Research Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2013, Volume 1, Issue 9
ISSN : 2321–3647(online)

Formulation and Characterization of Mouth Dissolving Tablet of Levocetrizine Hydrochloride

Anisree.G S[1]*, Nishma Poolat[2], Femina.K[2], Anu.V[2], Rauof.P[2] .
1. Head, Department of Pharmaceutics, Jamia Salafiya Pharmacy College, Malappuram-673637, Kerala, India
2. Research student, Department of Pharmaceutics, Jamia Salafiya Pharmacy College, Malappuram-673637, Kerala, India

ABSTRACT

Mouth dissolving tablets one of the novel approaches in improving patient compliance. Levocetrizine hydrochloride the non-sedative antihistamine drug commonly used for the treatment of allergic rhinitis. Tablet containing levocetrizine with Doshion P54 (C) resin and different superdisintegrants like Sodium starch glycolate, crospovidone, and polacrilin potassium were used for the manufacturing of tablet. Direct compression technique is used for manufacturing of tablet. Combinations of excipients were incorporated to formulate the tablet. Effect of the combinations were studied to optimize the formulation. Compatibility between the drug and excipients were performed with the help of 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 drug with Sodium Starch Glycolate and Polacriline Potassium met all the evaluation parameters and thus selected as the optimized formulation. The optimized formulation was undergone for stability studies in predicting the shelf-life as per ICH guidelines and proved for its adequate shelf-life.

Key words: Mouth dissolving tablet , Levocetrizine hydrochloride, FTIR, ICH guidelines.

*Corresponding Author Email: anisreegs@gmail.com
Received 04 December 2013, Accepted 09 December 2013

Please cite this article in press as: Anisree GS. *et al.*, Formulation and Characterization of Mouth Dissolving Tablet of Levocetrizine Hydrochloride. American Journal of Pharmacy & Health Research 2013.

INTRODUCTION

Oral route one of the versatile route of administration for solid dosage forms. This route has two common and main disadvantages such as dysphagia and rejection of the dosage form due to unpalatable taste of drugs. To rectify these challenges innovative drug delivery systems have been developed. Among the novel approaches, mouth dissolving drug delivery system plays an important role.

One of the main advantage of mouth dissolving tablets[1] that, only a low quantity of water is enough to swallow the dosage form[2]. If water is not available, the tablet in contact with the saliva, the drug from the dosage form is quickly releases and leads to achieve the expected pharmacological action with in a few seconds. Mouth dissolving tablets are preferred for persons suffering from dysphagia, psychiatric disorders[3] as well as hospitalised patients suffering from a verity of disorders. Mouth dissolving tablets [MDT] are very beneficial for a patient with difficulties in swallowing and conditions where access to water is difficult.

Manufacturing of MDT[4] can be done by various techniques. Some of the principles are by increasing the porosity of the tablet and by decreasing the disintegration time. Superdisintegrants are commonly incorporated as the additive, that may swell or absorb water rapidly to disintegrate the tablets[5]. Mouth dissolving tablet may disintegrates instantaneously and dissolves in saliva. With the evidence of the above, the drug is absorbed rapidly and may leads to greater bioavailability as compared with conventional dosage forms.

Levocetrizine[6] Hydrochloride, one of the commonly used non-sedative antihistamine, is an isomer of cetrizine. It is commonly used for the treatment of seasonal allergic rhinitis. The main objective of the present work was to manufacture mouth-dissolving tablets of Levocetrizine hydrochloride by direct compression method and to characterize the formulation to identify the ideal formulation.

MATERIALS AND METHODS

Levocetrizine hydrochloride was obtained as a gift sample from Metrochem Pvt. Ltd, Hyderabad, directly compressible Sodium Starch Glycolate (SSG), Polacriline Potassium(PP) and Crospovidone(C) were obtained as gift samples from Cipla Laboratories,Mumbai, Solan and aspartame, mannitol were obtained from Nice chemicals, Bangalore. All other ingredients used were of analytical grade.

