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Formulation and Evaluation of Cetirizine HCl Mouth Fast Dissolving Tablets

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ABSTRACT

Mouth Fast Dissolving Tablets (MFDT's) have emerged as an alternative to conventional oral dosage forms to improve the patient compliance. Due to problem in swallowing ability with age, the pediatric and geriatric patients complain of difficulty to take conventional solid dosage forms . The MFDT's are solid dosage forms that dissolve or disintegrate rapidly in the oral cavity, which results in solution or suspension without the need of water. The main objective of this work is to formulate and evaluate Cetirizine HCl MFDT's using different concentrations of superdisintegrants like croscarmellose sodium (CCS), crospovidone (CP), sodium starch glycolate (SSG). Tablets were prepared by direct compression method and evaluated for hardness, friability, wetting time, disintegration time and percent drug release. FT-IR studies revealed that there was no interaction between Cetirizine HCl and the excipients used in the study. The results indicate that formulation prepared with 5% croscarmellose sodium was found to be optimized which provides maximum drug release (99%) and minimum disintegration time (less than 20sec). Stability studies of optimized formulation revealed that formulation is stable.

Keywords: Cetirizine HCl, Mouth Fast Dissolving Tablets, superdisintegrant.

INTRODUCTION

Tablet is most popular among all dosage forms existing today because of convenience of self administration, compactness and easy manufacturing. However, patients especially elderly find it difficulty in swallowing tablets, capsules, fluids and thus do not comply with prescription which results in high incidence of noncompliance and ineffective therapy [1]. Patient convenience and compliance oriented research has resulted in bringing out many safer and newer drug delivery systems. Mouth Fast disintegration or dissolving tablets are of such examples, for the reason of rapid disintegration or dissolution in mouth with little amount of water or even with saliva

[2-4]. Significance of this drug delivery system includes administration without water, accuracy of dosage forms, ease of portability, alternative to liquid dosage forms, ideal for pediatric and geriatric patients and rapid onset of action [5-7].

Cetirizine hydrochloride (CTZ) is an orally active and selective H1-receptor antagonist used in seasonal allergic rhinitis, perennial allergic rhinitis and chronic urticaria. CTZ is a white, crystalline water soluble drug possessing bitter taste properties. Due to sore throat conditions, the patient experiences difficulty in swallowing a tablet type of dosage form. Thus, mouth fast dissolving tablets would serve as an ideal dosage form for the patients as well as paediatric patients who find it difficult to swallow the tablet.

MATERIALS AND METHODS

Cetirizine HCl was obtained as gift sample from Aurobindo Pharma, Hyderabad. Pearlitol® SD 200, a directly compressible vehicle, Crospovidone (CP), Croscarmellose Sodium (CS), Sodium Starch Glycolate (SSG) was purchased from, Nihal traders, Hyderabad, aspartame and peppermint flavor were from Himedia, Mumbai, colloidal silicon dioxide (Aerosil®) and talc from Span Pharma Private Limited (Hyderabad, India).

Method of preparation

Mouth fast dissolving tablets (MFDT's) were prepared by direct compression method according to formula given in **Table 1**. All the ingredients were passed through mesh # 40 except magnesium stearate. Magnesium stearate was passed through mesh # 60. Drug, pearlitol SD 200 and superdisintegrant were mixed by taking small portion of each in ascending order and blended to get a uniform mixture in a mortar. The other ingredients were weighed and mixed in geometrical order and tablets were compressed using 8mm round flat punches on a Cadmach single punch machine. A batch of 100 tablets each of 200mg weight was prepared.

Evaluation of tablets [8-11]

Weight variation:

Twenty tablets were selected at random and weighed and the average weight was determined by using a digital balance. Then individual tablets were weighed and compared with the average weight. Not more than two of the individual weights deviate from the average weight by more than the 7.5 %.

Thickness Variation

Six tablets from each batch were taken randomly and their thickness was measured using Vernier Calipers. The mean ± SD values were calculated.

Hardness

Hardness or crushing strength is the force required to break a tablet in diametric compression. Hardness of the tablets is determined by Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moving along the gauze in the barrel at which the tablet fractures indicates the hardness of the tablet. Six tablets from each batch were taken randomly and their hardness was determined.

