CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.8170970

Available online at: http://www.iajps.com *Research Article*

FORMULATION AND CHARACTERISATION OF ORAL DISINTEGRATING TABLETS OF LAMOTRIGINE USING NOVEL SUPER DISINTEGRANTS

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Abstract:

Orally disintegrating tablets are a vital tool in keeping our children and elderly population healthy. Their ease of use and accurate dosing allow higher patient compliance and more reliable therapeutic effects. Superdisintegrants are the fundamental element contained in orally disintegrating tablets and are responsible for their unique ability to quickly disintegrate and dissolve on the surface of the tongue without the use of any additional liquid. In order to determine the most effective type and optimal amount of superdisintegrants for orally disintegrating tablets manufactured by direct compression, the following tablet parameters were tested hardness, thickness, friability, disintegration time, and wetting time. three superdisintegrants were tested, namely: Solutab, Polyplasdone XL and Locust bean gum and the most efficient superdisintegrant was selected based on the above mentioned studies. From the results obtained, it can be concluded that the tablet formulation (F3) showed the promising formulation also the hardness, friability, disintegration time and dissolution rate of prepared tablets were found to be acceptable according to standard limits.

Key words: Lamotrigine, Solutab, Polyplasdone XL, Locust bean gum and Mouth dissolving tablets.

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Please cite this article in press K . Bhanu yaswanth et al, ***Formulation And Characterisation Of Oral Disintegrating Tablets Of Lamotrigine Using Novel Super Disintegrants.,*** *Indo Am. J. P. Sci, 2023; 10 (06).*

INTRODUCTION:

The oral route of administration isconsidered as the most widely accepted routebecause of its convenience of selfadministration, compactness and easy manufacturing. But the most evidentdrawback of the commonly used oral dosageforms like tablets and capsules is difficulty inswallowing, leading to patients incompliance particularly in case of pediatric and geriatric patients.[1] but it also applies to people whoare ill in bed and to those active workingpatients who are busy or traveling, especiallythose who have no access to water.[2]Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Orally disintegrating tablets are appreciated by a significant segment of populations particularly who have difficulty inswallowing. It has been reported that Dysphagia.[3](difficulty in swallowing) is common among all age groups and morespecific with pediatric, geriatric populationalong with institutionalized patients ,psychiatricpatients and patients with nausea, vomiting, andmotion sickness complications. ODTs withgood taste and flavor increase the acceptabilityof bitter drugs by various groups of population.

This dosage form combines theadvantages of dry and liquid formulation. Somenovel ODT technology allow high drug loading,have an acceptable taste, offer a pleasant mouthfelling, leaving minimal residue in the mouthafter oral administration.ODT have beeninvestigated for their potential in improvingbioavaibility of poorly soluble drug throughenhancing the dissolution profile of the drugand hepatic metabolism drugs.Orally disintegrating tablets are alsocalled as orodispersible tablets, quickdisintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets,porous tablets, and rapimelts. However, of all the above terms, United Statespharmacopoeia (USP) approved these dosageforms as ODTs. Recently, European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing.

United States Food and Drug Administration (FDA) defined ODT as “A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue.” The disintegration time for ODTs generally ranges from several seconds to about a minute.

Drug selection criteria

The ideal characteristics of a drug for oral dispersible tablet include

- Ability to permeate the oral mucosa.
- At least partially non-ionized at the oral cavity pH.
- Have the ability to diffuse and partition into the epithelium of the upper GIT.
- Small to moderate molecular weight.
- Low dose drugs preferably less than 50 mg.
- Short half life and frequent dosing drugs are unsuitable for ODT.
- Drug should have good stability in saliva and water.
- Very bitter or unacceptable taste and odor drugs are unsuitable for ODT

Desired criteria for ODTs

- ODT should leave minimal or no residue in mouth after oral administration, compatible with pleasing mouth feel.
- Effective taste masking technologies should be adopted for bitter taste drugs.
- Exhibit low sensitivity to environment condition such as humidity and temperature.
- ODTs should dissolve / disintegrate in the mouth in matter of seconds without water.
- Have sufficient mechanical strength and good package design.
- The drug and excipients property should not affect the orally disintegrating tablets.
- Be portable and without fragility concern.

Advantages of ODTs

The advantages of ODTs include :

No need of water to swallow the tablet.

- Compatible with taste masking and have a pleasing mouth feel.
- Can be easily administered to paediatric,elderly and mentally disabled patients.
- No residue in the oral cavity afteradministration.
- Manufacturing of the tablets can be done using conventional processing and packaging equipments at minimum cost. Allow high drug loading.
- Accurate dose can be given as comparedto liquids.
- Dissolution and absorption of the drug isfast, offering a rapid onset of action.
- Advantageous over liquid medication in terms of administration as well as transportation. Some amount of drugs is absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, thus reducing first pass metabolism, whichoffers improved bioavailability and thusreduced dose and side effects.

- No risk of suffocation due to physicalobstruction when swallowed, thusoffering improved safety.
- ODTs are suitable for sustained andcontrolled release actives.
- Unit packaging.

