International Journal for Pharmaceutical Research Scholars (IJPRS)

V-7, I-2, 2018 ISSN: 2277 - 7873

RESEARCH ARTICLE

Formulation and Evaluation of Fast Dissolving Tablet of Lamotrigine

Madhuri T. Hivarkar*, Ravi D. Hole

[1] *Department of Pharmaceutics, Dattakala College Of Pharmacy, Swami-Chincholi, Tal-Daund Dist-Pune 413130 India.*

Manuscript No: IJPRS/V7/I2/00030, Received On: 28/04/2018, Accepted On: 08/05/2018

ABSTRACT

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Fast dissolving tablet of Lamotrigine was formulated by using various super-disintegrants like Cross carmellose sodium and Sodium starch glycolate in different proportions by sublimating agent like camphor. The values of pre-compression parameters of all formulation showed good flow properties and compressibility, so these can be used for tablet manufacture. The disintegration time for all formulations was considered to be within the acceptable limit. It observed that when sublimating agent like camphor was used disintegration time of tablet is decreased. The concept of formulating high porous fast dissolving tablets of Lamotrigine inclusion complexes using superdisintegrants by sublimation technique offers a suitable and practical approach in serving desired objectives of faster disintegration and dissolution characteristics.

KEYWORDS

Superdisintegrants, oral drug delivery, Fast Dissolving Tablet, Lamotrigine

INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms.

*Address for Correspondence:
Madhuri T Hivarkar
Department Of Pharmaceutics, Dattakala College Of Pharmacy, Dist-Pune 413130.
E mail ID: ravihole12@gmail.com

Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (ketosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Or dispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people[4]. Fast dissolving tablets areal so called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapid melts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva[5]. The faster the drug into solution, quicker the

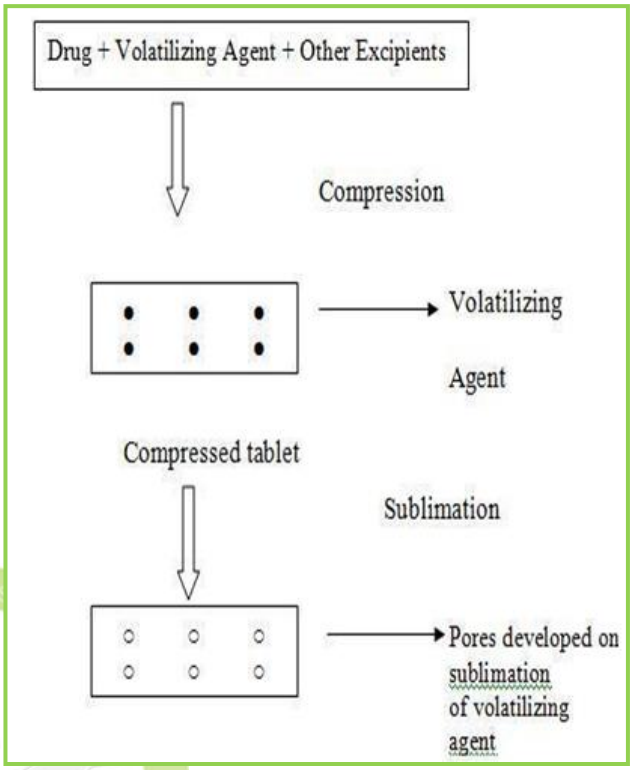
absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics[7]. Their growing importance was underlined recently when European pharmacopoeia adopted the term ―Orodispersible tablet‖ as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach in development of FDT is the use of superdisintegrants like cross linked carboxy methyl cellulose (crosscarmellose), sodium starch glycolate (primogel, explotab), polyvinyl pyrollidon (polyplasdone) etc, which provide instantaneous disintegration of tablet after putting on tongue, their by release the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pre gastric absorption of saliva

Containing dispersed drugs that pass down into the stomach. More ever, the amount of drug that is subject is to first pass metabolism is reduced as compared to standard tablet. The technologies used form manufacturing fast-dissolving tablets are tablet sublimation.

