

**Original Article**

**FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF LAMOTRIGINE USING DISCRETE SUPER DISINTEGRANTS AND COPROCESSED EXCIPIENTS**

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**ABSTRACT**

**Objective:** The present study was designed to formulate and evaluate the orodispersible tablets of lamotrigine after enhancing its solubility.

**Methods:** Lamotrigine was made into an inclusion complex with eudragit E 100 by kneading and mass extrusion method and later this mixture is compressed into orodispersible tablet using various super disintegrants and co-processed excipients to reduce the disintegration time for providing prompt action through rapid drug release.

**Results:** Lamotrigine ODTs containing F-melt (F1-3%, F2-5%) dispersed in lesser time of (9±0.11) and (21±0.58) compared to formulations with polyplasdone XL-10 and primellose as super disintegrants respectively with F1 showing short wetting time. The water absorption was also found to be more for formulation with 3% F-Melt.

**Conclusion:** Lamotrigine orodispersible tablets were prepared by direct compression technique by using 3% and 5% of three super disintegrants (F-melt, primellose and polyplasdone XL-10). Disintegration time of F1 (3% f-melt) formulation was found to be least (7 sec).

**Keywords:** Tablets of lamotrigine using, Coprocessed excipients

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**INTRODUCTION**

Orodispersible technique is the best way to delivery such kind of active pharmaceuticals which are required to elicit action immediately. Epilepsy is a neuronal disorder occurring all age groups and is a pathophysiological condition which requires immediate treatment [1]. Lamotrigine is chemically 3, 5-diamino-6-(2, 3-dichlorophenyl)-as-triazine, having a molecular formula C<sub>9</sub>H<sub>7</sub>N<sub>5</sub>Cl<sub>2</sub>, which is supposed to be acting by inhibiting voltage gated sodium channels and thus reducing the release of glutamate, an excitatory amino acid responsible in the initiation and dissemination of a seizure [2]. Lamotrigine shows good absorption profile but is poorly soluble in water. Thus it is required to formulate the dosage form, which modifies the solubility profile thus making it more bioavailable.

For this reason lamotrigine is complexed with eudragit E 100 by mass extrusion method. Then this complex is further blended with super disintegrants polyplasdone XL-10 or primellose or coprocessed excipient F-Melt and other excipients. Tablets were prepared by the direct compression method. Fast melting and taste-masking provide increased patient compliance. The combination of WOWTAB and pharmaburst technologies can help in providing faster disintegration as well as can provide better mouth feel [3]. WOWTAB fast-dissolving/disintegrating tablet formulation uses a combination of low and high mouldability saccharides for rapid dissolution and stronger binding property, respectively [4]. Pharmaburst technology utilizes co-processed excipient system, which works as a quick disintegrating matrix containing 85% of sugar polyol D-mannitol, < 10% silicon dioxide, < 10% sorbitol, 5% crospovidone produced by cospray drying leading to porous matrix enhancing compactibility and also wicking effect making disintegration to happen rapidly.

**MATERIALS AND METHODS**

**Materials**

Lamotrigine was obtained as a gift sample from Dr. Reddy's

Laboratories, (Hyderabad, India), eudragit E-100 by Evonik Degussa (Mumbai, India), polyplasdone XL-10 was a gift from ISP pharmaceuticals, (Covington, KY, USA), primellose and avicel pH 102 were gift samples from DFE Pharma (Goch, Germany), F-Melt was kindly donated by Fuji Chemical Industry Co., Ltd (Toyama-Pref, Japan), lubripharm (sodium stearyl fumarate) was gifted by SPI Pharma, (Bengaluru, India), the orange dry flavor was gifted by Capricorn Pharma private limited (Hyderabad, India) and ethanol and aerosil were procured from SD fine chemicals (Mumbai, India). All reagents and solvents were of analytical grade.

**Methods**

**Step 1: Preparation of lamotrigine inclusion complex with Eudragit E 100 by kneading and mass extrusion method**

Eudragit E100 and lamotrigine were taken in a mortar at a ratio of 1:1 (eudragit E 100: lamotrigine). To this small quantity of ethanol was added with trituration to get slurry like consistency [5]. Then slowly lamotrigine (API) was incorporated into the slurry and trituration was continued further for 15 min to get a soft mass of lamotrigine and eudragit E 100. The soft mass was then transferred to a syringe and extruded out and air dried at room temperature for 24 h, pulverized and passed through sieve no. 60 and was stored in a desiccator over fused calcium chloride.

