Research Article

EXPLORING THE TASTE MASKING EFFECT OF ION EXCHANGE RESINS IN ORODISPERSIBLE TABLETS OF LEVOCETIRIZINE HYDROCHLORIDE

K. Sampath Kumar ^{*1}, M. Ravindra Babu ², A.B. Sravani ³, D. Maheswara Reddy ¹, V. Vijay Kumar ¹

¹Assistant Professor, Santhiram College of Pharmacy, Nandyal, Kurnool (Dt), Andhra Pradesh, India

²Assistant Professor, Sree Vidyanikethan College of Pharmacy, Tirupati, Andhra Pradesh, India

³Assistant Professor, Creative Educational Society's College of Pharmacy, Kurnool, Andhra Pradesh, India

*Corresponding Author Email: sampathkatakam@gmail.com

Article Received on: 13/11/18 Approved for publication: 14/01/19

DOI: 10.7897/2230-8407.100127

ABSTRACT

The concept of formulating Orodispersible tablets containing Levocetirizine hydrochloride offers a suitable, practical approach to achieve fast release of the drug. Absorption of these tablets takes place direct into the systemic circulation which avoids the hepatic first pass metabolism of Levocetirizine hydrochloride which ultimately results in the improvement in the bioavailability. In the present study ODT tablets of Levocetirizine HCl were prepared by using different super disintegrants like cross povidone, starch 1500, MCC 102. Nine formulations were designed, using higher and lower level of super disintegrants and employing two and three super disintegrants at a time. In the FTIR studies, it was concluded that there was no interaction between drug and super disintegrants used in formulation. Formulation LF9 which consisted of 16.25 mg of Levocetirizine ionex complex, 7 mg of MCC 102, 4 mg of polyplasdone XL 10 and 67.88 mg of mannitol SD 100 showed better taste masking property with immediate disintegration and drug release.

Keywords: Orodispersible tablets, Levocetirizine hydrochloride, superdisintegrants.

INTRODUCTION

Many conventional drug delivery systems provide a provision for many drugs to release rapidly at the site of action through oral route. These immediate release products attain quick onset of action followed by rapid bioavailability which in turn shows the Pharmacodynamic actions. Tablets and capsules are the most widely used oral dosage forms among the human population because of its convenience in terms of self administration, pain avoidance, compactness and ease of handling. But one of the important drawbacks with this kind of dosage forms is dysphasia or difficulty in swallowing among all age groups¹. The size, surface and taste of the dosage forms are the common complaints behind these drawbacks. To fulfill these medical needs, a novel oral dosage form known as Oro Dispersible Tablets (ODTs) which disintegrate rapidly in saliva, usually within a matter of seconds, without the need to take it water. Drug dissolution and absorption, as well as onset of clinical effect and drug bioavailability, may be significantly greater than those as compared with conventional dosage forms. ODTs releases the medicament in the mouth for absorption through local oromucosal tissue and through pre-gastric (oral cavity, pharynx, and esophagus), gastric (stomach), and post-gastric (small and large intestine) segments of gastrointestinal tract (GIT)².

Levocetirizine Hydrochloride is a third- generation non-sedative anti histamine developed from the second generation anti histamine cetirizine. It is an orally active and selective H₁-receptor antagonist³. It is a BCS Class-I drug characterized by high solubility and high permeability which is suitable for the oro dispersibl resin. Levocetirizine ODT tablets were prepared using

different super disintegrants such as Vivapur type II, polyplasdone XL 10, starch 1500 etc, are used as a super disintegrants. Super disintegrants are used at various concentrations to study the effect on disintegration time, wetting time and dissolution⁴.

MATERIALS AND METHODS

Levocetirizine Hydrochloride, Orange flavor were obtained from Edict Pharma Ltd, Chennai. Poly plasdone XL 10, MCC 102, aspartame, Mannitol SD 100 were obtained from Natco Pharma Ltd, Hyderabad. Ionex WC 23, 29 were obtained from Phaex polymers pvt, Ltd. Starch 1500, Magnesium stearate and Cabosil were obtained from S.D. Fine chemicals Ltd, Mumbai. All the ingredients which are used in this formulation are of analytical grade.

