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Formulation and evaluation of mouth dissolving anti-allergic tablets of levocetrizine dihydrochloride

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ABSTRACT

The purpose of the research was to develop oral fast dissolving tablet of levocetrizine dihydrochloride. Oral fast dissolving tablet offer a solution for pediatrics, geriatrics; psychiatric or mentally ill people and those have difficulty in swallowing tablets/capsules resulting in improved patient compliance. So, mouth dissolving drug delivery systems (MDTs) have acquired an important position in the market by overcoming previously encountered administration problems and contributing to extention of patient life. MDTs have the ability of fast disintegrating and/or dissolving and releasing the drug as soon as they come in contact with saliva, thus avoiding the use of water in intake of dosage form. The aim is to formulate five formulation with increasing concentration of superdisintegrants by wet granulation method.

Keywords: Anti-allergic, Crosspovidone, MDTs, Superdisintegrants, MDDS, Dysphagia.

INTRODUCTION

Mouth dissolving drug delivery systems (MDDDS) are a new generation of formulations which combine the advantages of both liquid and conventional tablet formulations, and at the same time, offer added advantages over both the traditional dosage forms. They provide the convenience of a tablet formulation and also allow the ease of swallowing provided by a liquid formulation. MDDDS offer the luxury of much more accurate dosing than the primary alternative, oral liquids. This segment of formulation is especially designed for dysphagic, geriatric, pediatric, bed-ridden, travelling and psychotic patients who are unable to swallow or refuse to swallow conventional oral formulations [1-3].

Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva [4]. As they dissolve/disintegrate very fast when placed in the mouth, MDDDS are the most convenient dosage forms for dysphagic, pediatric and geriatric patients with swallowing problem. They do not require water for administration, thus are good alternative for travellers and for bed ridden patients. They simply vanish when placed in the mouth, so cannot be hidden in mouth by psychotic patients. These products not only increase the patient's compliance but also fetch large revenues to manufacturers due to line extension of the existing formulation.

In the recent past, several new advanced technologies have been introduced for the formulation of mouth dissolving tablets (MDTs) with very interesting features, like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients. The technologies utilized for fabrication of MDDDS include lyophilization [5], moulding [6], direct compression [7], cotton candy process [8], spray drying [9], sublimation [10], mass extrusion [11], nanonization [12] and quick dissolve film formation [13]. These techniques are based on the principles of increasing porosity and/or addition of superdisintegrants and water soluble excipients in the tablets. The formulations prepared from these techniques differ from each other on the basis of the factors like mechanical strength of final product, drug and dosage form stability, mouth feel, taste, rate of dissolution of the formulation in saliva, rate of absorption from saliva and overall drug bioavailability.

Levocetirizine dihydrochloride, is an orally active H1-receptor antagonist. The chemical name is (R)-[2-[4-[(4-chlorophenyl) phenylmethyl]-1-piperazinyl] ethoxy] acetic acid dihydrochloride. Levocetirizine dihydrochloride is the R enantiomer of cetirizine hydrochloride, a racemic compound with antihistaminic properties. The empirical formula of levocetirizine dihydrochloride is $C_{21}H_{25}ClN_2O_3$•2HCl. The molecular weight is 461.82 [14]. It does not prevent the actual release of histamine from mast cells, but prevents it binding to its receptors. Thus it prevents the release of other allergy chemicals and increased blood supply to the area, and provides relief from the typical symptoms of hay fever [15].

EXPERIMENTAL SECTION

Levocetrizine Dihydrochloride, MCC, Sachharin sodium, Magnesium stearate & all other chemicals was obtained from Morepen labs ltd ,Parwanoo(HP). All other chemicals and reagent were of analytical grade.

Formulation of MDTs

Five formulations were prepared by wet granulation method [16] using superdisintegrant such Crospovidone. API and all excipients were passed through sieve no.60 before granulation and lubrication. The required quantity of API and other excipients (except lubricants and glidants) were weighed and mixed uniformly. Then the mixture was made to a damp mass using starch paste. Then the prepared mass was passed through sieve no. 16. The prepared granules were dried in an oven at a temperature of 50oC for one hour. The granules obtained were lubricated by adding and mixing with talc, magnesium stearate and colloidal silicon dioxide. The lubricated

granules were evaluated and punched into tablets with an average weight of 200 mg, using 16 stations tabletting machine.

Table 1: Formulation of mouth dissolving tablets

Ingredient/per tablet(mg)	F1	F2	F3	F4	F5
Levocetrizine dihydrochloride	5	5	5	5	5
MCC	63	63	63	63	63
Sachharin Sodium	1	1	1	1	1
Starch paste	12	12	12	12	12
Magnesium stearate	2	2	2	2	2
Talc	1	1	1	1	1
Cab-o-sil	1	1	1	1	1
Crosspovidone	2	4	6	8	10
Mannitol upto	200	200	200	200	200

Table-2 Evaluation of lubricated granules of levocetrizine dihydrochloride

Batch	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Hausner ratio	Carr's index (%)	Angle of repose (θ)
F1	0.357	0.363	1.016	1.65	31.47
F2	0.344	0.354	1.029	2.82	31.13
F3	0.350	0.358	1.022	2.23	30.25
F4	0.370	0.387	1.045	4.39	31.47
F5	0.348	0.358	1.028	2.79	30.25

Evaluation of tablets

All the compressed tablets were evaluated for the following parameters. The results were shown in (Table 2-3)

Thickness: The thickness of the tablets was measured by using digital vernier calipers [17].

