RESEARCH ARTICLE

Fexofenadine Hydrochloride Dispersible Tablets: A Taste Masking Strategy using Ion Exchange Resin

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ABSTRACT

The pediatric population is more sensitive to allergies. Fexofenadine hydrochloride (FXD-HCL), a non-sedative antihistaminic drug, was chosen to create taste-masked patient-compliant pediatric dispersible tablets. Due to its bitter taste, fexofenadine hydrochloride is unsuitable for the formulation of dispersible tablets; therefore, Kyron T-134®, cation exchange resin was used to form a taste-masked complex with the drug to overcome its bitterness. The FXD HCL-resin complex was prepared using a kneading method and the complexation was confirmed by differential scanning calorimetry and FTIR studies. The FXD HCL-resin complex was evaluated for flow properties, degree of bitterness, assay and release study. Dispersible tablets were formulated by using a co-processed excipient, Granfiller-D211® containing croscarmellose sodium and crosspovidone, microcrystalline cellulose and mannitol. 22 factorial designs with two replicates optimized the dispersible tablets. The tablets, prepared using the direct compression technique on a single-stroke tablet compression machine, were elegant in appearance. Various pre and post-compression tests were conducted on all formulations. The tablets of hardness 3.5 kg/cm^2 showed friability, disintegration time, assay within the compendial limit and showed immediate release of a drug (NLT 60% in 10 min and NLT 80% in 30 minutes) in 0.001 N HCl (pH 3). The DSC thermogram indicated partial amorphization of the FXD HCL. Dispersible tablets of fexofenadine hydrochloride and Granfiller-D®211 at 1:4 proportion was stable for one month at ambient and accelerated storage conditions.

Keywords: Fexofenadine hydrochloride, Taste masking, Ion-exchange resin, Kyron T-134®, Dispersible tablets, Co-processed excipients, Granfiller-D®211.

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INTRODUCTION

The tablet formulation is a widely accepted dosage form in all age groups due to its ease of manufacturing, handling, and administration.Among the reported tablet manufacturing methods, direct compression is considered a simple and cost-effective alternative that simply compresses a dry powder containing drugs and excipients. The powder properties of the precompression blend, such as flowability, compressibility, and dilution potential, significantly impact the direct-compression process. To further improve excipient properties, co-processed excipient technology is developed, which is a novel single excipient that contains two or more excipients that interact at the sub-particle level without any chemical change, and it is widely accepted as safe for use in tablet formulations with multiple functionalities. They have an improvised performance in terms of flow, tablet ability, disintegration time, assay, and drug release performance.[1,2] Dispersible tablets are the chosen dosage form for pediatric populations since are dispersed in drinking water to form a smooth dispersion before administration, but they require several modifications in terms of organoleptic properties such as color, odor, and taste.[3] Several pediatric medications in the market have an unpleasant and nauseous taste, which limits comfort and compliance.[4] Fexofenadine hydrochloride (FXD HCL) is a non-sedative H1 antihistaminic drug used to treat allergic rhinitis and urticaria, but the bitter taste prevents children from adhering to the dosage regimen. It is an appropriate dosage form for pediatric patients due to specifically modified tablet formulations that take into account the physical and psychological aspects of children.[5,6] It has been reported that ion exchange resins can mask the bitterness of ionizable drugs. They are generally inert in nature, do not absorb in the body, and are easily eliminated. Furthermore, no organic solvents are used in the complexation process, making it appropriate for pediatrics. The drug resin complex that has formed blocks the drug from being released in the oral cavity and, as a result, the bitterness of the drug is not perceived. [7] There are various ion exchange resins reported in the literature used for taste