Preformulation

Drug excipients compatibility studies

The physico-chemical compatibility between Levocetirizine HCl and the excipients used in the research were tested by IR spectroscopy using Perkin Fourier Transform Infrared Spectrophotometer (Smilax Laboratories LTD, Hyderabad). The samples were scanned under diffuse reflectance mold and graph was plotted by KBr pellet technique. The spectra were recorded in the wave number region between 4400cm⁻¹ to 400cm⁻¹. The individual spectra obtained for Levocetirizine HCl, excipients were compared with the spectra of the physical mixture of Levocetirizine HCl and excipients⁵.

Flow properties⁶

Before compression all the solid powder ingredients were mixed and passed through sieve number 40 for particle size uniformity. The resultant powder mixture is subjected for flow properties such as bulk density, tapped density, Carr's index, angle of repose and Hauser's ratio.

Formulation of Citrizine ODTs**Tablet compression⁷**

To prepare the tablets, first Levocetirizine and Ionex WC23 complex has to be prepared. De ionized water was used as a vehicle to prepare this complex. 5% slurry of Ionex WC 23 was

prepared by stirring continuously. Drug was added slowly in small quantities while stirring the slurry within 15-30 min. Different ratios of drug and IONEX were prepared i.e., 1:0.5, 1:1, 1:1.5, 1:2, 1:2.25.

After complete addition of the drug while stirring and continued for 2 hours, so that most of the drug gets absorbed on the resin. Filter the drug resonant so formed. The resonant was washed with water. For the preparation of suspension, the supernatant was removed. For the preparation of tablets or capsules, the Resonant was dried at 60°C under vacuum. Pass the above resin complex mixture through 40 mesh. Pass remaining excipients through the same mesh. Resin complex and excipients are mixed thoroughly. So above mixed powders are subjected for direct compression.

Table 1: Scheme of formulation development

Ingredients	Ingredients (mg)								
	LF1	LF2	LF3	LF4	LF5	LF6	LF7	LF8	LF9
Levocetirizine HCl ionex wc 23	16.25	16.25	16.25	16.25	16.25	16.25	16.25	16.25	16.25
Mcc 102	5	6	7	—	—	—	—	6	7
Polypasdone XL 10	—	—	—	3	4	—	—	4	4
Starch 1500	—	—	—	—	—	7	9	9	—
Mannitol SD 100	73.88	72.88	71.88	75.88	74.88	71.88	69.88	59.88	67.88
aspartame	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3
Cabosil	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Mg.sterate	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8
Orange flavor	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27
Total wt (mg)	100	100	100	100	100	100	100	100	100

Development of the formulation in the present study was mainly based on the type of polymer, concentration of polymers, and the drug. Various polymers and excipients in different combinations were used so as to get tablet with good physical properties. Levocetirizine hydrochloride is a BCS class I (high solubility & high permeability) drug and dose taken is 5 mg. So, in the present study attempts were made to get good physical and release profile of the tablets⁸.

Evaluation of orodispersible tablets**Weight variation test⁹**

20 tablets were selected randomly from the lot and weighted individually to check for weight variation.

Thickness¹⁰

Thickness is an important characteristic feature eight variation. 20 tablets were taken and their thickness was recorded using digital vernier caliper.

Hardness¹¹

Tablet hardness can be roughly be determined by holding the tablet in between the fingers of the hand and throwing it lightly on the floor, if it does not break it indicates the proper hardness has been obtained. A number of hardness testers are used for determining the tablet hardness but Monsanto harness tester and Pfizer hardness tester are commonly used. The hardness of the tablet was determined using a Monsanto hardness tester. It is expressed in kg / cm².

Friability test¹²

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at a height of 6 inches in each revolution. Pre weighted

sample of tablets was placed in the friabilator and were subjected to the 100 revolutions.

$$\% \text{ Friability} = \text{loss in weight} / \text{Initial weight} \times 100$$

Drug content¹³

Three tablets of Levocetirizine Hcl containing the equivalent of 5mg of drug was collected randomly and powdered. The powder equivalent to 5mg of drug was weighed accurately, dissolved in 100mL of water. The solution was filtered and an aliquot corresponding to 100µg / mL was analyzed at 231nm.

