BCSIR

Available online at www.banglajol.info

Bangladesh J. Sci. Ind. Res. **48(2)**, 137-142, 2013

BANGLADESH JOURNAL OF SCIENTIFIC AND INDUSTRIAL RESEARCH

E-mail: bjsir07@gmail.com

Formulation and evaluation of loratadine mouth dissolving tablet

S. Shanmugam, Senthil* and T. Vetrichelvan

Department of Pharmaceutics, Adhiparasakthi College of Pharmacy, Melmaruvathur, Tamilnadu, India

Abstract

Loratadine 10 mg mouth dissolving tablet (MDT) was prepared by using super disintegrant such as sodium starch glycollate, crosscarmellose sodium, crospovidone at various concentration, aspartame was used as sweetening agent. The excipients were used for this study was based on the compatibillity studies. All the formulation was prepared by direct compression method. Among all the formulations crospovidone at 10 mg/tab gives 99.1% drug release at end of 12th min. It was considered as optimized batch. The optimized batch was processed for all the evaluation parameter and stability studies. The final formulations were packed in blister package.

Keywords: Loratadine; Mouth dissolving; Direct compression; Wetting time; Croscarmellose sodium

Introduction

The main problem with the common oral dosage form is that they have to be swallowed along with water and many patients find it difficult to swallow tablet, especially in elderly and pediatrics, because of the physiological changes associated with them. Due to this dysphasic condition, they do not comply with prescription, which results in accent non compliance. Thus MDTs are beneficial to patients who find it difficult to swallow tablet, moreover some of the drugs which are soluble in saliva are absorbed from the mouth and pharynx and esophagus as the saliva passes down in to stomach, which enhances bioavailabilty by avoiding first pass metabolism. Loratadine is a long acting selective peripheral H1 antogonist that has been used as anti-cholinergic effect. The objective of the present study was to formulate and evaluate Loratadine by using super disintegrants to develop a new dosage form.

Materials and methods

Loratadine, sodium starch glycolate, croscarmellose sodium and crospovidone were obtained as a gift samples from Madras Pharmaceuticals, Chennai. All other reagents and solvent used were of analytical grade.

Methods

Direct Compression

The mouth dissolving tablets were prepared by direct compression method with the use of three different superdisintegrants namely Croscarmellose sodium, Sodium starch glycolate, Crospovidone in the ratio of 5:2, 5:3 and 5:4. Microcrystalline cellulose, Mannitol was used as a diluents and mixture of Aerosil and Magnesium sterate (1:1) was used as glidant and lubricant respectively. The composition of mouth dissolving loratadine is shown in Table I.

Accurate quantity of drug and all ingredients were weighed according to formula shown in Table I and powder except Aerosil and Magnesium sterate was blended homogeneously in mortor and pestle for 15 minutes. Prepared powder blend was passed through sieve no. #60. Finally Aerosil and Magnesium sterate passed from sieve no. #30 added and was further mixed for 10 minutes.

Accurately weighed 200 mg homogeneously mixed powder blend was fed manually and compressed with constant compression force and hardness on 16 stations Cadmach tablet compression machine with 9 mm, breakthrough, and flat faced punches. Total nine formulations were prepared.

Experimental Work

Formulation and characterization of powder blend

Method

Accurate quantity of drug and all ingredients were weighed according to formula shown in Table I and powder except aerosil and magnesium sterate was blended homogeneously in mortor and pestel for 15 minutes. Prepared powder blend was passed through sieve No.#60. Finally aerosil and magnesium sterate passed through sieve No. #30 was added and

*Corresponding author. e-mail: senthilpharma84@gmail.com

Table I. Formulation composition of mouth dissolving loratadine tablets with superdisintegrants