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maksing of drugs. Dasankoppa FS and coworkers formulated chewable tablets with Indion 204 and Tulsion 335® as the ion exchange resin and clarithromycin.[8] Jain *et al*., designed a novel sustained ciprofloxacin HCL microbeads using ciprofloxacin HCL -Tulsion 344® complex.[9] Sharma and Soni *et al*., worked on overcoming the poor palatability of tapantadol with the help of Kyron T-134® and Tulsion 355®.[10] Sivaneswari and coworkers used Duolite AP 143® to prepare a taste-masked pediatric suspension of levetiracetam.[11] Indion 204® was used to mask the taste of etoricoxib by Patra *et al*.,[12] Panraksa *et al*., used Dowex-50® cation exchange resin to mask the taste of nizatidine.[13] Bhise coworkers worked on taste masking of diphenhydramine with cation resins such as Indion 234 and Indion 343®.[14] In the present study, FXD HCL resin complex was prepared using ion exchange resin Kyron T-134® by kneading method. The orodispersible tablets were formulated using direct compression method with suitable co-processed excipient. The optimization was carried out by a 2^2 factorial design and the optimised batch was evaluated for stability study as per ICH guidelines.

MATERIALS AND METHODS

Materials fexofenadine hydrochloride was provided by Virupaksha Chemical Pvt. Kyron T-134®, a resin was obtained as gift samples from Corel Pharma Chem., Baroda. Granfiller-D® 211, a co-processed excipient was received from Arihant Innochem Pvt. Ltd. Mumbai. Magnesium stearate was procured from Crest Cellulose Pvt. Ltd. Aerosil was purchased from Evonik Industries AG, Methanol AR grade and Acetonitrile were purchased from Loba Chemie Pvt. Ltd.

Methods

Preformulation studies

- *Analytical method development of FXD HCL*

The standard plot of FXD-HCL was developed in methanol and 0.001 N HCL at 220 nm between 5 to 40 mg/mL using a double beam UV-1800 Shimadzu spectrophotometer for determining pH-dependent solubility, assay, content uniformity and release studies.

Stability indicating high-performance liquid chromatography method was developed on Baker bond C18 column with 250 *4.6 mm; 5 mm dimension using Shimadzu HPLC system. The system composed of a UV detected and lab solution software. A mixture of acetonitrile and phosphate buffer pH 6.8 was used as the mobile phase at a flow rate of 1-mL/minute and a wavelength of 220 nm. Forced degradation studies of FXD HCL was carried out in acidic stress condition of 1N hydrochloric acid solution, alkaline stress condition of 1N sodium hydroxide solution, oxidative stress condition of 3% hydrogen peroxide solution and thermal degradation condition of 80ºC for 24 hours. The degradant peaks were recorded using the HPLC method.

- *pH dependent solubility of FXD HCL*

Excess amount of FXD HCL was added to a predetermined volume of pH solution in the range pH 1.2 to 8 buffer and shaken for 24 hours in orbital shaker. The dispersion was centrifuged for 15 minutes at 5000 rpm. Methanol was used to dilute the supernatants and analyze them using a UV spectrophotometer at 220 nm.[15-17]

- *Flow characterization of co-processed excipient*

The co-processed excipient was assessed for its flow characteristics, such as angle of repose, bulk density,tapped density, Carr's index and Hausner's ratio.[18]

Formulation and Evaluation of a FXD HCL-resin Complex

- *Preparation of FXD HCL-resin complex*

FXD HCL and Kyron T-134® complex at 1:2 proportion was prepared by the kneading method.[19–21] Kyron T-134®was allowed to swell in deionized water in a mortar for 30 minutes. FXD HCL was added to it and kneaded for 10 minutes with the help of a pestle to form a smooth paste. Sucralose and vanilla flavour were mixed with the same paste and kneaded for additional 5 minutes. The complex was dried at a temperature not exceeding 80ºC. The dried paste was scraped and sieved through #40 mesh.

