Research article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

Formulation and Evaluation of Mouth Dissolving Film of Fexofenadine Hydrochloride

Kunal N. Patel[*1], Krushika J. Patel[2] and Chirag. J. Patel[3]

[*1] Professor, Shree Swaminarayan Sanskar Pharmacy College, Zundal, Gandhinagar, Gujarat, India.
[2]PG Student, Shree Swaminarayan Sanskar Pharmacy College, Zundal, Gandhinagar, Gujarat, India.
[3]Principal, Shree Swaminarayan Sanskar Pharmacy College, Zundal, Gandhinagar, Gujarat, India.

ABSTRACT:

The present research work is to develop mouth dissolving film of Fexofenadine Hydrochloride by solvent casting method using different concentration of HPMC 5cps as film former & Polyethylene glycol 400 as plasticizer. Drug – Excipient compatibility study by FTIR shows no interaction between drug and excipients. The films were characterized for various physic-chemical parameters such as film weight, thickness, folding endurance, surface pH, tensile strength, % elongation, drug content, disintegration time, *in vitro* drug release studies. A 3^2full factorial design was applied to study the combined effect of HPMC 5cps and Polyethylene glycol 400. The formulation containing combination of two independent variables such as concentration of HPMC 5cps (X_1) and Concentration of polyethylene glycol 400 (X_2). Tensile strength (Y_1), Disintegration time (Y_2) and % CDR at 10 min. (Y_3) were selected as dependent variables. The results show that independent variables had a significant effect on the dependent variables. Besides studying the effect of the two factors on the various response variables, this study helped in finding the optimized formulation with good tensile strength, disintegration time and % CDR. Regarding all the parameters evaluated, the formulation FH6 containing HPMC 5cps (300mg) and Polyethylene glycol 400 (150mg) in combination was found to be effective & stable mouth dissolving film of Fexofenadine Hydrochloride. Hence, it was selected as optimized batch. Stability study conducted as per ICH guidelines & the optimized batch was found to be stable.

KEYWORDS: Fexofenadine Hydrochloride, Mouth Dissolving Film, HPMC 5cps, Polyethylene glycol 400, 3^2Full Factorial design.

*** Corresponding Author**

Dr. Kunal N.Patel

Professor,

Department of Pharmaceutics,

Shree Swaminarayan Sanskar Pharmacy College,

Zundal, Gandhinagar-382421, Gujarat, India

Mob. : 09586855668 Email Id- k.gadhiya1983@gmail.com

INTRODUCTION:

The oral route is greatest chosen & patient-advantageous methods for drug administration. The greater part of the medications are being taken as tablets and capsules by patients, comprising grown up, geriatric and pediatric patients. Nonetheless, around 26 – 50% of patients discover it hard to swallow tablets and hard gelatin capsules. These patients, predominantly incorporate elderly, pediatric patients and others which join the rationally ill, formatively disabled, patients who are uncooperative, on decreased fluid-intake plans or nauseated, and travelers who might not approach water. Transmucosal routes of drug delivery offer different benefits above oral administration for systemic drug delivery. These benefits incorporate by pass of first pass effect, avoidance of pre-systemic elimination inside the GI tract, and, less enzyme action.[1]

To attain rapid onset of action in order to treat unexpected surprising disorders. Unique exceptional nature of accommodation in dosing and portability of thin films gained a quick acceptance in administering the drugs in young and geriatric patients successfully. Disintegrates immediately when taken orally in saliva, within a few seconds without need of water or chewing. Subsequently patient compliance is more in patients with trouble in swallowing and chewing. Bioavailability of drug is more prominent than the conventional tablet dosage form bypassing first pass metabolism. Aside from above mouth dissolving films can withstand friable nature when contrasted with oral dispersible tablets. Oral films are flexible and less fragile as compared to ODTs. Hence, there is ease of transportation and during consumer handling and storage.[2]

Fexofenadine Hydrochloride is the 2nd and 3rd generation antihistamine drug used to treat hay fever and allergic symptoms. It does not readily pass through the blood-brain so it causes less drowsiness than first-generation histamine-receptor antagonists. The mechanism of action includes, it completes with free histamine to bind at H1-receptors in the large blood vessels, GI tract and bronchial smooth muscle. Fexofenadine Hydrochloride is a BCS class II drug having low bioavailability of 30-40% and a half-life of 14 hours. It undergoes hepatic first pass metabolism. Use for children aged 6 to 11 years in doses of 30mg twice daily for the treatment of allergic rhinitis or urticaria. Therefore, the aim of the investigation is to formulate and evaluate mouth dissolving film of Fexofenadine Hydrochloride.[3,4]

MATERIALS AND METHODS:

Fexofenadine Hydrochloride was obtained as gift sample from Sreekara Organic, Hyderabad; HPMC 5cps were obtained from Colorcon Pvt. Ltd., Goa; Polyethylene glycol 400 was obtained

from Avantor Performance Material, Gujarat; Sodium saccharine was obtained from Chemdyes Corporation, Gujarat; Methanol was obtained from Avantor performance material, Gujarat.

Drug-Excipients Compatibility Study by FT-IR[5]

The Fourier transform infrared spectrum of moisture free powdered sample of 1:1 ratio of Fexofenadine Hydrochloride with excipients was recorded on IR spectrophotometer by potassium bromide (KBr) pellet method. The spectra were scanned over a frequency range 3200-600 cm^{-1}. The characteristic peaks of different functional groups were compared with standard peaks.

3^2 Full Factorial Experimental Design[6,7]

Design experiment is a very efficient way to enhance the value of research and to minimize the process development time. The need to develop design is because traditional experiments involve a good deal of efforts and time, especially when complex formulation are to be developed. A full factorial 3^2 design was used for optimization of formulation. It is a suitable for investigating the quadratic response and for constructing a zero-order polynomial model, so enabling optimization of the time and site specific CDR process. A third level for a continuous factor facilitates investigation of a quadratic relationship between the response and each of the factor. To systemically study the effect of two independent variables i.e. concentration of HPMC 5cps(X_1) and concentration of Polyethylene glycol 400(X_2) on the characteristics of films i.e. responses tensile strength, disintegration time, and *in vitro* drug release, 3^2 full factorial design was applied.

A statistical model incorporating interactive and polynomial terms is used to evaluate the response. Polynomial equation generated by this design is as follow:

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

Where Y is the dependent variable, B_o is the arithmetic mean response of the nine runs, and b_1 to b_2 are the regression coefficients. 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 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. The response values are subjected to MLRA (Multiple linear regression analysis) to find out relationship between the factors used and response values obtained.

