International Journal of Chemistry and Pharmaceutical Sciences

Journal Home Page: www.pharmaresearchlibrary.com/ijcps

Research Article Open Access

Formulation and Evaluation of Lamotrigine Mouth Dissolving Tablets

Dr. B. Venkateswara Reddy[1]*, K.V. Ramana Reddy[2], Ayesha Sultana[1]

[1]*Department of Pharmaceutics, St.Paul's College of Pharmacy, Turkayamjal (V), Hayathnagar (M), R.R.Dist-501510, India.*
[2]*Sree Datta Institute of Pharmacy, Sheriguda (v), Ranga Reddy Dist-501510, India*

A B S T R A C T

In the present work an attempt has been made to develop fast disintegrating tablets of Lamotrigine. New generation super disintegrants Solutab, Explotab and Polyplasdone XL was selected. All the formulations were prepared by direct compression method using 6mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets have shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F4 formulation showed maximum % drug release i.e., 100.4 % in 10 min hence it is considered as optimized formulation. The F4 formulation contains Solutab as superdisintegrant in the concentration of 20 mg.

Keywords: Bore wells drinking water, Dissolved salt, TDS, Kathlal tehasil.

A R T I C L E I N F O

CONTENTS

Article History: Received 15 February 2015, **Accepted** 25 March 2015, **Available Online** 27 April 2015

***Corresponding Author**
Dr. B. Venkateswara Reddy
Department of Pharmaceutics,
St.Paul's College of Pharmacy, Turkayamjal (V),
Hayathnagar (M), R.R.Dist-501510, India.
Manuscript ID: IJCPS2521

PAPER-QR CODE

Citation: B. Venkateswara Reddy, et al. Formulation and Evaluation of Lamotrigine Mouth Dissolving Tablets. *Int. J. Chem, Pharm, Sci.*, 2015, 3(4): 1648-1652.

1. Introduction

Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Drug delivery systems are becoming increasingly sophisticated as

pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance [1]. Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, ease of administration lead to high levels of patient compliance [2]. It is always the aim of a scientist or a dosage form designer to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in NDDS aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance. Mouth Dissolving Tablet (MDT) is one among such approaches [3]. Mouth Dissolving Tablet disintegrates and dissolves rapidly in the saliva, within a few sec without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 10 sec to 3 min. Most of the MDTs include certain super disintegrants and taste masking agents [4]. Lamotrigine is an anti-convulsant drug used in the treatment of epilepsy and bipolar disorder [5]. It is well absorbed with bioavailability of 98%, but the half life of the drug ranges from 23-37 hours [6], therefore there is a need to develop a delivery system which releases the drug in short time. Thus the present research work is aimed at developing a mouth dissolving tablets of Lamotrigine.

2. Materials and Methods

Materials: Lamotrigine was obtained from SURA labs Hyderabad. Solutab, Explotab and Polyplasdone XL were purchased from Merck Specialities Pvt Ltd, Mumbai, India. Magnesium stearate, talc and microcrystalline cellulose were purchased from Degussa India Pvt. Ltd., Mumbai L.R.

Methods

Formulation development: Lamotrigine mouth dissolving tablets were prepared by direct compression method using the ingredients as shown in table 1. All the ingredients were weighed accurately. Required quantity of drug and excipient mixed thoroughly in a polybag. The blend is compressed using rotary tablet machine-8 station with 6mm flat punch, B tooling. Each tablet is designed to contain 2.5 mg Lamotrigine.

Evaluation studies:

Precompression evaluation studies:

The powder blend of the formulations are evaluated for bulk density, tapped density, carr's index, hausner's ratio and angle of repose to determine their flow and compressibility properties [7].

Post compression evaluation studies:

Hardness test: This is the force required to break a tablet in a diametric compression. Hardness of the tablet is determined by Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moves along the gauze in the barrel fracture. It is expressed in kg/cm^2.

Tablet size and Thickness:

Control of physical dimensions of the tablets such as size and thickness is essential for consumer acceptance and tablet-tablet uniformity. The diameter size and punch size of tablets depends on the die and punches selected for making the tablets. The thickness of tablet is measured by Vernier Callipers scale. Tablet thickness should be controlled within a ±5%. In addition thickness must be controlled to facilitate packaging [7].

Friability:

This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting. Initial weight of 20 tablets is taken and these are placed in the friabilator, rotating at 25rpm for 4min. The difference in the weight is noted and expressed as percentage. It should be preferably between 0.5 to 1.0%.

% Friability = $(W_1-W_2)/W_1$ X 100

Where, W_1= weight o f tablets before test, W_2 = weight of tablets after test

Weight variation of Tablets: It is desirable that all the tablets of a particular batch should be uniform in weight. Twenty tablets were taken randomly and weighed accurately. The average weight was calculated. If any weight variation is there, that should fall within the prescribed limits as given in the table-2.