Evaluation of FXD HCL-resin Complex

- *FT-IR of the FXD HCL-resin complex*

Infrared spectra of FXD HCL, Kyron T-134® and FXD HCL-resin complex were obtained using FT-IR (Shimadzu IR infinity) in 4000 to 400 cm^{-1} wavenumber range by preparing pellets on a KBr press. The obtained spectra were compared to the standard spectra of the FXD HCL to confirm the drug-resin complex formation.[22]

- *Differential Scanning Calorimetry studies (DSC)*

FXD HCL-resin complexation was confirmed using DSC as a tool.An aluminum pan containing 40 µL of sample was thermally scanned from 30 to 250°C by a Mettler DSC 1 (Mettler Toledo, USA) at a heating rate of 10°C/minute. Thermograms obtained were evaluated using the Stare software.

- *Bitterness evaluation of the FXD HCL-resin complex*

The taste of FXD HCL and FXD HCL-resin complex was determined by the (APL/MIS-2709) (Stp-btr-001-00) an inhouse method of bitterness testing at Arbro Pharmaceuticals Pvt. Ltd. (New Delhi).

- *Practical yield*

The practical yield was calculated by weighing FXD HCL-resin complex recovered from each formula in relation to the sum of the starting material.

- *Flow characterization of the FXD HCL-resin complex[18,23]*

The FXD HCL-resin complex was assessed for its flow characteristics, such as angle of repose, bulk density,tapped density, Carr's index and Hausner's ratio.

- *Content of FXD HCL in FXD HCL-resin complex*

FXD HCL-resin complex containing 30 mg of FXD HCL was sonicated for 30 minutes in methanol. The methanolic solution of the supernatant after centrifuging the dispersion for

15 minutes at 5000 rpm was analyzed for FXD HCL content using a double beam UV-1800 Shimadzu spectrophotometer at 220 nm in triplicates.

Formulation and optimization of FXD HCL Dispersible Tablets

- *Procedure for dispersible tablets*

The FXD HCL-resin complex was blended with Granfiller-D® 211, aerosil and magnesium stearate and was directly compressed using single stroke tablet punching machine (Royal artist, Mumbai) using a 9 and 11 mm round flat bevelled punch.

- *Optimization of dispersible tablets*

The optimization of dispersible tablets was carried out using a 2^2 factorial design. The levels of co-processed excipient (A) and magnesium stearate (B), which may influence the angle of repose of the pre compressed blend and disintegration time Y1 and Y2 respectively of the dispersible tablets were tested at 2 levels, low and high as shown in Table 1. The formulation details for DoE batches are shown in Table 2.

Evaluation of FXD HCL dispersible tablets

- *Precompression evaluation of the FXD HCL dispersible tablet blend*

The dispersible tablet blends were assessed for angle of repose (n = 3), bulk density, tapped density, Carr's index and Hausner's ratio.

- *Post compression evaluation of FXD HCL dispersible tablets*[24]

The tablets were randomly selected and measured for *hardness* with a Monsanto hardness tester. Tablet dimensions were measured by a vernier calliper. The tablets were weighed and Weight variation was calculated as per United States Pharmacopeia (USP) to determine the average weight. Veego friability test apparatus was used to check the friability of the tablets as per USP. Disintegration time and fineness of dispersion was determined as per Indian Pharmacopoeia (IP) 2018.

- *Content of FXD HCL*

The powder obtained after crushing 10 tablets was weighed in an amount equivalent to one tablet, mixed with methanol and sonicated for 30 minutes. The supernatant obtained after centrifuging the solution for 15 minutes at 5000 rpm was diluted with methanol and analyzed for drug content using double beam UV-1800 Shimadzu spectrophotometer at 220 nm lambda max in triplicates.

- *Release study*[25]

Release studies of FXD HCL dispersible tablets was performed in triplicate using the USP apparatus type II (paddle) in 900 mL 0.001 N HCL (pH3) at a paddle speed of 50 rpm and temperature 37 ± 0.5°C. A 5ml aliquot was removed at predetermined time intervals, filtered using Whatman filter paper diluted with 0.001 N HCL (pH 3) and analysed by UV at 220 nm.