Table 1: Selection of independent variables and Dependent variables

Independent variable		**Dependent variable**		
X_1	**X_2**	**Y_1**	**Y_2**	**Y_3**
Concentration of HPMC 5cps (mg)	Concentration of Polyethylene glycol 400 (mg)	Tensile strength (kg/cm^2)	Disintegration time (sec)	%CDR at 10 min (%)

Table 2: Selection of Levels for Independent Variables and coding of variable

Levels	Coded value	Independent Variable	
		Concentration of HPMC 5cps (mg) X_1	Concentration of Polyethylene glycol400 (mg) X_2
Low	-1	200	125
Intermediate	0	250	150
High	+1	300	175

Table 3: Composition of 3^2 Factorial Design Batches (FH1 to FH9)

Ingredients	FH1	FH2	FH3	FH4	FH5	FH6	FH7	FH8	FH9
Fexofenadine Hydrochloride	300	300	300	300	300	300	300	300	300
HPMC 5cps	200	250	300	200	250	300	200	250	300
Polyethylene glycol 400	125	125	125	150	150	150	175	175	175
Sodium saccharine	50	50	50	50	50	50	50	50	50
Methanol	7	7	7	7	7	7	7	7	7

Film was prepared by using specified polymer by solvent casting method. The specified amount of polymer was weighed and dissolved in 5ml of solvent for overnight to get a uniform dispersion of different % (w/v) solutions. Drug and sodium saccharine were dissolved in 1ml of methanol in a separate beaker. The drug solution was added to the polymer solution. Specified amount of plasticizer was added in the above mixture and the resulting solution was degassed so as to remove air bubbles formed. The bubble free solution was casted on to a petridish of surface area 38cm^2. It was dried for 24 hours at room temperature. The film was removed from the petridish very carefully and observed for any imperfections.

Evaluations of Films:

Weight Variation[8]

For evaluation of film weight, three films (2cm x 2cm) of every formulation are taken and weighed individually on a digital balance (Shimadzu AUX - 220). The average weights are calculated.

Thikness[8]

The three films of each formulation were taken and the film thickness is to be measured using micrometer screw gauge (Mlabs) at three different places, and the mean value is to be calculated.

Tensile Strength[9,10]

Tensile strength of the film was determined with digital tensile tester, which consists of two load cell grips. The lower one is fixed and upper one is movable. The test film of specific size 7 × 2cm was fixed between these two cell grips and force was gradually applied till the film breaks.

$$\text{Tensile strength} = \frac{\text{Break Load} \times 100}{\text{Film width} \times \text{Film thickness}}$$

Percentage Elongation[10]

The percentage elongation was carried out by using Hounsfield universal testing machine. It consists of two load cells grips. The lower one is fixed and upper one is movable. The test film of specific size 7 × 2cm was fixed between these two cell grips and force was gradually applied till the film breaks. The readings were taken from the instrument.

$$\%\, Elongationatbreak = \frac{\text{Increase in lenght} - \text{Original length}}{\text{Original length} \times 100}$$

Folding Endurance[11]

The folding endurance was determined by repeatedly folding one film at the same place till it breaks. The number of times the film could be folded at the same place without breaking gives the value of the folding endurance.

Content Uniformity[10]

The film were tested for content uniformity. Films of size one square inch was cut, placed in 100ml volumetric flask and dissolved in phosphate buffer pH 6.8, volume was made upto 100ml with phosphate buffer pH 6.8. Solution was suitably diluted. The absorbance of the solution was measured at 226.2nm.

Disintegration Time[11]

A film is placed onto 10 ml distilled water taken in petri dish. Time taken by the film to dissolve completely is considered as the disintegrating time.

***In-vitro* Dissolution Studies**[12]

In vitro dissolution study was carried out using USP type II (basket type) apparatus with Phosphate buffer pH 6.8 as a dissolution medium. The temperature was maintained at 37±0.5^{0}C with 50 rotations per minute. 5ml of aliquots were withdrawn at different time intervals and same amount of fresh dissolution medium was replaced to maintain sink condition. The aliquots were analyzed for drug content at λmax 226.2 nm wavelength using UV-spectrophotometer (Electro double beam S.L.210). The cumulative percentage drug release was calculated and reported.

Surface pH of Films

The surface pH of the mouth dissolving films was determined in order to investigate the possibility of any side effects *in vivo*. As an acidic or alkaline pH may cause irritation to the oral mucosa, it was determined to keep the surface pH as close to neutral as possible. A combined glass

electrode was used for this purpose. The mouth dissolving film was allowed to swell by keeping it in contact with 1 ml of distilled water for 1 hr at room temperature.

Statistical Analysis[13]

Statistical Analysis of the 3^2 factorial design batches was performed by multiple regression analysis using Microsoft excel. In this design 2 factors were evaluated, each at 3 levels, and experimental trials were performed at all 9 possible combinations. To evaluate the contribution of each factor with different levels to the response, the two-way analysis of variance (ANOVA) was performed using the Design Expert® Software Version 11 (STAT – EASE) demo version software. To graphically demonstrate the influence of each factor on the response, the response surface plots, Normal plot of residual, Two- Dimensional counter plot, 3-D graph, and overlay plot, were generated using the Design Expert® Software Version 11 (STAT – EASE) demo version software.

Checkpoint Analysis[14]

A checkpoint analysis was performed to confirm the role of the derived polynomial equation and contour plots in predicting the responses. Values of independent variables were taken at 3 points and the theoretical values of tensile strength, disintegration time and %CDR at 10min were calculated by substituting the values in the polynomial equation.

Optimization of Formulation[15]

The computation for optimized formulation was carried using software, Design Expert® Software Version 11(STAT – EASE). The optimized formulation was obtained by applying constraints (goals) on dependent (response) and independent variables (factors). The models were evaluated in terms of statistically significant coefficients and R^2 values. Various feasibility and grid searches were conducted to find the optimum parameters. Various 3- D response surface graphs were provided by the Design Expert software. The optimized formulation factors were evaluated for various response properties.

Accelerated Stability Study[16]

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and enables recommended storage condition, re-test periods and shelf life to be established. Stability studies were carried out on optimized film formulation. A Formulation was stored at accelerated stability condition 40ºC ± 2ºC / 75 ± 5 %RH for 1 month. After 1 month samples were withdrawn and tested with regards to the parameters i.e. tensile strength, disintegration time and *in-vitro* drug release and compared with initial results.

RESULT AND DISCUSSION:

Drug and Excipients Compatibility Study by FTIR

Drug and excipients compatibility study was performed using FT-IR spectrophotometer. Here, the peak of pure Fexofenadine Hydrochloride was correlate with the peak of drug in presence of other excipients. In all the FT-IR spectra, identical peak of Fexofenadine Hydrochloride was not varied then of its original peak. So, it would be concluded that, the drug is compatible with all the excipients used in the formulation.