S.NO	Tablet ingredient(mg/tablet)	Formulation code								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Loratadine	10	10	10	10	10	10	10	10	10
2	Croscarmellose sodium	4	6	8	-	-	-	-	-	-
3	Sodium starch glycolate	-	-	-	4	6	8	-	-	-
4	Crospovidone	-	-	-	-	-	-	4	6	8
5	Micro crystalline cellulose	74	72	70	74	72	70	74	72	70
6	Mannitol	100	100	100	100	100	100	100	100	100
7	Colloidal silicon dioxide (Aerosil)	4	4	4	4	4	4	4	4	4
8	Aspartame	6	6	6	6	6	6	6	6	6
9	Magnesium stearate	2	2	2	2	2	2	2	2	2
10	Strawberry	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

further mixed for 10 minutes. The powder blend was evaluated for angle of repose, bulk density, tapped density, Compressibility Index and Hausner ratio (Bankar *et. al*., 1996).

Angle of Repose

Angle of repose was determined using cylinder method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (θ) was calculated using the formula

$$\theta = \tan^{-1}(r/h) \quad (1)$$

Method

Weighted quantity of loratadine was passed through funnel kept at height at 9 cm from base. The powder forms heap and touches the tip of the funnel. The radius was measured and angle of repose was calculated.

Standard Relationship between Angle of Repose (θ) and Flow ability

Angle of repose (θ)	Flowability
< 20	Excellent
20-30	Good
30-34	Passable*
> 40	Very poor

*Adding glidant for improving flow

Bulk density

Apparent bulk density (ρ_b) was determined by pouring blend into a graduated cylinder. The bulk volume (V_b) and weight of the powder (M) was determined. The bulk density was calculated using the formula.

$$\rho_{b=} M/V_b \text{or} \quad (2)$$

BD = Weight of the powder/Volume of the powder.

Tapped density

It was determined by placing a graduated cylinder, containing a known mass of drug excipients blend, which was tapped for a fixed time until the powder bed volume has reached a minimum. The minimum volume (V_t) occupied in the cylinder and the weight (m) of the blend was measured. The tapped density (ρ_t) was calculated using the following formula.

$$\rho_{t = m} / V_{tor} \quad (3)$$

TBD = Weight of the powder/Tapped volume of the powder

Compressibility Index

The simplest way for measurement of free flow of powder is compressibility, a indication of the case with which a material can be induced to how is given by compressibility index (I) which is calculated as follows

Carr's compressibility index (%) = [(TBD-BD)/ TBD x 100

(4)

Standard values of Carr's index are as follows:

Carr's index	Flowability
5-15	Excellent
12-16	Good
18-21	Fair Passable
23-35	Poor
33-38	Very poor
> 40	Very very poor

For all the formulations bulk density, tupped density, angle of repose, Corr's index and Hansne's ratio are shown in Table II.

Table II. Evaluation of powder blends of loratadine

Formulation Code	Bulk density(g/mL)	Tapped density(g/mL)	Angle of repose(θ)	Carr's index (%)	Hausner's ratio
F1	0.45±0.0125	0.50±0.0231	31.78±1.8815	11.19±0.00	0.8880±0.00
F2	0.43±0.0165	0.49±0.0099	30.67±0.9514	11.45±0.00	0.8854±0.00
F3	0.45±0.0042	0.50±0.0063	34.53±1.7870	9.56±0.00	0.9043±0.00
F4	0.41±0.0105	0.47±0.0124	28.42±1.2725	12.26±0.00	0.8773±0.00
F5	0.45±0.0090	0.52±0.0213	33.78±1.4577	13.79±0.00	0.8620±0.00
F6	0.47±0.0120	0.54±0.0217	29.04±1.1461	12.69±0.00	0.8730±0.00
F7	0.46±0.0103	0.50±0.0107	33.65±0.5445	9.65±0.00	0.9034±0.00
F8	0.48±0.0134	0.56±0.0216	28.66±1.673	14.18±0.00	0.8581±0.00
F9	0.43±0.0171	0.48±0.0263	26.59±0.4705	10.31±0.00	0.8968±0.00

The value below 15% indicates a powder will usually give rise to good flow characteristics, whereas above 25% indicate poor Flow ability.

Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula;

Hausner's ratio= ρ_t / ρ_b

Where, ρ_t is tapped density and ρ_b is bulk density

A hausner's ratio less than 1.25 indicates good flow while greater than 1.5 indicates poor flow.

