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RESEARCH ARTICLE

Formulation and Evaluation of Fast Dissolving Tablet of Levocetrizine using Direct Compression Technique

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Abstract:

In this investigation fast dissolving tablets of Levocetrizine HCl were prepared using different super disintegrants by direct compression method. Fast dissolving tablets prepared by direct compression and using super disintegrants like Croscarmellose sodium and crospovidone in different concentration and evaluated for the pre-compression parameters such as bulk density, compressibility, angle of repose etc. The prepared batches of tablets were evaluated for hardness, weight variation, friability, drug content, disintegration time and in-vitro dissolution profile and found satisfactory. Among all, the formulation F6 containing super disintegrant crospovidone was considered to be best formulation, which release up to 98.89% in 5 min.

Keywords: Levocetrizine HCl; Mouth dissolving tablet; super disintegrants; Dissolution rate.

INTRODUCTION

Many patients, especially elderly find it difficulty in swallowing tablets, capsules ,thus do not comply with prescription , which results in high incidence of noncompliance and in effective therapy convince and compliance oriented research has resulted in bringing out many safer and newer drug delivery systems[1]. Fast dissolving tablets is one of such example, for the reason of rapid disintegration or dissolution in mouth with little amount of water or even with saliva. Significance of this drug delivery system includes administration without water, accuracy of dosage, ease of portability, alternative to liquid dosage forms ideal for pediatric and geriatric patients and rapid onset of action[2].

Recently, useful dosage forms, such as rapidly disintegrating or dissolving tablets, have been developed and applied clinically. When such tablets are placed in the oral cavity, saliva quickly penetrates into the pores to cause rapid tablet disintegration.[3-5] Currently, it has been has been revealed that a fast dissolving tablet prepared by a technique like lyophilization[6], vacuum drying technique[7], direct compression method[8,9], disintegrant addition technique[10] and sublimation technique by using sublime agent like camphor, menthol.[11, 12]

Levocetirizine dihydrochloride with texture acceptable to patients and with sufficient structural integrity by using sublimation technique. Levocetirizine dihydrochloride is levo active form of Cetirizine dihydrochloride which is a racemic mixture. Levocetirizine dihydrochloride is second generation piperazine derivative, potent H1 selective agent with fewer side effects. In case of allergic or histaminic reaction a rapid action of the drug is required. The characteristics of these tablets benefits in terms of patient compliance, rapid on-set of action, increased bio-availability, (sometimes bi-pass first pass effect) and good stability make these tablets popular as a dosage form of choice.[13]

In the present study, an attempt had been made to prepare fast dissolving tablets of Levocetrizine HCl in the oral cavity with enhanced dissolution rate & hence improved patient compliance5.

MATERIALS AND METHODS

Materials

Levocetrizine HCl was obtained as gift sample from Torrent Pharma, Ahmadabad, India, Croscarmellose sodium, Crospovidone gift sample form Zydus cadila, Ahmadabad, India, Lactose, Mannitol were purchased from Cosmo chemical, Pune, magnesium sterarate, talc,

saccharin were purchased from rankem and all other chemicals/ Solvents used were of analytical grade.

Methods

Preparation of Mixed Blend of Drug and Excipients

All the Ingredients were passed through mesh 60. Required quantity of each ingredient was taken for each specified formulation and all the ingredients were co-grind in a mortar and pestle. The powder blend was evaluated for flow properties such as Bulk density, Tapped density, Compressibility index and Hausner's ratio.

Preparation of Tablets

The ingredients (except magnesium stearate) were mixed homogenously and co grind in a mortar and pestle. Finally magnesium stearate was added and mixed for 5 min. The mixed blend of drug and excipients was compressed using cadmach single punch tablet punching machine to produce convex faced tablets weighing 200 mg each with a diameter of 8mm. a minimum of 50 tablets were prepared for each batch. The Composition of fast dissolving tablet of Levocetrizine HCl was summarized in Table 1.