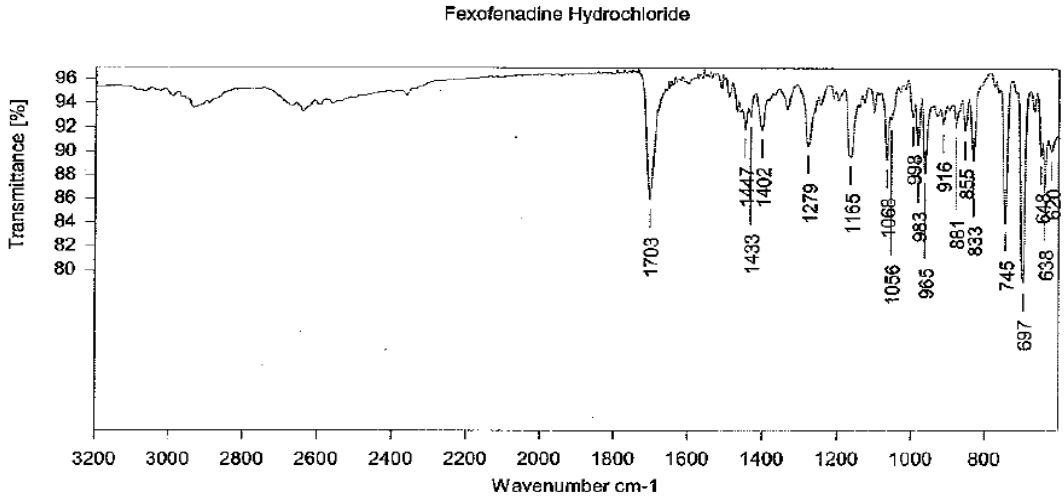


Figure 1: FT-IR Spectra of Fexofenadine Hydrochloride

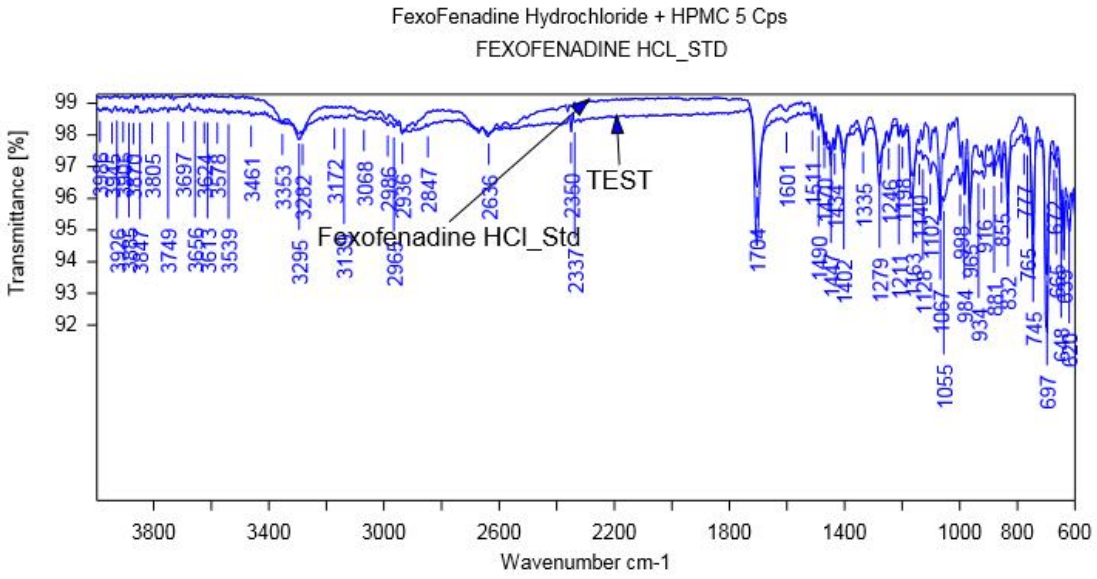


Figure 2: FTIR Spectra of mixture of Fexofenadine Hydrochloride and HPMC 5cps

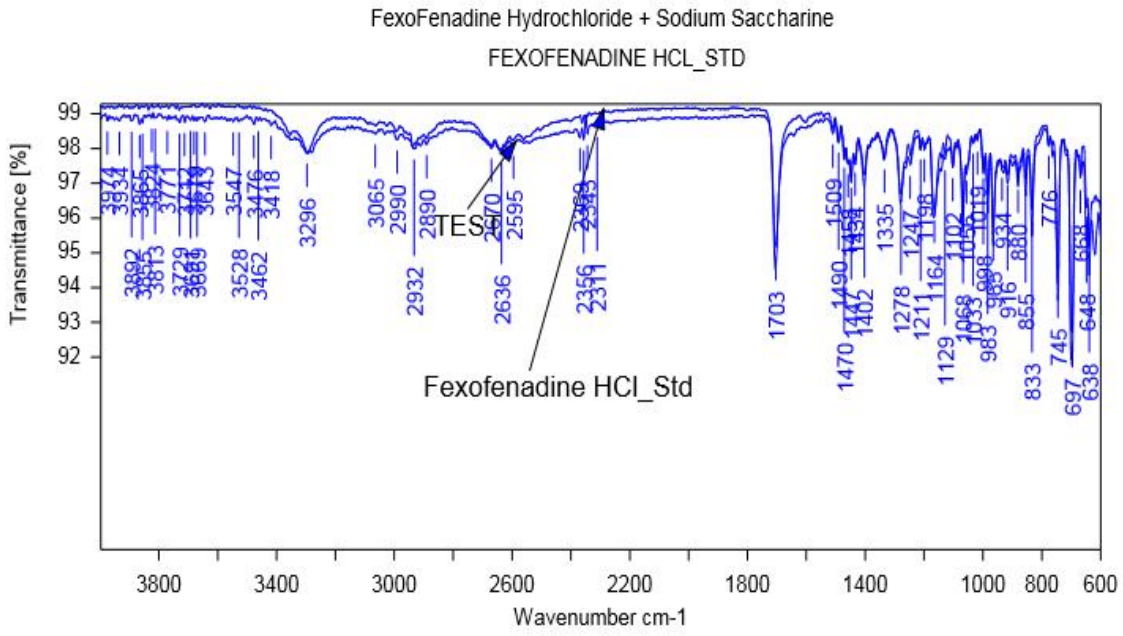


Figure 3: FTIR Spectra of mixture of Fexofenadine Hydrochloride and Sodium Saccharine

Evaluation of films:

The observed result of weight variation, thickness, folding endurance, surface pH, tensile strength, % elongation, disintegration time and drug content were showed in table 4. The result revealed that the weight of the films varied with polymer concentration. The weight of the film was found to be in the range of 69.9 ± 0.26 to 86.7 ± 0.69mg. The thickness of the films was found to be in the range of 0.11 ± 0.17 to 0.25 ± 0.23mm. The folding endurance of the films was found to be batch FH1 to FH6 more than 200 times and batch FH7 to FH9 less compare to other batches. The surface pH of the films was found between 6.6-6.8. The surface pH of all the formulations was close to the neutral pH. Tensile strength and percentage elongation varied with different concentrations of polymers. The results of tensile strength and percentage elongation of all formulations are 2.59 ± 0.11 to 6.46 ± 0.13 kg/cm^2 and 6.59 ± 0.19 to 22.15 ± 0.36%. The increased in polymer concentration showed increase in tensile strength with decrease in percentage elongation. The disintegration time of the films was found to be in the range of 46 to 53sec. %Drug content of the films was in between 92.25 ± 0.15 to 98.26 ± 0.35%. That indicating drug was uniformly distributed in the films.