Following conventional techniques are used for preparation of fast dissolving drug delivery system[7-9]

Sublimation

The slow dissolution of the compressed tablet containing even highly water-soluble ingredients is due to the low porosity of the tablets. Inert solid ingredients that volatilize readily (e.g. urea, ammonium carbonate, ammonium bicarbonate, hexa Methylene tetramine, camphor etc.) were added to the other tablet ingredients and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates porous structures. Additionally, several solvents (e.g. cyclohexane, benzene) can be also used as pore forming agents,



MATERIAL & METHODS

Table no-1

Sr no.	Name of Ingredient	Supplier
1	Lamotrigine	Abottpharmapvt. Ltd., Goa
2	Sodium StarchGlycollate	Yash Scientific Enterprises, Pune
3	Crosscarmellose Sodium	Kurla Complex, Mumbai
4	β-Cyclodextrin	Ozone international, Mumbai
5	Aerosil	Yash Scientific Enterprises, Pune
6	Camphor	Yash Scientific Enterprises, Pune
7	Directly Compressible Lactose	Yash Scientific Enterprises, Pune

Method

A) Preformulation Study

B) Organoleptic Characteristics

C) Physico-chemical Characterization

1 Bulk Density

2 Tapped Density

3 Carr's index

4 Hausner's Ratio

5 Angle of Repose

D) Calibration curve of Drug

E) Formulation & Evaluation of Tablet

1. Hardness

2. Disintegration Time

3. Thickness

4. Friability

5. Wetting Time

6. Drug Content

7. Weight Variation

8. *Invitro* Drug Release (Dissolution Study)

Formulation procedure of tablet (direct compression)

In process of direct compression techniques, the all ingredients were accurately weighed and passed through sieve no.40 then mixed together and then compressed using 6 mm flat punch on Cemach R&D Tablet press 10 station compression machine. Hardness of the tablet was maintained at 3-3.5 Kg/cm^2. Tablet weight was maintained at 170 to 180 mg. All the product and process variables like mixing time and hardness were kept as practically constant.

Table no-2

Sr No.	Name of ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
1	**Lamotrigine**	25	25	25	25	25	25
2	**β-cyclodextrin**	25	25	25	25	25	25
3	**Sodium starch glycolate**	21	26.25	31.5	-	-	-
4	**Crosscarmellose sodium**	-	-	-	21	26.25	31.5
5	**Direct compressible**	10.7	5.45	0.2	10.7	5.45	0.2
6	**Camphor**	7	7	7	7	7	7
8	**Total weight**	90	90	90	90	90	90

RESULTS AND DISCUSSION

In this study fast dissolving tablet of Lamotrigine were prepared by direct compression. Method and effect of different superdisintegrating and sublimating agent camphor on *in vitro* release were evaluated.

Organoleptic Characteristics

Organoleptic characteristics like colour, odour, and taste were studied. The Lamotrigine complies with specifications. The results are illustrated in table

Table No.3 Organoleptic properties of Lamotrigine

Sr. No	Properties	Specification	Lamotrigine
1	Appearance	White	White
2	Description	Crystalline	Crystalline
3	Odour	Odourless	Odourless
4	Taste	Bitter	Bitter

Physical characterization

The powder bed was evaluated for the blend property like Bulk density, Tapped density, Carr's index, Hausner's ratio and Angle of repose.

Batch code	Bulk density (gm/ml) ± SD	Tapped density (gm/ml) ± SD	Carr's index % ± SD	Hausner's ratio % ± SD	Angle of repose (^{0}) ± SD
F1	0.6032± 0.03	0.6912 ± 0.01	14.25 ± 0.20	1.1124 ± 0.02	20.07 ± 0.54
F2	0.6133 ± 0.05	0.6999 ± 0.02	14.09 ± 0.39	1.1358 ± 0.07	19.45 ± 0.85
F3	0.6258 ± 0.01	0.7134 ± 0.06	15.00 ± 0.13	1.1425 ± 0.06	19.39 ± 0.29
F4	0.6078 ± 0.07	0.7088 ± 0.09	15.04 ± 0.75	1.1298 ± 0.04	20.14 ± 0.17
F5	0.6125 ± 0.02	0.7032 ± 0.05	14.58 ± 0.09	1.1340 ± 0.03	20.73 ± 0.65
F6	0.6289 ± 0.08	0.7155 ± 0.04	14.99 ± 0.67	1.1536 ± 0.01	20.10 ± 0.44

Calibration curve of Drug

Stock solution of 100 µg/ml was prepared in 0.1 ml N HCL, from which dilution were made to obtain 2, 4, 6, 8, 10 µg/ml solution. Absorbance of these solutions when measured at ƛmax 267 nm and the results are given Table.

