Original Research Paper

Volume-7 | Issue-12 | December-2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 86.18

Pharmaceuticals

FORMULATION AND *IN -VITRO* EVALUATION OF ORALLY DISINTEGRATING TABLETS OF LEVOCETIRIZINE HYDROCHLORIDE

B. Deepika* Department Of Pharmaceutics Nalanda College of Pharmacy, Cherlapally, Nalgonda (Dist), T. S-508001*Corresponding Author

L. Srilatha Department Of Pharmaceutics Nalanda College of Pharmacy, Cherlapally, Nalgonda (Dist), T. S-508001

Kandukoori Naga Raju Department Of Pharmaceutics Nalanda College of Pharmacy, Cherlapally, Nalgonda (Dist), T. S-508001

ABSTRACT Levocetirizine Hydrochloride is an anti-allergic agent under the class of anti-histamines. In current research work oral disintegrating tablets of Levocetirizine Hydrochloride were prepared with Sodium starch glycolate, L-HPC LH 11, Crospovidone as superdisintegrants in different concentrations using direct compression method. The blend was examined for the pre-compression parameters and the values obtained were within prescribed USP limits. The prepared tablets were evaluated for various parameters like Thickness, weight variation, hardness, friability, disintegration time, drug content, water absorption ratio, wetting time, and *in vitro* drug release. The values obtained in post-compression parameters were within the prescribed USP limits. Based on the results obtained, the formulation containing 10% Crosspovidone (CP3) was identified as an ideal and better formulation because it had exhibited faster wetting time, good taste and faster disintegration time (19.6 sec) when compared to all other formulations. The *in vitro* drug release of optimized formulation CP3 was found to be 98% at the end of 15 min, 50 % of drug was released within 3.5 min and 90 % of drug was in 9.4 min. The results concluded that oral disintegrating tablets of Levocetirizine hydrochloride shown enhanced dissolution rate, which improves bioavailability, effectiveness and hence better patient compliance.

KEYWORDS : Levocetirizine hydrochloride, oral disintegrating tablets, Crosspovidone.

Introduction

Oral drug delivery has been known for decades. This route of administration is mostly used among all the routes that have been utilized for the systemic delivery of drugs via various pharmaceutical dosage forms. The reasons are, oral route achieved such popularity may be in part of its ease of administration as well as the traditional belief that by oral administration the drug is well absorbed as the foodstuffs that are ingested daily. In fact, the development of a pharmaceutical product for oral delivery, irrespective of its physical form involves varying extents of optimization of dosage form characteristics within the inherent constraints of GI physiology. Oral dosage forms are taken per orally for a local effect in the mouth, throat (or) gastrointestinal tract or for a systemic effect in the body after absorption from the mouth or gastrointestinal tract.

These dosage forms are classified into two main groups based on the physical state of the dosage forms, solid oral dosage forms (tablets, capsules or powders) and liquid oral dosage forms (solutions, syrups, suspensions and emulsions).[3] Drinking water will play an important role in the swallowing of oral dosage forms. This is due to the inconvenience in swallowing conventional dosage forms such as tablets when water is not available in the case of motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic conditions and bronchitis. [4] Difficulty in swallowing (dysphasia) is a common problem in all age groups, especially the elderly and pediatrics because of the physiological changes associated with these age groups. For these reasons tablets which can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Over the last 30 years, orally disintegrating tablets (ODTs) are gaining considerable importance. These tablets disperse in the saliva within a short period of time. Saliva containing the dispersed drug is then swallowed through the esophagus as the saliva passes down into the stomach.[5].

Levocetirizine hydrochloride is an anti- allergic agent under the class of Antihistamines and is used for treatment of Allergic rhinitis, chronic idiopathic urticaria and seasonal year round allergies and relieve from itching caused by hives (patches of red, swollen, itchy skin). As the drug is bitter in taste it is difficult to increase the patient compliance mouth dissolving tablets are preferred.

Materials and Methods:

Levocetirizine hydrochloride, Mannitol SD 200, MCC pH 101, Crospovidone (Kollidone-CL), L-HPC, LH 11, sodium starch glycolate (primogel), Aspartame (Granular), Strawberry flavor, Aerosil 200, Magnesium stearate were obtained from Hetero Labs Limited, Jadcherla, Hyderabad.

Method of preparation:

Orodispersible tablets were prepared by direct-compression method,the composition of different tablet blends used in the study are shown in table-1.Tablets containing 20mg of equivalent drug, diluents and superdisintegrants were accurately weighed and passed through sieve # 40. All of the above ingredients were taken in a clean, dried plastic container and mixed geometrically and blended for 15min with constant acceleration. Aerosil and magnesium stearate were passed through sieve # 60, mixed and blended with initial mixture in a same plastic container for 5min. The powder blend was compressed into tablets on eight-station rotary punch tableting machine (Cadmach machinery co. pvt ltd. Ahmedabad).