Table 4: Evaluation of Factorial Batches FH1 to FH9

Formulation Code	Weight variation (mg)	Thickness (mm)	Folding endurance	Surface pH	Tensile strength (kg/cm^2)	Percentage Elongation (%)	Disintegration time (Sec)	Drug Content (%)
FH1	75.5 ± 0.23	0.12 ± 0.12	>200	6.68 ± 0.04	4.86 ± 0.19	15.65 ± 0.14	53 ± 0.25	93.28 ± 0.65
FH2	80.3 ± 0.56	0.18 ± 0.23	>200	6.82 ± 0.01	5.37 ± 0.14	13.14 ± 0.25	48 ± 0.16	95.26 ± 0.25
FH3	86.7 ± 0.69	0.25 ± 0.15	>200	6.62 ± 0.02	5.9 ± 0.17	11.11 ± 0.18	47 ± 0.23	97.56 ± 0.18
FH4	73.6 ± 0.35	0.11 ± 0.17	>200	6.76 ± 0.11	6.14 ± 0.21	22.15 ± 0.36	48 ± 0.18	96.68 ± 0.35
FH5	77.2 ± 0.61	0.13 ± 0.19	>200	6.62 ± 0.05	6.28 ± 0.08	20.78 ± 0.23	47 ± 0.12	97.23 ± 0.26
FH6	79.8 ± 0.19	0.15 ± 0.22	>200	6.85 ± 0.04	6.46 ± 0.13	19.23 ± 0.17	45 ± 0.09	98.26 ± 0.35
FH7	69.9 ± 0.47	0.14 ± 0.11	78	6.79 ± 0.06	2.59 ± 0.11	8.32 ± 0.26	46 ± 0.14	92.25 ± 0.15
FH8	71.3 ± 0.16	0.15 ± 0.18	89	6.72 ± 0.05	3.27 ± 0.23	7.26 ± 0.22	48 ± 0.18	92.89 ± 0.21
FH9	74.3 ± 0.26	0.23 ± 0.21	106	6.81 ± 0.07	3.96 ± 0.18	6.59 ± 0.19	52 ± 0.13	93.56 ± 0.32

All values are expressed as mean ± standard deviation, n=3

In Vitro Drug Release Study of Factorial Batches FH1 to FH9

Table 5: *In vitro* Drug Release Study of 3^2 Factorial design FH1 to FH9

Time (min)	FH1	FH2	FH3	FH4	FH5	FH6	FH7	FH8	FH9
0	0	0	0	0	0	0	0	0	0
5	67.32± 6.44	69.25± 5.21	72.54± 6.98	68.21± 4.22	70.26± 6.33	75.48± 4.21	57.23± 4.11	63.29± 5.44	67.59± 4.83
10	73.45± 4.26	77.19± 6.56	84.62± 6.44	76.29± 6.59	78.89± 4.29	86.89± 5.44	62.14± 5.26	69.26± 5.41	76.63± 4.63
15	85.96± 4.11	84.65± 5.36	89.29± 5.82	79.22± 6.11	85.38± 4.98	94.31± 5.79	74.28± 5.89	79.87± 4.88	85.98± 5.89
20	89.26± 5.88	90.24± 5.76	94.33± 5.51	84.18± 5.53	91.55± 5.84	96.94± 6.10	80.41± 5.97	84.26± 6.58	91.29± 5.15
25	92.35± 5.31	93.41± 4.52	97.16± 4.25	89.59± 5.23	93.87± 5.65	99.17± 5.55	88.82± 6.37	89.54± 6.29	94.78± 6.27
30	96.51± 5.98	95.62± 6.88	98.36± 5.31	94.28± 4.52	96.54± 6.35	99.84± 5.75	93.67± 6.23	94.89± 5.88	96.70± 6.22

All values are expressed as mean ± standard deviation

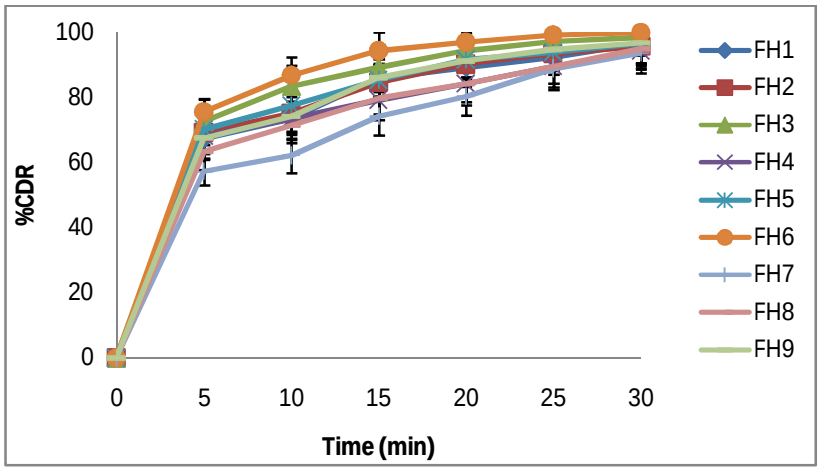


Figure 4: Dissolution Profiles of Factorial Batches (FH1 to FH9)

The results obtained in the *in vitro* drug release for the formulations FH1 to FH9 is tabulated in table 5. From the drug release study, it was observed that as the concentration of polymer increases, it gives better drug release. This might be due to the increase concentration of polymer, results in formation of strong matrix layer caused by more intimate contact between the particles of HPMC results in decrease in mobility of drug particles in swalloen matrices, which leads to better drug release. Batches FH3 & FH6 shows 85% drug release within 10 mins and complete drug release within 30 mins. From all the evaluation parameters, it has been seen that FH6 formulation fulfill all the characteristics of mouth dissolving films. So FH6 formulation was selected as best formulation.