Disintegration test¹⁴

The time for disintegration of ODTs was generally less than one minute and actual disintegration time that patient can experience ranges from 5-30 seconds. The method needs to be modified for ODTs as disintegration is required without water; thus the test should mimic disintegration in salivary contents. Distilled water (800 mL) was used as the immersion fluid, and was heated and maintained at a temperature of 37°C. The water temperature was constantly monitored by a thermometer. A digital stopwatch was used to measure the disintegration time to the nearest second. Only one tablet was analyzed at a time in order to ensure maximum accuracy. At the end of each test, the basket rack assembly and the plastic disk were thoroughly washed and dried to remove any traces of the tablet excipients and water. A total of six tablets were tested for each concentration and the values reported are mean ± standard deviation.

Wetting time¹⁵

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small Petridish (ID = 6.5 cm) containing 6 mL of Sorenson's buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch and the standard deviation also determined.

Figure 1: Texture analyzer apparatus for disintegration test

Fig: A-F- Shows wetting process at 5 sec interval. The wetting process was completed at 30 secs.
Figure 2: Wetting Time evaluation for Levocetirizine HCl ODT tablets

Dissolution test¹⁶

In-vitro dissolution study was performed by using USP dissolution apparatus type-II (paddle) at 50rpm. Phosphate buffer (pH 6.8) was used as dissolution medium and temperature was maintained at $37 \pm 0.5^\circ \text{C}$. 5mL of dissolution media is taken as sample by using a syringe (which consists of muslin cloth at the

tip of the syringe) at different time intervals i.e., 5, 10, 15, 20, 25, 30, min. Simultaneously 5mL of phosphate buffer was replaced. The collected samples were used to determine the amount of drug content present in the samples by using UV spectrophotometer and absorbance was measured at 231 nm.

$$\% \text{ drug released} = \text{concentration} \times \text{dilution factor}$$

RESULTS

Preformulation parameters – FTIR

Figure 3: FTIR spectrum of Drug+Ionex WC 23

Figure 4: FTIR Spectrum of Drug+MCC 102

Figure 5: FTIR Spectrum of Drug+Polypladone XL 10

Table 2: Flow properties

S.No	Formulation code	Bulk density	Tapped density	Carr's Index	Hausner's ratio	Angle of repose
1	LF 1	0.58±0.004	0.76 ±0.008	23.68±0.924	1.31±0.033	20.58±0.34
2	LF 2	0.58±0.002	0.71 ±0.004	18.30±1.090	1.22±0.009	24.97±0.56
3	LF 3	0.62± 0.004	0.76 ±0.004	18.42±1.456	1.22±0.010	23.74±0.009
4	LF 4	0.58± 0.002	0.76 ±0.002	23.68±0.910	1.31±0.002	21.78±0.010
5	LF 5	0.55 ±0.001	0.76±0.002	22.153±1.170	1.29±0.008	21.78±0.016
6	LF 6	0.62±0.002	0.71±0.003	25.70±0.699	1.33±0.010	22.21±0.014
7	LF 7	0.58±0.003	0.83 ±0.006	23.68 ±0.890	1.31±0.004	20.61±0.006
8	LF 8	0.58 ±0.004	0.76 ±0.005	30.12 ±0.004	1.43±0.005	21.50±0.004
9	LF 9	0.58 ±0.002	0.71 ±0.002	18.30 ±1.092	1.22±0.006	21.76±0.016

Table 3: Evaluation of formulations

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (kp)	Friability (%)	Disintegration (sec)	Wetting time (sec)
LF1	101.79±2.72	2.90±0.03	4.08±0.34	0.17±0.01	28.22±0.50	52.02±0.32
LF2	102.69±2.72	2.83±0.03	4.5±0.34	0.25±0.09	26.79±1.34	52.38±2.37
LF3	102.45±5.03	2.80±0.06	4.78±0.77	0.24±0.01	25.6±3.93	53.71±3.05
LF4	104.18±3.80	2.81±0.06	4.78±0.77	0.16±0.01	21.04±0.80	49.99±0.69
LF5	102.5±1.84	2.94±0.02	4.02±0.88	0.28±0.08	20.18±0.04	50.04±0.70
LF6	103.23±4.73	2.86±0.11	4.02±0.88	0.31±0.02	27.01±0.02	49.17±0.11
LF7	103.23±4.73	3.03±0.03	4.09±0.34	0.28±0.06	24.45±3.18	54.32±1.77
LF8	100.65±2.95	2.64±0.01	4.88±0.36	0.25±0.10	18.92±2.50	48.72±1.35
LF9	100.85±5.64	2.81±0.04	4.67±0.31	0.17±0.12	16.78±1.64	37.55±1.43