- *DSC*

An aluminum pan containing 40 µL of dispersible tablet blend was thermally scanned from 30 to 250 °C by a Mettler DSC 1 (Mettler Toledo, USA) at a heating rate of 10°C/ minute Thermograms obtained were evaluated using the Star^e software.

Evaluation of Stability of FXD HCL Dispersible Tablets

The FXD HCL dispersible tablets were packed in PVC laminated aluminium foil and kept in a stability chamber at a temperature of 25 ± 2ºC/ 60%RH and 40 ± 2ºC/ 75% RH. The tablets were examined for uniformity of content, disintegration time and release study.

Table 1: Levels of independent variables

Independent variable	*Low level (-1)*	*High level (+1)*
X1-Co-processed excipient (mg)	120	180
X2-Magnesium stearate (%)	1	2

Table 2: Factorial design batches for dispersible tablets.

	Quantity (mg/tablet)							
Composition	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*
FXD HCL-resin complex	100.5	100.5	100.5	100.5	100.5	100.5	100.5	100.5
GNF-D®211	120	120	180	180	120	120	180	180
Aerosil® 200	2.2	2.2	2.8	2.8	2.2	2.2	2.8	2.8
Magnesium stearate	2.2	4.41	2.8	5.61	2.2	4.41	2.8	5.61
Wt. of tablet	225	227	286	289	225	227	286	289
Punch size (mm)	9	9	11	11	9	9	11	11

RESULTS

Preformulation Studies

Analytical method development

The standard plot of FXD HCl in methanol and 0.001 N HCL showed good correlation between absorbance and concentration with regression equation y = 0.039x - 0.0424,r^2 0.9998 and y = 0.0253x + 0.0059, r^2 0.997, respectively. The calibration equation was further used to analyze samples for assay and release.

A regression equation y = 37156x – 64915, r^2 0.9979 in the concentration range of 1 to 100 mg/mL indicated stable HPLC method development. The chromatograms of FXD HCL in different solution showed well-separated FXD HCL and degradation peaks at different retention times. The degradation studies revealed that FXD HCL is more stable in acidic and thermal stress conditions than alkaline and oxidative conditions

pH dependent solubility of FXD HCL

FXD HCL showed solubility increase from pH 1.2 to pH 3 and further decrease in solubility was seen till pH 7.4 as seen in

Figure 1. A maximum solubility of FXD HCL was observed in 0.001 N HCL (pH 3) and the least solubility was observed in PBS (pH 6.8) which agrees with Rosa and co-workers report on the solubility of FXD HCL.[15]

Flow characterization of co-processed excipient

The angle of repose of GNF-D®211 was found to be 35.84° ± 1.51. The bulk density and tapped density were 0.363 ± 0.032 g/mL and 0.469 ± 0.027 g/mL respectively. The Carr's index was 22.53 ± 2.19 and Hausner's ratio was 1.29 ± 0.035. The flow was found to be good to passable. This data coincides with the technical data of GNF-D®211.[26]

Formulation and Evaluation of a FXD HCL-resin Complex

FTIR of FXD HCL-resin complex

A FT-IR spectrum of FXD HCL revealed peak 1705 cm^{-1} depicting -C–O stretching. C–N stretching at 1277 cm^{-1} and another at 3296 cm^{-1} represented –OH stretching. The elimination of 1705 and 1277 cm^{-1} peaks in FXD HCL-resin complex spectra confirmed complex formation, wherein FXD HCL's amino group interacts with the carboxylic group of Kyron T-134®, which agrees with the results reported by D. Suares and co-workers for the complexation of FXD HCL and Kyron T-314®.[22] The FTIR spectra of fexofenadine hydrochloride, drug resin complex and resin is provided in Figure 2.

