

Research Article

Design and Evaluation of Mouth Dissolving Tablet of Levocetirizine Hydrochloride

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Abstract: The purpose of this research work was to develop mouth-dissolving tablet of Levocetirizine hydrochloride. Tablet containing drug and excipients were prepared by direct compression method. Excipients in combinations were incorporated to achieve the aim. Effect of different combinations was studied to optimize the ideal formulation. Drug excipients interaction studies were carried out by FTIR spectral analysis. The tablets were evaluated for their hardness, wetting time, disintegrating time and dissolution parameters. It was concluded that the tablets having the combination of croscopolvidone and microcrystalline cellulose met all the evaluation parameters and thus selected as the optimized formulation. Optimized formulation was undergone for stability testing as a parameter to predict the shelf life as per ICH guidelines and proved for its adequate shelf life.

Keywords: Levocetirizine hydrochloride, Mouth dissolving tablet, Optimized formulation, ICH guidelines.

INTRODUCTION

Oral route of delivery of drugs remains to be the most convenient and preferred route for administration. This route of administration has two main challenges such as dysphagia and delivery of unpalatable drugs. To rectify these challenges, innovative drug delivery systems have been developed. Among the novel approaches, mouth dissolving drug delivery system [1] plays an important role.

Mouth dissolving tablets are the dosage forms which disperse upon contact with the mucosal surface of the oral cavity and quickly release their components without modification or need of water before swallowing [2]. Mouth dissolving tablets are preferred for people suffering from dysphagia; institutional psychiatric patients as well as hospitalised patients suffering from a variety of disorders [3] Mouth dissolving tablets [MDT] are very beneficial for patients with difficulties in swallowing and conditions where access to water is difficult.

Mouth dissolving tablets[4] can be formulated using various methods. Some of the methods involve increasing the porosity of the tablet and decreasing the disintegration time. Superdisintegrants for the manufacturing will swell or absorb water rapidly to disintegrate the tablets[5]. This type of dosage form disintegrates instantaneously and dissolves in saliva. Due to the above said reason, the drug is absorbed rapidly and may leads to greater bio availability as compared with conventional dosage system.

Levocetirizine [6], one of the non-sedative anti histamine, is an isomer of cetirizine. It is commonly used for the treatment and symptomatic relief of allergy especially for seasonal allergy. The main objective of the present work was to develop mouth dissolving Levocetirizine hydrochloride tablets by direct compression method and to study the effect of functionality differences of the different additives and their combinations used in the tablet formulation

MATERIALS AND METHODS

Materials

Levocetirizine hydrochloride was obtained as a gift sample from Metrochem Pvt. Ltd, Hyderabad; directly compressible microcrystalline cellulose, Croscopolvidone, Cross carmellose sodium were obtained from Nanhang industrial, China, Solan; Aspartame and Mannitol were obtained from Lobacheme, Bangalore. All other chemicals used were of analytical grade.

Experimental Part

Mouth dissolving tablets of Levocetirizine hydrochloride was prepared by direct compression method. Accurately weighed ingredients were finely powdered and kept separately. The weighed ingredients were mixed by the principle of geometrical order to obtain a uniform mixture. The different ratios of the mixture are represented in Table 1 and the formulations were identified as F1, F2, F3, F4, F5 and F6 respectively. Each batch of powder mixture was undergone for compression using sixteen station single rotary tableting machine (ChamundaPharma machinery

pvt. Ltd., Ahmedabad) using biconvex round punches. The obtained tablet were collected and stored in well-

closed amber coloured bottle for evaluation.

Table 1: Formulation chart for mouth dissolving tablet of Levocetirizine hydrochloride

Sl. No	Ingredients (mg/Tab)	F1	F2	F3	F4	F5	F6
1.	Levocetirizine	5	5	5	5	5	5
2.	Cross providone	40		40	20		20
3.	Cross carramellose sodium	20	40		40	20	
4.	Avicel 102		20	20		40	40
5.	Mannitol	20	20	20	20	20	20
6.	Aerosil	5	5	5	5	5	5
7.	Magnesium stearate	5	5	5	5	5	5
8.	Aspartame	3	3	3	3	3	3
9.	Flavour (peppermint)	2	2	2	2	2	2
Total weight		100	100	100	100	100	100

Evaluation of Tablets

Calibration curve

Calibration curve of Levocetirizine [7] hydrochloride in acetate buffer pH 6.8

Accurately weighed Levocetirizine was dissolved to make the solution in range of 2 to 16 μ g/mL using the buffer solution. Absorbance of each concentration was measured using U.V. Spectrophotometer (Shimadzu) at 231 nm and the absorbance was plotted against concentration of drug solution.

Compatibility studies [8]

Compatibility between the drug and the excipients were studied using Fourier Transform Infrared (FTIR) spectrophotometer (Shimadzu) using KBr disc method.

Physical characterisation [9]

The stored tablet were analysed for the different parameters such as weight variation, hardness, and percentage friability.