**Step 2: Preparation of lamotrigine orodispersible tablets by direct compression method**

Lamotrigine ODTs were prepared by direct compression method. Different formulations of lamotrigine orodispersible tablets were designed to be prepared by direct compression technique using three super disintegrants, (F-Melt, primellose, and polyplasdone XL-10). Super disintegrants were varied with 2 different concentrations (i.e., 3, 5, respectively), keeping all other ingredients constant. Formulations designed are assigned with formulation codes shown in table 1.

Table 1: Formulation codes

Super disintegrant used	Concentration (%)	Formulation code
F-Melt type c	3	F1
	5	F2
Primellose	3	F3
	5	F4
Polyplasdone XL-10	3	F5
	5	F6
Marketed formulation	-	M
Pure drug	-	P

Drug-polymer complex, super disintegrants, avicel pH 102, aspartame, orange flavor were accurately weighed and passed through a 40-mesh screen to get uniform size particles and mixed in a glass mortar for 15 min. The obtained blend was lubricated with aerosil and glidant (sodium stearyl fumarate) was added and mixing

was continued for further 5 min. The resultant mixture was directly compressed into tablets by using 9 mm round flat-faced punch on a rotary tableting machine. Compression force was kept constant for all formulations. Composition of lamotrigine orodispersible tablets is shown in table 2

Table 2: Composition of lamotrigine or dispersible tablet

Materials (mg)	F1	F2	F3	F4	F5	F6
Drug-polymer complex	50	50	50	50	50	50
F-Melt Type C	7.5	12.5	-	-	-	-
Polyplasdone XL-10	-	-	-	-	7.5	12.5
Primellose	-	-	7.5	12.5	-	-
Aerosil	5	5	5	5	5	5
Lubripharm	2.5	2.5	2.5	2.5	2.5	2.5
Aspartame	5	5	5	5	5	5
Orange Flavor	2.5	2.5	2.5	2.5	2.5	2.5
Avicel pH 102	177.5	172.5	177.5	172.5	177.5	172.5
Total weight of tablet (mg)	250	250	250	250	250	250

#### Evaluation of pre-compression parameters of powder blend

##### Angle of repose

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

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

##### % Compressibility index or carr's index

The simplest way for measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility index which was determined by the formula

$$\text{Carr's index} = \rho_t - \rho_b / \rho_t * 100$$

Where  $\rho_t$  = tapped density and  $\rho_b$  = bulk density.

##### Hausner's Ratio (H)

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

$$\text{Hausner's ratio} = \frac{\rho_t}{\rho_b}$$

Where  $\rho_t$  = tapped density and  $\rho_b$  = bulk density

#### Evaluation of post compression parameters of lamotrigine ODTs

Different quality control tests were performed for all the ODT formulations to check whether these have met the specifications given in USP along with other *in vitro* tests like wetting time and water absorption ratio.

##### Weight variation test

20 tablets were randomly selected from each formulation and their individual weights and average weight of all 20 tablets was

calculated by weighing on an electronic balance (Shimadzu, AUX 220, Shimadzu Corp, Japan) [6]. The mean $\pm$ SD was noted.

##### Thickness

Randomly 10 tablets were taken from each formulation and their thickness was measured using a digital Vernier caliper (Mitutoyo Corp, Kawasaki, Japan). Average thickness and standard deviation values were calculated. The tablet thickness should be controlled within a  $\pm 5\%$  variation of standard value [7].

##### Hardness

The tablet hardness of different formulations was measured using the Monsanto hardness tester. The tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger was placed in contact with the tablet, and a zero was taken. The upper plunger was then forced against the spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture is recorded, and the zero force reading is deducted from it. Generally, a minimum hardness of 4 kg/cm<sup>2</sup> is considered acceptable for uncoated tablets. The hardness for ODTs should be preferably 1-4 kg/cm<sup>2</sup> [8].

##### Friability

This test was performed using a laboratory friability tester known as Roche friabilator. 20 tablets were weighed and placed in a plastic chambered friabilator attached to a motor, which revolves at a speed of 25 rpm, dropping the tablets from a distance of 6 inches with each revolution. The tablets were subjected to 100 revolutions for 4 min. After the process, these tablets were de-dusted and reweighed. Percentage loss of tablet weight was calculated. Friability values below 1% are generally acceptable.

$$\% \text{ friability} = \frac{W_1 - W_2}{W_1} * 100$$

Where  $W_1$  = Initial weight of 10 tablets and  $W_2$  = Final weight of 10 tablets [9].