Table: 1 Composition of fast dissolving tablet of Levocetrizine HCl

Sr. no.	Ingredients	F1	F2	F3	F4	F5	F6
1.	Levocetrizine HCl	100	100	100	100	100	100
2.	Crosscarmellose sodium	50	50	50	-	-	-
3.	Crosspovidone	-	-	-	50	50	50
4.	Lactose	20	20	20	20	20	20
5.	Mannitol	10	10	10	10	10	10
6.	Magnesium stearte	10	10	10	10	10	10
7.	Talc	10	10	10	10	10	10
Total Weight		200mg	200mg	200mg	200mg	200mg	200mg

EVALUATION OF LEVOCETRIZINE FAST DISSOLVING TABLETS

Weight variation test[14]

Twenty tablets were selected at a random and average weight was determined. Then individual tablets were weighed and was compared with average weight.

Hardness [15]

The crushing tolerance of tablets was measured using an Electrolab hardness tester model EL 500. Determinations were made in triplicate.

Drug estimation

10 tablets were taken their weight accurately. Average weight is calculated and equivalent to 25 mg of drug was taken for estimating the drug content in the total tablet. It was within official limit.

Percentage of drug content is calculated by: Y/X ×100

Where Y = Actual drug content (mg)

X = Labeled amount of drug (mg)

Tablet Friability [16]

The friability of the tablets was measured in a Roche friabilator. Tablets of a known weight or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1%. Determination was made in triplicate.

The friability (f) is given by the formula:

(Initial weight- Final weight) / (Initial weight)] x 100

In-vitro Disintegration test [17]

Disintegration time was determined using the disintegration apparatus USP (E.I. Instrument, Haryana, India) distilled water at 37°C±2°C was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

In-vitro Dissolution test [18]

Drug release profile was evaluated ***in vitro*** using a dissolution test apparatus (E.I. Instrument, Haryana, India). The USP Type II (paddle type) method was selected to perform the dissolution profile of Levofloxacin hydrochloride. The dissolution for all the formulations was carried out according to US Pharmacopoeia for 12 h in 0.1N HCl first two hours and then media was changed into phosphate buffer pH 6.8 for remaining 6 hours. The temperature was maintained at 37 ± 0.5°C and a constant paddle rotation speed of 50 rpm. Samples (10 ml) were withdrawn at regular intervals and filtered through membrane filter (pore size 0.22 μm).

Concentration of Levocetrizine was determined spectophotometrically at 234 nm (Systronics 1700 UV- is Spectrophotometer).

Actual amount of released drug was determined from the calibration curve.

Accelerated Stability Study of Best Batch [19,20,21]

In order to determine the change in in-vitro release profile on storage, stability study of batch F5 was carried out at 40$_0$ C in a humidity chamber having 75% RH. Samples were withdrawn at regular intervals during the study of 60 days. Formulation is evaluated for change in invitro drug release pattern, hardness and disintegration time.

RESULTS AND DISCUSSION

Six formulations of Levocetrizine HCl were prepared with varying concentration of two super disintegrants: Croscarmellose Sodium, Crospovidone, and mannitol were used as diluents (Table 1). For each formulation, blend of drug and excipients were prepared and evaluated for various parameters. The evaluation of blend properties as shown in Table-2.

Table: 2. Evaluation of Blends. (Micromeritics property of Blends)

Micromeritics Property of blends	F1	F2	F3	F4	F5	F6
Angle of repose (Θ)	25.32	28.21	24.23	24.34	22.42	26.12
Bulk density (g/cm^3)	0.46	0.84	0.42	1.09	0.58	0.48
Tapped density (g/cm^3)	0.53	0.91	0.46	1.12	0.64	0.52
Carr's index (%)	13.20	7.69	8.69	8.47	9.37	7.69
Hausner's Ratio	1.15	1.08	1.09	1.02	1.10	1.08

