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Formulation and In Vitro Evaluation of Immediate Release Tablet of Fexofenadine Hydrochloride.

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ABSTRACT

The pivotal motif of the present research work is to develop immediate release tablets of Fexofenadine hydrochloride. The rate of dissolution and bioavailability of the Fexofenadine HCL may be increased by using superdisintegrant in its immediate release tablets. Direct compression method was adapted to prepare the tablets by using lactose, microcrystalline cellulose as filler, crospovidone and sodium starch glycolate as superdisintegrant in different concentration (2-8%). Tablet were prepared and evaluated for Hardness, friability, weight variation, content uniformity, wetting time, disintegration time and in-vitro drug release. Disintegration time decreased with increase in the level of crospovidone. Whereas, disintegration time increased with increase in the level of sodium starch glycolate. The results indicate that the selected batch of tablet formulation containing crospovidone provides DT between 3-6 minutes with sufficient crushing strength and accepted friability. It was concluded that immediate release tablet for Fexofenadine hydrochloride can be formulated for fast treatment of allergic rhinitis

Keywords: Fexofenadine Hydrochloride, Crospovidone, Sodium starch glycolate, Microcrystalline cellulose, Immediate Release

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INTRODUCTION

The oral route of drug administration is the most common and preferred method of delivery due to convenience and ease of ingestion. From a patient's perspective, swallowing a dosage form is a familiar means of taking medication. As a result, patient compliance and hence drug treatment is typically more effective with orally administered medications as compared with other routes of administration. The concept of immediate release tablets emerged from the desire to provide patient with more conventional means of taking their medication when emergency treatment is required. Most of the technologies for the manufacture of immediate release tablets use superdisintegrants so that the tablet disintegrates quickly [1, 2]. The disintegration of the solid oral dosage form which will increase the wettability of the drug. This highlights the importance of proper choice of superdisintegrants i.e. crospovidone, sodium CMC, alginic acid and there consistency of performance which are of critical importance to increase the rate of dissolution and hence its bioavailability [3].

Fexofenadine HCl is a second-generation non-sedating histamine H1 receptor antagonist widely used in seasonal allergic rhinitis. Fexofenadine hydrochloride is a white to off-white crystalline powder. It is freely soluble in methanol and ethanol, slightly soluble in chloroform and water. As it is included in class III of the Biopharmaceutical Classification System (BCS), the use of superdisintegrating agent might be necessary to improve the absorption, thereby increasing the bioavailability. There are various factors (hardness, concentration of disintegrants etc.) affecting the disintegration time (DT) and rate of dissolution of the drug [4,5].The present investigation deals with the development of an effective and immediate release of Fexofenadine hydrochloride having adequate hardness, low disintegration time. Its insolubility in water makes it an ideal candidate for immediate release tablets with regards to bioavaibility.

MATERIALS AND METHODS:

Fexofenadine HCl was obtained as a gift sample from Bajaj Health Care Pvt. Ltd., Mumbai (India). Sodium starch glycolate, Crospovidone, and microcrystalline cellulose were obtained from Sigma Aldrich Mumbai (India). All other chemicals, additives and solvent like ethanol and methanol were obtained from Loba Chemie, Mumbai.

Evaluation of Powder Blend

Bulk Density

It is the ratio of total mass of powder to the bulk volume of powder. Bulk volume was measured by pouring the weighed powder (passed through standard sieve # 20) into a measuring cylinder

and initial volume was noted. This initial volume was called the bulk volume. From this the bulk density was calculated according to the formula mentioned below. It is expressed in gm/ml and is given by

Bulk density = M/ Vb

Where, M and Vb are mass of powder and bulk volume of the powder respectively [6].

Tapped Density

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 500 times and the tapped volume was noted. It is expressed in gm/ml and is given by

Tapped density = M / Vt

Where, M and Vt are mass of powder and tapped volume of the powder respectively [6].

Flow properties of powder blend [7, 8]

The flow properties of blend (before compression) were characterized in terms of angle of repose, Carr's index and Hausner ratio.

For determination of angle of repose (θ), the blend were poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2.0 cm above hard surface. The blends were poured till the time when upper tip of the pile surface touched the lower tip of the funnel. Angle of repose was calculated using following equation.

$$\tan \theta = (h/r)$$

Where, h = height of pile; r = radius of pile

Carr's index (or) % compressibility [8]

It indicates powder flow properties. It is expressed in percentage and is given by

C.I. = (Tapped Density – Bulk Density / Tapped Density) × 100

Hausner ratio

Hausner ratio is an indirect index of ease of powder flow [8]. It was calculated by the following formula.

