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Formulation and In Vitro Evaluation of Fexofenadine HCl Fast Dissolving Tablets

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ABSTRACT

A fast-dissolving drug delivery system is a tablet that dissolves or disintegrates in the oral cavity without the need of water or chewing. These are novel types of tablets that disintegrate/dissolve/ disperse in saliva within few seconds. According to European Pharmacopoeia, the Oral Dissolving Tablet should disperse/disintegrate in less than three minutes. The basic approach used in development of Fast Dissolving Table is the use of super disintegrant like Crospovidone, which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. Crospovidone is a disintegrating agent at the 4-8% level and is an effective binder–disintegrant in tablets prepared using wet granulation. Furthermore, swelling properties paired with particle size distribution make the finer grades of Crospovidone work efficiently in fast-disintegrating formulation. Powders are evaluated for flow properties like Angle of Repose, Carr's consolidation index and Hausner ratio were found to be within acceptance criteria to indicate good flow properties. Five tablets of each formulation with varying concentration of Crospovidone were evaluated for different parameters like Hardness, Thickness, Friability, Weight variation and Disintegration time were found to be within acceptance criteria. The F3 containing 7.2% w/w of Crospovidone was found to be promising and has shown an in vitro disintegration time of 20 sec when compared to control which shows 300 sec. By increasing super-disintegrant concentration for different formulations, our results reveal that the F3 has shown better release compared to control in 20 mins.

Keywords: Fast Dissolving Tablet, Fexofenadine HCl, Crospovidone, Direct Compression method.

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INTRODUCTION

Chemically Fexofenadine is 2-[4-[1-hydroxy-4-[4-(hydroxy-diphenyl-methyl)-1-piperidyl]-butyl] phenyl]-2- methyl-propanoic acid. Fexofenadine is an antihistamine drug used in the treatment of hay fever and similar allergy symptoms. Fexofenadine, like other second and third-generation antihistamines, does not readily pass through the blood-brain barrier, and so causes less drowsiness than first-generation histamine-receptor antagonists. United States Food and drug administration (FDA) defined fast dissolving tablet (FDT) as "A solid dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue." A fast-dissolving drug delivery system[1] is a tablet that dissolves or disintegrates in the oral cavity without the need of water or chewing. The development of Fast dissolving tablets has been formulated for pediatric, geriatric, and bedridden patients and may not have access to water. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing of conventional tablets may be difficult[2]. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients[3-4]. These are also called melt-in-mouth tablets, repimelts, porous tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets. These are novel types of tablets that disintegrate/dissolve/ disperse in saliva within few seconds[5]. According to European Pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach used in development of FDT is the use of Superdisintegrants like Cross linked carboxymethyl cellulose (Croscar-meliose), Sodium Starch Glycolate (Primogel, Explotab). Polyvinylpyrrolidone (Polyplasdone) etc., which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. FDTs can be prepared by different methods as direct compression, freeze-drying, spray drying, sublimation and wet granulation method[6-8] and Effervescent[9] method. The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and also due to pre-gastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subject to first pass metabolism is reduced as compared to standard tablets[10-12]. The poor availability and less solubility of the drug is a major problem for developing a dosage form. The dissolution enhancement can be done by using super disintegrants. The important one among them is Crospovidone.

MATERIALS AND METHODS

Instruments:

Hot air oven (Scientific Kemi Engineering corporation sector India), Friability apparatus (Electrolab), Hardness apparatus (Monsanto), UV-Visible Spectrophotometer (Systronics UV-Visible Spectrophotometer 118), Punching machine (Dolphin Industries pvt Ltd Bombay), Disintegration apparatus (Electrolab), Dissolution apparatus (D.B.K Instruments Bombay), Electronic balance (LC-GC), Sieves (Sethi Equipments).

Chemicals:

Fexofenadine gift sample was procured from Aurobindo Pharma. The Crospovidone was gifted from Basf - India. Talc, Sodium Stearyl Fumarate was procured from Lobachem. Methanol was obtained from S.D. Fine Chemicals.

Calibration Curve of Fexofenadine:

10 mg of pure drug was dissolved in methanol to get a concentration of 1000 µg/ml (Stock). From this Stock solution 0.1, 0.2, 0.3, 0.4 and 0.5 ml of the solution was taken in to separate 10 ml volumetric flasks and diluted with phosphate buffer pH 6.8 to get a concentration of 10,20,30,40 and 50 µg/ml. And the absorbances measured by using SYSTRONICS UV-Visible Spectrophotometer 118. The Statistical Data of the drug is given in Table 1.