Friability:
This test is performed to evaluate the ability of a tablet to withstand abrasion in packing, handling and transporting purpose. Twenty sample tablets were rotated at 25rpm for 4 minutes by a USP-type Roche friabilator, then reweighed after removal of fines and the percentage weight loss was calculated according to the following formula. The tablets were found to pass the friability test, if the percentage weight loss was found to be less than 1%.

$$\% \text{ Friability} = (W_0 - W)/W_0 \times 100$$

Where W_0=initial weight of twenty tablets
W= weight of 20 tablets after 100 revolutions

Water Absorption Ratio (R)
A piece of tissue paper folded twice was placed in a small petri dish containing 6ml of water. The weight of the tablet prior to placement in the petri dish was noted (Wb) utilizing a Shimadzu digital balance. The wetted tablet was removed and reweighed (Wa). Water absorption ratio, R, was then determined according to the following equation.

$$R = 100 \times (Wa - Wb) / Wb$$

Where Wb and Wa were tablet weights before and after water absorption, respectively.

Wetting Time
Five circular tissue papers were placed in a Petri dish of 10 cm diameter. Ten milliliters of water containing 0.5% nigrosine, a water-soluble dye, was added to the petri dish. The dye solution was used to identify complete wetting of the tablet surface. A tablet was carefully placed on the surface of the tissue paper in the petridish at 25^0C. The time required for water to reach the upper surface of the tablets and to completely wet them was noted as the wetting time. This test was carried out in replicate of three. Wetting time was recorded using a stopwatch.

Drug content uniformity
Six prepared tablets from each batch were powdered and the blend equivalent to10 mg of cetirizine was weighted and dissolved in suitable quantity of methanol. The solution was filtered, suitably diluted and drug content was analyzed spectrophotometrically at 239 nm [12]. Each sample was analyzed in triplicate.

Mouth feel
To know mouth feel of the tablets, selected human volunteers were given placebo tablets and the taste sensation felt was evaluated.

***In Vitro* Disintegration Time**
In vitro disintegration time (DT) of the orally disintegrating tablets was determined. 10 mL of water at 25^oC was placed in a petri dish of 10 cm diameter. The tablet was then carefully positioned in the center of the petri dish and the time required for the tablet to completely disintegrate into fine particles was noted. Determination was carried out in replicates of six tablet (n=6) and mean value was recorded.

Dissolution study

Dissolution study was carried using USP Type II dissolution apparatus. Three tablets were taken from each formulation and the dissolution was carried out in pH 6.2 buffer solution as dissolution medium (pH of saliva). 5ml samples were collected at 2, 5, 10, 15 and 25 minute time intervals and after proper dilution they were analyzed at 239 nm against the blank pH 6.2 buffer solution using an Elico UV Double Beam Spectrophotometer.

Stability studies:

The optimized formulation was subjected for stability studies at accelerated conditions of a temperature 40^{o}C and a relative humidity of 75% and analyzed at 0, 10, 20 and 30 days for their physical appearance, hardness, disintegration time, wetting time and friability.

Table 1: Formulation of different batches

Ingredients	Amount (mg/tablet)												
	F_0	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Cetirizine HCl	10	10	10	10	10	10	10	10	10	10	10	10	10
Sodium starch glycolate	-	5	10	15	20	-	-	-	-	-	-	-	-
Croscarmillose sodium	-	-	-	-	-	5	10	15	20	-	-	-	-
Crospovidone	-									5	10	15	20
Pearlitol SD 200	154	149	144	139	134	149	144	139	134	149	144	139	134
Sorbitol	20	20	20	20	20	20	20	20	20	20	20	20	20
Aspartame	4	4	4	4	4	4	4	4	4	4	4	4	4
Other excipients	12	12	12	12	12	12	12	12	12	12	12	12	12

Other excipients:-Magnesium stearate -2mg, Aerosil-2mg, Talc-2mg, Flavour-6mg, Total tablet weight-200mg, Batch size-100 tablets.