Table 1: Formulation of Levicitirazine hydrochloride

SNO	Ingredients	CP1	Cp2	CP3	SSG1	SSG2	SSG3	Lh1	LH2
1	Levocetirizine hydrochloride	5.9	5.95	5.95	5.95	5.95	5.95	5.95	5.95
2	MCC pH 101	104.55	99.55	94.55	104.55	99.55	94.55	104.55	99.55
3	Mannitol SD 200	30	30	30	30	30	30	30	30
4	Crospovidone	05	10	15	----	----	----	----	----
5	Sodium Starch Glycollate	----	----	----	05	10	15	----	----
6	L-HPC, LH 11	----	----	----	----	----	----	05	10
7	Aspartame	2	2	2	2	2	2	2	2
8	Straw Berry flavour	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
9	Aerosil 200	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
10	Mg. Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Evaluation of Tablets:

Precompression parameters:

Characterization of tablets for physicochemical parameters

The prepared mouth dissolving tablets were evaluated for their physicochemical parameters like weight variation, hardness, thickness, friability and drug content.

Hardness test: The tablets to be tested are held between a fixed and a moving jaw of hardness test apparatus (Monsanto) and reading of the indicator is adjusted to zero. The screw knob was moved forward until

the tablet breaks and the force required to break the tablet was noted.

Tablet thickness:
The thickness in millimeters (mm) was measured individually for 10 pre weighed tablets by using digital verniercalipers (Mitutayo) The average thickness and standard deviation were reported.

Weight variation test:
Randomly selected 20 tablets from each batch and weighed using digital electronic balance. The average was calculated. It passes the test for weight variation, if not more than two of the individual tablet weights deviate from the average weight by more than the allowed percentage deviation and none deviate by more than twice the percentage shown. The tablets weight variation limits as per USP mentioned in table.

Friability:
Friability test was performed using Roche friabilator. Ten tablets were weighed and placed in the friabilator, which was then operated for 25 revolutions per minute. After 100 revolutions the tablets were dusted and reweighed. The percentage friability was determined using the formula.

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

Drug content:
Ten tablets were weighed from each formulation, powdered and equivalent to 5 mg of Levocetirizine hydrochloride were weighed and dissolved in 100ml of 0.1N HCl and filtered. The filtrate was made up to a volume of 200 ml with 0.1NHCl. The solutions were suitably diluted with 0.1NHCl and the drug content was estimated spectrophotometrically at 231.5 nm using 0.1NHCl as a blank.

Disintegration test:
The disintegration time was measured using disintegration apparatus. 6 tablets are placed in the tubes of the basket with bottom mesh was immersed in water bath at 37 ± 2^{0}C. The time required for complete disintegration of the tablet in each tube was determined using digital watch equipped with in the instrument

Wetting time:
A piece of tissue paper (12×10.75 cm) folded twice was placed in a Petri dish (internal diameter=9 cm) containing 10 ml of buffer solution simulating saliva, pH 6.8 in which methylene red (water soluble dye) was dissolved. The dye solution was used to identify the complete wetting of the tablet surface and noted the wetting time.

Water absorption ratio:
water absorption ratio = (wa-wb)/100
A tablet was weighed and was carefully placed on the paper at room temperature (Wb). The wetted tablet was reweighed (Wa). Tablet was wetted as per the procedure and water absorption ratio, R, was then determined according the equation mentioned below

***In vitro* Dissolution study:**
The prepared tablets was studied for dissolution test by USP type II apparatus (paddle) using 900 mL of dissolution medium (0.1 N HCl), at a speed of 50 rpm and at a temperature of 37±0.5 ºC. 10 mL aliquots were withdrawn at regular intervals of 3, 5, 07, 11, 13, and 15 minutes, the same volume of fresh dissolution medium was a replaced. Samples were filtered through Nylon filter paper (0.45µm), and the absorbance was recorded at 231 nm. The percentage drug released at each time point was calculated and a graph was plotted. The t50% and t90%values were obtained by the *in vitro* drug release graph.

Results and Discussion:
Compatibility Studies:
FTIR spectra are used to determine the drug-polymer compatibility; table shows the FTIR spectra of pure Levocetirizine Hcl and mixture of pure drug and disintegrating agents. The spectra of pure Levocetirizine hydrochloride shows characteristic peaks at 1742 cm^{-1} due to stretching vibrations of –COOH group, the peak at 2947 cm^{-1} due to CH2 stretching and the peaks at 758 cm^{-1}due to C-CL stretching. The similar peaks were also observed in the spectra of mixture of Levocetirizine HCl and polymers with slight deviations. This indicates that the drug is stable and there is no drug-excipient interaction.