Wetting time [10]

This parameter is very much useful in predicting the disintegration time of the tablet. Here the tablet was placed on a filter paper that placed in a petridish containing 10 ml of water. The time taken for complete wetting of the tablet was noted and recorded.

Drug content [11]

Randomly selected five tablets from each batch were weighed and crushed to make a powder. An amount of powder equivalent to 5 mg of Levocetirizine was weighed and dissolved in a 50 ml standard flask containing buffer solution pH 6.8 and allowed to extract the contents. After 30 minutes, the solution was filtered and suitable dilutions were made. Suitably diluted solution was undergone for measuring the absorbance and the drug content was tabulated.

In-vitro disintegration time [12]

Disintegration time measures the time taken to disintegrate the tablet. Six tablets were collected in a random from each batch. Each tablet from each batch were placed in the disintegration apparatus as specified in the I P. Buffer solution pH 6.8 was used as the medium which was maintained at a temperature of 37 \pm 2 $^{\circ}$ C. The test was carried out for 30 cycles and the time was recorded.

In-vitro dissolution studies [13]

Dissolution test was carried out using dissolution apparatus USP Type-II using buffer pH 6.8 as the dissolution medium, maintained at a temperature of 37 \pm 0.5 $^{\circ}$ C. Randomly selected three tablets from each batch were taken for the evaluation. Aliquot amount of solution was withdrawn in every 5 minutes. The filtered solution was analysed for the drug concentration by measuring absorbance at 231nm using U.V Spectrophotometer. The measured absorbance was tabulated and the amount of drug present was recorded.

Stability studies [14]

Accelerated stability studies were carried out for the optimized formulation in predicting the shelf life. The study was carried out by ICH guidelines at a temperature 40 $^{\circ}$ C/75%RH.

RESULTS AND DISCUSSION

Direct compression method was utilized here for the manufacturing of mouth dissolving tablet of Levocetirizine hydrochloride. Different batches of tablets were manufactured using different combination of superdisintegrants. Primary evaluation tests of the tablets were carried out and from the results, it is clear that the technique adopted is suitable of the process.

Compatibility studies were carried out to study the chemical interaction between drug and the excipients. After interpreting the FTIR spectra, there was no interaction observed for the drug while combining with the excipients. From the FTIR spectral analysis, the drug is compatible with the excipients.

The prepared tablets were taken for hardness evaluation using Monsanto Hardness tester. From the results, the hardness of the tablets were found in the range of 3.5kg/cm² to 4.00kg/cm², proved for its adequate strength. Weight variation test performed for each tablet and the obtained report showed that the tablets having the weights in the range of 95 to 105 mg. All the tablets passed the weight variation test as the average percentage weight variation within the limit of IP standards.

Thicknesses of the tablet were measured and the obtained report proved that all the tablet having

uniform thickness. Wetting time is closely related to the inner structure of the tablet. The wetting time of the prepared formulation were found in the range of 20 to 40 seconds. The formulation F6 showed the wetting time 20 second that facilitates faster dispersion in the mouth. Drug content of the prepared tablets were carried out for all the batches. The samples were analysed and the percentage drug content were found out. The report reveals the drug content in the range of 95.83±0.26% to 98.98±0.38% of the Levocetizine hydrochloride. The various results are reported in Table 2.

Table 2: Various physical parameters of the mouth dissolving tablets of Levocetizine Hydrochloride

Sl. No	Evaluation Parameters	Formulation Identity					
		F1	F2	F3	F4	F5	F6
1.	Thickness * (mm)	1.63 ± 0.26	1.38 ± 0.3	1.56 ± 0.18	1.62 ± 0.26	1.68 ± 0.18	1.86 ± 0.21
2.	Weight variation*(mg)	100.52 ±0.21	98.32 ±0.18	95.56 ± 0.21	100.13 ±0.21	98.53 ±0.11	98.6 ±1.63
3.	Friability* (%)	0.51 ± 0.13	0.52 ±0.26	0.62 ±0.21	0.68 ±0.19	0.53 ±0.20	0.52 ±0.26
4.	Hardness* (kg/cm ²)	3.5 ± 0.13	3.2 ±0.21	4.0 ±0.21	3.2 ± 0.16	3.4 ± 0.21	3.6 ± 0.18
5.	Wetting time* (sec)	24.6 ±0.21	40.4 ±0.28	39.6 ±0.18	27.3 ±0.21	22.5 ±0.19	20.3 ±0.19
6.	Disintegration* (sec)	67.12 ±0.18	72.36 ±0.26	26.48 ±0.16	35.32 ±0.26	46.45 ±0.28	25.02 ±0.26
7.	Drug content* (%)	95.83 ±0.26	96.26 ±0.16	97.38 ±0.23	96.56 ±0.28	97.11 ±0.26	98.98 ±0.38

* n=3 observations ± SD

In-vitro disintegration time is measured by the time taken to undergo complete disintegration. Rapid and uniform disintegration of tablets were observed in all the formulations. The report shows the disintegration time for all the formulations in the range of 25 to 72 seconds fulfilling the official standards. Based on the *in-vitro* disintegration time, the formulation with the combination of microcrystalline cellulose and crosspovidone (F6) showed a fast disintegration time of 25 second. Thus the formulation can be selected as the ideal formulation.