Limitations of ODTs

It includes

- The tablets commonly have insufficient mechanical strength. Hence, conscientious handling is necessary.
- The tablets may leave an unpalatable taste and grittiness in the oral cavity if not formulated properly.
- Drugs which have large doses, can cause problems to formulate them into ODTs.
- Patients who simultaneously take anticholinergic drugs are not suitable candidates for ODTs.[11,12]

Challenges in the formulation of ODTs

- Mechanical strength and disintegration time: Disintegration time will extend if the mechanical strength is more, so a good cooperation between these two parameters is always necessary.
- Taste masking: Efficient taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.
- Mouth feel: The particles produced after disintegration of the ODT should be very small. ODT should not leave any residue in the mouth after oral administration. Addition of flavors and cooling agents like menthol enhance the mouth feel.
- Sensitivity to environmental conditions: ODTs should have low sensitivity to environmental conditions such as humidity and temperature.

Cost: The technology adopted for an ODT should be acceptable in terms of cost of the final product.

MATERIALS

Lamotrigine- Procured From Aurobindo pharma Ltd, Hyderabad, India. Provided by SURA LABS, Dilsukhnagar, Hyderabad, Solutab- S.D. Fine Chemicals. Pvt Ltd, Mumbai, India, Polyplasdone XL- S.D. Fine Chemicals. Pvt Ltd, Locust bean gum- S.D. Fine Chemicals. Pvt Ltd, Aspartame- S.D. Fine Chemicals. Pvt Ltd, Talc- S.D. Fine Chemicals. Pvt Ltd, Mg striate- S.D. Fine Chemicals. Pvt Ltd, MCC- S.D. Fine Chemicals. Pvt Ltd.

METHODOLOGY

Buffer preparation:

Preparation of 0.2 M Potassium dihydrogen orthophosphate solution: Accurately weighed 27.128 gm of monobasic potassium dihydrogen orthophosphate was dissolved in 1000 ml of distilled water and mixed.

Preparation of 0.2 M sodium hydroxide solution : Accurately weighed 8 gm of sodium hydroxide pellets were dissolved in 1000 mL of distilled water and mixed.

Preparation of pH 6.8 phosphate buffer : Accurately measured 250 mL of 0.2 M potassium dihydrogen orthophosphate and 112.5 mL of 0.2 M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Analytical method development forLamotrigine:

a) Determination of absorption maxima

A spectrum of the working standards was obtained by scanning from 200-400 nm against the reagent blank to fix absorption maxima. The λ_{max} was found to be 304 nm. Hence all further investigations were carried out at the same wavelength.

b) Construction of standard graph

100 mg of Lamotrigine was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/mL (1000µg/mL) 1 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10µg/ml). From this stock solution aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8ml, 1 ml, were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 2, 4, 6, 8 and 10µg/ml respectively. The absorbance of each concentration was measured at respective (λ_{max}) i.e., 304nm.

Formulation development:

Drug and different concentrations of super disintegrants (Solutab, Polyplasdone XL and Locust bean gum)and required ingredients were accurately weighed and passed through a 40-mesh screen to get uniform size particles and mixed in a glass motor for 15 min.

- The obtained blend was lubricated with magnesium stearate and glidant (Talc) was added and mixing was continued for further 5 min.
- The resultant mixture was directly compressed into tablets by using punch of rotary tablet compression machine. Compression force was kept constant for all formulations.

Table 1: Formulation table showing various compositions

INGREDIENTS (MG)	FORMULATION CODES								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lamotrigine	25	25	25	25	25	25	25	25	25
Solutab	25	50	75	-	-	-	-	-	-
Polyplasdone XL	-	-	-	25	50	75	-	-	-
Locust bean gum	-	-	-	-	-	-	25	50	75
Aspartame	15	15	15	15	15	15	15	15	15
Talc	6	6	6	6	6	6	6	6	6
Mg streate	5	5	5	5	5	5	5	5	5
MCC	74	49	24	74	49	24	74	49	24
Total Weight (mg)	150	150	150	150	150	150	150	150	150

RESULTS AND DISCUSSION:

Preparation of Calibration Curve of Lamotrigine: The regression coefficient was found to be 0.998 which indicates a linearity with an equation of Y= 0.066 X-0.013. Hence Beer-Lambert's law was obeyed.