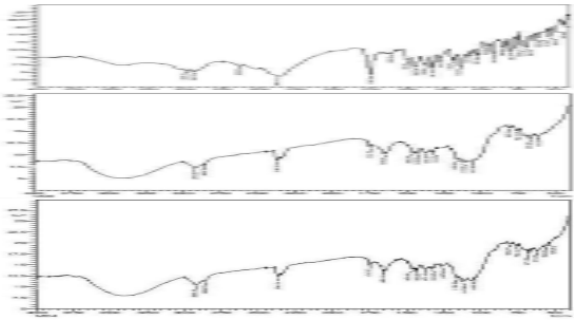

Fig: FTIR spectra of Levocetirizine hydrochloride, physical mixture and optimized formulation Evaluation of zidovudine powder mixture and matrix Tablets:

The powder prepared for compression of matrix tablets were evaluated for their flow properties. The bulk density was within the range of 0.37 to 0.50 gm/cm3 . Tapped density ranged between 0.598-0.648 gm/cm3. Angle of repose was within the range of 28. 10 to 34. 96. Compressibility index was found to be 14.71-16.82 and Hausner ratio ranged from 1.17-1.22 for powder of different formulations (Table-2). These values indicate that the prepared granules exhibited good flow properties.

Table: Physical Properties of powder blends

Formulation	Bulk density (g/ml)	Tapped density (g/ml)	Compressability index (%)	Hausners ratio	Angle of repose (Θ)
CP1	0.510	0.598	14.71	1.172	35.1
CP2	0.515	0.610	15.57	1.184	38.1
CP3	0.522	0.628	16.17	1.203	39.2
SSG1	0.524	0.628	16.52	1.198	37.2
SSG2	0.528	0.631	16.32	1.195	38.9
SSG3	0.534	0.648	16.82	1.22	40.9
L-HPC1	0.511	0.606	15.67	1.185	35.2
L-HPC2	0.515	0.622	15.59	1.184	38.9
L-HPC3	0.522	0.638	15.83	1.188	40.1

Table: Physical properties of prepared tablets.

Formulation	Weight variation (mg)	Hardness	Friability (%)	Drug content	Thickness (mm)	Disintegration time (sec)
CP1	152.6 ± 1.07	5.86 ± 0.29	0.289	96.6 ± 1.79	2.65 ± 0.0206	40.6 ± 1.37
CP2	150.2 ± 1.50	5.71 ± 0.40	0.438	98.2 ± 1.05	2.61 ± 0.0214	26.5 ± 1.50
CP3	151.1 ± 1.52	5.71 ± 0.27	0.349	98.1 ± 1.86	2.64 ± 0.0210	19.6 ± 0.74
SSG1	150.2 ± 1.32	5.81 ± 0.22	0.450	95.3 ± 1.49	2.64 ± 0.0216	74.3 ± 1.79
SSG2	150.9 ± 1.44	5.69 ± 0.39	0.364	95.1 ± 1.67	2.63 ± 0.0201	31.0 ± 1.91
SSG3	150.6 ± 1.42	5.86 ± 0.29	0.348	95.3 ± 1.49	2.64 ± 0.0214	24.6 ± 1.97
LH1	150.0 ± 1.45	5.81± 0.25	0.312	94.5 ± 0.95	2.58 ± 0.0208	46.5 ± 1.11
LH2	150.5 ± 1.28	5.85 ± 0.31	0.278	96.1 ± 1.34	2.61 ± 0.0198	29.1 ± 1.57
LH3	150.1 ± 1.30	5.81 ± 0.25	0.371	94.0 ± 1.29	2.59 ± 0.0211	52.6 ± 1.38

All the prepared tablets showed good elegance in appearance. The hardness of the tablets of all formulations was within the range of 5.6 to 5.8 kg/cm^2, indicating good mechanical resistance of the tablets. The variation in weight was within the range of ±0.22% complying with pharmacopoeia specifications. The disintegration time of *Levocetirizine Hydrochloride* in all formulations was ranging from 19.6-74.3 sec, the drug content in all the formulations was found to be in between 94.0 to 98.2 indicating content uniformity was within the limits (±10%). The thickness and diameter of tablets was found to be in the range of 2.58 to 2.65 mm and 6.1 to 6.2 mm respectively, which showed uniform thickness and diameter. The particle loss in the friability test was below 1% for all the formulations, which is an indication of good mechanical resistance of tablets. The wetting time of all the formulations was in the range 28.6 sec to 79.2sec.