Table 4: *Invitro* dissolution studies

Time (min)	%CDR								
	LF1	LF2	LF3	LF4	LF5	LF6	LF7	LF8	LF9
0	0	0	0	0	0	0	0	0	0
5	81.5	82.2	83.2	81.7	83.7	83.5	84.2	83.2	85.0
10	89.9	91.3	91.0	85.0	94.2	91.3	91.8	94.4	94.9
15	90.8	91.8	91.8	91.5	94.9	91.8	92.5	95.2	96.2
20	91.1	93.1	93.0	93.3	96.3	93.1	94.0	96.0	97.1
25	92.6	93.4	93.8	95.1	96.3	93.4	95.5	96.8	98.1
30	93.5	94.5	95.2	96.2	97.4	94.5	96.8	97.8	99.3

Table 5: Stability studies

S.NO	Test	Specifications	Initial	Period in Months		
				1	2	3
1	Description	White to off white un coated tablets.	Complies	Complies	Complies	Complies
2	Taste	Good taste of the tablet	good	good	good	good
3	Hardness(kp)	Between 4-4.8	4.5	No change	No change	No change
4	Wt variation	100-105 mg	102	No change	No change	No change
5	Thickness (mm)	2- 2.8	2.5	2.5	2.5	2.5
6	Disintegration (sec)	Nmt 30 sec	18.54	19.24	19.51	19.64

Table 6: In-vitro dissolution data for formulation after Stability studies LF9

IN-VITRO DRUG RELEASE DATA	
TIME (min)	% CDR
0	0
5	83.25
10	84.43
15	91.19
20	93.37
25	95.03
30	96.44

DISCUSSION

FTIR Studies

FTIR spectrum for API and other excipients were taken individually. The physical mixture of API and excipients spectrum was also taken. The functional groups present in the individual ingredients were reflected in the physical mixture and there are no extra functional groups other than the functional groups present in the individual ingredients. This gives a conclusion that there is no interaction between API and excipients.

Flow properties

Flow properties like bulk density, tapped density, carr's index, angle of repose and hausner's ratio were conducted and the results shown that the flow properties of the mixture of powders are excellent.

Evaluation of ODTs

The values of weight variation and friability were found to be within the limits of ODTs stated in the Indian Pharmacopoeia. Thickness of the tablets varied from 2.80 mm to 3.03 mm. Hardness of the tablets varied from 4.02-4.88 kp which are within the limits only. The % friability and disintegration time values also within the limits of ODTs.

In-vitro dissolution data

The invitro dissolution studies of all nine formulations were carried out in The United States Pharmacopoeia (USP II) rotating paddle apparatus. The amount of drug release was highest for F9 formulation which was 99.3 as it contains highest amount of different super disintegrants.

Formulations LF1, LF2, and LF3 showed 93.54, 94.57, and 95.23 % of drug release in 30 mins, respectively. As the concentration of MCC 102 reached maximum level (up to 7%) in LF3 and could not be increased further, to achieve 100% drug release, various other super disintegrants were employed in different concentrations.

The tablets of LF4, LF5 showed 96.22, 97.41, of drug release in 30 minutes. Drug release profile of all these formulations did not show 100 % drug release within much less time. Polyplasdone XL 10 releases the drug from tablet by rapid capillary uptake of water and pronounced hydration with little tendency to form gel. However, Polyplasdone XL10 used alone in the above formulations unable to release the drug within much less time and the aim was not achieved. Hence further attempts were made to improve the formulation.

Drug release profile of LF6 & LF7 of the formulations mentioned above closer to the 100 % drug release. As both showed 94.57 % & 96.81 % in 30 min, as compare to other formulations as Starch 1500 acts by the swelling actions which helps in release of the drug. This is the general mechanism of action for tablet disintegration.

In formulation LF8 and LF9, LF8 showed slow drug release due to presence of starch 1500 in maximum concentration which could hinder drug release due to swelling action. LF9 showed maximum drug release (99.38%) due to presence of highest concentrations of MCC 102 and polyplasdone XL 10 which could facilitate drug release by disintegration and rapid capillary action.

Stability studies

Accelerated Stability studies for LF9 shows that after conducting the stability studies for 3 months the resultant formulation complies with the specifications of initial formulation in terms of colour, taste, weight, hardness, thickness and disintegration time.