In-vitro dissolution studies were also carried out to optimise the ideal formulation. Test was carried out by USP Type II apparatus. The dissolution of Levocetizine hydrochloride from the tablet is recorded in Table 3 and the corresponding plots are represented in Figure.No.1.From the parameters the formulation F6 showed good release profile for the time specified and selected as the ideal formulation. The uniformity in the release profile may be due to the presence of super disintegrants in the correct ratio for the formulation. Thus it is selected as the ideal formulation.

Table 3: *In-vitro* dissolution profile of Levocetizine mouth dissolving tablets

Sl. No.	Time (min.)	Percentage Cumulative Drug Release*					
		F1	F2	F3	F4	F5	F6
1.	0	0	0	0	0	0	0
2.	5	26.46±0.12	30.56±0.13	20.11±0.14	28.56±0.09	19.56±0.08	39.46±0.12
3.	10	39.86±0.09	48.32±0.11	39.56±0.21	40.28±0.15	48.28±0.13	67.53±0.16
4.	15	59.53±0.14	62.83±0.14	54.13±0.07	63.88±0.19	70.56±0.14	86.56±0.14
5.	20	73.66±0.18	79.56±0.09	70.56±0.15	86.29±0.21	84.16±0.17	97.63±0.15
6.	25	89.81±0.07	85.58±0.11	85.16±0.21	96.73±0.14	94.38±0.07	98.92±0.12
7.	30	96.63±0.11	97.56±0.17	96.52±0.11	97.56±0.11	95.26±0.12	98.92±0.09

* n=3 observations ± SD

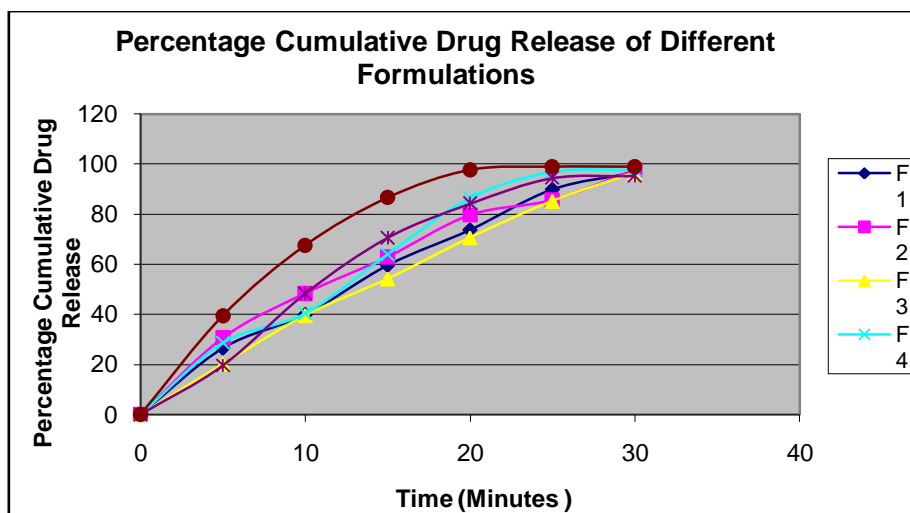


Figure 1: Percentage cumulative drug release from different formulations

Stability study for the optimized formulation was carried out for a period of 30 days at 40°C/75% RH according to ICH guidelines, in predicting the shelf life of the formulation. Physical appearance and drug content of the formulation were studied during this

period. From the results, it was found that the ideal formulation does not have major degradation and can be predicted for a good shelf life. The obtained results were tabulated in Table 4.

Table 4: Stability testing parameters of the optimised formulation

Time(days)	Physical appearance	Drug content*(%)
0	Good	98.56± 0.18
15	Good	98.26 ±0.26
30	Good	98.13 ±0.51

* n=3 observations ± SD

CONCLUSION

Mouth dissolving tablets of Levocetirizine hydrochloride were successfully developed by direct compression method. All the physical parameters were found within the approved range. *In-vitro* disintegration and dissolution parameters revealed that the excipients are suitable for the manufacture of mouth dissolving tablet. Among this, the formulation denoted as F6 exhibited 98.92% of drug release within 25 minutes and showed low disintegration time. Thus formulation F6 was found as the ideal formulation, have the combination of Crosspovidone and Microcrystalline cellulose. Accelerated stability studies were carried out for the optimized formulation to predict the shelf life. The formulation exhibited no change for its physical appearance and drug content. From the above findings the formulation F6 selected as ideal formulation that having the combination of Crosspovidone and Microcrystalline cellulose with the drug utilized for the release of Levocetirizine hydrochloride as mouth dissolving tablet.

ACKNOWLEDGEMENT

We thank the Director and Principal, JamiaSalafiya Pharmacy College, Pulikkal for the timely support to carry out this work in a successful manner.

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