Evaluation of loratidine MDTs

Appearance

The tablets were visually observed for capping, chipping and lamination.

Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets were calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviate from the average weight. The results are shown in Table III.

Thickness uniformity

Three tablets were selected randomly from each batch and thickness was measured by using Vernier Caliper. The results are shown in Table III.

Hardness

Hardness or tablet crushing strength (Fo) the force required to break a tablet in a diametric compression was measured using Monsanto Hardness Tester.

Table III. Evaluation of dimension, hardness and friability, drug content, weight variation of mouth dissolving loratadine tablets

Formulation	Dimension		Hardness	Friability	Drug content	Weight variation
Code	Thickness (mm)	Diameter	(kg/cm^2)	(%)	(%w/w)	(mm)
F1	2.90±0.10	7.86±0.20	3.26± 0.05	0.8±0.05	98.50±0.11	204.6± 1.18
F2	2.9±0.17	7.73±0.32	3.36± 0.11	0.8±0.15	98.75±0.01	205.15 ± 1.59
F3	2.76±0.25	7.83±0.24	3.26± 0.15	0.9±0.1	98.25±0.15	206.15 ± 1.63
F4	2.80±0.10	7.96±0.20	3.36± 0.15	0.9±0.13	95.25±0.13	207.15 ± 1.53
F5	2.70±0.17	7.76±0.32	3.33± 0.25	0.8±0.07	98.50±0.06	207.10 ± 1.61
F6	3.0±0.10	7.80±0.45	3.4± 0.10	0.8±0.09	97.70±0.23	205.10 ± 1.48
F7	2.86±0.11	7.93±0.35	3.4± 0.10	0.8±0.06	97.75±0.14	206.40 ± 1.66
F8	2.96±0.05	7.76±0.30	3.4± 0.10	0.9±0.10	98.75±0.17	207.15 ± 1.53
F9	2.8±0.10	7.83±0.20	3.0± 0.10	0.9±0.11	98.75±0.01	201.55 ± 1.63

For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm^2. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted in kg/cm^2 (Bankar *et. al.*, 1996). The results are shown in Table III.

Friability

Friability of the tablets was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and roping the tablets ata height of 6 inches in each revolution. Preweighed sample of tablets was placed in the Friabilator and were subjected to 100 revolutions. Tablets were dedusted using a soft muslin cloth and reweighed, the friability (F) is given by the formula (Bankar *et. al.*, 1996). The results are shown in Table III.

$$\% F = (\text{Initial wt.} - \text{Final wt.} / \text{Initial wt.}) \times 100.$$

Content uniformity

The Loratadine content in the tablets was estimated as follows.

The tablet powder were weighed equivalent to 10 mg of Loratadine and dissolved in 100 mL of methanol and assayed for drug content using UV-Visible spectrophotometer at 275.00 nm (Anonymous, 2007).

Disintegration time

The Disintegration time of the tablets was determined as per Indian Pharmacopoeia monograph. The test was carried out using USP Disintegrate Test apparatus, (Veego scientific VTD-DV). It consists of an apparatus in which 6 tablets was introduced into each of six cylindrical tubes, the lower end of which was covered by a 0.025 in wire mesh. The tubes were then raised and lowered through a distance of 5.3 to 5.7 cm in a test fluid phosphate buffer pH 6.8 and 0.1N HCl pH 1.2 as a disintegrating media maintained at 37^o ± 2^{o}C. and the time in second taken for complete disintegrate of the tablet with no palpable mass remaining in the apparatus was measured in seconds (Anonymous 2007; Chaudhari *et. al*., 2005). The results are shown in Table IV.

Wetting time of water absorption Ratio

The wetting time characteristic of the loose disintegrant powder allows an evaluation of both the intrinsic swelling and the wettability of the super disintegrants. Wetting time of the ODT is important parameter, which needs to be assessed to give an insight into the disintegrate properties of the tablets; a lower wetting time implies a quicker disintegrate of the tablet. Wetting time was performed at room temperature (Chaudhari *et. al*., 2005; Gattani *et. al*., 2009).