### Drug content

3 tablets were randomly selected, weighed and finely powdered and the quantity of powder equivalent to one tablet was added to 100 ml of 6.8 pH phosphate buffer in a conical flask. A conical flask was then placed on a rotary shaker. An aliquot of the solution was centrifuged and the supernatant was filtered through a 0.22 $\mu$  filter. Absorbance of the resulted supernatant solution was measured using U. V Visible double beam spectrophotometer at a wavelength of 308 nm against 6.8 pH phosphate buffer as blank. Concentrations and amount of drug present in one tablet were calculated with the help of calibration curves [10-12].

### Wetting time

A piece of tissue paper folded twice was placed in a small petridish containing 6 ml of water. Water-soluble dye phenolphthalein was added to the petridish. The dye solution was used to identify the complete wetting of the tablet surface [13, 14]. A tablet was carefully placed on the surface of tissue paper in the petridish at room temperature. The time required for water to reach the upper surface of the tablets and completely wet them was noted as the wetting time. To check for reproducibility, the measurements were carried out in triplicates (n=3). The wetting time was recorded using a stopwatch.

### Water absorption ratio (r)

The weight of the tablet before keeping in the petridish was noted ( $W_b$ ) using shimadzu digital balance. The wetted tablet from the petridish was taken and reweighed ( $W_a$ ) using the same [15]. The Water absorption ratio, R, was determined according to the following equation

$$R = \frac{W_a - W_b}{W_b} * 100$$

Where  $W_a$ = Weight of the tablet after absorption and  $W_b$ = Weight of the tablet before absorption.

### In vitro dispersion time

*In vitro* dispersion time was determined by placing one tablet in a beaker containing 10 ml of pH 6.8 phosphate buffer at 37 $\pm$ 0.5  $^{\circ}$ C and the time required for complete dispersion was determined. To check for reproducibility, the measurements were carried out in triplicates (n=3). The dispersion time was recorded using a stopwatch [13].

### In vitro disintegration time

A piece of tissue paper folded twice was placed in a small petridish containing 6 ml of pH 6.8 phosphate buffer. A tablet was carefully

placed on the surface of tissue paper in the petridish at room temperature. The time required for water to reach the upper surface of the tablets and completely wet them and break down into small particles was noted as the *in vitro* disintegration time. To check for reproducibility, the measurements were carried out in triplicates (n=3). The disintegration time was recorded using a stopwatch [16, 17].

### In vitro dissolution studies

#### Method

Dissolution test was carried out by using USP type II apparatus. The paddle was rotated at 50 rpm. 6.8 pH phosphate buffer was used as dissolution medium (900 ml) and was maintained at 37 $\pm$ 1  $^{\circ}$ C. Samples of 5 ml were withdrawn at predetermined intervals (1, 3,5,10,15,20,25,30,45,60 min), filtered and replaced with 5 ml of fresh dissolution medium. The collected samples were suitably diluted with dissolution fluid, where ever necessary and were analyzed for the drug at 308 nm by using ultra violet double beam spectrophotometer. Each dissolution study was performed for three times and mean values were taken [18-20].

### Fourier transform infrared spectroscopy (FTIR)

FTIR studies were performed on drug, drug-polymer complex. F-melt, optimized formulation using Shimadzu FTIR (Prestige, India). The samples were analyzed between wave numbers 4000 and 400  $cm^{-1}$ .

### Stability studies

#### Moisture uptake studies

Moisture uptake studies for ODT were conducted to assess the stability of the formulation. Ten tablets from each formulation were kept in a desiccator over calcium chloride at 37  $^{\circ}$ C for 24h. The tablets were then weighed and exposed to 75% relative humidity, at room temperature for two weeks. The relative humidity was achieved by was achieved by keeping saturated sodium chloride solution at the bottom of the desiccator for 3 d. One tablet as control (without super disintegrants) was kept to assess the moisture uptake due to other excipients. Tablets were then weighed and the percentage increase in weight was recorded [21-24].

## RESULTS AND DISCUSSION

### Evaluations of precompression parameters of lamotrigine ODTs

Precompression parameters were measured as per standard procedure and the values obtained are as shown in table 3.