Table 2: Calibration curve data of Lamotrigine in pH 6.8 phosphate buffer

Concentration	Absorbance
0	0
2	0.158
4	0.286
6	0.415
8	0.551
10	0.675

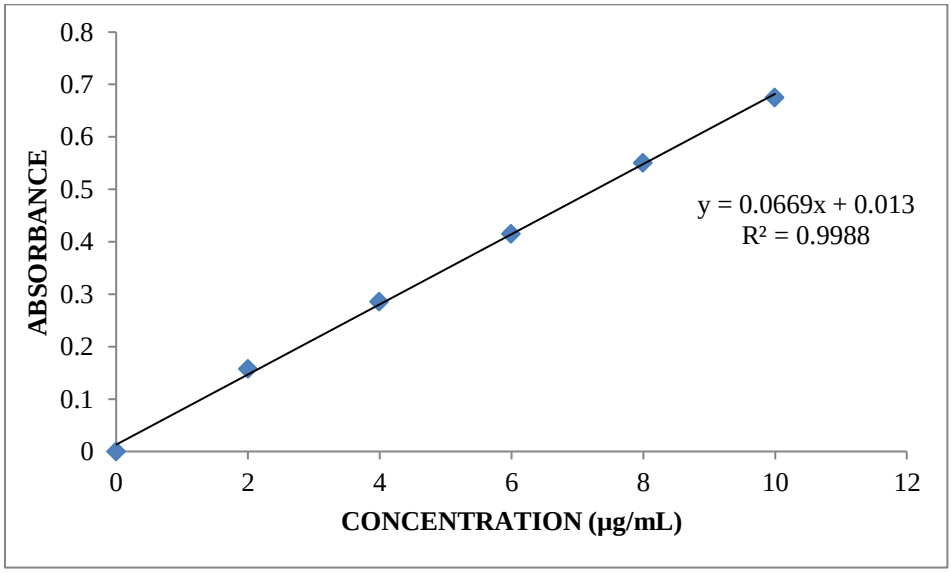

Fig 1: Standard curve of Lamotrigine

Evaluation of pre-compression parameters of powder blend

Table 3 : Evaluation of pre-compression parameters of powder blend

Formulation Code	Angle of Repose	Bulk Density(gm/mL)	Tapped Density (gm/mL)	Carr'sIndex(%)	Hausner's Ratio
F1	23.172º±0.051	0.490±0.103	0.588±0.048	16.896±0.095	1.201±0.183
F2	22.483º±0.063	0.487±0.042	0.580±0.067	16.034±0.405	1.191±0.082
F3	21.668º±0.044	0.475±0.132	0.569±0.133	16.520±0.278	1.197±0.073
F4	19.578º±0.027	0.466±0.053	0.558±0.025	16.487±0.322	1.196±0.064
F5	23.435º±0.077	0.585±0.065	0.678±0.041	13.71±0.461	1.15±0.033
F6	21.247º±0.081	0.564±0.003	0.652±0.083	13.49±0.587	1.15±0.050
F7	20.839º±0.062	0.547±0.074	0.641±0.052	14.66±0.372	1.17±0.028
F8	19.631º±0.043	0.520±0.122	0.622±0.035	16.39±0.241	1.19±0.091
F9	21.356º±0.053	0.576±0.068	0.664±0.033	13.25±0.321	1.15±0.056

- For each formulation blend of drug and excipients were prepared and evaluated for various pre compression parameters described earlier in methodology chapter.
- The bulk density of all formulations was found in the range of 0.466±0.053 - 0.585±0.065 and tapped densiy was in the range of 0.558±0.025 - 0.678±0.041
- The Carr's index and Hausner's ratio was calculated from tapped density and bulk density.

Evaluations of post compression parameters of Lamotrigine mouth dissolving tablets

Table 4: Evaluation of post compression parameters of Lamotrigine Mouth dissolving tablets

Formulation codes	Average weight (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	148.53	4.1	0.35	3.96	97.45
F2	149.23	4.8	0.61	3.14	99.31
F3	146.92	4.2	0.24	3.59	96.80
F4	148.75	4.5	0.50	3.82	98.45
F5	147.80	5.0	0.74	3.23	99.12
F6	148.21	4.6	0.49	3.40	95.21
F7	150.03	5.3	0.20	3.72	98.38
F8	146.92	4.1	0.73	3.51	96.90
F9	148.67	4.9	0.11	3.17	97.49

Weight variation and Thickness : All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown above. The average tablet weights of all the formulations were noted down.

Hardness and friability: All the Mouth Dissolving formulations were evaluated for their hardness using Monsanto hardness tester and the results are shown above. The average hardness for all formulations was found to be between (4.1 – 5.3) kg/cm^2 which was found to be acceptable. Friability was determined to evaluate the ability of the tablets to with stand the abrasion during packing, handling and transpoting. All the Mouth dissolving formulations were evaluated for their percentage friability using Roche friabilator and the results are shown above. The average percentage friability for all the formulations was between 0.11 – 0.74 which was found to be within the limit.

Drug content : All formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown above. The assay values for all formulations were found to be in the range of (95.21 – 99.31). According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the Mouth dissolving formulation comply with the standards given in IP.

Table 5: Evaluation of post compression parameters of Lamotrigine mouth dissolving tablets

Formulation	Disintegration time*(seconds)	Wetting time* (seconds)	*In vitro* dispersion time*(sec)	% Water absorption ratio*
F1	54	63	57	96
F2	35	58	43	98
F3	21	26	24	99
F4	45	59	42	97
F5	30	43	31	99
F6	28	31	28	98
F7	51	65	49	95
F8	46	57	42	98
F9	32	40	36	98