***Invitro* dissolution study:**

The in vitro drug release of crospovidone containing formulationsi.e. (CP1, CP2 and CP3) was in the range 88±1.41% to 98±0.82% as the concentration of crospovidone increases the drug release also increases with respect to time.CP3 had shown maximum drug release 98±0.82% at the end of 15mins. These results suggests that the crospovidone containing tablets were disintegrated rapidly compared to other formulations because of the viscosity and hydration capacity of polymer very low due to less density and high porosity that provides rapid disintegration property to the formulation. As the concentration of crospovidone increases the disintegration time of the formulation had decreases. Generally crospovidone having high molecular weight compared to all other disintegrate but the structure of polymer was linear and hydroxyl groups had not present in the structure, which provides low viscosity and low hydration capacity to the polymer. CP3 had shown maximum drug release 98±0.82% at the end of 15mins, which also shown 50% of drug release (t50%) in 3.5 min, and (t50%) of drug released in 9.4 min. The in vitro drug release of promising (optimized) formulation (CP3) had shown maximum drug release 98±0.82% at the end of 15mins. As the results suggested that the concentration super disintegrate increases disintegrating capacity also increases, so that drug release increases with respect to time.

The in vitro drug release of commercial IR tablet had shown maximum drug release 85±0.62% at the end of 15mins. As the results suggested that the tablet contains film coated and the tablet was prepared by wet granulation process. In this IR formulation had shown high disintegration time, that was the reason for least drug release at the end of 15mins.

Hence, overall increase in the dissolution rate of all the optimized formulations described in terms of dissolution parameters with respect to marketed tablet possibly due to shorter disintegration time and wetting time to produce a large surface area for dissolution.

Table: Percentage Drug Release of all formulations

Time (mins)	CP1	CP2	CP3	SSG1	SSG2	SSG3	LH1	LH2	LH3
0	0	0	0	0	0	0	0	0	0
3	26 ±1.03	30±1.21	45±0.75	20±1.51	22±1.38	34±0.75	25±0.75	28±0.52	12±0.52
5	33±0.98	46±0.98	61±0.41	27±052	38±1.72	44±0.75	38±0.82	46±0.82	26±0.52
7	48±0.98	68±0.84	78±1.03	40±1.33	55±0.89	68±0.82	44±0.55	69±0.75	34±0.52
9	62±1.03	77±0.82	86±0.55	54±0.63	69±1.03	76±0.98	65±0.63	80±0.55	46±0.82
11	62±1.03	82±0.98	90±0.89	62±1.26	78±1.17	81±0.75	78±0.52	85±0.52	62±075
13	78±1.1	87±0.75	94±0.75	66±0.84	82±1.37	86±0.89	80±0.82	88±0.52	71±0.81
15	85±1.37	87±0.75	98±0.82	76±0.55	87±1.03	90±0	82±0.52	93±0.52	79±0.55
t50% Value	7.3 min	5.4 min	3.5 min	8.8 min	6.6 min	5.4 min	7.4 min	6.3 min	7.5 min
t90% Value	---	13.2 min	9.4 min	----	----	15.0 min	---	14.2 min	---

Conclusion

The conclusion drawn from the present investigation is given below. Preformulation studies of *Levocetirizine hydrochloride* were performed. The FTIR analysis revealed that the excipients were compatible with Levocetirizine hydrochloride. Nine batches of oral disintegrating tablets of *Levocetirizine hydrochloride* were successfully prepared by direct compression method using three types of super disintegrating agents such as crospovidone, sodium starch glycolate and L-HPC LH 11 in different concentration. The prepared tablets were evaluated for different evaluation parameters. Disintegration time decreased with the increase in the concentration of superdisintergrants from 3.3 % w/w to 10 w/w but L-HPC LH 11had shown increased disintegration time with the increase in the concentration .Based on the results obtained, the formulation containing 10 % crospovidone (CP3) was identified as ideal and better formulation among all formulations because it had exhibited faster wetting time, good taste and faster disintegration time when compared to all other formulations. The *in vitro* drug release of promising formulation (CP3) was found to be 98% within 15 min. The 50 % of drug released within 3.5 min, and 90 % of drug released in 9.4 min. The promising formulation had compared with commercial IR tablets. The results concluded that oral disintegrating tablets of *Levocetirizine hydrochloride* shown unpalatable taste with enhanced dissolution rate, will lead to improved bioavailability, improved effectiveness and hence better patient compliance.