Experimental Part

Mouth dissolving tablets of Levocetrizine hydrochloride were prepared using superdisinegrats

such as Sodium Starch Glycolate (SSG), Polacriline Potassium (PP) and Crospovidone(C) by direct compression method. Accurately weighed ingredients were finely powdered and kept separately. The weighed ingredients were mixed with drug by the principle of geometrical order to form a uniform mixture. The different ratios of the mixture are represented in Table no: 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 16 station tablet punching machine (Cadmach) using biconvex round punches. The collected tablets were stored in a well-closed amber coloured container for its characterization.

Table No.1 Formulation chart for mouth dissolving tablet of Levocetrizine hydrochloride

Sr.No	Ingredients (mg/Tab)	F1	F2	F3	F4	F5	F6
1	Levocetrizine	5	5	5	5	5	5
2	Sodium Starch Glycolate	40		40	20		20
3	Polacriline Potassium	20	40		40	20	
4	Crospovidone		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 (in mg)	100	100	100	100	100	100

Evaluation of Tablets

(a) Calibration curve of Levocetrizine[7] hydrochloride in acetate buffer pH 6.8

Accurately weighed Levocetrizine was dissolved to make a solution in the concentration between 2 to 16µg/mL using the acetate buffer solution pH 6.8. Absorbance of each concentration was measured using U.V. Spectrophotometer (Shimadzu) at 231 nm and the absorbance was plotted against concentration of drug solution.

(b) Compatibility studies[8]

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

(c) Characterisation of tablets[9]

The stored tablets were analysed for different physicochemical parameters such as weight variation, hardness, percentage friability, wetting time, disintegration time and dissolution time parameters.

i) Wetting time[10]

Here each tablet from each batch 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.

ii) 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 Levocetrizine was weighed and dissolved in the 50 ml of 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.

d) *In-vitro* disintegration time[12]

Disintegration of the tablets were done to measure the time to disintegrate the tablet. Six tablets were collected in a random from each batch. The selected tablets 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±2ºC. The test was carried out for 30 cycles and the time was recorded to disintegrate the tablets (in seconds).

e) *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±0.5°C. Randomly selected three tablets from each batch were taken for the evaluation. Aliquot amount of drug 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.

f) 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 40°C/75%RH.Periodical evaluation of the tablets were carried out for their physical appearance and drug content.

RESULTS AND DISCUSSION

Levocetrizine mouth dissolving tablets were formulated by direct compression method. Different batches of tablets were manufactured using different combination of superdisintegrants. Primary evaluation parameters of the tablets were carried out and from the results, it is proved that compression technique is suitable for the manufacturing process.

Compatibility studies were carried out to identify the chemical interaction between drug and the excipients. After interpreting the FTIR spectra, it is clear that there was no interaction occurred for the drug excipients combinations. From the FTIR spectral analysis, it is proved for the suitability of the drug and excipients for this dosage form.

Various physicochemical evaluations were conducted for the tablets. Hardness of the tablets were done by using Monsanto Hardness tester. From the evaluation the hardness were found in the range of 3.5kg/cm^2 to 4.0 kg/cm^2, proved for its adequate physical strength. Weight variation test performed for each tablet and from the reports 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.

Thickness of the tablet was done 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 21 to 40 seconds. The formulation F4 showed a wetting time 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 96.73±0.08% to 98.98±0.38% of the Levocetrizine hydrochloride. The various results are reported in Table No: 2.

Table. No.2 Various physical parameters of the mouth dissolving tablets of Levocetrizine Hydrochloride

Sr. 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)	105.52 ±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)	4.0 ± 0.13	3.2 ±0.21	3.6 ±0.21	3.2 ± 0.16	3.4 ± 0.21	3.5 ± 0.18
5	Wetting time* (sec)	21.3 ±0.21	36.4 ±0.28	25.5 ±0.18	31.3 ±0.21	33.5 ±0.19	40.3 ±0.19
6	Disintegration* (sec)	28.12 ±0.18	27.26 ±0.26	26.48 ±0.16	25.32 ±0.26	26.45 ±0.28	25.22 ±0.26
7	Drug content* (%)	96.73 ±0.08	96.26 ±0.16	97.38 ±0.23	98.98 ±0.38	97.11 ±0.26	96.56 ±0.38

