VOLUME-7, ISSUE-2, FEBRUARY-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Science

Formulation and Evaluation of Mouth Dissolving Tablets of CetrizinediHCl

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ABSTRACT

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. Advantages of this drug delivery system include administration without water. Some drug are absorbed from mouth, pharynx and esophagus as the saliva passes down in to the stomach and in such cases bioavailability of drug is increased, pre-gastric absorption can result in improved bioavailability and as a result to reduce dosage form, improved reduction of unwanted effects.

KEYWORDS : CTZ, Mouth Dissolving Tablets, H1-receptor antagonist

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. 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.

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.

Mouth dissolving tablet disintegrate or dissolve in saliva and are swallowed without the need for water. They offer an advantage over swallowing tablets and capsules. Difficulty to swallow is particularly experienced by pediatric and geriatric patients. Technique that are frequently employed in the preparation of mouth dissolving tablets include, freeze drying, sublimation, spray drying, moulding, mass extrusion and direct compression.Cinnarizine is a H1-receptor antagonist that is widely used in the treatment of motion sickness, vomiting and vertigo. It is water insoluble and tasteless. Hence it was select as a model drug for the preparation of mouth dissolving tablets. In the present work effervescent, superdisintegrant addition and sublimation technique were tried for formulation of tablets. Superdisintegrant addition method was found as best and further study carried out using three superdisintegrants in different ratios [1]. Certain innovative drug delivery systems, like 'Mouth Dissolving Tablets' (MDT) have been developed. These are novel dosage forms which dissolve in saliva within a few seconds, when put on tongue. Such MDTs can be administered anywhere and anytime, without the need of waterand are thus quite suitable for children, elderly and mentally disabled patients [2]. This report summarizes the details of ingredients used in preparation of mouth dissolving tablets; conventional manufacturing techniques for mouth dissolving tablets; patented technologies for preparation of mouth dissolving tablets;evaluation of mouth dissolving tablet; and mechanism of action of mouth dissolving tablets [3].

Methods to improve patient's compliance have always attracted scientists towards the development of fancy oral drug delivery systems. Apart from the conventional methods of fabrication, this review also provides the detailed concept of some unique patented technologies like Zydis, Lyoc, Quicksolv, Orasolv, Durasolv, Flashtab, Oraquick,Wowtab and Zipletalongwith their advantages & limitatons[4].

Enormous work has been done in this field, wherein some of the researchers have developed their own methods of evaluation.In the absence of any available standardized method, the author's recommendation on critical issues in the field may be considered[5].

Material and Method

CetrizinediHCl was obtained as a gift sample from Cipla Ltd., MIDC Patalganga, Raigad, Maharashtra, India. All other ingredients such as Crospovidone (CP), Croscarmellose Sodium (CS), Sodium Starch Glycolate (SSG), Microcrystalline Cellulose (MCC) were obtained from Departmental Lab of UDCT, Dr. B.A.M. University, Aurangabad, India. All ingredients used were of analytical grade.

Fast dissolving tablets of CetrizinediHCl were prepared by direct compression method according to the formula given in Table-2. All the ingredients were weighed and kept separately. Then the weighed ingredients were mixed in geometrical order with weigh CetrizinediHCl and blend together to get uniform mixture. Then tablets were compressed using 6.5mm sizes biconvex round punch to get tablet using Compression machine.

Table 1

Ingredients	Amounts (mg/tablet)									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Cetrizine di HCl	10	10	10	10	10	10	10	10	10	10
Crospovodine	10	-	5	5	-	-	10	-	5	5
Croscarmellose Sodium	-	10	-	5	-	5	-	5	-	5
Sodium Starch Glycolate	-	-	5	-	10	5	-	5	5	-
Microcrystalline Cellulose	75	75	75	75	75	75	72	72	72	72
Saccharin	2	2	2	2	2	2	2	2	2	2
Other Excipients	3	3	3	3	3	3	6	6	6	6

Table -2: Equipment used for evaluation of CetrizinediHCl MFDT :

Sr No.	Test	Equipment
1	Weight variation	High Precision Balance
2	Hardness	Monsanto Hardness Tester
3	Thickness	Vernier Caliper
4	Friability	Roche Friabilator
5	Dissolution	USP Type II Dissolution Apparatus

Evaluation of CetrizinediHCl Mouth Dissolving Tablets

Evaluation of bulk powder :

Angle of repose

The angle of repose of granules was determined by the funnel method. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$\tan\theta = h/r$

Where h and r are the height and radius of the powder cone[1].

Bulk Density

Both loose bulk density and tapped bulk density were determined and calculated by using the following formulas.