A piece of tissue paper of 10 cm folded twice was placed in small petri dish of diameter 10 cm containing 6 mL of water. A tablet was put on the paper and the time required for water to reach upper surface of tablet was noted. The results are shown in Table IV.

For water absorption ratio the same wetted tablet was taken out from petri dish and weighed. Water absorption ratio (R) was determined by using following equation.

$$R = 100 \times W_a - W_b / W_b$$

Where,

W_b =Weight of tablet before water absorption

W_a = Weight of tablet after water absorption

In-vitro Dissolution studies

Dissolution profiles of Loratadine tablets were determined using the USP Type II Dissolution Test apparatus (Veego scientific VDA-8DR) set with a paddle speed of 100 rpm.

Table IV. Disintegration time, water absorption ratio and wetting time studies of mouth dissolving Loratidine tablet

Formulation code	Disintegration time(sec)±SD	Wetting time(sec) ± SD	Water absorption ratio(%) ± SD
F1	25±3.2863	25±3.2863	81.26 ± 0.98
F2	19±1.4142	20±2.0000	90.28 ± 3.98
F3	15±1.4142	17±1.4142	117.40 ± 1.88
F4	30±1.8973	42±1.8973	78.45 ± 5.92
F5	22±1.4142	31±1.4142	84.44 ± 2.96
F6	18±1.4142	23±2.2803	96.66 ± 1.41
F7	20±2.000	26±2.0000	84.24 ± 6.02
F8	15±1.4142	17±1.4142	96.66 ± 5.40
F9	12±1.8973	11±1.4142	125.80 ± 5.10

Dissolution was performed in 900 mL of 0.1N HCl maintained at 370± 0.5°C. Aliquot of dissolution medium, 5 mL was with drawn at 3, 6, 9, up to 12 min with 5 minutes interval, and filtered through Whatmann filter paper. The amount of drug dissolved was determined by UV-Visible spectrophotometer (Shimadzu-1700 Pharmaspec UV-VIS Spectrophotometer) by measuring the absorbance of the sample at 275 nm. An equal volume of fresh medium, prewarmed at 37°C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Three trials for each batch were performed and average percentage drug release was calculated by using PCP disso V3 software (Anonymous 2007; Gattani 2009; Lachman *et. al.,* 1991). The results are shown in Table V.

Uniformity of drug content

One tablet was crushed and transferred to a 50 mL volumetric flask, 20 mL of methanol was added, shaken well to dissolve the drug. The volume was made up to 100 mL with water and filtered. Then 5 mL of the filterate was diluted to 50 mL with water again from that 5 mL was taken and diluted to 50 mL with water. The results are shown in Table IV.

Stability study of tablets for formulation F9

Optimized formulation F9 sealed in blister packaging and various replicates were kept in the humidity chamber maintained at 40°C and 75 % RH for three months. At the end of the study the samples were analysed for the drug content and release studies and other physical parameter. The results of stability study after three month are given in The results are shown in Table VI.

Results and discussion

Pre-compression parameter (all formulation) of the drug excipients blend has been carried out such as Bulk density, Tapped density, Angle of repose and Carr's index. For F9 formulation the obtained value of Angle of repose (θ) was 26.59, Haussner's ratio 0.8968 and Carr's index 10.31 indicating good flow properties. All the parameters were falls within the limits. Then all the formulations have been evaluated for post- compression parameters. The thickness of all the tablets found in range of 2.8 – 3.0 mm for all the formulations within the prescribed limits of IP 1996 (±5%). The tablet hardness was found to be 3-3.4 kg/cm^2, the friability of all the formulations were found to be between 0.8 - 0.9, which was found to be within the official requirement (i.e. not more than 1%). This value is indicator that the tablets were mechanically stable. The drug content estimation data for all the batches were found to be within the limits (i.e. 95.25 – 99.50). Formulation F9 possess good disintegrating property among all the formulation which was observed during in-vitro disintegration, wetting time, *in vitro* dispersion time.