DSC

The calorimetric determination of FXD HCL depicted a characteristic sharp endothermic peak at 205ºC as shown in Figure 3, which is not significantly evident in the thermogram of the FXD HCL-resin complex and indicates the partial amorphization of the FXD HCL, thereby indicating interaction and complex formation.[27-29]

Bitterness evaluation of the FXD HCL-resin complex

The bitterness values of FXD HCL and FXD HCL resin complex were found to be 1.31 and 1.14% w/w respectively. The FXD HCL-resin complex was found to efficiently mask the taste of FXD HCL in a 1:2 proportion of drug and resin, which is as per the results reported by D. Suares *et al.*[22]

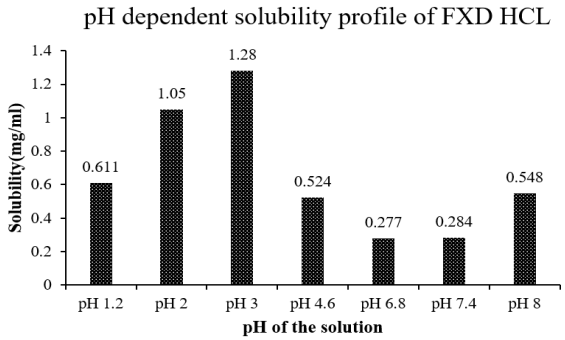

Figure 1: Solubility profile of FXD HCL

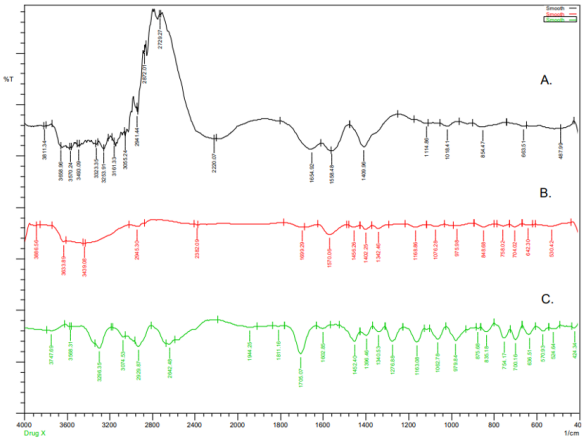

Figure 2: Observed FTIR spectrum of A. Kyron T-134®, B. FXD HCL-resin complex and C. FXD HCL

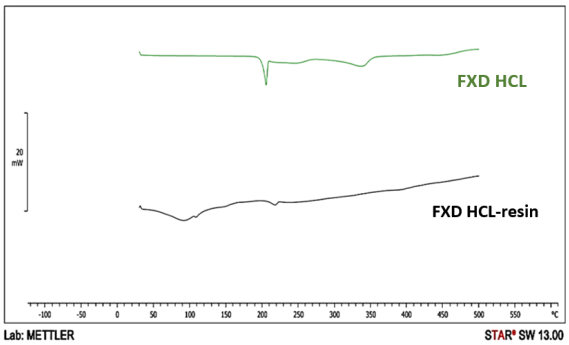

Figure 3: DSC Thermogram

Practical yield

The practical yield of the FXD HCL resin complex was 98 ± 1.12%.

Flow characterization of the FXD HCL-resin complex

The angle of repose of FXD HCL-resin complex was 35.1° ± 0.93, bulk density,tapped density and Carr's index were 0.358, 0.486 g/mL, 26.33 respectively, whereas Hausner's ratio was 1.36. The Carr's index and Hausner's ratio indicate a poor powder flow that requires further enhancement by the addition of glidant.

Assay of the FXD HCL-resin complex

The percent assay was 103% ± 1.01, which is satisfactory.

Formulation and Optimization of FXD HCL Dispersible tTablets

The amount of co-processed excipients and magnesium stearate was optimized using the quality by design method, which has a significant impact on the angle of repose of the pre compressed blend and disintegration time of the dispersible tablets. The DoE formulations were assessed for flow properties and found to be excellent as the angle of repose was less than 30º. All formulations were passing uniformity of weight test. The friability (< 1%), uniformity of content and assay (95–105%) for all the FXD HCL dispersible tablets were found to be within the limit as per IP and USP.[25] The results of the DoE formulations are reported in Tables 3 and 4.