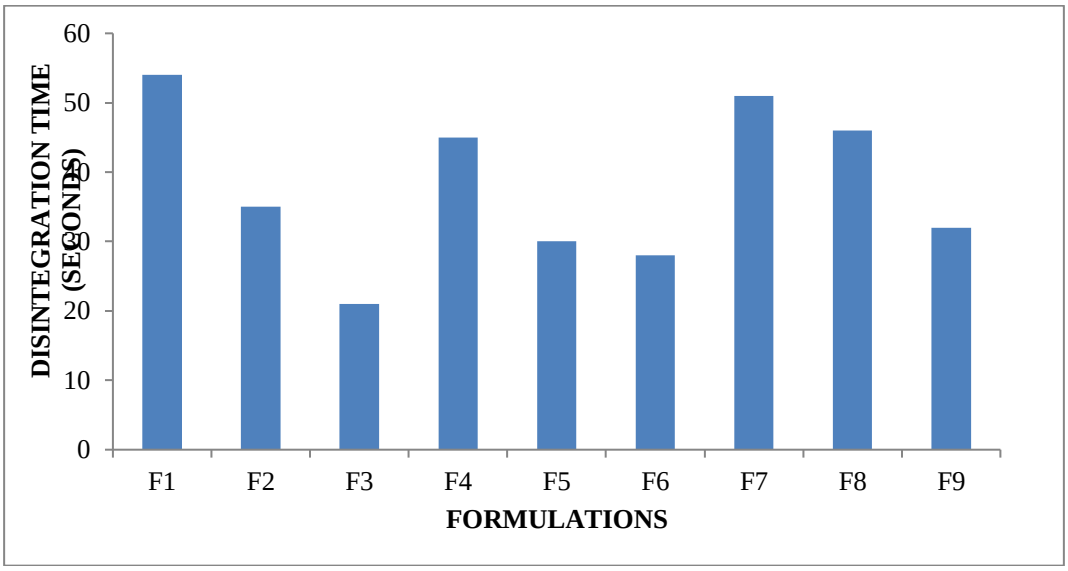

Figure 2 :*In vitro* Disintegration time graph

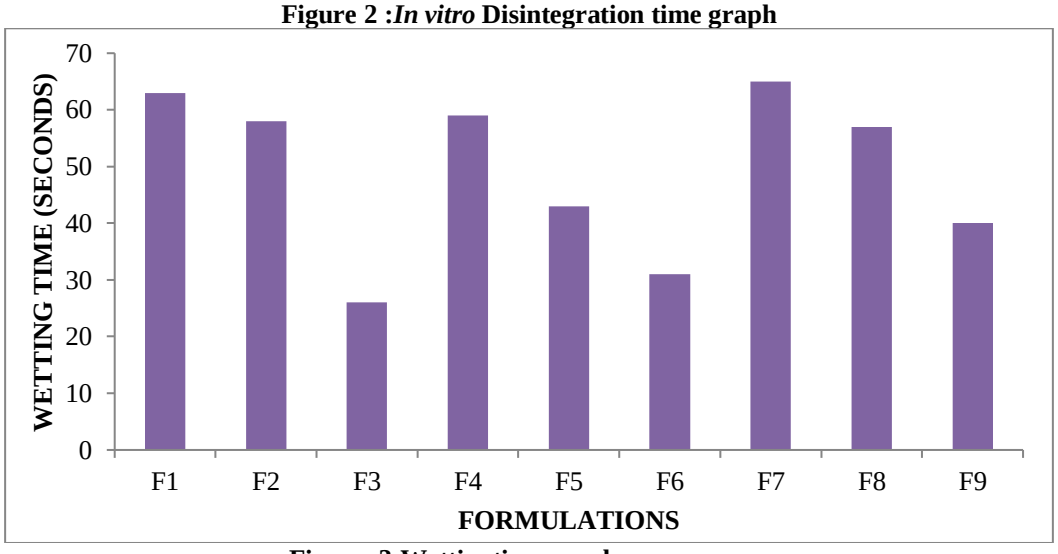

Figure 3:Wettingtime graph

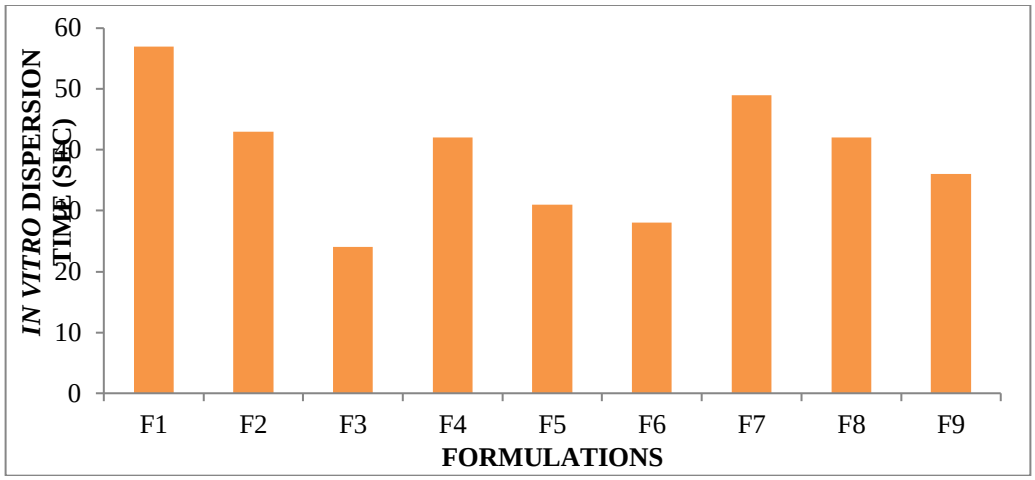

Figure 4:*In vitro* dispersion time

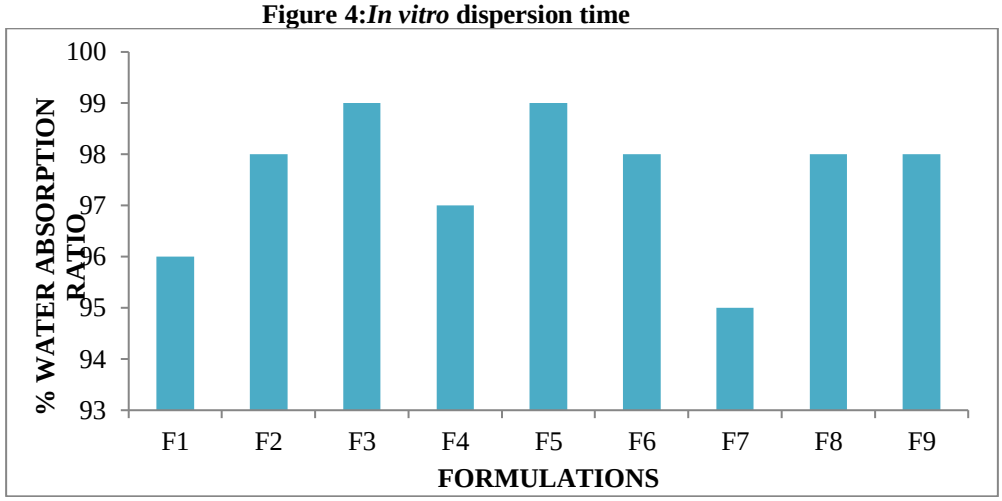

Figure 5: Water absorption ratio graph

***In vitro* disintegration time:** *In vitro* disintegration studies showed from 21 to 54 secs. These results indicate that the F3 formulation which shown less disintegration time than remaining formulations.

Wetting time: Wetting time to the time required to wet completely when kept motionless on the tissue paper in a petridish.

- All the FDT formulations were evaluated for their wetting time as per the procedure described in the methodology section, and the results are shown in table.
- The average wetting time for all the formulations was in the range of **(26 to 65)** seconds.
- It was also observed that formula F3 which had the least wetting time also had the minimum disintegration time showing a strong correlation between disintegration time and wetting time.

***In vitro* dispersion time:** Lamotrigine Mouth Dissolving Tablets F6 formulation dispersed time was 24 secs. It was known that less dispersion time than other formulation.

The *In vitro* dispersion time for all formulation was found to be in a range of **24 to 57** seconds

Water Absorption ratio: All the formulations were evaluated for water absorption ratio according to the procedure described in methodology section and the results are shown in table.

- The maximum water absorption ratio was shown by formulation F3 showed **99 %.**
- Water absorption ratio is proportional to dissolution rate profile as higher the water absorption ratio Higher the dissolution

***In vitro* drug release studies of Lamotrigine**

Table 6: Dissolution data of Lamotrigine

Time (Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	31.86	38.25	43.61	40.23	43.95	38.95	41.10	38.80	21.29
10	43.14	50.23	56.25	56.72	61.10	53.43	57.14	50.64	46.17
15	52.93	64.12	70.71	68.39	76.43	67.32	73.38	65.25	69.38
20	68.30	76.90	88.63	74.18	85.21	85.01	89.14	74.40	73.05
30	78.41	87.35	98.75	86.24	92.87	97.14	96.30	86.76	86.14