Hausner ratio = Tapped Density / Bulk Density

Preparation of immediate release tablets of Fexofenadine HCL

All the excipients used to formulate into tablets were passed through sieve # 40 and mixed in geometric dilution. Drug-excipient mixture equivalent to 120 mg of drug were compressed on Cadmach rotary 08 station tablet press machine and the same hardness was used for all the tablets. The formula for different batches were given in table 1

Table 1: Formulae used in the preparation of tablet

Ingredients (mg per tab.)	F1	F2	F3	F4	F5	F6
Fexofenadine HCL	120mg	120mg	120mg	120mg	120mg	120mg
Crospovidone	08mg	16mg	24mg			
Sodium starch glycolate	-	-	-	7.5mg	14mg	21mg
Microcrystalline cellulose	50mg	50mg	50mg	50mg	50mg	50mg
Magnesium stearate	3mg	3mg	3mg	3mg	3mg	3mg
Lactose	169mg	161mg	153mg	169.5mg	163mg	156mg
Total Weight	350mg	350mg	350mg	350mg	350mg	350mg

Evaluation of immediate release tablets of Fexofenadine HCL

Uniformity of weight

Twenty tablets were taken and their weight was determined individually and collectively on digital weighing balance. The average weight of one tablet was determined from the collective weight [9].

Hardness

Hardness was determined by taking six tablets from each formulation, using a Monsanto Hardness Tester [9].

Friability

The friability of sample of six tablets ware measured using a Roche Friabilator. Six pre-weighed tablets were rotated at 25 rpm for 4 minutes. The tablets were then reweighed after removal of fine's using 60 mesh screen and the percentage of weight loss was calculated [9].

$$\% \text{ Friability} = (\text{Loss in weight} / \text{Initial weight}) \times 100$$

Wetting time [10]

A piece of paper folded twice was kept in a Petri dish (internal diameter 5.5 cm) containing 6 ml of purified water. A tablet having a small amount of Rosaline dye powder on the upper surface was placed on the tissue paper. The time required to develop a red colour on the upper surface of the tablet was recorded as the wetting time.

Disintegration time

Disintegration time was measured in distilled water according to the USP method at 37 ± 0.5^{o}C temperature. The disintegration time of 6 individual tablets were recorded and the average was reported [11].

Content uniformity

Twenty tablets were powdered, and 10 mg equivalent weight of Fexofenadine HCL tablet powder was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 10 ml of 0.01N HCL was added and shaken for 10 min. Then, the volume was made up to100 ml with

0.01N HCL. The solution in the volumetric flask was filtered, diluted, and analyzed spectrophotometrically at 256 nm.

Dissolution study

In vitro release of Fexofenadine HCL from tablets was monitored by using 900 ml of 0.01 N HCL, at 37±0.5° and 50 rpm using programmable dissolution tester USP II. Aliquots of 10 ml were withdrawn from the dissolution apparatus at time intervals of 2min and the samples were replaced with fresh dissolution medium. Absorbance of these solutions was measured at 256 nm. The percent drug release was calculated using the calibration curve of the drug in 0.01 N Hydrochloric acid [12, 13].

RESULTS AND DISCUSSION

Evaluation of Powder Blend

Since, the flow properties of the powder mixture are important for the uniformity of mass of the tablets, the flow of the powder mixture was analyzed before compression to tablets. Low Hausner`s ratio (≤1.29), compressibility index (≤21.68) and angle of repose (≤22.13) values indicated a fairly good flowability of powder mixture [14]. As the tablet powder mixture was free flowing, tablets produced were of uniform weight with acceptable weight variation due to uniform die fill. All results are shown in Table 2

Hardness (3.63-4.41 kg/cm^2) and friability loss (0.37-0.83 %) indicated that tablets had a good mechanical resistance [15]. All result shown in Table 3

Table 2: Different evaluation results of powder blend

Evaluation parameter	F1	F2	F3	F4	F5	F6
Bulk density (gm/ml)	0.632±3.2	0.659±1	0.783±0.3	0.689±0.14	0.619±091	0.698±1.3
Tapped density (gm/ml)	0.712±0.32	0.678±0.87	0.881±0.87	0.725±2.8	0.721±2.1	0.721±0.45
Angle of repose	20.21±0.5	19.21±0.3	18.13±0.4	20.91±0.2	22.13±0.2	19.23±0.4
% compressibility	16.72±1.3	16.23±0.3	15.23±0.7	18.68±1.7	18.02±2.1	17.33±0.8
Hausner's Ratio	1.27±1.2	1.11±0.1	1.03±0.2	1.23±0.2	1.29±0.1	1.24±0.4

* Each value represent mean S.D. ± (n=3)

Table 3: Evaluation of prepared immediate release tablet of Fexofenadine HCL

Batch Code	Average Weight (mg) *	Hardness (kg/cm2) *	Friability (%)*	Disintegration Time (min) *	Wetting Time (sec) *
F1	350±0.07	4.32±0.02	0.41±0.03	4.5±2.00	65±1.00
F2	353±0.23	4.01±0.04	0.37±0.90	2.50±0.33	54±0.12
F3	352±0.21	3.63±0.32	0.57±0.33	2.24±1.20	35±0.87
F4	351±0.11	3.94±0.01	0.83±0.32	2.49±1.54	57±0.98
F5	350±0.40	4.41±0.12	0.63±0.76	3.11±0.91	65±0.56
F6	350±0.30	4.41±0.13	0.48±0.87	5.90±0.34	69±0.12

* Each value represent mean S.D. ± (n=6)

Drug content was found to be high (≥92.3%) and uniform (coefficient of variation between 0.89-2.56%) in all the tablet formulations.