Table 2: Evaluation parameters of all formulations

Parameters	Formulation Code												
	F_0	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**	**F_8**	**F_9**	**F_{10}**	**F_{11}**	**F_{12}**
Disintegration Time(sec)**	188 ±2	36 ±2	21 ±1.2	27 ±1.4	29 ±1.33	31 ±2	18 ±2.2	25 ±1.3	28 ±2.3	35 ±1.22	27 ±1.32	30 ±1.5	32 ±1.23
Water Absorption ratio (%) **	12.1	13.3	16.88	18.24	18.2	13.68	17.22	17.0	17.25	16.1	19.18	21.34	22.34
Wetting time (sec) **	176	33	21	25	28	27	18	24	22	31	22	27	28
Weight variation (%)#	200.32 ± 0.65	200.01 ± 0.91	200.03 ± 0.71	200.34 ± 0.51	199.32 ± 0.8	200.03 ± 0.61	200.13 ± 0.56	199.34 ± 0.50	199.12 ± 0.82	200.3 ± 0.90	200.11 ± 0.66	200.22 ± 0.59	199.19 ± 0.78
Thickness (mm) *	3.2 ±0.21	3.1 ±0.22	3.2 ±0.32	3.4 ±0.21	3.33 ±0.33	3.1 ±0.22	3.2 ±0.32	3.4 ±0.21	3.33 ±0.33	3.1 ±0.22	3.2 ±0.32	3.4 ±0.21	3.33 ±0.33
Hardness (Kg/cm^2)*	3.3 ±0.36	3.1 ±0.22	3.0 ±0.2	2.9 ±0.43	2.8 ±0.33	3.22 ±0.32	3.32 ±0.12	3.55 ±0.41	3.2 ±0.53	3.0 ±0.13	3.1 ±0.12	2.9 ±0.49	2.8 ±0.29
Friability (%)#	0.92	0.91	0.93	1.01	1.12	0.93	0.91	1.11	1.34	0.97	0.94	0.91	1.22
Content Uniformity (%)*	100.24 ±0.32	99.23 ±0.36	99.99 ±0.22	100.36 ±0.16	99.11 ±0.62	98.23 ±0.31	99.89 ±0.2	100.16 ±0.14	99.41 ±0.52	99.43 ±0.43	99.89 ±0.62	101.36 ±0.11	99.01 ±0.15
Taste /mouth feel*	Pala table	Pala table	Pala table	Pala Table	Pala table	Pala table	Pala table	Pala table	Pala table	Pala table	Pala table	Pala table	Pala table

**Each value was an average of six determinations, **Each value was an average of three determinations, # Each value was an average of twenty determinations*

RESULTS AND DISCUSSION

Mouth fast dissolving tablets of Cetirizine Hydrochloride were prepared by direct compression method using sodium starch glycolate, croscarmellose and crospovidone as superdisintegrants in different concentrations and Pearlitol as directly compressible diluent.

Aspartame was used to enhance palatability. Twelve formulations and a control formulation (without superdisintegrant) were prepared.

The values of different physical tests were given in **Table 2.** The tablets obtained were of uniform weight, with acceptable official limits i.e., below ± 7.5%. Drug content was found to be in the range to 99 to 102%, which is within acceptable limit. Hardness of tablet were found to be in the range of 2.8 - 3.6 Kg/ cm^2. Friability was found to be below 1% which indicates good mechanical strength of the tablets. Water absorption ratio and wetting time which are critical parameters for evaluation of performance of a MFDT's were found to be in the range of 13-22% and 16-33 sec respectively. All the formulations found to have much faster wetting time compared to the control with significant increase in the water absorption capacity.

The disintegration time (DT) for the formulations prepared with sodium starch glycolate (F_1 to F_4) was found to range from 21 to 36 sec. In case of formulations prepared with croscarmillose sodium (F_5 to F_8) the DT was found to range from 18 to 31 sec whereas prepared with crospovidone (F_9 to F_{12}) DT was found to range from 27 to 35 sec. Among all the formulations F_6 and F_2 were found to be promising as the DT was found to be 18 and 21sec, which facilitates their faster dispersion in the mouth which is subjected to further studies for optimization. From the results use of croscarmellose sodium in direct compression method resulted in hydrophilicity and swelling which in turn causes rapid disintegration. The rapid dissolution might be due to fast breakdown of particles of superdisintegrants.

Table 3: *In vitro* Drug release studies of the selected formulations

Time(Min)	**F_0**	**F_2**	**F_6**
0	0	0	0
2	1.1	5.21	5.51
5	23.45	33.74	35.42
10	42.11	67.25	67.89
15	56.91	90.41	90.11
25	68.9	96.7	98.99

In vitro drug release studies were performed on the selected formulations (F_6 and F_2) along with the control (F_0). The results were tabulated in **Table 3**. The percentage drug release for the formulations F_0, F_2 and F_6 was found to be 68.9%, 96.7% and 98.99% respectively at the end of 25 minutes. Among the two formulations F_2 and F_6, as the DT in case of F_6 is 18 sec which is less than F_2 and percent drug release is 98.99% which is more than F_2 , formulation F_6 prepared with croscarmilose sodium was found to be optimized **(Fig 1)**.