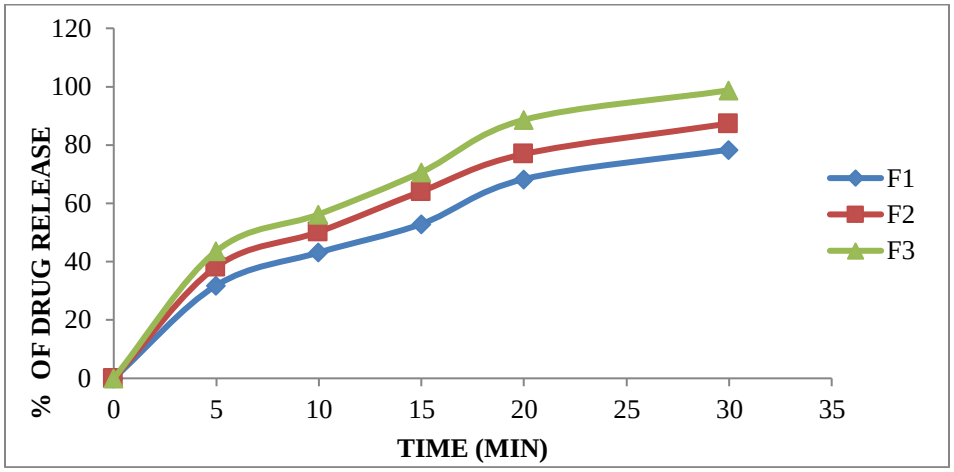

Fig 6: Dissolution profile of formulations F1, F2, F3

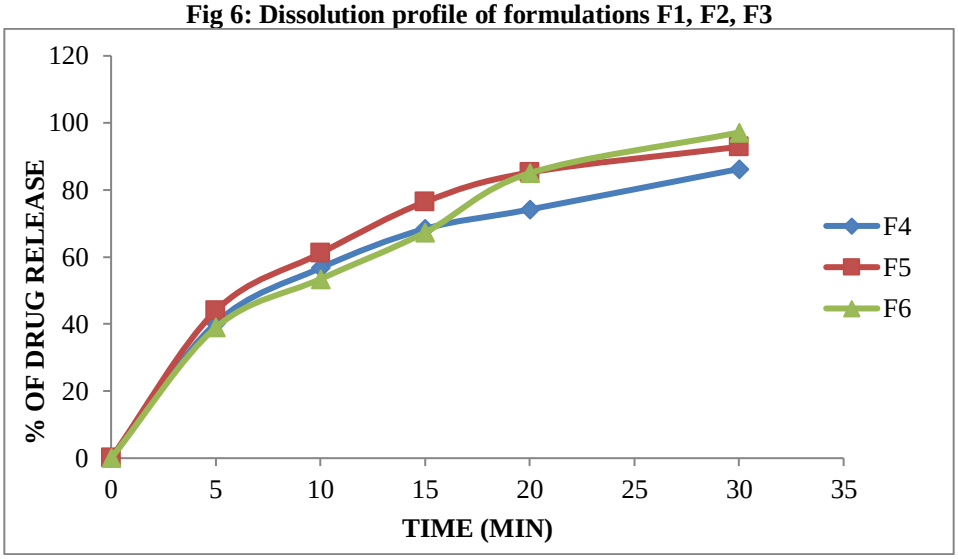

Fig7 : Dissolution profile of formulations F4, F5, F6

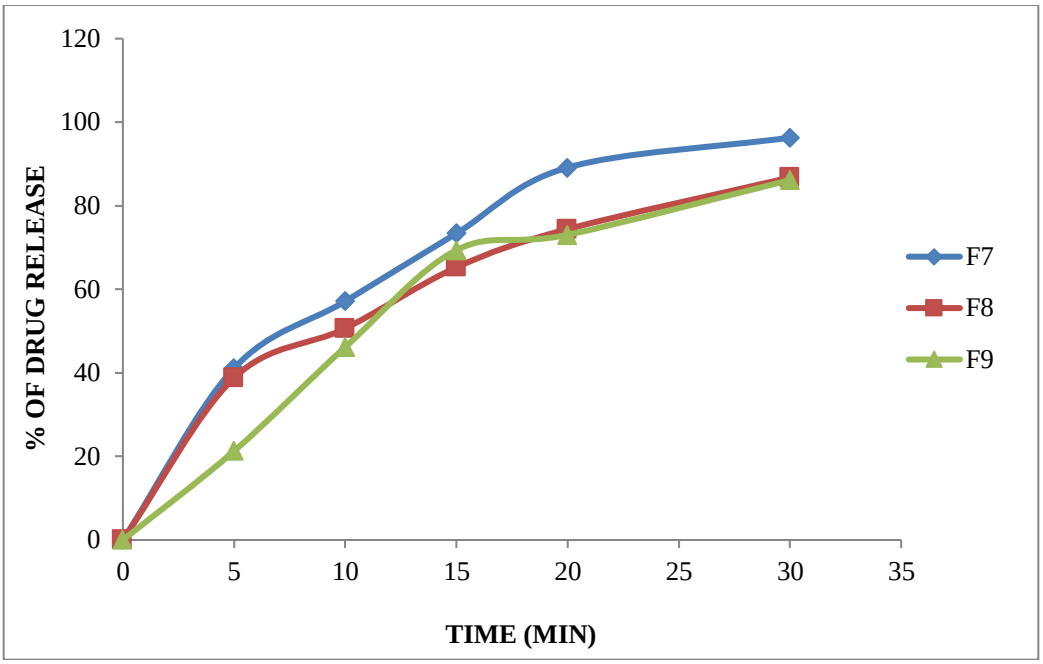

Fig 8: Dissolution profile of formulations F7, F8, F9

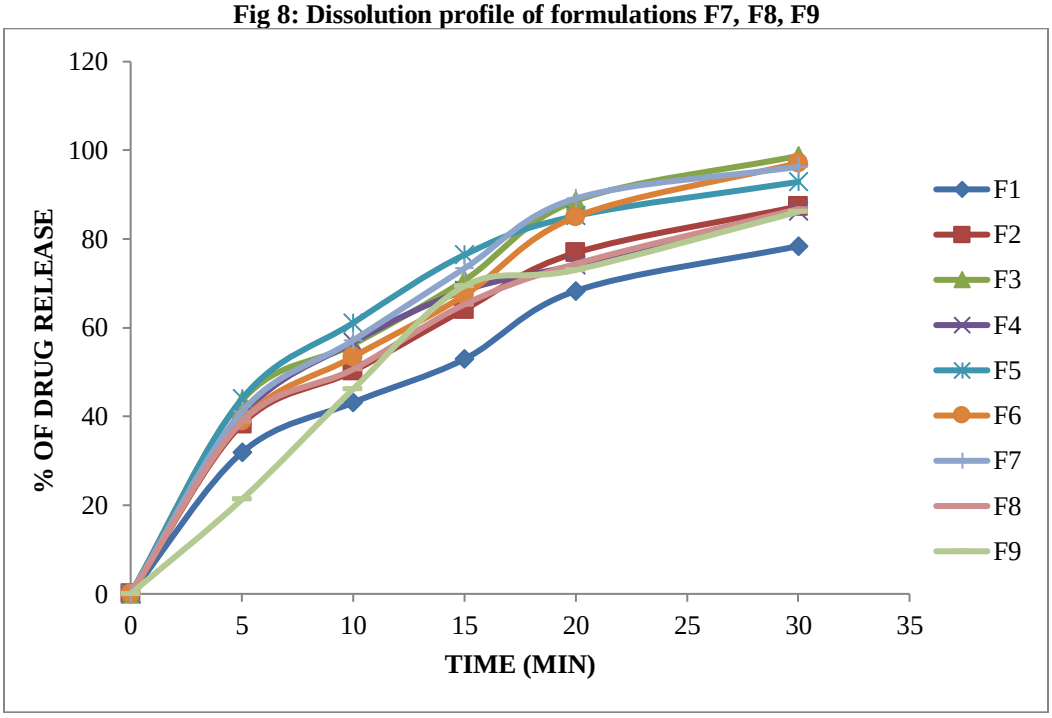

Fig.9 : Dissolution profile of all formulations F1-F9

The F3 formulation shows 98.75 % drug release in 30 min while using 75 mg concentration of Solutab and disintegration time is 21 sec. In which increase of concentration of Solutab improved dissolution and decreased disintegration so it was optimized formulation. Finally Concluded that F3 formulation was the optimized Formulation.