Statistical Analysis

The 3^2 full factorial design was applied to study the effect of independent variables such as concentration of HPMC 5cps (X_1) & PEG-400 (X_2) on dependent variables such as Tensile Strength (Y_1), Disintegration time (Y_2) and %CDR at 10min. (Y_3). Various models, such as linear, 2FI, quadratic and cubic, were fitted to the data for these responses simultaneously using the Design Expert software and adequacy and good fit of the model was tested using analysis of variance (ANOVA). Results of Analysis of variance (ANOVA) for Tensile Strength, Disintegration time and %CDR at 10min. are tabulated in Table 6 to 8.

A mathematical relationship in the form of polynomial equation for Tensile Strength, Disintegration time and %CDR at 10min. are as follows:

$$\mathbf{Y_1 = 6.29+0.4550X_1-1.05X_2+0.0825X_1X_2+0.0117X_1^2-1.97X_2^2,\ R^2= 0.9836}$$

$$\mathbf{Y_2 = 45.67-0.1667X_1-0.3333X_2 + 3.00X_1X_2+0.5000X_1^2 + 3.00X_2^2,\ R^2= 0.9222}$$

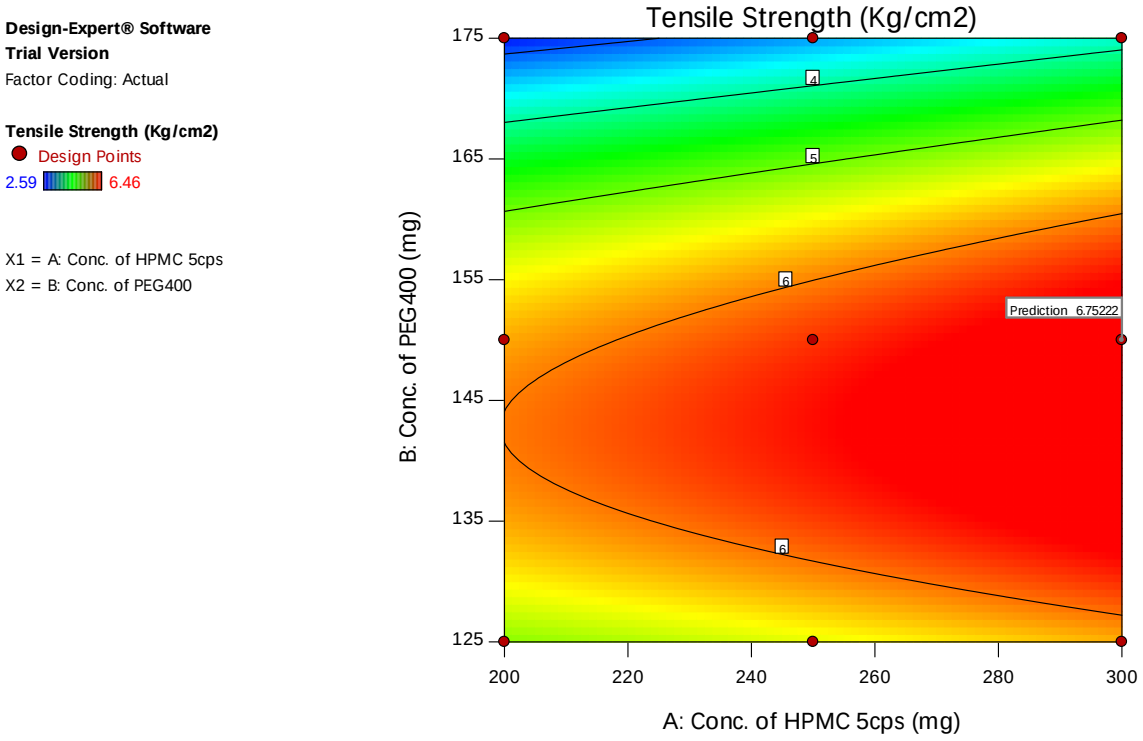
$$\mathbf{Y_3 = 79.65 + 6.04X_1- 4.54X_2 +0.8300X_1X_2 + 1.56X_1^2 – 6.81X_2^2,\ R^2= 0.9912}$$

The high r^2 value indicating the adequate fitting of the linear model. The polynomial equations can also be used to draw conclusions considering the magnitude of co-efficient and the

mathematical sign it carries; i.e. positive or negative. The positive coefficient of variable X_1 i.e. concentration of HPMC 5cps for responses Tensile Strength (Y_1) indicates that, as the concentration was increased, the Tensile Strength was increased. The negative coefficient of variable X_1 i.e. concentration of HPMC 5cps and X_2 i.e. concentration of PEG-400 for response disintegration time (Y_2) indicates that, as the concentration was decreased, the disintegration time was also decreased. Similarly, The positive coefficient of variable X_1 i.e. concentration of HPMC 5cps and negative coefficient of variable X_2 i.e. concentration of PEG-400 for response %CDR at 10min. (Y_3) indicate better drug release from mouth dissolving film. The data clearly indicate that the dependent variables are strongly dependent on the independent variables. The relationship between the variables was further elucidated by using the response surface plot (Figure 5 to 7).

Table 6: ANOVA Response Surface Quadratic Model Y_1

Source	Sum of Squares	Df	Mean Square	F- value	p- value
Model	15.65	5	3.13	35.97	0.0070
X_1 – Conc of HPMC 5cps	1.24	1	1.24	14.27	0.0325
X_2 – Conc of PEG 400	6.64	1	6.64	76.23	0.0032
X_1X_2	0.0272	1	0.0272	0.3127	0.6150
X_1^2	0.0003	1	0.0003	0.0031	0.9589
X_2^2	7.75	1	7.75	89.01	0.0025
Residual	0.2612	3	0.0871		
Cor Total	15.92	8			