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

Formulation	Bulk density* (g/ml)	Tapped density* (g/ml)	Carr's index* (%)	Angle of repose* ( $^{\circ}$ )	Hausner's ratio*
F1	0.64 $\pm$ 0.03	0.59 $\pm$ 0.03	6.02 $\pm$ 0.05	25 $\pm$ 0.02	0.91 $\pm$ 0.02
F2	0.62 $\pm$ 0.01	0.58 $\pm$ 0.02	6.08 $\pm$ 0.06	26 $\pm$ 0.05	0.92 $\pm$ 0.07
F3	0.62 $\pm$ 0.08	0.58 $\pm$ 0.05	7.50 $\pm$ 0.01	28 $\pm$ 0.04	0.93 $\pm$ 0.03
F4	0.60 $\pm$ 0.03	0.56 $\pm$ 0.04	7.45 $\pm$ 0.02	29 $\pm$ 0.05	0.92 $\pm$ 0.05
F5	0.55 $\pm$ 0.05	0.50 $\pm$ 0.03	7.21 $\pm$ 0.04	27 $\pm$ 0.03	0.96 $\pm$ 0.06
F6	0.54 $\pm$ 0.02	0.53 $\pm$ 0.01	7.53 $\pm$ 0.05	29 $\pm$ 0.01	0.96 $\pm$ 0.06

\*Results are the mean of 3 observations $\pm$ SD.

For each formulation blend of drug and excipients were prepared and evaluated for various Precompression parameters and the bulk density of all formulations was found in the range of (0.54 $\pm$ 0.020-0.64 $\pm$ 0.03) and tapped density was in range of (0.50 $\pm$ 0.03-0.59 $\pm$ 0.03). The Carr's index and Hausner's ratio was calculated from tapped density and bulk density. The powder blend of all six formulations with Hausner's ration<1.25 and Carr's index<14 indicates excellent flow ability of all powder blends. The flow properties for all the powder blends were excellent as evidentially proved by the angle of repose values obtained, which ranged between (25.02  $^{\circ}$ -29.05  $^{\circ}$ ) better than that of pure drug.

### Evaluations of post-compression parameters of lamotrigine ODTs

The prepared tablets were characterized for various tests and the results were as shown in table 4.

#### Weight variation and thickness

All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 4. The average tablet weight of all the formulations was found to be between (248.4 $\pm$ 0.78 to 250.3 $\pm$ 0.55). The maximum allowed percentage weight variation for tablets weighing 80-250 mg by I. P is 7.5% and no formulations are exceeding this limit. Thus all the formulations were found to comply with the standards given in I. P.

Table 4: Evaluation of post-compression parameters of lamotrigine orodispersible tablets

Formulation	Weight variation*	Thickness (mm)**	Hardness*** Kg/cm <sup>2</sup>	% Friability*	Drug content***
F1	248.4±0.78	3.16±0.08	3.2±0.11	0.33±0.21	102.43±0.5
F2	250.2±0.63	3.13±0.1	3.1±0.19	0.36±0.03	101.07±0.8
F3	249.8±0.6	3.14±0.1	3.2±0.15	0.54±0.15	101.75±0.3
F4	250.3±0.55	3.18±0.08	3.1±0.18	0.59±0.11	101.13±0.7
F5	249.6±0.52	3.15±0.05	3.1±0.22	0.63±0.19	99.69±0.21
F6	249.2±0.4	3.14±0.07	3.3±0.13	0.65±0.08	99.94±0.48

\*Results are the mean where n is 20±SD, \*\*Results are the mean where n is 10±SD and \*\*\*Results are the mean where n is 3±SD

### Hardness

All the ODT formulations were evaluated for their hardness, using Monsanto hardness tester. The average hardness for all the formulations was found to be between (3.1±0.18 to 3.3±0.13) Kg/cm<sup>2</sup> which was found to be acceptable, the hardness for F4 (3.1±0.18 Kg/cm<sup>2</sup>) was found to be least and for F6 (3.3±0.13 Kg/cm<sup>2</sup>) was found to be the highest of all the formulations.

### Friability

All the ODT formulations were evaluated for their percentage friability using Roche friabilator and the results are shown in table 8.3. The average percentage friability for all the formulations was between (0.33±0.21% to 0.65±0.08 %), which was found to be within the limit.