Table No 5 Calibration curve of lamotrigine in 0.1 N HCL

Sr. No.	Concentration (µg/ml)	Absorbance at 267 nm ±SD
1	0	0 ± 00
2	2	0.1927± 0.00015
3	4	0.2360± 0.00023
4	6	0.2924± 0.00011
5	8	0.3207± 0.00046
6	10	0.3913± 0.00078

Calibration curve

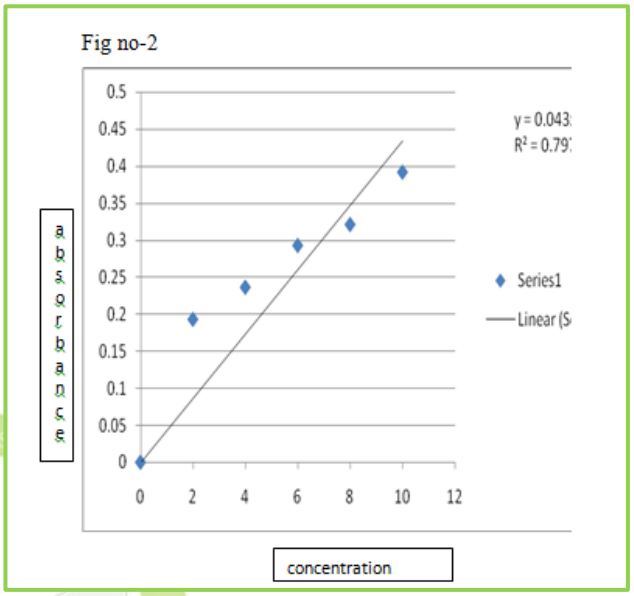


Figure 2: Standard calibration curve of Lamotrigine in 0.1 N HCl

Evaluation of compression characteristics of formulations

Tablets of all batches were evaluated for weight variation, hardness, thickness and friability results were tabulated in Table.

Tablet No.6 Post compression properties of tablets F1 to F6

Batch code	Weight variation (mg) ± SD	Hardness (kg/cm^2) ± SD	Thickness (mm) ± SD	Friability ± SD%
F1	0.090 ± 0.02	12.25 ± 0.28	5.02 ± 0.03	0.63 ± 0.02
F2	0.090 ± 0.01	13.20 ± 0.90	5.05 ± 0.08	0.52 ± 0.02
F3	0.090 ± 0.03	13.00 ± 0.26	5.06 ± 0.02	0.73 ± 0.01

F4	0.090 ± 0.02	13.10 ± 0.13	5.07 ± 0.05	0.89 ± 0.03
F5	0.090 ± 0.03	13.23 ± 0.58	5.03 ± 0.04	0.75 ± 0.04
F6	0.090 ± 0.01	13.05 ± 0.10	5.04 ± 0.01	0.45 ± 0.03

Evaluation of various Parameters of Tablets

The tablets were evaluated for disintegration time, wetting time, and drug content. Results obtained were given in Tablet.

Table No.7 other post compression parameters of tablets F1 to F6

Batch code	Disintegration time (s)± SD	Wetting Time (s) ± SD	Drug content ± SD
F1	58.05 ± 0.07	62.37 ± 0.54	95.49 ± 1.11
F2	53.14 ± 0.04	59.48 ± 0.34	96.76 ± 0.92
F3	45.38 ± 0.03	56.35 ± 0.12	98.48 ± 1.07
F4	15.20 ± 0.10	57.01 ± 0.89	97.68 ± 1.15
F5	17.02 ± 0.07	55.42 ± 0.45	95.21 ± 1.01
F6	08.20 ± 0.03	53.32 ± 0.75	101.23 ± 1.05