Table 1: Composition for mouth dissolving tablets of lamotrigine

Ingredients	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Lamotrigine	2.5	2.	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Solutab	5	10	15	20	-	-	-	-	-	-	-	-
Explotab	-	-	-	-	5	10	15	20	-	-	-	-
Polyplasodne XL	-	-	-	-	-	-	-	-	5	10	15	20
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Mg. Stearate	2	2	2	2	2	2	2	2	2	2	2	2
MCC pH102	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight(mg)	100	100	100	100	100	100	100	100	100	100	100	100

Table 2: Acceptance criteria for tablet weight variation

Average weight of tablet(mg)	Maximum % difference allowed
130 or Less than	± 10
130-324	± 7.5
More than 324	± 5

Assay:

10 tablets were weighed and triturated. The tablet triturate equivalent to 10 mg of the drug was weighed accurately, dissolved in pH 1.2 buffer and diluted to 100 ml with the same. Further dilutions were done suitably to get a concentration of 10 µg/ ml with simulated gastric fluid pH 1.2. Absorbance was read at 304 nm against the reagent blank, and the concentrations of lamotrigine in µg/ ml was determined by using the regression equation [8].

$$Y = 0.007x + 0.001$$

Drug content in mg / tablet = conc. µg/ml * dilution factor

% Drug content = drug content in mg * 100 / label claim

Disintegration test:

Disintegration time is considered to be one of the important criteria in selecting the best formulation. To achieve correlation between disintegration time in-vitro and in-vivo, several methods were proposed, developed and followed at their convenience. One tablet was placed into each tube and the assembly was suspended into the 1000ml beaker containing water maintained at 37±2^{o}c and operated the apparatus for 15 minutes. The assembly was removed from the liquid and the tablets were observed. If one or two tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not less than 16 of the total of 18 tablets tested are disintegrated [9].

***In-vitro* Dissolution study:**

Dissolution media was taken as 0.1N HCL and was placed in the vessel and USP II Paddle apparatus was assembled. The medium was allowed to equilibrate to a temperature of 37±0.5°C. Tablet was placed in the basket and placed in the vessel and operated for 30min at 50 rpm. At definite time intervals, 5 ml of the fluid was withdrawn, filtered and again 5ml of the fluid was replaced. Suitable dilutions were done with the dissolution fluid and the samples were analyzed using UV spectrophotometer at 304nm [10].

3. Result and Discussion

Pre-compression parameters:

The results are given in Table-3.The values for angle of repose were found in the range of 25°-30°. Bulk densities and tapped densities of various formulations were found to be in the range of 0.41 to 0.50 (gm/cc) and 0.50 to 0.58 (gm/cc) respectively. Carr's index of the prepared blends was in the range of 13.79% to 18.24% and hausner's ratio in the range of 1.16 to 1.22. From the result it was concluded that the powder blends had good flow properties and these can be used for tablet manufacture.

Table 3: Precompression results of the power blend

Formulations	Bulk Density (g/cm^2)	Tap Density (g/cm^2)	Carr's Index (%)	Hausner's ratio	Angle of Repose (Ɵ)
F_1	0.45	0.55	18.18	1.22	27.91
F_2	0.47	0.55	14.54	1.17	28.23
F_3	0.50	0.58	13.79	1.16	29.34
F_4	0.46	0.55	16.36	1.19	26.71
F_5	0.50	0.58	13.79	1.16	29.34
F_6	0.47	0.55	14.54	1.17	28.23
F_7	0.50	0.58	13.79	1.16	29.34
F_8	0.41	0.50	18	1.21	26.78
F_9	0.41	0.50	18	1.21	26.78
F_{10}	0.42	0.51	18.24	1.20	26.68
F_{11}	0.48	0.56	18.12	1.21	26.70
F_{12}	0.41	0.54	18.11	1.22	26.71

Post compression Parameters:

Hardness test:

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table-4. The results showed that the hardness of the tablets is in range of 2.3 to 2.8kg/cm^2, which was within IP limits.

Thickness: Thickness of three tablets of each batch was checked by using vernier caliper and data shown in Table-4. The result showed that thickness of the tablet is ranging from 3.45 to 3.64mm.

Friability: Tablets of each batch were evaluated for percentage friability and the data's were shown in the Table-4. The average friability of all the formulations lies in the range of 0.30 to 0.54% which was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Weight variation test: Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table-4. The average weight of the tablet is approximately in range of 109 to 98.5, so the permissible limit is ±10% (110-90mg). The results of the test showed that, the tablet weights were within the pharmacopoeia limit.

***In vitro* disintegration time:** Tablets of each batch were evaluated for in vitro disintegration time and the data's were shown in the Table-4. The results showed that the disintegration time of prepared tablets were in the range of 12.66 to 30.33 seconds.

Assay: Assay studies were performed for the prepared formulations. From the assay studies it was concluded that all the formulations were showing the % drug content values within 97.23 -100.94 %.