Table1: Statistical Data of Calibration Curve

Parameter	Method
λ_{max}	259.0nm
Linearity Range (µg/ml)	10-50
Correlation coefficient (r^2)	0.9996
Regression equation (Y)	0.0168X - 0.002
Slope (b)	0.0168
Intercept (a)	0.002

Preparation of Fast Dissolving Tablets:

The tablets were prepared by Effervescent method. All the ingredients were weighed accurately. All the ingredients were sifted through # 44 mesh separately. Fexofenadine and Crospovidone were accurately weighed and mixed them according to geometric dilution. To that above mixture lactose, Sodium Stearyl Fumarate, aspartame was added. The citric acid and sodium bicarbonate were taken in a china dish separately and heated slightly to 80^0C for some time. This pre heated citric acid and sodium bicarbonate mixtures were added to the above mixture. The powder was mixed well and passed through Sieve No # 44. Finally the lubricant, talc was mixed and the tablets are compressed. 40 tablets of each 4 formulations were prepared by using the formula in Table 2.

Table 2: Formula for Different Formulations

Ingredient	Control (mg)	F1 (mg)	F2 (mg)	F3 (mg)
Fexofenadine	30	30	30	30
Sodium bicarbonate	20	20	20	20
Citric acid	15	15	15	15
Crospovidone	_	4	8	16
Aspartame	12.5	12.5	12.5	12.5
Sodium Stearyl Fumarate	2.5	2.5	2.5	2.5
Talc	12.5	12.5	12.5	12.5
Lactose	157.5	153.5	149.5	141.5
Total Tablet weight	250.0	250.0	250.0	250.0

Evaluation of Powders (Pre Formulation Studies):

Bulk density:

Both loose bulk density (LBD) & tapped bulk density (TBD) were determined. A quantity of 2 g of powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 second intervals. The tapping was continued until no further change in the volume was noted. LBD & TBD were calculated using the following formulas.

LBD = weight of the powder / volume of the packing

TBD = weight of the powder / tapped volume of the packing

Compressibility Index:

The compressibility index of the granules was determined by Carr's compressibility Index

Carr's index (%) = [(TBD – LBD) * 100] / TBD

LBD = weight of the powder / volume of the packing

TBD = weight of the powder / tapped volume of the packing

Angle of Repose:

The angle of repose of granules was determined by the funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured & angle of repose was calculated using the following equation

$$\tan\varphi = h/r$$

Where, h & r are the height & radius of the powder cone.

Hausner Ratio (HR):

It is defined as the ratio of the tapped density to bulk density it can also be calculated by using the formula by using Carr's consolidation index

Hausner ratio = Tapped density / Bulk density

Evaluation of Tablets (Post Formulation Studies):

Weight uniformity:

20 randomly selected tablets were weighed individually and the average weight and the standard deviation were calculated.

Hardness:

Hardness of tablets was measured using Monsanto hardness tester. The tablet to be tested is held between a fixed and moving plunger and reading of indicator is adjusted to zero. The force applied to the edge of the tablet is gradually increased by moving the screw knob forward until the tablet breaks. The reading is noted from the scale which indicates pressure required in kg /cm2.

Thickness:

The thickness is measured by using vernier calipers. 3 tablets are taken and are placed between the two upper jaws and the thickness was measured as replicate of three sets. After adjusting the calipers to zero reading the negative/ positive correction value is noted and the values are estimated.

Friability:

Friability of the tablets was determined using Roche friabilitor at 25 rpm/min for 4 min. 10 tablets were weighed and loss in weight (%) was calculated.

Friability = (W1 – W2) / W1 X 100

Weight of 10 Tablets = W1, Weight of 10 Tablets after friability = W2

Disintegration Time:

The disintegration time for six tablets of each formula was measured in distilled water at 37ºC ± 2ºC which was used as a disintegration media as per I.P. The average time and standard deviation were calculated for each.

Dissolution Studies:

Dissolution of Fexofenadine fast dissolving tablets was studied in Apparatus I as per I.P. employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 phosphate buffer at 37±0.5º as dissolution medium. One tablet was used in each test. Aliquots of dissolution medium (5 ml) were withdrawn at specific intervals of time and analyzed for drug content by measuring the absorbance at 259 nm. The volume withdrawn at each time interval was replaced with fresh

quantity of dissolution medium. Cumulative percent of Fexofenadine released was calculated and plotted against time.