Tablet wetting initial **Tablet wetting after 53.32 sec**

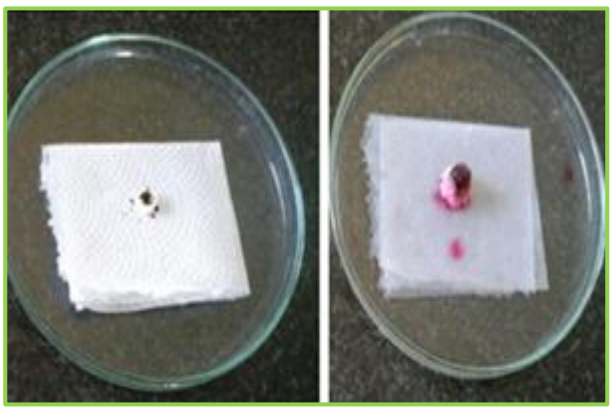


Figure 3: wetting time of fast dissolving tablet of Lamotriginre

***In vitro* Drug Release (Dissolution Study)**

Dissolution test were carried out using USP Type dissolution test apparatus at 37 ± 0.5^0C and rpm speed. 900 ml of 0.1 N HCl was used as dissolution medium. Two tablets from each tablets were tested individually in 0.1 N HCl with sample withdraw 5 ml. Collected samples were analysed at ƛ max 267 nm using 0.1 N HCl as blank. The percentage drug release was found to formulation F1 to F6 are given in following tables.

Table No.7 *In vitro* drug release data of formulation F1 (n=2)

Time (min)	Absorbance (267nm)	Concentration (µg/ml)	Cumulative drug release	Percentage CDR (%)
0	0	0	0	0
1	0.0415	1.22	0.048	4.8
2	0.1737	5.18	0.20	20.43
5	0.3995	11.75	0.47	47.00
15	0.5805	17.07	0.68	68.28
30	0.8298	24.40	0.97	97.60

Table No.8 *In vitro* drug release data of formulation F2 (n=2)

Time (min)	Absorbance (267nm)	Concentration (µg/ml)	Cumulative drug release	Percentage CDR (%)
0	0	0	0	0
1	0.0761	2.23	0.08	8.9
2	0.1908	5.61	0.22	22.44
5	0.38.37	11.28	0.45	45.12
15	0.5638	16.58	0.66	66.32
30	0.8344	24.54	0.98	98.16

Table No.9 In *vitro* drug release data of formulation F3 (n=2)

Time (min)	Absorb-ance (267nm)	Concⁿ (µg/ml)	Cumulative drug release	Percentage CDR (%)
0	0	0	0	0
1	0.0625	1.83	0.07	7.35
2	0.2248	6.61	0.26	26.44
5	0.4158	12.22	0.48	48.88
15	0.5960	17.52	0.70	70.08
30	0.8495	24.98	0.99	99.92

Table No.10 In *vitro* drug release data of formulation F4 (n=2)

Time (min)	Absor-bance (267nm)	Concⁿ (µg/ml)	Cumulative drug release	Percentage CDR (%)
0	0	0	0	0
1	0.0305	0.89	0.03	3.5
2	0.2348	6.90	0.27	27.62
5	0.4009	11.79	0.47	47.16
15	0.6010	17.67	0.70	70.68
30	0.8489	24.96	0.99	99.84

Table No.11 in *vitro* drug release data of formulation F5 (n=2)

Time (min)	Absorbance (267nm)	Concⁿ (µg/ml)	Cumulative drug release	Percentage CDR (%)
0	0	0	0	0
1	0.0238	0.7	0.02	2.8
2	0.1983	5.83	0.23	23.32
5	0.3785	11.13	0.44	44.52
15	0.5969	17.55	0.70	70.20
30	0.8239	24.23	0.96	96.92

Table No.12 In *vitro* drug release data of formulation F6 (n=2)

Time (min)	Absorb-ance (267nm)	Concⁿ (µg/ml)	Cumulative drug release	Percentage CDR (%)
0	0	0	0	0
1	0.0843	2.47	0.09	9.9
2	0.2248	6.61	0.26	26.44
5	0.4475	13.16	0.52	52.64
15	0.6308	18.55	0.74	74.20
30	0.8399	24.70	0.98	98.81