Table 4: Results of post compression study

FD	Wt.variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Assay (%)
F_1	105	2.5	3.59	20.33	0.43	97.23
F_2	104	2.6	3.64	22.66	0.34	98.55
F_3	101	2.5	3.59	30.3	0.49	98.16
F_4	109	2.6	3.58	12.66	0.47	101.4
F_5	99.4	2.3	3.59	30.33	0.49	98.16
F_6	102	2.7	3.64	22.66	0.34	98.55
F_7	101	2.5	3.59	30.13	0.49	100.8
F_8	107	2.6	3.56	17.00	0.34	99.25
F_9	102	2.5	3.56	17.00	0.30	99.25
F_{10}	103	2.4	3.55	15.99	0.43	98.6
F_{11}	102.4	2.8	3.45	15.00	0.54	100.94
F_{12}	98.5	2.5	3.54	16.76	0.43	98.5

***In-vitro* Dissolution studies:**

The results of *in-vitro* dissolution studies are represented in table-5. In most of the formulations complete drug release was found to be within 25mins. Various disintegrants have shown various drug release profile out of all the formulations, the formulation with more amount of disintegrants have shown maximum drug release within 15-20mins. The formulation F4 containing Solutab as disintegrant was found to be the best with 100.4% of drug release in 15mins. Irrespective of super disintegrate type the disintegration time decreases and Dissolution time also decreases as the concentration of super disintegrate increases.

Table 5: *In-Vitro* dissolution studies

Time (mins)	Cumulative %drug release											
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
2	13.5	32.9	37.6	54.9	12.8	31.4	33.7	37.9	12.84	21.45	25.41	22.4
4	24.7	44.4	55.8	78.8	26.4	43.5	48.9	51.4	34.71	39.47	43.17	41.6
6	35.8	55.5	67.9	94.1	37.6	57.1	67.4	67.8	48.46	50.51	55.84	58.4
10	57.4	70.1	78.4	100.4	51.1	73.5	83.7	76.1	56.82	67.49	74.98	66.7
15	68.2	88.0	91.4	-	62.4	81.6	91.2	95.2	76.41	80.14	86.54	89.3
20	81.6	95.6	98.2	-	77.5	90.4.	96.4	100.2	84.3	89.18	94.94	99.7
25	90.1	98.5	-	-	90.9	97.9	99.5	-	92.4	95.84	98.15	-
30	96.4	-	-	-	95.4	-	-	-	97.71	99.45	-	-

4. Conclusion

Lamotrigine mouth dissolving tablets were successfully prepared by employing various disintegrants like Solutab, Explotab and Polyplasodne XL. Direct compression method was used to prepare the tablets and initially the powder blend was subjected to precompression studies and found that powder exhibited good flow properties. The post compression evaluation indicated that the developed formulations were fulfilling the required specifications. Out of 12 formulations developed formulation F4 containing solutab in a concentration of 20mg showed good results in terms of quick disintegration time and maximum drug release of 100.2% at the end of 10mins. So it is considered as the optimized formulation, which releases the drug within 10mins of administration.

5. References

1. Aulton E. Micheal. Modified release peroral dosage forms, Pharmaceutics - The Science of Dosage form Design, New York: Churchill Livingston, pp. 575.
2. Chein YW. Oral Drug Delivery and Delivery Systems. 2nd ed. New York: Marcel Dekker, 1992.
3. Kaur T, Bhawandeep G, Sandeep K, Gupta GD. Mouth dissolving tablets: A novel approach to drug delivery. Int J Curr Pharm Res., **2011**, 3(1): 1-7.
4. Deshika R, Viness P, Yahya EC, Lisa CT. Rapidly disintegrating oramucosal drug delivery technologies. Pharm Dev Tech., **2009**, 14(6): 588-601.
5. Rambeck B, Wolf P. Lamotrigine clinical pharmacokinetics. Clin Pharmacokinet., **1993**, 25(6): 433-43.

6. Victor Biton. Pharmacokinetics, toxicology and safety of lamotrigine in epilepsy. Expert Opinion on Drug Metabolism & Toxicology, **2006,** 2(6): 1009-1018.
7. Lachman L, Liberman HA and Kanig JL. Theory & practice of industrial pharmacy. 3rd ed. Mumbai: Varghese publishing house, **1991**, pp. 296-302.
8. C.Patil and S.Das. Effect of various superdisintegrants on the drug release profile and disintegration time of lamotrigine orally disintegrating tablets. African journal of pharmacy and pharmacology, **2011**, 5(1):76-82.
9. B.Venkateswara Reddy, N.Theja Vinod Kumar, K.Navaneetha. Formulation and evaluation of dispersible tablets of olmesartan medoxomil. European journal of biomedical and pharmaceutical sciences, 2015, 2(1):250-260.
10. P.K.Lakshmi, Swetha Reddy, C. Kishore, B. Satish Reddy. Formulation and Evaluation of Oral Disintegrating Tablets of Lamotrigine Solid Dispersions. Iranian Journal of Pharmaceutical Sciences, **2013**, 9(1):1-12.