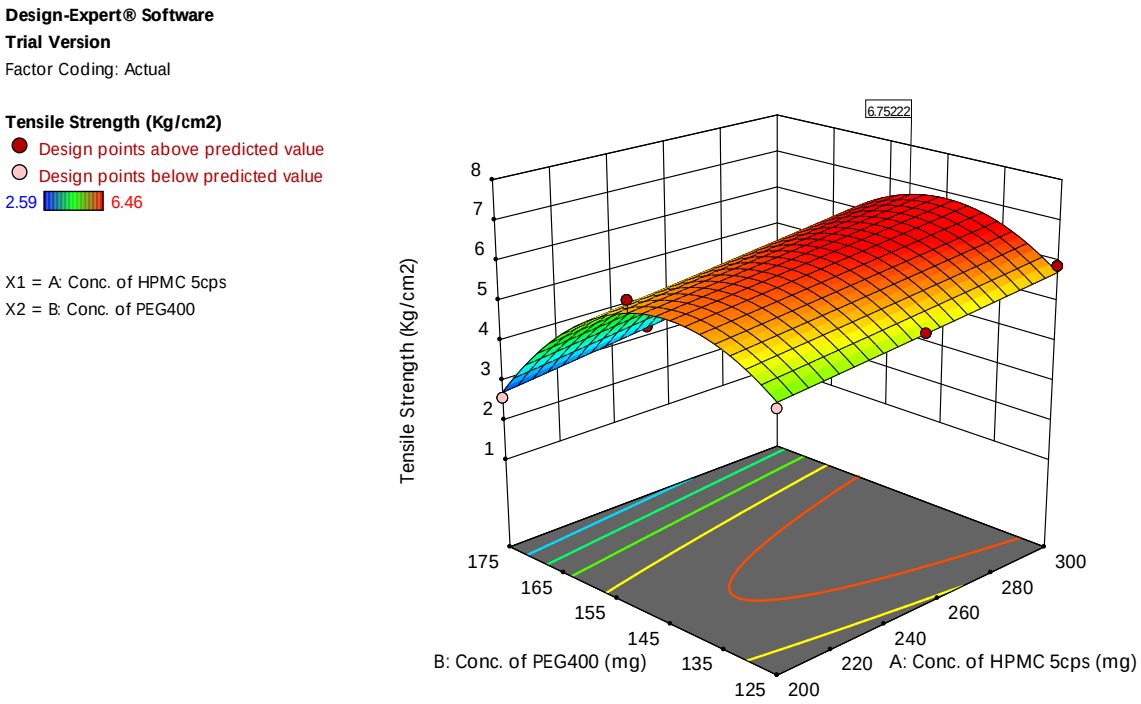
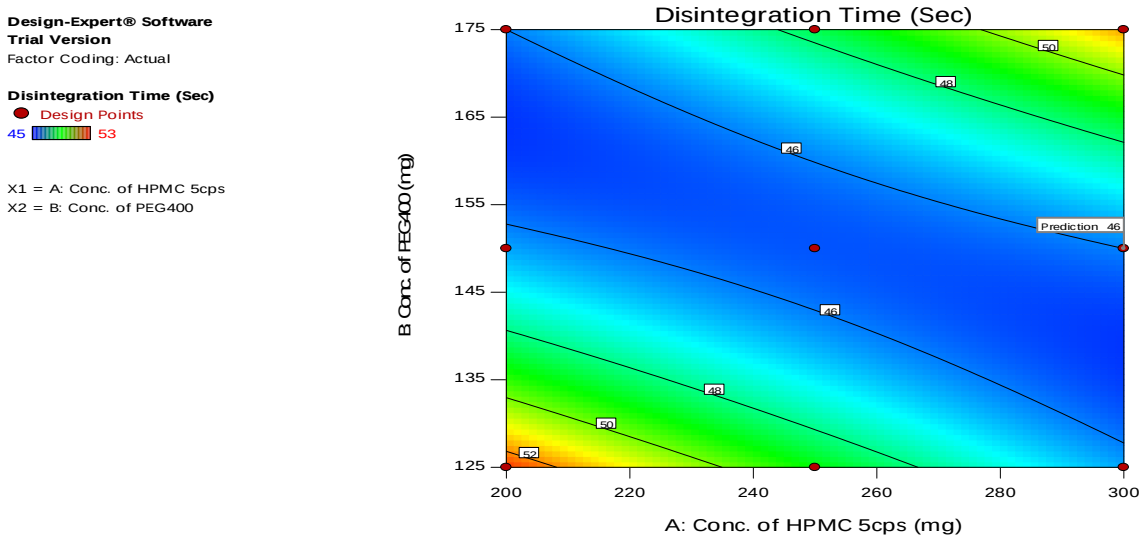


Figure 5: 2D and 3D Curve shows effect of HPMC 5cps (X_1) & Polyethylene glycol 400 (X_2) on Tensile strength (Y_1)

Table 7: ANOVA Response Surface Quadratic Model for Y_2

Source	Sum of Squares	Df	Mean Square	F- value	p- value
Model	55.33	5	11.07	7.11	0.0686
X_1 – Conc of HPMC 5cps	0.1667	1	0.1667	0.1071	0.7649
X_2 – Conc of PEG 400	0.6667	1	0.6667	0.4286	0.5594
X_1X_2	36.00	1	36.00	23.14	0.0171
X_1^2	0.5000	1	0.5000	0.3214	0.6104
X_2^2	18.00	1	18.00	11.57	0.0424
Residual	4.67	3	1.56		
Cor Total	60.00	8			



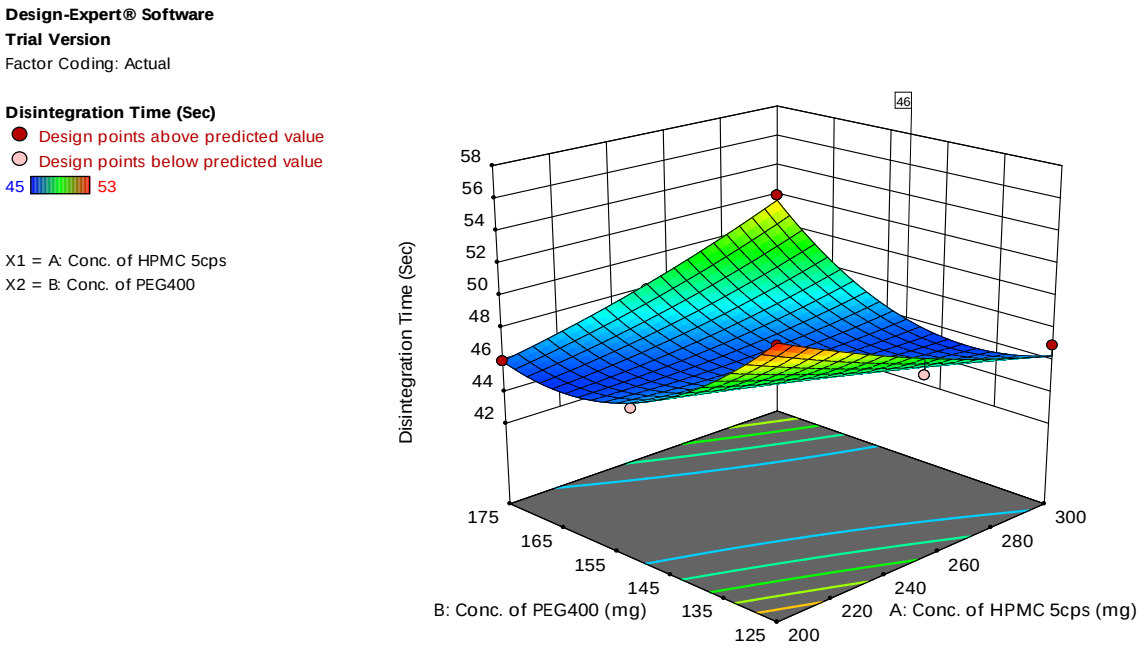


Figure 6: 2D and 3D Curve shows the effect of HPMC 5cps (X_1) & Polyethylene glycol 400 (X_2) for Disintegration time (Y_2)