The FTIR spectrum was shown in **Figure 2** and **Figure 3**. Based on the FTIR studies, there appears to be no possibility of interaction between Cetirizine and croscarmellose sodium used in the study as no change or shifts in the characteristic peaks of drug was noticed.

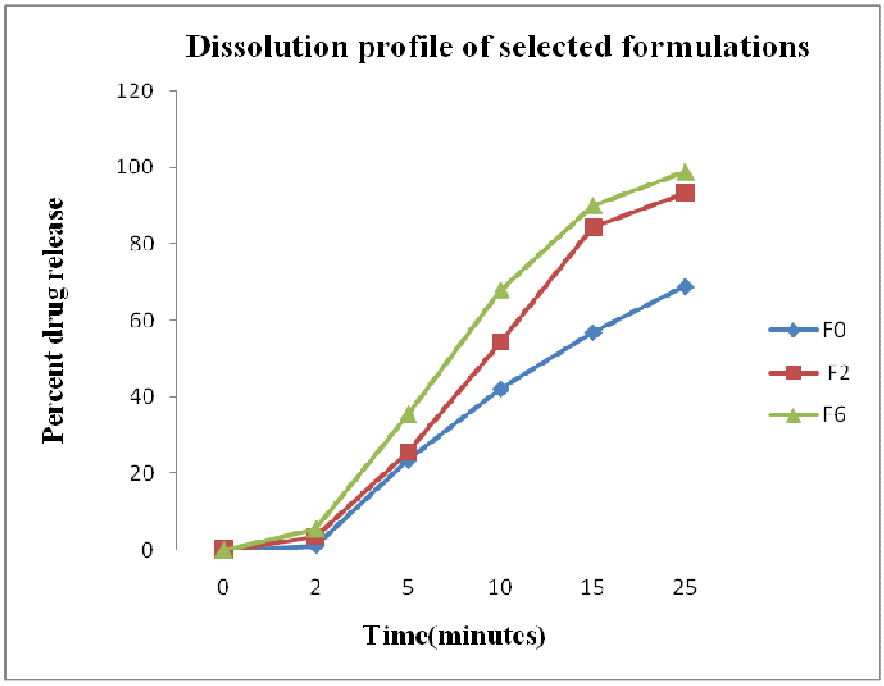

Figure 1: *In vitro* Percent Drug release vs. time profile

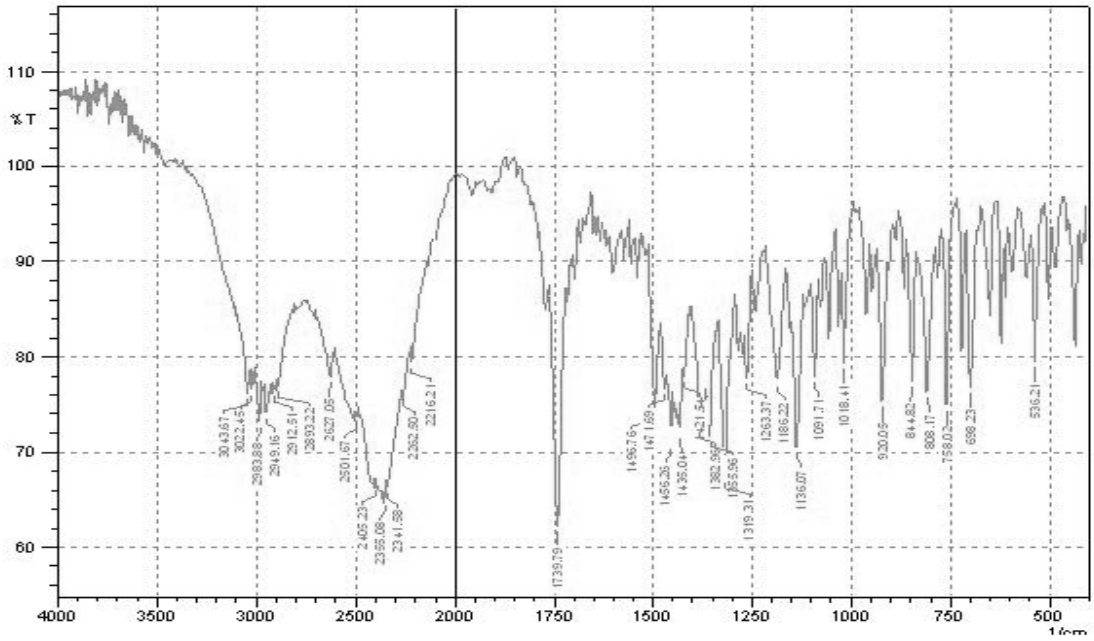

Figure 2: FT-IR spectrum of Cetirizine Hydrochloride

The stability studies of the optimized formulation (F_6) were conducted to assess its stability with respect to its physical appearance, hardness, DT, wetting time and friability. The results are given in **Table 4.** The results of the stability study indicated that the tablets showed no change in physical appearance during the study period. There were no observed differences in hardness,