References:

1. Ghosh TK, Jasti BR. Theory and practice of contemporary pharmaceutics. CRC press, Fourth edition, 150-155, 282-367, 2005.
2. Yoela BS, Pisal SS, Paradker AR, Mahadhik KR.New drug delivery systems for elderly, Indian Drugs, 312-18, 2000.
3. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form,J Pharm Pharmacol, 50, 375-382, 1998,.
4. VenkatewarluV. Biopaharmaceutics and pharmacokinetics textbook, Pharmed press, Hyderabad, second edition, 331-33, 2005.
5. Subrahmanyam CVS. Essentials of physical pharmacy text book, Vallabhprakashan, Delhi, 6theddtion, 368-80, 2013.
6. AbolghasemJouyban.Solubility Prediction Methods for drugs/drug like molecules, Recent Patents on Chemical Engineering, 1, 220-231, 2008.
7. www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2007-D-0365-gdl.pdf, accessed Aug. 20, 2009.
8. The free encyclopaedia, European Pharmacopeia 6th edddition. Strasburg, France, 2007.
9. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets, developments, technologies, taste-masking and clinical studies,Crit Rev Ther Drug Carrier Sys, 2, 1433-1476, 2004.
10. Tasbira Jesmeen, Riaz Uddin Orodispesible tablets A short review, Stamford journal of pharmaceutical sciences, 4(1), 96-99, 2011.
11. Rakesh Pahwa. Orally Disintegrating Tablets - Friendly to Paediatrics and Geriatrics, Scholars Research Library. Archives of Applied Science Research, 2 (2), 35-48, 2010.
12. Chatap VK.. "A Review on Taste masking Methods on Bitter Drugs", pharmainfo.net, 5, 2007.
13. Rasmachereson. Bioavailability, bioequivalence and drug selection, Basic pharmacokinetics review, 8, 1-8, 1996.
14. Jhon D Smart. Drug delivery using buccal-adhesive systems, Advance drug delivery reviews, 11, 253-70, 1993.
15. Sallam E, Ibrahim H, Abuahab R, Shubair M, Khalil E. Evaluation of fast disintegrants interfenadine tablets containing a gas-evolving disintegrant, Drug DevInd Pharm,24, 501-507, 1998.
16. Mahaveer Pr. Khinchi,GuptaM.K, DilipAgarwal, Natasha Sharma, ShailendraWadhwa. Orally Disintegrating Tablets,A Future Prospectus, Int J Pharm Sci Bio, 1(2), 71-79, 2010.
17. Reeta Rani Thakur, Sonia Narwal.Orally disintegrating preparations: recent advancement in formulation and technology, Journal of Drug Delivery and Therapeutics, 2(3), 87-96, 2012.
18. Yourong Fu, et al. Orally Fast Disintegrating Tablets Developments, Technologies, Taste-Masking and Clinical Studies. Critical Reviews, in Therapeutic Drug Carrier Systems,21(6):433–47, 2004.
19. Atish s. Mundada.The technologies used for developing orally disintegrating tablets, A review, Acta Pharm, 61, 17–139, 2011.
20. Yang S, Fu Y, Jeong SH, Park K. Application of poly(acrylic acid) super porous hydrogel microparticles as a super-disintegrant in fast-disintegrating tablets, J Pharm Pharmacol, 56(4), 429–436, 2004.
21. AnasBahnassi. Formulation and Evaluation of Aceclofenac Fast Dissolving Tablets Using Foam Granulation Technique. Indo Global Journal of Pharmaceutical Sciences, 2(4), 342-347, 2012.
22. Bradoo R, Shahani S, Deewan B, Sudarshan S. Orally disintegrating drug delivery system. J Am Med Assoc India, 4(10), 27-31, 2001.
23. Mahaveer Pr. Khinchi, GuptaM.K, DilipAgarwal, Natasha Sharma, Shailendra Wadhwa. Orally Disintegrating Tablets: A Future Prospectus, Int J Pharm Sci Bio, 1(2), 71-79, 2010.
24. Shalini Sharma and Shaila Lewis, Taste Masking Technologies.A Review. International Journal of Pharmacy and Pharmaceutical Sciences, 2(2), 6-13, 2010.
25. Mahaveer Pr. Khinchi, M.K.Gupta, DilipAgarwal, Natasha Sharma, Shailendra Wadhwa, Orally Disintegrating Tablets: A Future Prospectus, Int J Pharm Sci Bio, 1(2), 71-79, 2010.
26. Reeta Rani Thakur, Sonia Narwal. Orally disintegrating preparations: recent advancement in formulation and technology, Journal of Drug Delivery & Therapeutics, 2(3), 87-96, 2012.