### Drug content

All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 4. The assay values for all the formulations were found to be in the range of (99.69±0.219 to 102.43±0.5). 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 ODT formulations comply with the standards given in IP.

### In vitro disintegration time

*In vitro* disintegration studies showed that ODTs containing F-Melt (F1-3%, F2-5%) showed lesser disintegration time of (7±0.78) and (13±0.63) compared to formulations with Polyplasdone XL-10 and Primellose as super disintegrants respectively. These results indicate that increasing the concentration of F-Melt in the tablets results in the formation of more cohesive tablets that are less likely to break up or dissolve easily in water. These results are further confirmed by wetting time in which tablets containing 3% F-Melt showed significantly short wetting time (2.16±0.08) compared to tablets containing 5% F-Melt (8.13±0.1) short wetting time is indicative of the highly porous nature of the tablet matrix. The

disintegrating time of formulations containing F-Melt was lower than those containing Primellose and Polyplasdone XL-10, which might be attributed due to its rapid water absorbing nature involving both wicking and swelling mechanisms, and delayed disintegration time for other super disintegrants due to their tendency to gel more than F-Melt. The *in vitro* disintegration time for all formulation was between 7 to 30 seconds as shown in fig. 1.

### Wetting time

Wetting time corresponds to the time required to wet completely when kept motionless on the tissue paper in a petridish. All the ODT formulations were evaluated for their wetting time as per the procedure described in the methodology section, and the results are shown in fig. 2. The average wetting time for all the formulations was in the range of (2.16±0.08 to 21.15±0.05) seconds. The formulation F1 (3% F-Melt) have shown lowest wetting time of (2.16±0.08) seconds and the formulation F5 (3 % Polyplasdone XL-10) have shown highest wetting time of (21.15±0.05) seconds. It was also observed that formula F1 which had the least wetting time also had the minimum disintegration time showing a strong correlation between disintegration times and wetting time.

### In vitro dispersion time

Lamotrigine ODTs containing F-Melt (F1-3%, F2-5%) dispersed in lesser time of (9±0.11) and (21±0.58) compared to formulations with Polyplasdone XL-10 and Primellose as super disintegrants respectively. These results are further confirmed by wetting time in which tablets containing 3% F-Melt showed significantly short wetting time (2.16±0.08) compared to tablets containing 5% F-Melt (8.13±0.1). Short wetting time is indicative of the highly porous nature of the tablet matrix. The *in vitro* dispersion time for all formulation was found to be in a range of 9 to 120 seconds.

### Water absorption ratio

All the formulations were evaluated for water absorption ratio and the results were as shown in fig. 4. The maximum water absorption ratio was shown by formulation F1 (96±0.78).

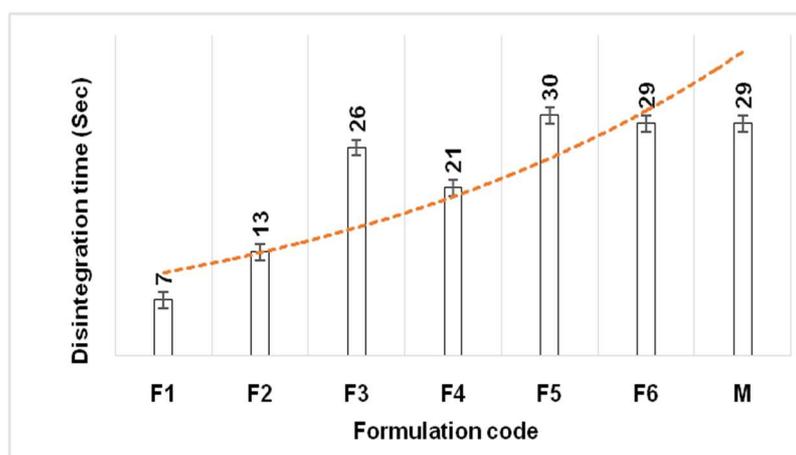


Fig. 1: Comparison of *in vitro* disintegration time of formulations comprising 3% and 5% of super disintegrants (F-Melt, Primellose and Polyplasdone XL-10) and marketed formulation

Table 5: Evaluation of other post-compression parameters of lamotrigine or dispersible tablets compared with marketed tablets