FTIR RESULTS:

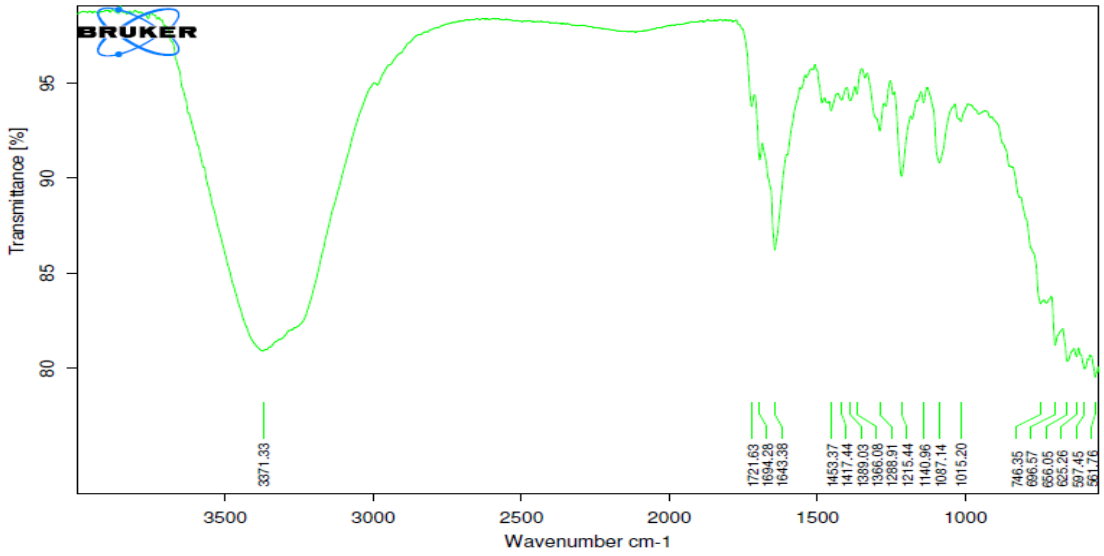

Fig 10: FTIR of Lamotrigine Pure drug

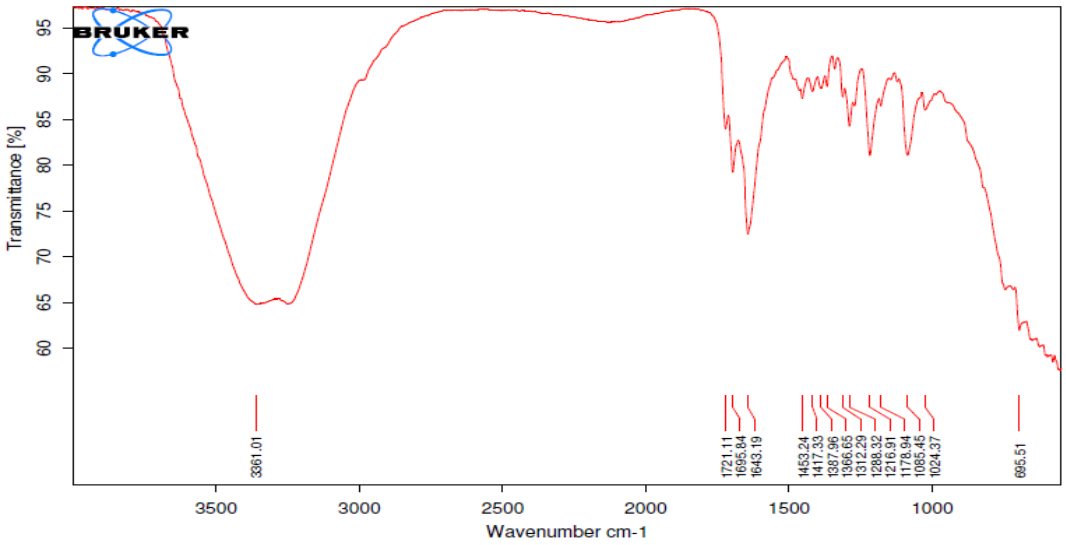

Fig 11: FTIR of Lamotrigine optimized formulation

Lamotrigine was mixed with proportions of excipients showed no colour change providing no drug-excipient interactions.