Table 3: Evaluation of DoE formulation of FXD HCL dispersible tablets

Sr. no	*Parameters*	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*
				I. Precompression evaluation of powder blend					
i.	Angle of repose (°)	Results reported in Table 5							
ii.	B.D (g/mL)	0.375	0.4	0.374	0.377	0.389	0.4	0.391	0.394
iii.	T.D (g/mL)	0.511	0.524	0.507	0.51	0.538	0.504	0.538	0.526
iv.	%Carr's index	26.67	23.66	26.09	26.15	27.69	20.63	27.27	25.09
v.	Hausner's ratio	1.36	1.31	1.35	1.35	1.38	1.26	1.37	1.33
				II. Post compression evaluation of tablets					
vi.	Hardness (kg/cm^2)	3–4	3–4	3–4	3–4	3–4	3–4	3–4	3–4
vii.	Diameter (mm)	9.13 ± 0.15	9.2 ± 0.1	11.29 ± 0.02	11.31 ± 0.03	9.11 ± 0.1	9.25 ± 0.05	11.18 ± 0.16	11.3 ± 0.015
viii.	Thickness (mm)	3.2 ± 0.1	3.1 ± 0.1	2.06 ± 0.15	2.1 ± 0.05	3.12 ± 0.11	3.08 ± 0.14	2.13 ± 0.15	2.24 ± 0.28
ix.	Average wt. (mg)	224.9 ± 1.85	225 ± 4.22	286.2 ± 3.15	290.7 ± 3.5	225 ± 4.22	228 ± 3.09	285.9 ± 2.28	288.7 ± 2.8
x.	%Friability	0.178	0.13	0.139	0.07	0.176	0.09	0.07	0.138
xi.	DT (sec)	Results reported in Table 5							
xii.	%Assay	96 ± 0.027	99.66 ± 0.0	101.9 ± 0.04	96.13 ± 0.03	95.11 ± 1.07	98.89 ± 1.45	101.07 ± 4.9	96.47 ± 1.23

Note: B.D: Bulk density, T.D: Tapped density, CI: Carr's index, DT: Disintegration time

Table 4: Optimization of FXD HCL dispersible tablets through Design Expert software

Sr. No.	*A: Granfiller-D®211(mg)*	*B: Magnesium stearate (mg)*	*Angle of repose (°)*	*Disintegration time (Sec)*
1	120	2.2	25.54	148.5
2	120	4.4	21.34	139.4
3	180	2.8	12.26	75.8
4	180	5.61	29.05	78
5	120	2.2	21.52	129.7
6	120	4.4	20.74	139.4
7	180	2.8	13.89	74.62
8	180	5.61	25.54	80

Table 5: ANOVA for the angle of the repose of powder blend

Source	*Sum of Squares*	*df*	*Mean Square*	*F-value*	*p-value*	
Model	217.23	3	72.41	18.39	0.0084	Signi ficant
A-Co-processed excipient	73.91	1	73.91	18.77	0.0123	
B-Magnesium stearate	46.31	1	46.31	11.76	0.0265	
AB	115.06	1	115.06	29.22	0.0057	
Pure Error	15.75	4	3.94			
Cor Total	232.98	7				

Determination of impact of independent factors on the angle of repose of the powder blend of FXD HCL dispersible tablets by ANOVA.

The model F-value of 18.39 and $p < 0.05$ imply the model is significant, as shown in Table 5. A polynomial equation describing the impact of changing A and B on the dependent variables was obtained. Angle of Repose = +18.95-3.34 A+2.16 B+3.41 AB. In this case, A, B and AB are significant model terms. Figure 4 shows the contour plot and 3D response curve for angle of repose.

Determination of impact of independent factors on the disintegration time of FXD HCL dispersible tablets by ANOVA.

