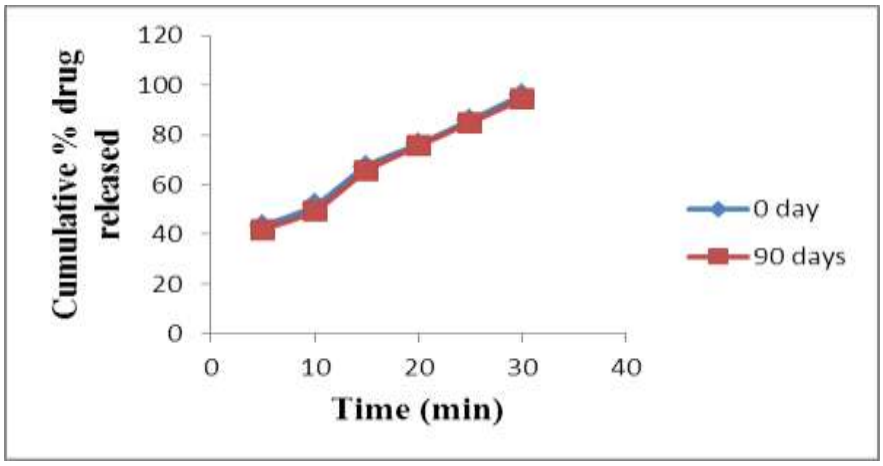

Figure 21: Comparision of drug release before and after stability

The similarity factor was calculated for the comparison of the dissolution profile before and after stability studies. The f2 value according to Moore and flanner equation was found to be 76.09 that was more than 50, indicating a close similarity between both the dissolution profiles.

CONCLUSION

The results of 3^2 full factorial design revealed that the amount of camphor and crospovidone significantly affect the dependent variables such as disintegration time, and percentage friability. Thus it is concluded that by adopting the systematic formulation approaches, an optimum point can be reached in the shortest time with minimum effort.

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