CONCLUSION:

- ✓ The purpose of the study was to formulate and evaluate mouth dissolving tablets of Lamotrigine.
- ✓ The results of Fourier Transmission Infra-Red spectroscopy confirm that both drug and excipients are compatible with each other and and are devoid of interactions.
- ✓ The results of precompression studies like angle of repose, bulk density, tapped density, compressibility index and hausner's ratio reveals that the prepared powder blends of all formulations possess good flow properties.
- ✓ The tablets were prepared by direct compression method using superdisintegrants like Solutab (F1 to F3), Polyplasdone XL (F4 to F6), Locust bean gum (F7 to F9) in different concentrations. Aspartame is used as sweetener for additional taste masking and Microcrystalline cellulose as diluent. The tablets obtained were of uniform shape and size.
- ✓ The prepared tablets were subjected to post compression evaluations and the results indicate that, The hardness, thickness and Friability of all the tablets are uniform, which ensures that all the

tablets were of uniform size and shape with good resistance against mechanical damage.

- ✓ The tablets of all formulations contains uniform amount of drug, which ensures content uniformity for tablets of all formulations.
- ✓ The tablets were within the limits of weight variation test, which in turn indicate uniform distribution of contents of the powder blends of each formulations.
- ✓ The friability of all the tablets was found to be < 1%, which indicates the good mechanical resistance.
- ✓ The tablets of all formulations were found to have minimum wetting time and maximum water absorption ratio which is the desired characteristic of fast dissolving tablets, which enables faster disintegration of tablets.
- ✓ The disintegration time of all tablets were found to be less than 21 sec, which ensures faster disintegration.

Amongst all the formulations, formulation containing Solutab as superdisintgrants is fulfilling all the parameters satisfactorily. It has shown excellent *in vitro* disintegration compared to other superdisintegrants.

Apart from all the formulations, F3 formulation showed maximum drug release (98.75%) at the end of 30 min.

CONCLUSION:

It was concluded, that Lamotrigine can be successfully formulated as mouth dissolving tablets using various super disintegrants in different concentrations by direct compression method. The formulation containing 1:3 ratio of Solutab as super disintegrant was found to be outstanding than other formulations in terms of disintegration time and rate of dissolution.

REFERENCES:

1. Velmurugan S and Sundar Vinushitha.Oral Disintegrating Tablets: An Overview.International Journal of Chemical and Pharmaceutical Sciences 2010, Dec., Vol.1 (2).
2. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. Journal of Pharmacy and Pharmacology. 1998; 50(4):375-82.
3. Lindgren S, Janzon L. Dysphagia; Prevalence of swallowing complaints and clinical findings. Medical clinics of North America., 1993; 77: 3-5.
4. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies. Critical Review in Therapeutic Drug Carrier System. 2004;21:433-76.
5. Brown D. Orally Disintegrating TabletsTaste over Speed. Drug Delivery Technology. 2003; 3:58-61.
6. Kumaresan C, Orally Disintegrating Tablet - Rapid Disintegration, Sweet Taste, And Target Release Profile, pharmainfo.net sep9 2008.
7. Reddy L. H, Ghosh B, and Rajneesh. Fast dissolving drug delivery systems: a review of the literature. Indian Journal of Pharmaceutical Science. 2002; 64(4): 331-336.
8. Seager H. Drug-deliver products and the zydis fast-dissolving dosage form. Journal of Pharmacy and Pharmacology. 1998;50: 375-382.
9. Parijat Pandey, Mandeep Dahiya.Oral Disintegrating Tablets: A Review.International Journal of Pharma Research & Review, Jan 2016;5(1):50-62.
10. .Seager H. Drug delivery products and the zydis fast dissolving dosage form. Journal of Pharmacy and Pharmacology 1998;50(4): 375-382
11. Habib W, Khankari R, Hontz J. Fast dissolving drug delivery system. Critical Reviews in Therapeutic Drug Carrier Systems 2000; 17(1):61-72.
12. Gafiţanu E, Dumistracel I, Antochi S. Formulations and bioavailability of propyphenazone in lyophilized tablets. Revista Medico-chirurgicala a Societatii De Medici Si Naturalisti Din Iasi 1991;95(1- 2):127-128.
13. Bharadwaj S, Jain V, Sharma S, Jat RC, Jain S. Orally Disintegrating Tablets: A Review. Drug Invent Today 2010;2(1):81-88.
14. Vani R, Rasheed A. Formulation and evaluation of hydrochlorothiazide and ramipril mouth dissolving tablet using different superdisintegrants. International Journal of Pharma Sciences and Research 2014;5(1):207-212.
15. Parkash V, Maan S, Deepika, Yadav SK, Hemlata, Jogpal V. Fast disintegrating tablets: Opportunity in drug delivery system. Journal of Advanced Pharmaceutical Technology and Research 2011;2(4):223-235.
16. Ashish P, Harsoliya MS, Pathan JK, Shruti S. A review - Formulation of mouth dissolving tablet. International Journal of Pharmacology and Clinical Sciences 2011;1(1):1-8.
17. Shukla S, Mishra DK, Jain DK. New insights in the field of fast dissolving tablets. Journal of Hormonized Research in Pharmacy 2015;4 (3):213-226.
18. Bera A, Mukherjee A. A detailed study of mouth dissolving drug delivery system. Acta

ChimicaPharmceutica and Indica 2013;3(1): 65-93.
19. Reddy AM, Babu PS, Harshita B, Sravya R. Conventional and patented technologies in oral dispersible tablets: a review. Journal of Chemical and Pharmaceutical Sciences 2013; 6(4):286-292.
20. Siddiqui MN, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization an evaluation: an overview. International Journal of Pharmaceutical Sciences Review and Research 2010;4(2):87- 96.