* n=3 observations ± SD

In-vitro disintegration time was measured by the time taken to undergo complete disintegration. Rapid and uniform disintegration of tablets were observed in all the formulations. The result shows the disintegration time for all the formulations in the range of 25 to 28 seconds fulfilling the official standard. Based on the *in-vitro* disintegration time, the formulation having drug combination with Sodium Starch Glycolate and Polacriline Potassium (F4) showed a fast

disintegration time. Thus from the physicochemical evaluation and disintegration time parameters 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 Levocetrizine hydrochloride from the tablet is recorded in Table.No.3 and the corresponding plots are represented in Figure.No.1.From the evaluation parameters the formulation F4 showed good release profile for the time specified and got the supportive measure in selecting the ideal formulation. The uniformity in the release profile may be due to the presence of super disintegrants in the correct ratio in the formulation. Thus it is selected as the ideal formulation.

Table. No: 3 *In-vitro* dissolution profile of Levocetrizine mouth dissolving tablets.

Sr. 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	19.58±0.09	19.56±0.08	20.46±0.12
3	10	37.86±0.09	48.32±0.11	40.56±0.09	38.51±0.15	47.28±0.13	36.35±0.16
4	15	57.53±0.14	62.83±0.09	54.13±0.07	58.82±0.19	70.56±0.14	52.56±0.14
5	20	72.66±0.18	79.56±0.09	67.56±0.15	79.66±0.21	85.16±0.17	76.86±0.15
6	25	89.81±0.07	85.58±0.22	85.16±0.09	88.51±0.14	91.38±0.17	88.15±0.12
7	30	95.63±0.18	96.56±0.14	96.52±0.15	98.78±0.11	94.26±0.12	96.12±0.23

* n=3 observations ± SD

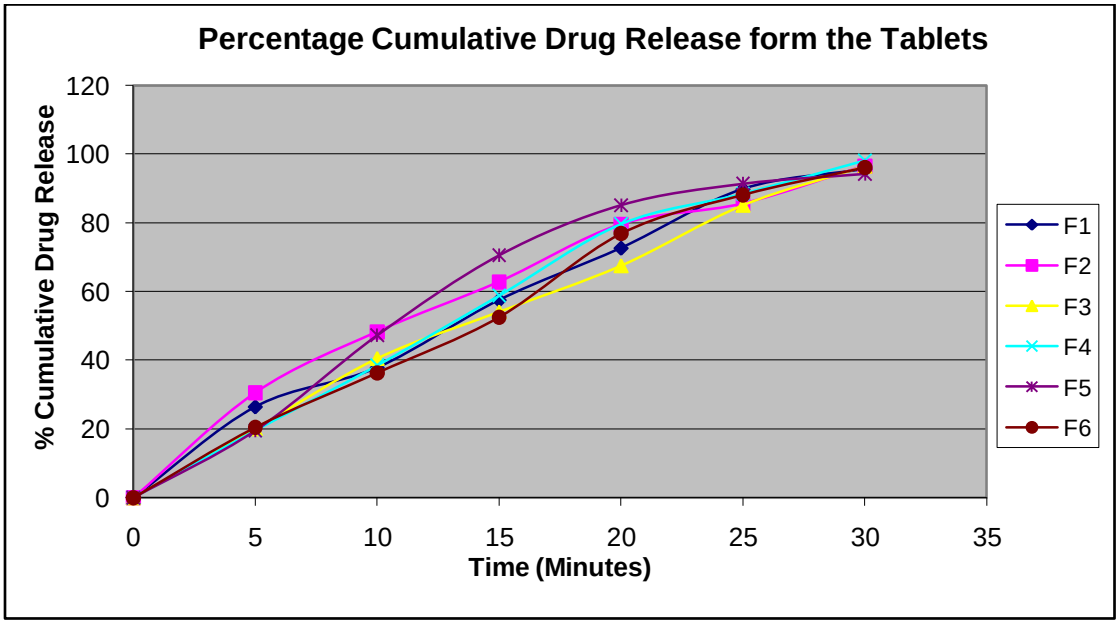

Figure:1 Figure showing Percentage cumulative drug release from different formulations.