Table 8: ANOVA Response Surface Quadratic Model for Y_3

Source	Sum of Squares	Df	Mean Square	F- value	p- value
Model	443.02	5	88.60	67.28	0.0028
X_1 – Conc of HPMC 5cps	219.13	1	219.13	166.39	0.0010
X_2 – Conc of PEG 400	123.58	1	123.58	93.83	0.0023
X_1X_2	2.76	1	2.76	2.09	0.2438
X_1^2	4.85	1	4.85	3.68	0.1509
X_2^2	92.71	1	92.71	70.39	0.0036
Residual	3.95	3	1.32		
Cor Total	446.97	8			

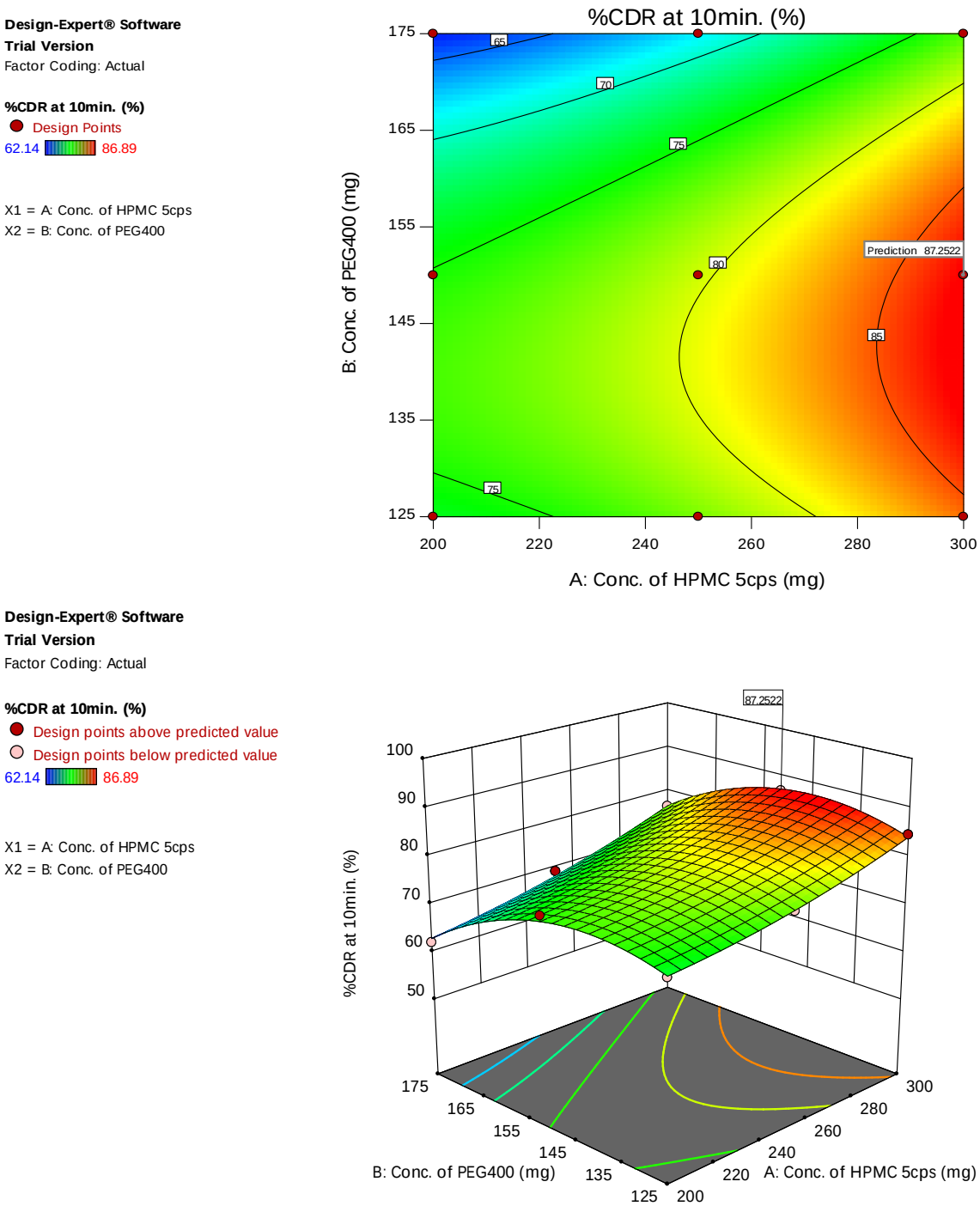


Figure 7: 2D and 3D Curve shows effect of HPMC 5cps (X_1) & Polyethylene glycol 400 (X_2) for % CDR at 10 min (Y_3)

Checkpoint Analysis

Table 9: Checkpoint Batches with Predicted and Measured value of Tensile Strength, Disintegration time and % CDR

Batch code	X_1	X_2	Tensile strength (Y_1)		Disintegration time (Y_2)		% CDR at 10 min (Y_3)	
			Measured	Predicted	Measured	Predicted	Measured	Predicted
FH10	0	0.5	5.25	5.27	46.21	46.25	75.70	75.67
FH11	0.5	1	3.59	3.54	49.85	49.87	72.25	72.12
FH12	1	0.5	5.80	5.78	48.11	48.08	83.75	83.69

When measured tensile strength, Disintegration time and %CDR at 10 min values were compared with predicted tensile strength, Disintegration time and %CDR at 10 min values, the values were found significant. Thus, it can be concluded that the obtained mathematical equation is valid for predicted values.