RESULTS AND DISCUSSION:

1.Powders for Effervescent compression were prepared and evaluated for flow properties like Angle of Repose, Carr's consolidation index and Hausner ratio were found to be within in acceptance criteria to indicate good flow properties. The values are shown in Table 3.

Table 3: Evaluation of Powder (Pre Formulation Studies)

Formulation	Angle of repose	LBD (gm/ml)	TBD (gm/ml)	Carr's index	HR
Control	26.71±0.05	0.57±0.01	0.65±0.02	12.30±0.5	1.14±0.04
F1	29.35±0.06	0.60±0.02	0.70±0.02	14.28±0.8	1.16±0.03
F2	24.89±0.04	0.58±0.01	0.67±0.01	13.43±0.6	1.15±0.01
F3	25.23±0.05	0.61±0.03	0.71±0.03	14.08±0.3	1.16±0.02

n=3(all the values are average of three determinations)

2. Powders were punched into tablets by direct compression method and five tablets of each formulation were evaluated for different parameters lie Hardness, Thickness, Friability, Weight variation and Disintegration time were found to be within acceptance criteria. The values shown in Table 4.

Table 4: Evaluation of Tablets of Different Formulations

Formulation	Hardness(kg/cm^2)	Friability (%)	Thickness (mm)	Weight variation (mg)	Disintegration time (sec)
Control	2.53 ± 0.2	0.6±0.02	0.45	250 ±5	300 ±0.5
F1	2.76 ± 0.2	0.58±0.02	0.47	252 ±4	60 ±0.4
F2	2.5 ± 0.2	0.59±0.02	0.46	251 ±4	30 ±0.2
F3	2.6 ± 0.2	0.58±0.02	0.45	250 ±5	20 ±0.2

n=5 (all the values are average of five determinations)

3. The disintegration time for the formulation F3 was found to be 20 ±0.2.

4. By increasing super-disintegrant concentration for different formulations, our results reveal that cumulative release of F3 has shown better release compared to control, F1, and F2 in 20 min. Cumulative release profile of formulations shown in figure 1. The values are shown in Table 5. The formulation F3 shown a release of 75.35% drug with in 20 min.

Table 5: Cumulative Release of Different Formulations

Time(min)	Control	F1	F2	F3
5	5.176	5.88	6.96	12.853
10	23	27.141	32.49	36.066
15	45	50.353	53.9	57.49
20	50.35	62.853	68.213	75.35

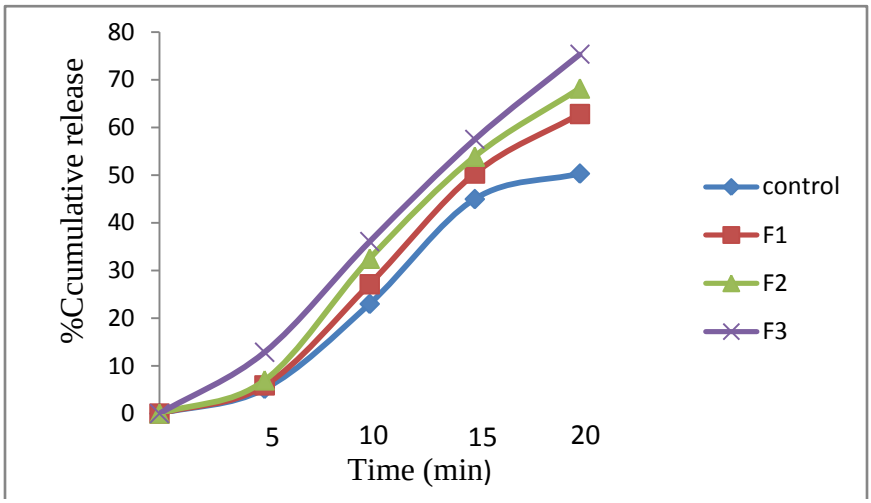

Figure1: Cumulative Release profile of different formulations.

CONCLUSION

The F3 containing 7.2% of Crospovidone was found to be promising and has shown an in vitro disintegration time of 20±0.2 sec when compared to control which shows 300 sec. By increasing super-disintegrant concentration for different formulations, our results reveal that the F3 has shown better release compared to control in 20 min. Fast dissolving delivery system have started gaining popularity and acceptance with increased consumer choice, for the reason of rapid disintegrate or dissolution, self administration even without water or chewing. The concept of formulating Fexofenadine Fast dissolving tablets by simultaneous employment of super-disintegrant and Effervescent technique offers suitable and practical approach in serving desired objective in Allergic patients.

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