Stability study for the optimized formulation was carried out for a period of 30 days at 40ºC/75% RH according to ICH guidelines, in predicting the shelf life. Physical appearance and drug content of the optimised formulation were studied during the time schedule. From the results obtained, it was found that the ideal formulation does not have major degradation and the formulation have an adequate shelf life. The obtained results were tabulated in Table.No.4.

Table. No 4 Stability testing parameters of the optimised formulation

Time (days)	Physical appearance	Drug content* (%)
0	Good	98.56± 0.17
15	Good	98.06 ±0.16
30	Good	97.83 ±0.08

* n=3 observations ± SD

CONCLUSION

Mouth dissolving tablets of Levocetrizine hydrochloride were successfully developed by direct compression method. Characterization of the tablets was also carried out to identify the optimized formulation. All the physical parameters were found with in the approved range. *In-vitro* disintegration, and dissolution parameters revealed that the excipients are suitable for the manufacture of mouth dissolving tablet. The formulation denoted as F4 exhibited 98.78% of drug release with in 30 minutes and showed a low disintegration time. Thus formulation F4 was selected as the ideal formulation, having the drug with Sodium Starch Glycolate and Polacriline Potassium combination. Accelerated stability study was carried out for the optimized formulation to predict the shelf life. During the evaluation, the tablet was examined for its physical appearance and drug content. The formulation exhibited no change for its physical appearance and drug content. From the above findings the formulation F4 selected as ideal formulation. Thus the combination is suitable for the manufacturing of mouth dissolving tablet of Levocetrizine hydrochloride.

ACKNOWLEDGEMENT

The authors would like to thank the Director, Principal and all the staffs of J S P C, Malappuram, Kerala who directly or indirectly helped us for the successful completion of the work in a good manner.

REFERENCES

1. Aulton,M E.,Pharmaceutics,The design and manufacture of medicines.Churchill Levingstone,Newyork,2007,353-356.
2. Tasbira J, Riaz U, Orodisposible tablets: A short review SJ Pharmaceutical science 2011, 4(1),96-99.

3. Badgugar BP and Mundada AS, The technologies used for developing orally disintegrating tablets; A Review Acta Pharm 2011, 61,117-139.
4. Kuchekar BS, Arumugam V**.** Design of fast dissolving tablets. *Indian J Pharm Edu Res*, 2001;35:150-152.
5. Chang R, Guo X, Burnside. B, Fast dissolving tablets. Pharmaceutical technology 2000, 24 (6), 52-58
6. John Martin, British national formulary,58th edn,2009,171-172.
7. Manis.K,sharad.V, Preparation and evaluation of fast dissolving tablet of Levocetrizine hydrochloride. International journal of pharmacy and pharmaceutical science 2010: 2(3),109-111.
8. Willard ,Instrumental methods of analysis, sixth edition CBS Publishers. 199-209.
9. Kumar S, Bajpai M., Formulation and Evaluation of mouth dissolving tablets of Sildenafil citrate.J.Pharma Sci Technol.2010,2(4),202-206.
10. Shirwaikar A A,Ramesh A.,Fast disintegrating tablets of atenolol by dry granulation method,In.j.Pharm.Sci,2004,66,422-426.
11. Senthilnathan.B, Anusha.R., Formulation development and evaluation of Venlafaxine hydrochloride oro disposable tablets. International Journal of pharmaceutical science and research 2011. 2(4) 913-921.
12. Sumanta.M,Ashok.KP., Formulation and evaluation of fast disposable aceclofenac tablets, effects of functionality of super disintegrants. Journal of global pharma. technology 2009;90-96
13. Jones RJ, Ali.R.S.The influence of formulation and manufacturing process parameters on the charectoristics of lyophilized orally disintegration tablets. Pharmaceutics 2011,3, 440.
14. Ashish P., A Review-Formulation of mouth dissolving tablet.Int.J.PharmClin Sci 2011,1(1),1-8.