DT, wetting time and friability before and after the storage period. This indicates that the optimized formulation is fairly stable.

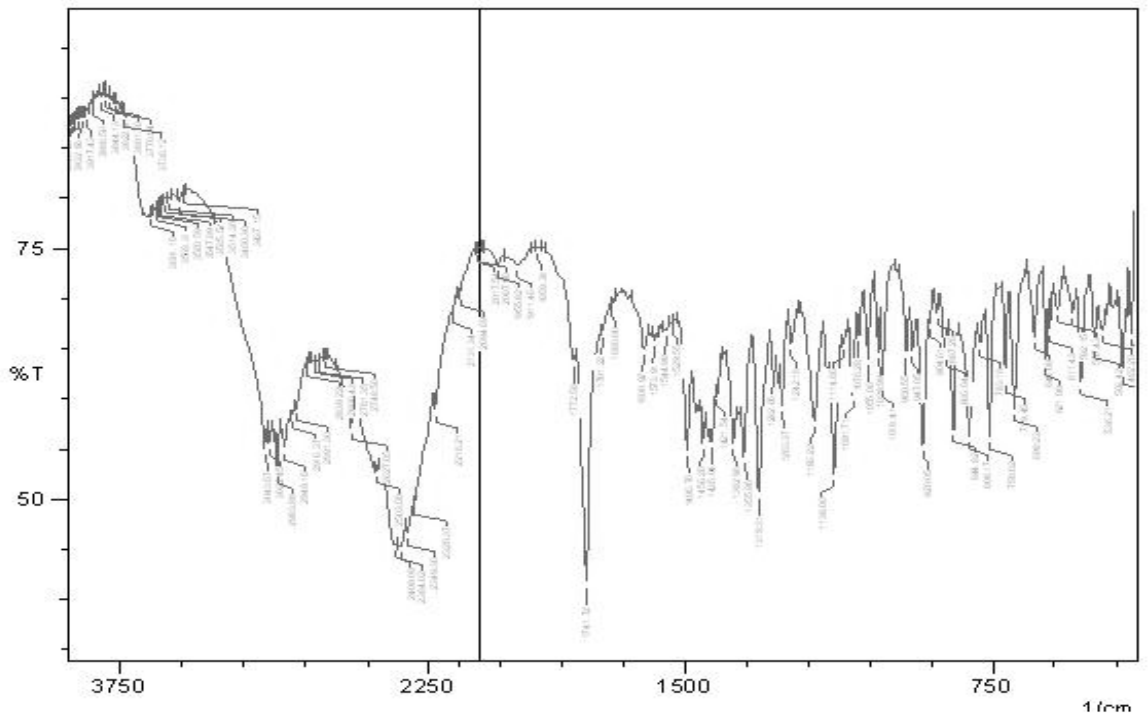

Figure 3: FT-IR spectrum of Cetirizine Hydrochloride along with Croscarmellose sodium

Table 4: Stability study of optimized formulation F_6

Tested after time (days)	Hardness (Kg/cm^2)	Disintegration Time(Sec)	Wetting Time (Sec)	Friability (%)
0	3.32 ± 0.2	18 ± 2.2	18 ± 1.4	0.31
10	3.32 ± 0.8	17 ± 1.3	18 ± 1.1	0.4
20	3.31 ± 0.6	17 ± 1.1	17 ± 0.7	0.45
30	3.0 ± 0.5	18 ± 1.13	18 ± 0.9	0.34

CONCLUSION

The prime objective of the study was to develop Cetirizine hydrochloride mouth fast dissolving tablets by using commonly available excipients and conventional technology. From the above study, it was concluded that by employing commonly available pharmaceutical excipents such as superdisintegrants, hydrophilic excipients and proper filler a mouth fast dissolving tablets of Ceterizine hydrochloride can be developed which can be commercialized.

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