In this case, A is a significant model term. ANOVA for disintegration time of dispersible tablets is given in Table 6. The effect of varying A and B on the dependent variables was determined using statistical equations. Disintegration time 107.80-31.45A+1.01B. Figure 5 shows the contour plot and 3D response curve for disintegration time.

The data obtained from DoE batches were analysed using Design-Expert® 13 software.As seen from the ANOVA table, co-processed excipient and magnesium stearate have a significant impact on the angle of repose. The contour plot and 3D response surface curve for the same indicates that as the amount of co-processed excipient increases and the level of magnesium stearate reduces, the obtained value of the angle of repose is small, as indicated by the blue color in the contour plot, which is desirable. Magnesium stearate has a great impact on the flow properties of the blend as explained by Yüksel *et al.* They discovered that increasing magnesium stearate concentration can negatively affect the flow properties of the tableting mass.[1,30] ANOVA of disintegration time shows that the co-processed excipients have a major impact on tablet disintegration, whereas magnesium stearate does not have a severe impact. The contour plot and 3D response surface curve for the same indicates that as the amount of co-processed excipient increases, the disintegration time decreases, as indicated in green to blue colour from left to right, whereas

Table 6: ANOVA for disintegration time of dispersible tablets

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	7716.18	2	3858.09	104.35	< 0.0001	Signi ficant
A-Co-processed excipient	7011.89	1	7011.89	189.65	< 0.0001	Signi ficant
B-Magnesium stearate	10.81	1	10.81	0.2923	0.6120	Not sig nificant
Residual	184.87	5	36.97			
Lack of Fit	4.81	1	4.81	0.1068	0.7602	Not sig nificant
Pure Error	180.06	4	45.02			
Cor Total	7901.04	7				

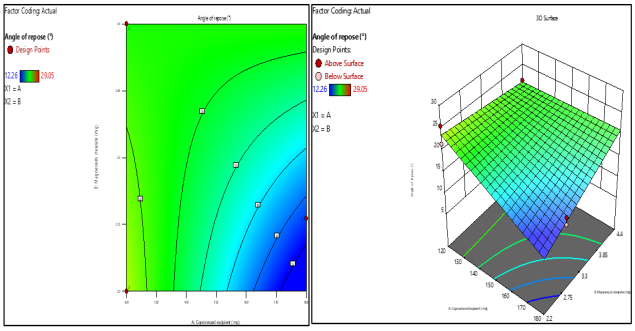

Figure 4: Contour plot and 3D response curve for angle of repose of powder blend

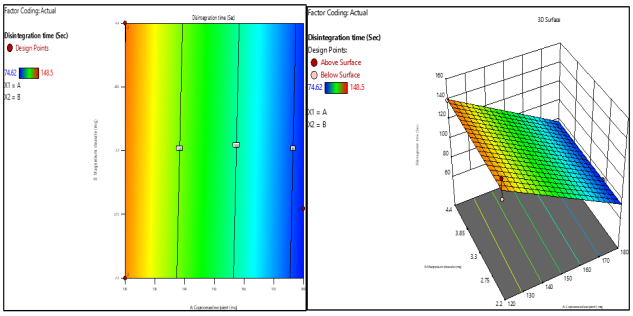

Figure 5: Contour plot and 3D response curve for disintegration time of tablet

magnesium stearate has no severe impact on disintegration time.[31] The overlay plot is shown in Figure 6.

The overlay plot of the optimization design was obtained by considering the desired angle of repose of the powder blend and disintegration time of FXD HCL dispersible tablets.Formula F1 was selected as the optimized formulation with angle of repose 25° and disintegration time of 148 seconds.

Release study

All the FXD GNF-D®211 dispersible tablets showed an immediate drug release pattern in 0.001 N HCL (pH 3) i.e., NLT 60% within 10 minutes and NLT 80% within 30 minutes.[25] The release pattern of GNF-D®211 based dispersible tablets is shown in Figure 7 (n = 3).