Formulation containing crospovidone F9 was showing better drug release at end of 12th mins (99.1%). All the formulations were subjected to evaluation studies and from these formulation showed good matrix integrity and drug release rate. Overall results significance that crospovidone in the ratio 10 mg/tablet acts as good disintegrate for fast dissolving tablets. *In-vitro* dissolution results proved formulations F9 were better choice among all the formulations. Stability studies were conducted for all the formulation at 45 °C/75% RH and 50°C for a period of three months as per ICH guidelines.

During the study period several parameters like Hardness, In-vitro disintegration, Drug content uniformity and Wetting time were evaluated for possible instability problems. No significant changes in parameter were observed throughout the study period.

Table V. *In vitro* dissolution profile data for mouth dissolving loratadine tablets for all formulations

Formulation code	Percentage drug release ± S.D of mouth dissolving loratadine tablets at the following time intervals			
	3 minutes	6 minutes	9 minutes	12 minutes
F1	72.91±0.6266	76.42±0.7985	85.50±-0.6221	88.14±0.2214
F2	76.34±0.9868	80.88±0.9421	87.34±0.8546	91.79±1.0974
F3	78.31±1.0102	83.81±0.9072	90.01±1.7596	93.54±0.9073
F4	70.20±1.9053	74.05±0.5212	80.16±1.0627	85.43±1.0627
F5	72.58±0.4653	79.36±1.5224	83.30±2.9131	87.89±1.3618
F6	76.13±0.9595	80.97±1.3054	87.52±0.5105	90.96±0.6814
F7	76.07±0.3220	81.24±0.9209	87.09±0.1330	91.92±0.6291
F8	81.11±1.0369	85.20±0.8182	90.13±2.2305	96.17±2.1127
F9	85.42±1.6733	91.78±0.9055	97.01±1.5832	99.10±0.9422

Table VI. Uniformity of drug content and % drug release of mouth dissolving loratadine tablets at initial and after 3 months stability studies at 40ºC / 75% RH

Formulation code	% drug content w/w (initial month)	% drug content w/w (after 3rd month)	% drug release
		At 40ºc/75%RH	At 40ºC/75% RH
F1	98.50	97.50	87.88±0.298
F2	98.75	97.75	91.26±0.411
F3	98.25	96.50	92.98±0.085
F4	95.25	96.25	84.08±0.024
F5	98.50	96.00	86.72±0.116
F6	97.70	95.50	90.45±0.561
F7	97.75	98.00	90.78±0.312
F8	98.75	95.50	95.07±0.611
F9	99.50	97.50	98.99±0.571

In-vitro dissolution and Wetting time parameters signified that crospovidone in ratio 10 mg per tablet act as good disintegrates prepared by direct compression method. Overall combination F9 were found to be an excellent mouth dissolving tablets with good taste.

Acknowledgement

We heartly express our sincere thanks to Madras Pharmaceuticals, Chennai for providing samples carryout research work and Ideal Analytical and Research institution Pondichery for carrying out FTIR spectras.

References

Anonymous. (2007), Indian Pharmacopoeia. Published by the Controller of Publication, Govt. of India, Ministry of Health and Family Welfare, New Delhi 2007, pp 1045.

Bankar GS and Rhodes CT (1996), Modern Pharmaceutics, 3rd edition, Marcel Dekker, Inc. New York, 1996, pp 668-669.

Chaudhari PD, Chaudhari SP and Kolhe SR (2005), Formulation and evaluation of Famotidine MDT, *Indian Drugs,* **42**(10): 641 - 649.

Gattani SG, Kakade BG and Patil AB (2009), Formulation and evaluation of Ondansetron Hydrochloride mouth dissolving Tablets, *Indian Drugs,* **46** (1): 44 - 60.

Lachman L, Lieberman HA and Kanig JL (1991), The theory and practice of Industrial Pharmacy, 3rd edition, Varghese Publishing House, Mumbai, 199, pp 67-71, 183-184.

Received: 21 March 2012; Accepted: 24 September 2012 .