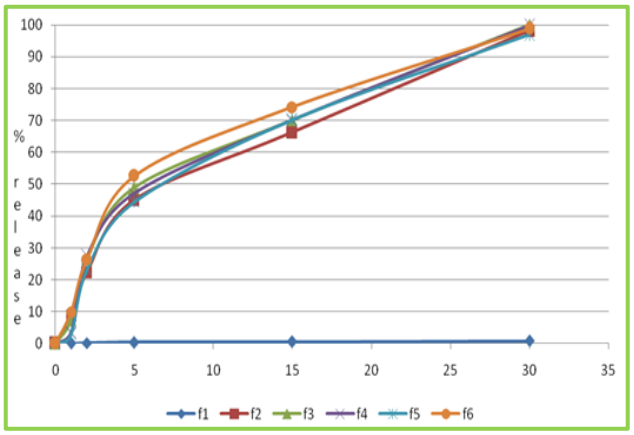


Figure no-4 dissolution profile of formulation F1 to F6

CONCLUSION

The results obtained so far encouraged as to derive following conclusion,

- Fast dissolving tablet of Lamotrigine was formulated by using various superdisintegrants like Crosscarmellose sodium and Sodium starch glycolate in different proportions by sublimating agent like camphor.
- The values of pre-compression parameters of all formulation showed good flow properties and compressibility, so these can be used for tablet manufacture.
- The disintegration time for all formulations was considered to be within the acceptable limit. It observed that when sublimating agent like camphor was used disintegration time of tablet is decreased.
- Wetting time studies showed that wetting time was rapid in formulations containing camphor followed by CCS and SSG. It was found that as the concentration of CCS and SSG was increases, then wetting was reduces.
- The post compression parameters of all formulations were determined and the values were found to be within IP limits.
- *In-vitro* disintegration of F3 gives rapid disintegrating time and wetting time.
- As result of this study, it may be concluded inclusion the complexation techniques may be useful to enhance solubility and dissolution rate.
- The concept of formulating high porous fast dissolving tablets of Lamotrigine inclusion complexes using superdisintegrants by sublimation technique offers a suitable and practical approach in serving desired objectives of faster disintegration and dissolution characteristics.

REFERENCES

1. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy.
2. Third Edition, Varghese Publication House, Bombay, India 1987: 296-300.
3. Amin, A. F., Shah, T. J., Bhadani, M. N., & Patel, M. M. (2005). Emerging trends in orally disintegrating tablets.
4. Prakash Goudanavar et al. (2011). Development and characterization of lamotrigineorodispersible tablets Inclusion complex with hydroxypropyl β cyclodextrin‖ *International Journal of Pharmacy and Pharmaceutical Sciences*, *3*(3), 208-214
5. Seager, H. (1998). Drug-delivery products and the Zydis fast-dissolving dosage form. *Journal of pharmacy and pharmacology*, *50*(4), 375-382.
6. Remon, J. P., & Corveleyn, S. (2000). *U.S. Patent No. 6,010,719*. Washington, DC: U.S. Patent and Trademark Office.
7. Masaki, K., Intrabuccaly disintegrating preparation and production thereof, *US Patent No.5, 466*, 464, 1995.
8. Pebley, W.S., Jager, N.E., Thompson, S.J., Rapidly disintegrating tablets, US Patent No.5, 298, 261, 1994.
9. Amrutkar, P. P., Patil, S. B., Todarwal, A. N., Wagh, M. A., Kothawade, P. D., & Surawase, R. K. (2010). Design and evaluation of taste masked chewable dispersible tablet of lamotrigine by melt

granulation. *International Journal of Drug Delivery*, *2*(2).

10. Allen Jr, L. V., & Wang, B. (1996). *U.S. Patent No. 5,587,180*. Washington, DC: U.S. Patent and Trademark Office.
11. Biradar, S. S., Bhagavati, S. T., & Kuppasad, I. J. (2006). Fast dissolving drug delivery systems: a brief overview. *The internet journal of pharmacology*, *4*(2), 26-30.
12. Zade, P. S., Kawtikwar, P. S., & Sakarkar, D. M. (2009). Formulation, evaluation and optimization of fast dissolving tablet containing tizanidine hydrochloride. *Int J Pharm Tech Res*, *1*(1), 34-42.
13. Sukhavasi, S., & Kishore, V. S. (2012). Formulation and evaluation of fast dissolving tablets of amlodipine besylate by using hibiscus rosa-sinensis mucilage and modified gum karaya. *International Journal of Pharmaceutical Sciences and Research*, *3*(10), 3975.
14. Patil, C., & Das, S. (2009). Effect of various superdisintegrants on the drug release profile and disintegration time of Lamotrigine orally disintegrating tablets. *African journal of pharmacy and pharmacology*, *5*(1), 76-82.
15. Swamy, P. V., Areefulla, S. H., Shirs, S. B., Smitha, G., & Prashanth, B. (2007). Orodispersible tablets of meloxicam using disintegrant blends for improved efficacy. *Indian journal of pharmaceutical sciences*, *69*(6), 836.
16. Shah S. D. (2010). M.Pharm thesis, Formulation and evaluation ofsublingual tablet of Sumatriptan succinate, Saurashtra University.