The most important parameter that needs to be optimized in the development of immediate release tablets is the disintegration time of tablets [16]. In the present study, all the tablets disintegrated in 3-6 min. shown in Table 3. It is observed that the disintegration time of the tablets decreased with increase in the level of crospovidone. However, disintegration time increased with increase in the level of sodium starch glycolate in the tablets. It indicates that increase in the level of sodium starch glycolate had a negative effect on the disintegration of the tablets. At higher levels, formation of a viscous layer by sodium starch glycolate [17] might have formed a thick barrier to the further penetration of the disintegration medium and hindered the disintegration or leakage of tablet contents. Thus, tablet disintegration is retarded to some extent with tablets containing sodium starch glycolate. Comparatively, disintegration times of the tablets is crospovidone <sodium starch glycolate. The disintegration times of crospovidone containing tablets are comparatively lower than those containing sodium starch glycolate. The faster disintegration of crospovidone tablets may be attributed to its rapid capillary activity and pronounced hydration[18]. Thus, these results suggest that the disintegration times can be decreased by using crospovidone.

Since the dissolution process of a tablet depends upon the wetting followed by disintegration of the tablet, the measurement of wetting time may be used as another confirmative test for the evaluation of immediate release tablets. However, wetting times decreased with increase in the level of crospovidone above 4%, as shown in Table 3. It is interesting to note that wetting time increased with increase in the level of sodium starch glycolate above 3% in the tablets, as shown in table 3. Thus wetting times of tablets with crospovidone < sodium starch glycolate. These results are in consistent with disintegration test results.

The influence of superdisintegrants on the dissolution of Fexofenadine HCL from the tablets is shown in figure.2. The dissolution increased with increase in the level of sodium starch glycolate and crospovodone. But dissolution is high for tablet containing crospovidone. The rapid increase in dissolution of Fexofenadine HCL with the increase in crospovidone may be attributed to rapid swelling and disintegration exhibits high capillary activity and pronounced hydration[17].While, tablets prepared with sodium starch glycolate, disintegrate by rapid uptake of water initially, but later dissolve slowly due to the formation of a viscous layer by sodium starch glycolate.

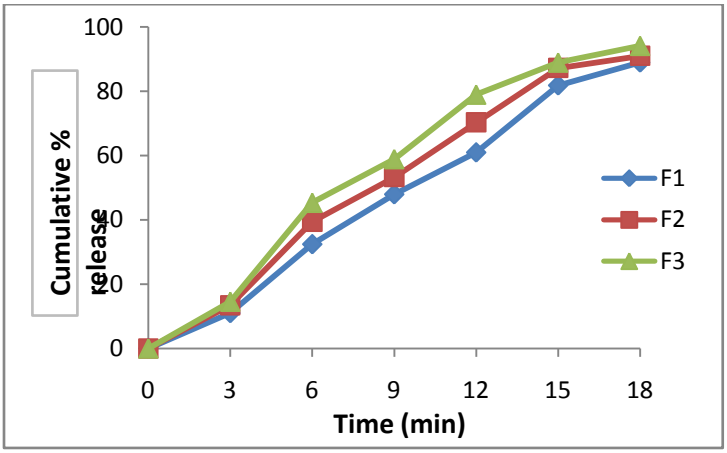

Figure.1: In-vitro dissolution profile for immediate release Fexofenadine Hydrochloride tablet containing Crospovidone

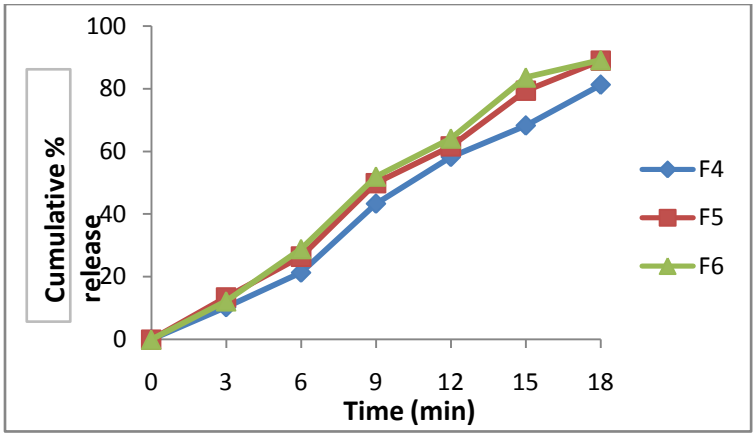

Figure.2: *In-vitro* dissolution profile for immediate release Fexofenadine Hydrochloride tablet containing Sodium Starch Glycolate

CONCLUSION

Immediate release tablet of Fexofenadine HCl as a promising approach to enhance the drug release profile using Superdisintegrants. The results showed that the release of the drug was depended on different superdisintegrants used, in that crospovidone can release drug faster compare to Sodium starch glycolate. So immediate release tablet of Fexofenadine hydrochloride show better drug release profile as compare to other formulations.

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