Uniformity of weight: 20 tablets were weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it was within permissible limits or not [17].

Hardness: Hardness of the tablet was determined using the Monsanto hardness tester [17].

Friability test: Tablets were preweighted placed in the apparatus, which was given 100 revolutions and the tablets were reweighed [17].

$$\text{Percentage friability} = \frac{\text{Initial weight-Final weight}}{\text{Initial weight}} \times 100$$

Drug content: 20 tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 5 mg of levocetrizine dihydrochloride was transferred into a 100 ml standard flask and volume was made up with methanol upto 50 ml. Further 5ml of the above

solution was diluted to 50 ml with methanol and absorbance of the resulting solution was observed at 231nm [17].

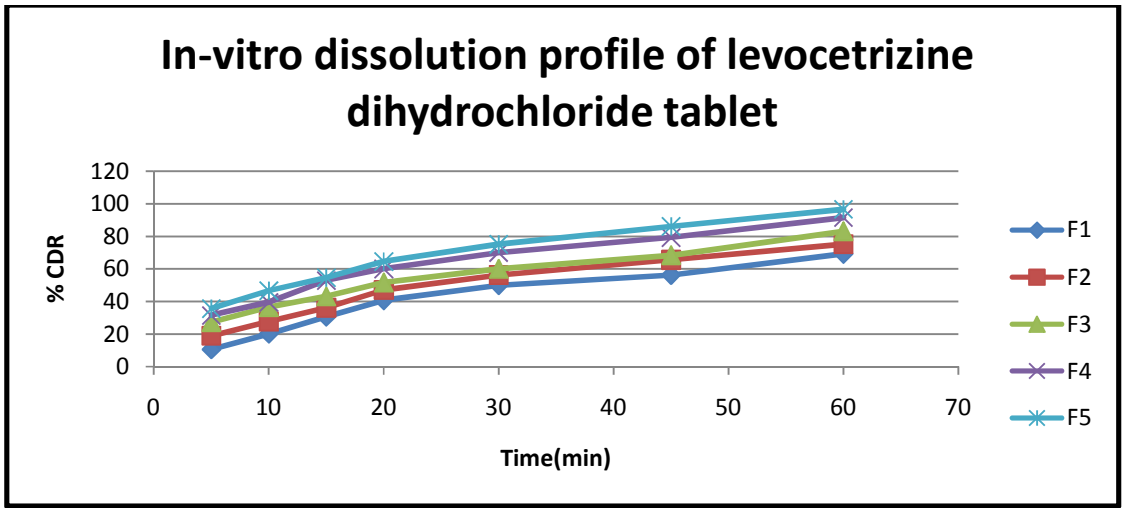
Disintegration test: Fast dissolving tablets should disintegrate within 3 mts. 6 tablets of each formulation were taken and placed in 6 tubes of disintegration apparatus. The time taken for complete disintegration was noted [17].

***In- vitro* dissolution studies:**The dissolution test [18] has been carried out for all the formulations. The in vitro drug release is performed using USP dissolution apparatus- II, 24 type paddle apparatus using 900 ml of 0.1 N HCL at paddle rotation of 50 rpm at 37±0.5ºC. 5 ml of the samples were withdrawn at predetermined time intervals of 5, 10, 15, 20, 30, 45, 60 mins for a period of 60 mins and replaced with the fresh medium of 0.1 N HCL. The samples were filtered through 0.45 mm membrane filter, suitably diluted and analyzed at 231 nm using double beam UV/Visible spectrophotometer. The content of drug was calculated.

RESULTS AND DISCUSSION

The lubricated granules parameters were satisfactory and showed good flowability. With this the granules were found to be free flowing material and showed suitability to be compressed as tablets of expected weight. Thickness ranged from 5.18 – 5.22 mm. Hardness was observed to be within the limit in the range of 4.3 – 4.5 kg/cm^2 Friability was observed between percent 0.40 – 0.65 % w/w hence within the limit of > 1%. The results of drug content for all formulations were found to be between 95 % – 101.0 % hence within the IP limit of 85.0 % -115.0 %.

Figure 1: In-vitro dissolution profile of levocetrizine dihydrochloride tablet



Disintegration time was found to be between 27 -123 seconds.The recommended limit for fast dissolving tablets is that it should disintegrate within 3 minutes. Therefore, all formulations are within this limit and pass the test. F-5 shows fast disintegration time of 27 seconds.

In vitro dissolution test reveals the release increases from 69.24% to a maximum of almost 96.52%. The maximum *in vitro* dissolution was found to be with formulation F-5 was found to contain maximum in vitro dissolution of 96.52%. Hence increases in concentration of crospovidone accounts for rapid drug release.

Table 3: Evaluation of levocetrizine dihydrochloride MDTS

Batch	Thickness (mm)	Hardness (kg/cm^2)	Drug content(mg)	Disintegration Time(sec)	Friablity (%w/w)	% CDR
F1	5.22	4.5	5.01	123	0.54	69.24
F2	5.19	4.4	5.08	90	0.59	75.11
F3	5.20	4.5	4.94	73	0.40	83.09
F4	05.22	4.4	5.03	52	0.65	91.48
F5	5.18	4.3	4.98	27	0.54	96.52

CONCLUSION

The results have shown that increase in the concentration of Crospovidone as a superdisintegrant (F1 to F5) shows results of fastest disintegration (27 secs) and maximum drug release (96.52%) within 60 minutes, when compared with other formulations.

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