Formulation	Disintegration time* (sec)	Wetting time*(sec)	In vitro dispersion time* (sec)	%Water absorption ratio*
F1	7±0.78	2.16±0.08	9±0.11	96±0.78
F2	13±0.63	8.13±0.10	21±0.58	88±0.63
F3	21±0.6	12.14±0.10	38±0.15	85±0.60
F4	26±0.55	17.18±0.08	41±0.32	81±0.55
F5	30.6±0.52	21.15±0.05	48±0.27	79.±0.52
F6	29.2±0.4	19.14±0.07	45±0.48	81±0.40
M	30.6±0.51	22.15±0.05	120±0.05	89.±0.05

\*Results are the mean where n is 3±SD

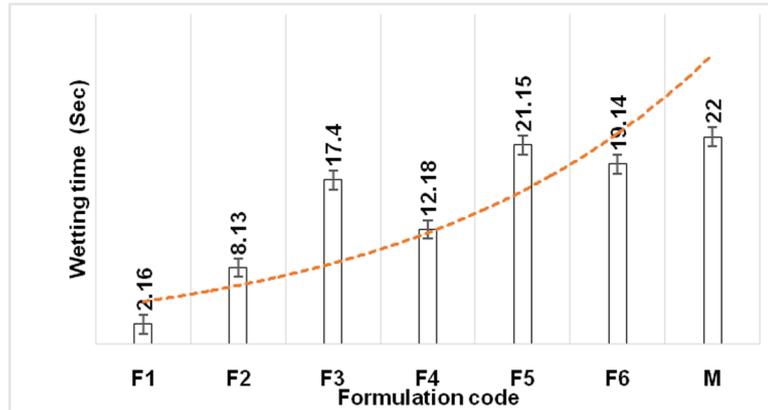


Fig. 2: Comparison of wetting time of formulations comprising 3% and 5% of super disintegrants (F-Melt, Primellose and Polyplasdone XL-10) and marketed formulation

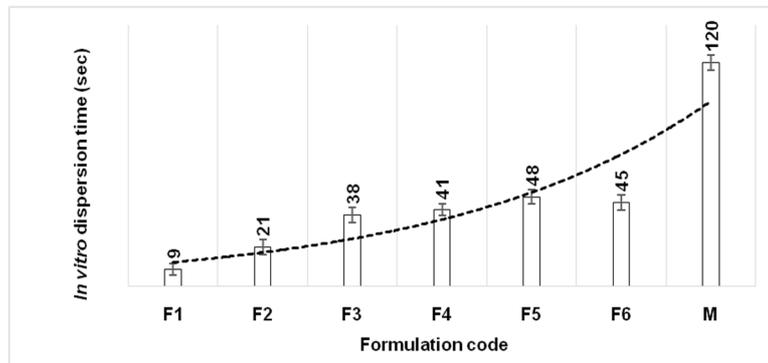


Fig. 3: Comparison of in vitro dispersion time of formulations comprising 3% and 5% of super disintegrants (F-Melt, Primellose and Polyplasdone XL-10) and marketed formulation

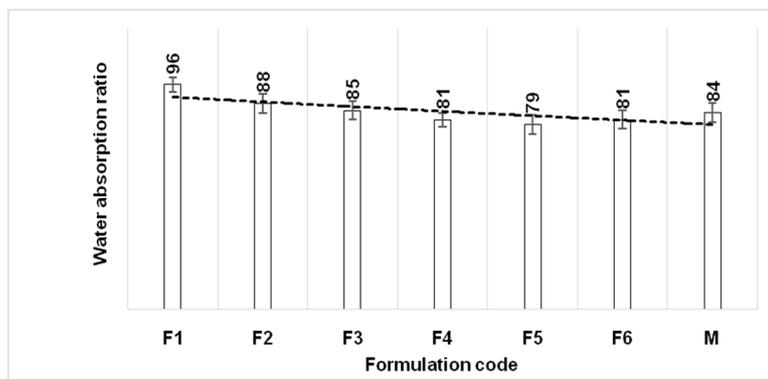


Fig. 4: Comparison of water absorption ratio of formulations comprising 3% and 5% of super disintegrants (F-Melt, Primellose and Polyplasdone XL-10) and marketed formulation

**In vitro drug release**

All the tablets prepared were subjected to *in vitro* dissolution studies in USP type II apparatus. The tablets prepared from three super disintegrants (F-Melt, primellose and polyplasdone XL-10) i.e., formulations (F1-F6) showed a drug release between (99-102%). Among six batches, batch F1 is selected as optimized batch because of its lowest disintegration time and highest drug release at 10 min when compared to other formulations. A short wetting time and highest water absorption ratio with no significant moisture uptake formulation F1 with 3% F-Melt was unique of all and considered to be optimized formulation as shown in table 6 and fig. 5.