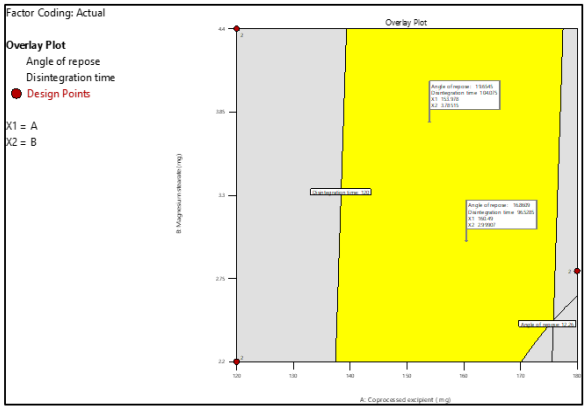

Figure 6: Overlay plot obtained from Design Expert® 13 software

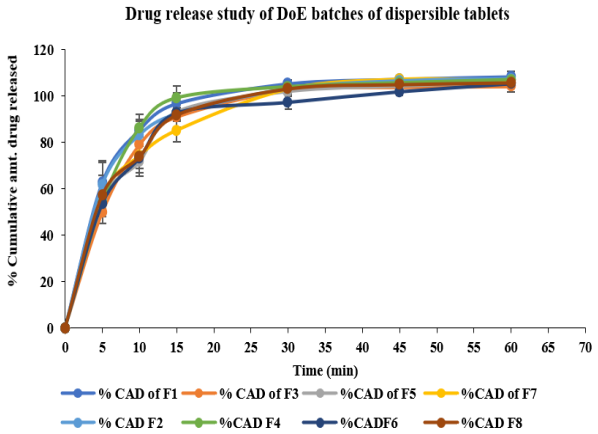

Figure 7: Release study profile of DoE formulations of FXD HCL dispersible tablets

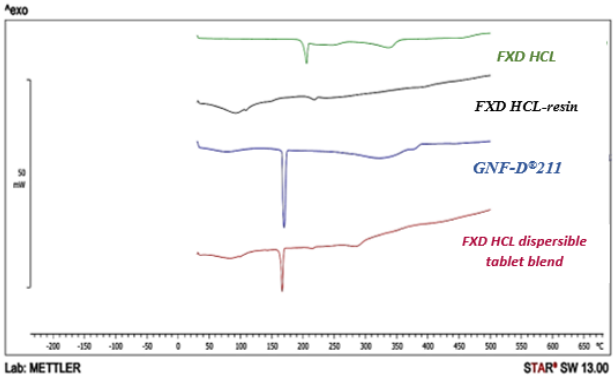

Figure 8: DSC Thermogram

DSC of an optimized dispersible tablet batch

The DSC thermogram of F1 formula of GNF-D®211 based FXD HCL dispersible tablets was compared with those of FXD HCL, FXD HCL-resin complex and GNF-D®211 as represented in Figure 8. There was an absence of a sharp endothermic peak of FXD HCL in the DSC thermogram of FXD HCL-resin complex and in the dispersible tablet blend. It indicates amorphization of FXD HCL in the FXD HCL-resin complex and tablet blend. Figure 8 depicts the DSC thermogram of FXD HCL, FXD HCL-resin complex, GNF-D®211, and dispersible tablet blend.

Stability Study of a GNF-D®211 Based FXD HCL Dispersible Tablet

The tablets were assessed for color, friability, disintegration time, assay and release profile after one month of exposure to 25 ± 2ºC/ 60%RH and 40 ± 2ºC/75% RH. There was no noticeable difference in the appearance, integrity, or uniformity of the content on the tablets (data not shown).

CONCLUSION

Granfiller-D®211, a coprocessed excipient, could be used to formulate dispersible tablets. FXD HCl, a bitter drug, was successfully incorporated into a dispersible tablet using taste masking ion exchange resin, Kyron-T134®. *In-vitro* assessment of the dispersible tablets confirmed the overall potential of combining Kyron-T 134® and Granfiller-D®211as a novel combination to improve FXD HCL delivery.

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