LBD = weight of the powder / volume of the packing

Tapped Bulk Density

It is the ratio of the weight of blend to the minimum volume occupied in measuring cylinder by powder. Measuring cylinder containing the porous mass of powder was tapped using tapped density apparatus.

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. Based on the apparent bulk density and the tapped den¬sity, the percentage compressibility of the powder mix¬ture was determined by the following formula.

Carr's index (%) = [TBD-LBD] X 100 / TBD

Evaluation of tablets

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 %.

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%.

$\%\ \text{Friability} = (W0-W)/W0 \times 100$

Where W0=initial weight of twenty tablets W= weight of 05 tablets after 75 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 was added to the petri dish. A tablet was carefully placed on the surface of the tissue paper in the petridish at 250C. 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.

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 25oC 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 2 tablets.

Dissolution study

Dissolution study was carried using USP Type II dissolution apparatus. Three tablets were taken rom 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 UV Double Beam Spectrophotometer.

Result and Discussion

Pre-formulation studies :

Development of calibration curve for Cetrizinedihydrochloridethe scanning of the drug solution in the UV range showed maximum absorbance at 231 nm and hence the calibration curve was developed at this wavelength.

Pre-compression studies :

The different pre-compression tests were performed**.**All the formulations prepared by the direct compression technique showed the angle of repose less than 30^0, which reveals good flow property.

The loose bulk density and tapped bulk density for the entire formulation blend varied from 0.44 gm/cm^3 to 0.49 gm/cm^3.

Hausner ratio of entire formulation showed between 1.20 to 1.30 indicates good flow properties

The results of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 17.85% to 24.13%.

Tablet characteristics :

The values of different physical tests are given in Table 4.1. The tablets obtained were of uniform weight, with acceptable official limits i.e., below ± 7.5. Hardness of tablet were found to be in the range of 2.5 - 4.0 Kg/ cm^2. Friability was found to be below 2% 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 11-27% and 13-48 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 was found to be 36-55 sec Among all the formulations F_2, F_4 and F_9 were found to be promising 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

Calibration curve of CetrizinediHCl

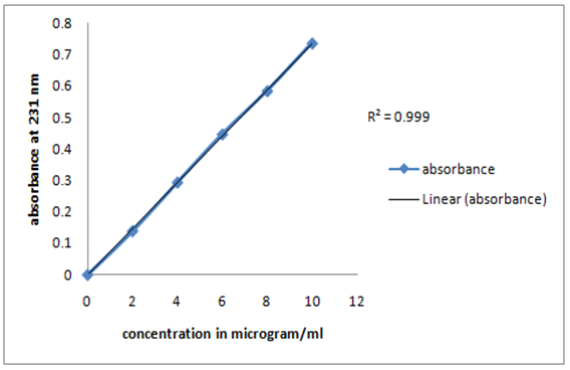

Table 4.1 :Formulation Batches

Parameters	Formulation Code									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Disintegration Time (sec)	57	37	47	27	45	46	48	55	36	40
Hardness (kg/cm^2)	2.5	2.6	3.7	2.1	3.0	4.0	2.5	3.0	3.5	3.0
Friability (%)	1.91	2.01	2.11	1.05	0.92	1.10	1.23	1.27	0.91	1.30
Wetting Time (sec)	38	36	30	35	13	18	30	25	20	28
Water Absorption Ratio (%)	11.2	14.6	11.7	18.24	12.8	13.4	12.2	10.6	13.7	11.8
Weight Variation (%)	97.4	83.8	95.4	92	93.2	107.8	101.20	102.90	100.80	105.3
Taste/ Mouth feel	Pala table	Pala Table	Pala Table	Pala Table	Pala Table	Pala Table	Pala Table	Pala Table	Pala Table	Pala table

In vitro drug release studies were performed on the selected formulations F_2, F_4 and F_9.

The results are tabulated in Table 4.2. The percentage drug release for the formulations F_2, F_4 and F_9 was found to be 88.9%, 96.3% and 89.9% respectively at the end of 25 minutes.

Table 4.2 : *In vitro* drug release of Cetirizine diHCl

Time (min)	F2	F4	F9
0	0	0	0
5	37.25	42.7	38.4
10	48.2	54.5	49.1
15	69.3	73.8	67.2
20	78.7	85.2	76.8
25	88.9	96.3	89.9

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. Orodispersible tablets of CetrizinediHcl were successfully formulated by employing direct compression method. Percentage weight variation and drug content uniformity were found to be within the approved range (Indian Pharmacopoeia Standards) for all the formulations.Wetting time parameters revealed that sodium starch glycolate, croscarmellose sodium, crospovidone alone and in combinations. This acts as superdisintegrants, reveals good results in all the formulations.

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