The powder blend was compressed using direct compression technique. Values for angle of repose were found in the range of 22.42 to 28.21°. Bulk density, was found in the range of 0.42-1.09 g/cm3 and the tapped density between 0.46-1.12 g/cm3. Using these two density data hausner's ratio and compressibility index was calculated. The powder blends of all formulations had hausner's ratio less than 1.15 indicates better flow property. The compressibility index was found between 7.69-13.20, which indicates a fairly good flow ability of the powder blend. The good flow ability of the powder blend was also evidenced with angle of repose (range of 25-27) which is below 40^0 indicating good flow ability. Tablets were prepared using direct compression technique. Since the powder material was free flowing, tablets were obtained of uniform weight due of uniform die fill, with acceptable weight variations as per I.P. The drug content was found in the range of 95.7% - 99.8% (acceptable limit) and the hardness of the tablets were fond below 1% indicating a good mechanical resistance of the tablets, and the parameters were found well within the specified limit for uncoated tablets. The in-vitro disintegration time (DT) of the tablets was found to less than 60 sec. Disintegration time of fast dissolving tablet was shown in table 3.

Table 3: EVALUATION OF TABLETS WITH SUPERDISINTEGRANTS

Code	D.T (sec)	Friability (%) ± S.D	Hardness (Kg/cm2) ± S.D	Wetting Time (sec)	Drug content (%)	Average Weight (mg)	Palatability
F1	55	2.5 ±0.22	4.5	11	97.3	596.3	Good
F2	40	1.02 ± 0.14	5.0	14	99.8	602.3	Good
F3	45	0.58 ± 0.24	4.0	15	95.7	612.5	Good
F4	50	1.26 ± 0.14	5.5	17	97.8	610.0	Poor
F5	45	1.2 ± 0.20	5.0	20	94.8	607.4	Fair
F6	40	1.03 ± 0.14	4.1	15	96.5	608.2	Good

The rapid disintegration was seen in the formulation containing Crospovidone rather than CCS. This is due to the rapid uptake of water from the medium, swelling and burst effect. Percentage drug content of all tablets was found in between 95.7 – 99.8% for CCS formulations (F1-F3) and 94.8 – 97.8 % for crospovidone formulations (F4-F6), which was within the acceptable limits. Dissolution profile of formulations (F1-F3) as shown in Table-4**.**

Table 4: Dissolution Profile Of Tablets By Using Crosscarmellose Sodium As Super Disintegrant

Time (Sec)	% of Drug release		
	F1	F2	F3
0	0	0	0
30	3.65	4.13	3.99
60	12.73	12.98	13.5
90	28.52	29.78	29.41
120	36.81	42.22	41.9
150	58.42	63.45	61.39
180	79.51	82.42	81.59
210	83.53	87.79	85.69
240	89.91	93.46	89.55
270	91.40	96.32	94.21
300	96.09	98.75	96.94

As concentration of CCS increased, there was a decrease in disintegration time and increases the dissolution of drug. More than 96.09 – 98.75 % drug was released from the formulations (F1 – F3) of CCS in 30, 60, 90, 120, 150, 180, 210, 240, 270 and 300 seconds respectively. Dissolution profile of formulations (F4-F6) as shown in Table-5**.** As concentration of crospovidone increased, there was a decrease in disintegration time and increases the dissolution of drug. More than 96.63 – 98.89 % drug was released from the formulations (F4 – F6) of crospovidone in 30, 60, 90, 120, 150, 180, 210, 240, 270 and 300 seconds respectively.

Table-5: Dissolution profile of tablets by using crosspovidone as super disintegrant

Time (Sec)	% of Drug release		
	F4	F5	F6
0	0	0	0
30	2.12	3.21	4.22
60	11.2	13.82	15.45
90	28.53	26.74	29.56
120	38.2	36.98	37.89
150	57.46	59.25	62.21
180	72.25	74.44	76.44
210	78.38	79.41	79.71
240	85.14	84.57	84.51
270	91.67	93.7	95.92
300	96.63	97.53	98.89

Therefore, it can be concluded that, the formulation F6 was better release pattern, was selected as the optimized formulation. Hence, Crospovidone shows higher percent drug release as compare to the CCS. The formulation was stable under accelerated conditions of temperature and humidity.

CONCLUSION

It was concluded that fast disintegrating tablets of Metformin HCl. can be successfully prepared selected super disintegrants in order to improve disintegrants/dissolution of the drug in oral cavity & hence better patient's compliance & effective therapy. Therefore, it can conclude that from our results, Crospovidone having better disintegrant properties than that of CCS.

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