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RESEARCH PAPER

FORMULATION AND EVALUATION OF TASTE MASKED ORODISPERSIBLE TABLET OF LEVOCETIRIZINE DIHYDROCHLORIDE

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The objective of present investigation was to prepare and evaluate taste masked orodispersible tablet of levocetirizine dihydrochloride using superdisintegrants crospovidone and sodium starch glycolate for the treatment of allergic rhinitis. The taste masking technique employed was ion-exchange resin whereas tableting was done using direct compression method. Prepared tablets were evaluated for weight variation, hardness, friability, content uniformity, wetting time, *in vitro* disintegration time, water absorption ratio and stability studies. Among developed formulations, disintegration time was found to be rapid in F4 formulation. The *in vitro* dissolution studies showed that F4 formulation released 99.73% of drug in 10 min. Moreover, F4 formulation was found to be stable and retained its original properties during the testing period.

Key words: Levocetirizine dihydrochloride, Orodispersible tablet, Direct compression, Superdisintegrant

INTRODUCTION

Oral route is the most preferred route of administration of drugs because of accurate dosage, self medication, low cost and ease of administration leading to high level of patient compliance. Many tablets and capsules are administered through a glass of water which may be inconvenient for some geriatric patients because of changes in various physiological and neurological conditions associated with aging including difficulty in swallowing or dysphagia, hand tremors etc (Hirani *et al* 2009; Desale *et al* 2011; Divate *et al* 2011; Mangal *et al* 2012). Solid dosage forms also present significant administration challenges in children, mentally challenged and uncooperative patients. Moreover, patients travelling with little or no access to water, limit utility to orally administered conventional tablets or capsules. Therefore, to fulfill the needs of such patients, recent advancements in technology have resulted in development of viable dosage alternative popularly known as orally disintegrating tablet (ODTs) which disintegrates tablet in mouth without water and in few seconds. The mouth dissolving tablet formulation is defined by the food and drug administration (FDA) as "A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue" (Garg and Gupta, 2013). Oral route of drug administration have wide acceptance upto 50-60% of total dosage forms (Bhowmik *et al* 2009). Sometimes people experience inconvenience in swallowing conventional dosage forms such as tablets when water is not available in the case of motion sickness (kinetosis) and the sudden episodes of coughing during the common cold, allergic conditions and bronchitis That's why tablets which can rapidly disintegrate in oral cavity have attracted great deal of attention.

Much work has been reviewed (Yadav *et al* 2014) and reported on mouth dissolving and orodispersible tablets for better therapeutic benefits as well as patient compliance (Dahiya *et al* 2011; Bhatere *et al* 2012; Bhimavarapu *et al* 2012; Prusty, 2014). Keeping in view the growing demand of orodispersible tablets, the present work was directed toward formulation development of levocetirizine dihydrochloride.

MATERIALS AND METHODS

Materials

Levocetirizine dihydrochloride was purchased from Paranami Drug Pvt Ltd. (Gujarat), Kyron T-134 was purchased from Corel Pharmaceuticals Ltd. (Gujarat), Colloidal silicon dioxide and talc were obtained from Signet Chemicals Corporation (Mumbai), sodium starch glycolate (SSG) was purchased from Accent Micro Chem. Ltd. (Gujarat), Crospovidone was purchased from Triveni Interchem Pvt. Ltd. (Gujarat), Microcrystalline cellulose was purchased from Albert David Ltd. (Gujarat).

Preparation and optimization of drug resin complex

Preparation of drug resin complex by batch method

The resins were first washed with distilled water till neutralization. Three hundred milligrams of resin was placed in a beaker containing 25 ml of deionised water and allowed to swell for 90 min. The pH of the resin solution was adjusted to 6.5 to 7.0 by using 1 M KOH solution then accurately weighed 100 mg of levocetirizine dihydrochloride was added to the resin solution and stirred for 2-3 h. During stirring, pH of the DRC was checked frequently and adjusted to 6.5 to 7.0 by using 1 M KOH solution. Then the mixture was filtered through whatman filter paper no. 41 and residue was washed with 75 ml of deionised water and put it for drying at 60°C for 3-4 h in oven (Sharma and Singh, 2011).

Optimization of drug resin complex (DRC)

Taste masking was done by complexing levocetirizine dihydrochloride with Kyron T-134 in different ratios 1:1, 1:2, 1:3, 1:4. Drug-resin complex were optimized by considering parameters such as optimization of resin concentration, optimization of swelling time, optimization of pH and optimization of temperature on maximum drug loading. The effects of variables were observed on maximum amount of the drug loading.

During preparation of drug resin complex (resinate), the other variables were kept constant. Resinate was evaluated for taste masking, thus results conclusively demonstrated successful masking of taste and rapid disintegration of the formulated tablets in the oral cavity (Gupta *et al* 2010).