CONCLUSION

The concept of formulating oro dispersible tablets containing Levocetirizine hydrochloride offers a suitable, practical approach to achieve fast release of the drug. Absorption of these tablets takes place direct into the systemic circulation which avoids the hepatic first pass metabolism of Levocetirizine hydrochloride which ultimately results in the improvement in the bioavailability. In the present study ODT tablets of Levocetirizine Hcl were prepared by using different super disintegrants as cross povidone, starch 1500, MCC 102. Nine formulations were designed, using higher and lower level of super disintegrants and employing two and three super disintegrants at a time. In the FTIR studies, it was concluded that there was no interaction between drug and super disintegrants used in formulation.

Formulation LF9 which consisted of 16.25 mg of Levocetirizine ionex complex, 7 mg of MCC 102, 4 mg of polyplasdone XL 10 and 67.88 mg of mannitol SD 100 showed better taste masking property with immediate disintegration and drug release fulfilling the objective of the study.

REFERENCES

1. Chang R, Guo X, Burnside B, Couch R. A review of fast dissolving tablets. *Pharmaceutical Technology* 2000; 12:52-8.
2. Bi Y, Sunada H, Yonezawa Y, Danjo K, Iida K. Preparation and evaluation of compressed tablets rapidly disintegrating in the oral cavity. *Chemical Pharma Bulletin* 1996; 44:2121-7.
3. Hinz B, Auge D, Rau T, Rietbrock S, Brune K, Werner U. Simultaneous determination of aceclofenac and three of its metabolites in human plasma by high-performance liquid chromatography. *Biomedical Chromatography* 2003; 17:268-75.
4. Legrand E. Aceclofenac in the management of inflammatory pain. *Expert Opinion on Pharmacotherapeutics* 2004; 5:1347- 57.
5. Mishra DN, Bindal M, Singh SK, Kumar SG. Spray dried excipient base: A novel technique for the formulation of orally disintegrating tablets. *Chemical Pharma Bulletin* 2006; 54:99-102.
6. Rowe RC, Sheskey PJ, Owen SC. *Handbook of Pharmaceutical Excipients*. 5th Edition, Pharmaceutical Press 2006; 532-34.
7. Fu Y, Jeong SH, Park K. Fast-melting tablets based on highly plastic granules. *Journal of Control Release* 2005; 109:203-10.
8. Setty CM, Prasad DVK, Gupta VRM. Development of fast dispersible aceclofenac tablets: Effects of functionality of superdisintegrants. *Indian Journal of Pharmaceutical Science* 2008; 70(2):180-85.
9. Omama AS, Mohammed AH, Nagia AM, Ahmed SZ. Formulation and optimization of mouth dissolve tablets containing rofecoxib solid dispersion. *Pharmaceutical Science and Technology* 2006; 7:55.
10. Gohel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. *Pharmaceutical Science and Technology* 2004; 5:36.
11. Suresh S, Pandit V, Joshi HP. Preparation and evaluation of mouth dissolving tablets of salbutamol sulphate. *Indian Journal of Pharmaceutical Science* 2007; 69:467-9.
12. Roser BJ, Blair J. Rapidly soluble oral dosage forms, methods of making the same and composition thereof. US patent 5762961; 1998.
13. Ahmed IS, Fatahalla FA. Pilot study of relative bioavailability of two oral formulations of ketoprofen in healthy subjects, a fast dissolving lyophilized tablet as compared to immediate release tablet. *Drug Delivery* 2007; 33:505-11.
14. Ahmed IS, Nafadi MM, Fatahalla FA. Formulation of fast dissolving ketoprofen tablet using freeze-drying in blister technique. *Drug Delivery* 2006; 32:437-42.

Cite this article as:

K. Sampath Kumar *et al.* Exploring the taste masking effect of ion exchange resins in orodispersible tablets of levocetirizine hydrochloride. *Int. Res. J. Pharm.* 2019;10(1):161-166
<http://dx.doi.org/10.7897/2230-8407.100127>

Source of support: Nil, Conflict of interest: None Declared

Disclaimer: IRJP is solely owned by Moksha Publishing House - A non-profit publishing house, dedicated to publish quality research, while every effort has been taken to verify the accuracy of the content published in our Journal. IRJP cannot accept any responsibility or liability for the site content and articles published. The views expressed in articles by our contributing authors are not necessarily those of IRJP editor or editorial board members.