Optimization of Formulation

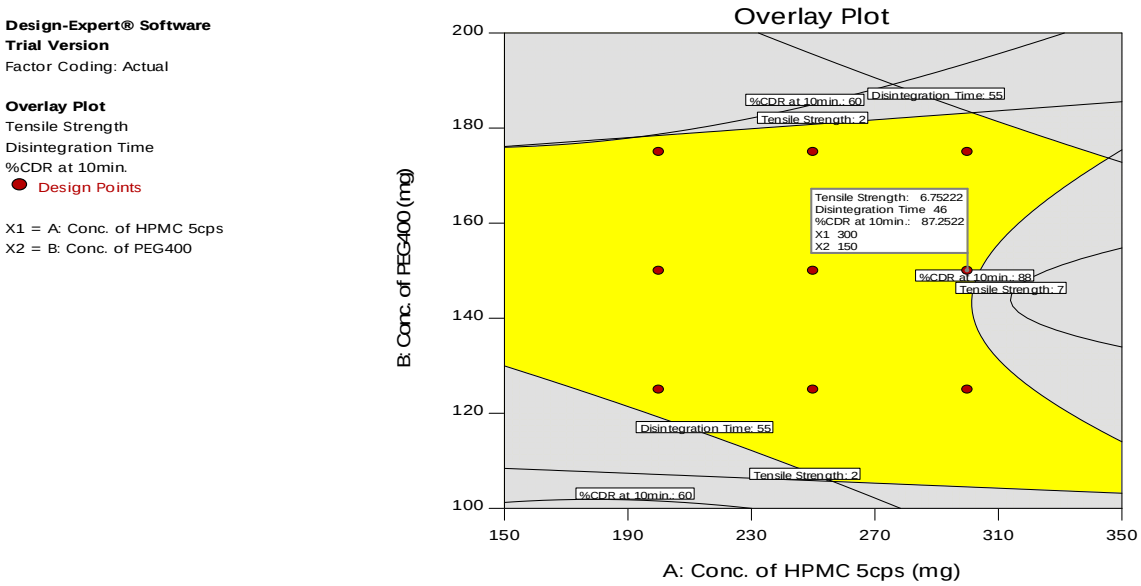


Figure 8 : Overlay Plot of Response Variables

An optimization technique using desirable approach to develop a new formulation with the desired responses. This was the most important part of the response surface methodology. The optimum formulation was selected based on the criteria of attaining Tensile strength, Disintegration time, & %CDR at 10 min. The overlay plot of responses generates an optimized area as per desired criteria of Tensile strength 67.52 kg/cm^2, Disintegration time 46 sec and % CDR at 10 min should be 87.25%. So, it can be concluded that by adopting systemic formulation approach one can reach to an optimum tensile strength, disintegration time and % CDR.

Stability Study

Table 10: Stability Study of Optimized formulation (FH6)

No. of Months	Tensile strength	Disintegration time	% CDR
0	6.46 ± 0.13	45 ± 0.09	86.89 ± 5.44
1	6.42 ± 0.08	45 ± 0.03	86.94 ± 4.98

All values are expressed as mean ± standard deviation

Stability Study of mouth dissolving film of Fexofenadine Hydrochloride was carried out for one month at specified condition. All data were mentioned in above table 10. The stability studies of optimized batch shown no significant changes in the Tensile strength, Disintegration time and % CDR when stored at temperature and humidity conditions of 40 ± 2^0C/ 75 ± 5% RH. So, it was considered that formulation having good stability.

CONCLUSION:

The Fast dissolving drug delivery system was potential to be an effective immediate release system over a long period of time & to avoid first-pass metabolism of Fexofenadine hydrochloride. The type & level of polymers used are important factors that can affect the drug release & also the physico-chemical properties of this mouth dissolving films. Regarding all the properties evaluated FH6 formulation was found to be best formulation containing mixture of HPMC 5cps and Polyethylene glycol to achieve the aim of this study. These films have good Tensile strength, Disintegration time, and % CDR. The stability studies were carried out according to ICH guideline which indicates that the selected formulation was stable.

ACKNOWLEDGRMENT:

We express our sincere thanks to Dr. Chirag J Patel, Principal and Shastri Shri Purushottam Charan Dasji, Managing Trustee of Shree Swaminarayan Sanskar Pharmacy College, Zundal, Gandhinagar, Gujarat for providing excellent facilities for research work.

REFERANCES:

1. Dahiya M, Saha S Shahiwala AF. A review on mouth dissolving films. Curr. Drug Del. 2009; 6: 469-476.
2. Komaragiri SD, Shaik F, Amaravathi V, Uttaradi A. Formulation and characterization of atenolol fast dissolving films.Ind. J. of Pharm. Sci. & Res. 2012; 2(2): 58-62.
3. Goankar UU, Bolmal UB, Gadad AP. Design and characterization of solid dispersed fexofenadine hydrochloride buccal film by central composite design. Int. J. Pharm. Sci. Res. 2016; 7(10): 4097-4109.
4. Gupta B, Kumar S. Fast dissolving tablets of fexofenadine hydrochloride by melt technology: formulation and characterization. Int. J. Pharm. Sci. Res. 2018; 9(3): 1226-1230.

5. Desale KY, Gaikwad PD, Bankal VH. Formulation and characterization of fexofenadine hydrochloride fast dissolving tablet by using various super-disintegrants. Int. J. Drug Dev. 2012; 4(1): 82-88.
6. Budheliya SR, Trivedi HJ, Patel BA, Patel KN, Patel MM. Formulation and evaluation of escitalopram oxalate orodispersible tablets using sublimation technique. Int. J. of Pharma. Res. and Health Sci. 2018; 6(2): 2528-2535.
7. Patel KN, Patel SS, Trivedi HJ, Patel BA, Patel MM. Design and characterization of donepezil hydrochloride sustained release matrix tablets. J. of Drug Del. and Ther. 2018; 8(3): 64-74.
8. Yasmeen BR, Mouli YC, Shaik F, Uttaradi A. Preparation and evaluation of oral fast dissolving films of citalopram hydrobromide. Int. J. of Biopharma. 2012; 3(2): 103-106.
9. Aggarwal J, Singh G, Saini S, Rana AC. Fast dissolving films: a novel approach to oral drug delivery. Int. Res. J. Pharm. 2011; 2(12): 69-74.
10. Kulkarni PK, Mudit D, Gunashekara K, Kulkarni A. Formulation and evaluation of mouth dissolving film containing rofecoxib. Int. Res. J. Pharm. 2011; 2(3): 273-278.
11. Komaragiri SD, Shaik F, Amaravathi V, Uttaradi A. Formulation and characterization of atenolol fast dissolving films. I. J. of Pharma. Sci. and Res. 2012; 2(2): 58-62.
12. Praveen T, Sindhu V, Bhavya S. Formulation and evaluation of oral dissolving films of fexofenadine. World J. Pharm. Pharm. Sci. 2017; 6(11): 814-827.
13. Ikram M, Gilhotra N, Gilhotra RM. Formulation and optimization of mucoadhesive buccal patches of Losartan potassium by using response surface methodology.Adv. Biomed. Res. 2015; 4: 239.
14. Patel KT, Mahajan AN, Shah DA. Studies in formulation development of chronotherapeutics dosage of model drug. Sch. Res. Lib.2011;3: 227-240.
15. Khinchi MP, Gupta MK, Bhandri A, Sharma N, Agrawa lD. Orally disintegrating film of famotidine prepared by solvent casting method using 3^2 full factorial design. Asian J. Pharm. Hea. Sci. 2011; 1:55-60.
16. ICH Guidelines Q1A (R2), Guidance for industry, stability testing of new drug substances and products, Word Health Organization, WHO Technical Report Series, No. 953,2009