Formulation of orodispersible tablet by direct compression method

Already prepared DRC along with other excipients put in rapid mix granulator and mixed for 10 min. (dry mix). Purified water was added and mixed for approx. 30 min. (wet mix), granules were formed. Wet granules were passed through multimill which was fitted with 10 sieve no. after then the wet granules were put in fluidized bed dryer and dried for 5 minutes at temperature of 60°C. Now granules were dried and dried granules passed from sieve no. 40 and sizing was done through cadmill using screen of 1.0 mm at slow speed. All the ingredients pass through sieve number 40 and blending was performed through rotacube mixer. All the five batches were prepared by direct compression method using single punch machine. The hardness of the tablet of each batch were tried to keep constant (2.4 kg/cm^2). The weight of the tablet of each batch was adjusted to 135 mg.

Evaluation of orodispersible tablets

The tablet was evaluated for its weight variation, friability, disintegration time**.** Dissolution study of tablets was carried out in simulated gastric fluid (Sharma and Chopra, 2012).

RESULTS AND DISCUSSION

In this research work, with levocetirizine dihydrochloride, drug resin concentration in 1:3 ratio showed maximum drug loading (**Table 1**).

Table 1. Effect of resin concentration on % drug loading method (n=3)

Resin	Drug + Resin ratio	% of drug loading (±S.D.)
Kyron T-134	1:1	79.15 ± 0.74
	1:2	86.37 ± 0.41
	1:3	92.12 ± 0.70
	1:4	91.09 ± 0.69

If further increase the resin concentration (1:4) leads to the saturation of complex formation therefore resin ratio (1:3) was selected as optimized batch. Among all the formulations, batch F4 showed least disintegration time and wetting time and maximum water absorption ratio therefore batch F4 was selected as optimized batch (**Table 2**).

Table 2. Evaluation of ODT

Formulation (±S.D.)	F1	F2	F3	F4	F5
Thickness (mm)	2.9 ±0.00	2.9±0.01	2.9± 0.04	2.9± 0.03	2.9 ± 0.02
Hardness (kg/cm²)	2.9 ± 0.119	2.6 ± 0.937	2.5 ± 0.856	2.4 ± 0.178	2.6 ± 0.763
Friability (%)	0.21 ± 0.511	0.27 ± 0.632	0.24 ± 0.705	0.18 ± 0.732	0.16 ±0.176
Weight variation	passes	passes	passes	passes	passes
Disintegration time (sec)	37 ± 0.773	35 ± 0.752	30 ± 0.731	25 ± 0.765	42 ± 0.653
Wetting time (sec)	24 ± 0.579	23 ± 0.374	21 ± 0.552	20 ± 0.413	28 ± 0.118
Water absorption ratio (%)	75.15 ± 0.41	75.93 ± 0.70	78.47 ± 0.54	87.12 ± 0.76	75.10 ± 0.31
Uniformity of drug content (%)	89.94 ± 0.85	95.11 ± 0.55	97.14 ± 0.70	98.97 ± 0.76	95.71 ± 0.39

Formulation F4 has the maximum *in vitro* drug release in 10 min as shown in **Figure 1** and **Table 3**.

The time intensity study for taste in human volunteers of the drug, DRC (Drug resin complex) showed that the degree of bitterness ultimately reaching to 0+ within 3 min which showed the palatability of the formulation concluding that the bitter taste of formulation has been successfully masked (**Table 4**).

Table 3. *In vitro* drug release data of five formulations

S. No.	Time (in min)	Cumulative % drug release				
		F1	F2	F3	F4	F5
1.	0	0	0	0	0	0
2.	1	55.567 ± 0.323	56.322 ± 0.473	59.631 ± 0.704	60.115 ± 0.793	61.763 ± 0.993
3.	2	65.965 ± 0.931	67.208 ± 0.734	70.131 ± 0.770	70.966 ± 0.543	69.611 ± 0.096
4.	3	78.516 ± 0.605	80.365 ± 0.119	80.216 ± 0.742	82.742 ± 0.563	80.745 ± 0.631
5.	4	81.330 ± 0.664	82.773 ± 0.867	85.117 ± 0.749	85.007± 1.587	86.752 ± 0.119
6.	5	84.085 ±0.194	84.324 ± 0.650	88.472 ± 0.943	89.801 ± 0.332	88.733 ± 0.864
7.	6	90.137 ± 0.421	92.333 ± 0.712	94.876 ± 0.417	95.519 ± 0.543	92.886 ± 0.385
8.	7	92.395 ± 0.528	93.121 ± 0.488	95.186 ± 0.435	96.831 ± 0.507	93.408 ± 0.411
9.	8	93.581 ± 0.256	95.067 ± 0.579	97.993 ± 0.701	98.430 ± 0.365	94.865 ± 0.710
10.	10	94.414 ± 0.791	96.743 ± 0.406	98.116 ± 0.862	99.732 ± 0.110	97.122 ± 0.830

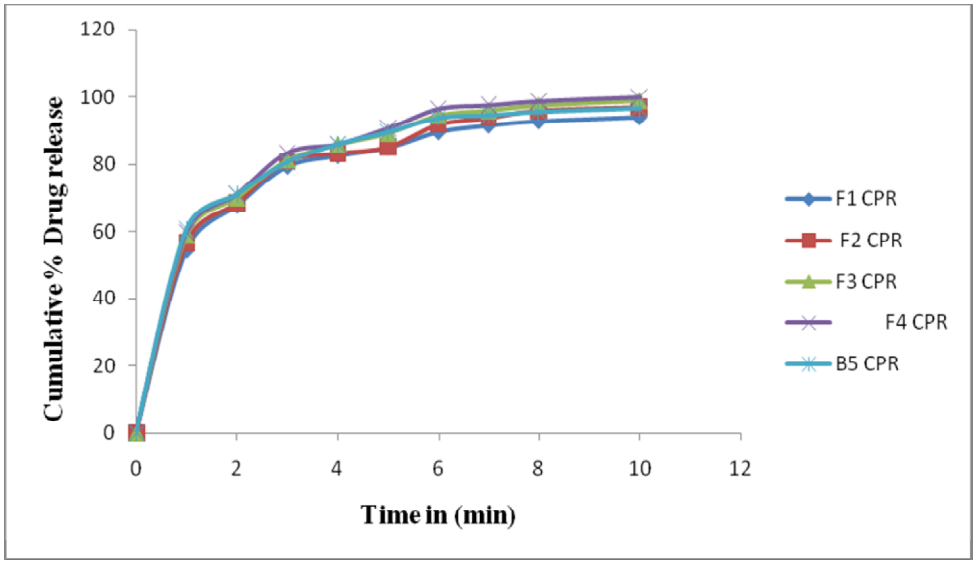

Fig. 1. *In vitro* drug release profile of all formulations

Table 4. Taste evaluation of ODT

Formulation of levocetirizine dihydrochloride	Degree of bitterness after time			
	10 sec	1 min	2 min	3 min
Pure drug	0.5	3	3	3
DRC	0	0	0.5	0.5
FDT	0+	0+	0+	0+

CONCLUSION

It was concluded that sodium starch glycolate at 3.5 % and crospovidone at 5 % concentration can be successfully employed to obtain the orodispersible tablets of levocetirizine dihydrochloride with desired properties.

REFERENCES

Bhatere D, Rathore D, Dahima R. Formulation development of mouth dissolving tablets of a poorly water soluble drug using sublimation technique. *Bull. Pharm. Res.* 2012; 2(1):5-9.

Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: An overview. *J. Chem. Pharm. Res.* 2009;1(1):163-77.

Bhimavarapu R, Chitra KP, Kanikanti D, Anne M, Meda H, Gowthami N. Effect of disintegrants on *in vitro* release of fenofibrate oro-dissolving tablets. *Bull. Pharm. Res.* 2012;2(1):10-4.

Dahiya S, Asati S, Mallurwar V. Formulation and evaluation of granisetron hydrochloride orodispersible tablets. *Bull. Pharm. Res.* 2011;1(2):41-6.

Desale KY, Bankar VH, Gaikwad PD, Pawar SP. Review on: Fast dissolving/disintegrating tablets. *Int. J. Pharm. Sci. Rev. Res.* 2011;11(1):152-8.

Divate S, Kavitha K, Sockan GN. Fast disintegrating tablets - An emerging trend. *Int. J. Pharm. Sci. Rev. Res.* 2011; 6(2): 18-22.

Garg A, Gupta MM. Mouth dissolving tablets: A review. *J. Drug. Deliv. Ther.* 2013;3(2):207-14.

Gupta A, Mishra AK, Gupta V, Bansal P, Singh R, Singh AK. Recent trends of fast dissolving tablet – An overview of formulation technology. *Int. J. Pharm. Biol. Arch.* 2010; 1(1):1-10.

Hirani JJ, Rathod DA, Vadalia KR. Orally disintegrating tablets: A review. *Trop. J. Pharm. Res.* 2009;8(2): 161-72.

Mangal M, Thakur N, Bansal R, Thakral S, Goswami M. Fast dissolving tablet: An approach for emergency treatment. *Int. J. Res. Ayur. Pharm.* 2012;3(3):377-80.

Prusty A. Formulation and in-vitro evaluation of amlodipine besylate HP-β-CD inclusion complex incorporated mouth dissolving tablets. *Bull. Pharm. Res.* 2014;4(3):124-8

Sharma V, Chopra H. Formulation and evaluation of taste masked mouth dissolving tablets of levocetirizine hydrochloride. *Iran. J. Pharm. Res.* 2012;11(2):457-63.

Sharma V, Singh L. Ion-exchange resins: A boon for pharmaceutical industry - An overview. *Int. J. Pharm. Sci. Rev. Res.* 2011;6(1):10-3.

Yadav AK, Sharma A, Saxena S, Kesarwani A. Mouth dissolving tablets: General overview and formulation aspects. *Bull. Pharm. Res.* 2014;4(1):43-57.

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