The % drug release for the optimized formulations F1 prepared by 3% of super disintegrant (F-Melt) at 10 min was found to be

100.49±0.05 which is better than marketed formulation and pure drug with 57.97524±0.02 and 55.75506±0.91. As lamotrigine orodispersible tablets are meant for fast action, especially for patients suffering from epileptic seizures need immediate treatment when they get seizures these ODTs show fast action and get immediate relief. Optimized formulation F1 has less quantity of super disintegrant but showed quicker dissolution rate as shown in fig. 6.

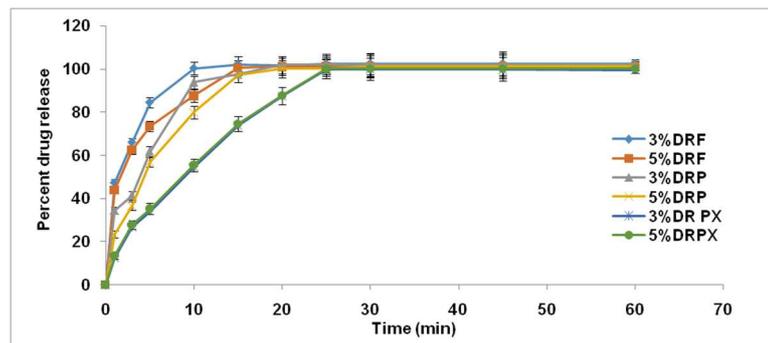
**Moisture uptake study**

The optimized formulation (F1) lamotrigine orodispersible tablets prepared with 3% F-Melt showed no moisture uptake as it is non-hygroscopic in nature, as shown in table 7.

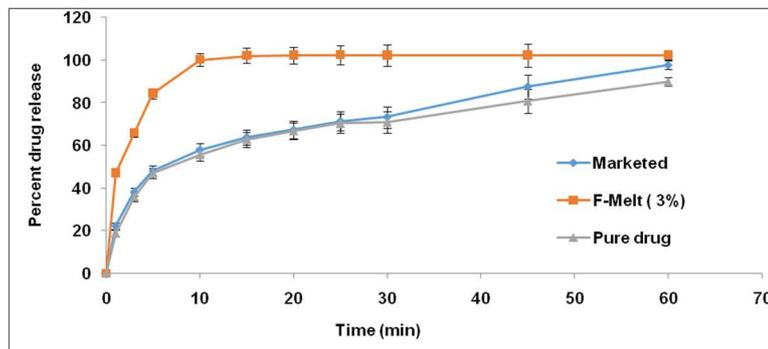
**Table 6: In vitro drug release profile of all six formulations of lamotrigine ODTs**

Time (min)	3%DRF*	5%DRF*	3%DRP*	5%DRP*	3%DRPX*	5%DRPX*
1	47.17±0.06	43.76±0.01	34.33±0.09	23.33±0.03	12.33±0.09	13.44±0.03
3	65.90±0.07	62.43±0.03	41.33±0.07	36.37±0.01	26.57±0.15	27.71±0.02
5	84.42±0.05	73.36±0.08	61.57±0.09	56.97±0.03	34.02±0.29	35.14±0.01
10	100.20±0.10	87.57±0.04	93.60±0.87	79.81±0.02	54.42±0.10	55.40±0.01
15	102.18±0.95	100.49±0.05	97.34±0.98	97.12±0.05	73.84±0.25	74.41±0.04
20	102.65±1.02	101.05±0.02	101.60±1.02	100.03±0.04	87.31±0.34	87.63±0.02
25	102.43±1.25	101.07±0.06	101.75±0.95	100.11±0.05	99.66±0.45	99.87±0.02
30	102.40±1.23	101.11±0.05	101.71±0.93	100.99±0.06	99.69±0.17	99.93±0.04
45	102.34±1.24	101.13±0.01	101.66±0.91	101.08±0.06	99.62±0.23	99.94±0.03
60	102.31±0.06	101.12±0.02	101.62±1.45	101.05±0.02	99.49±0.23	99.92±0.04

\*Results are the mean where n is 3±SD, DRF= Disintegrant F-melt, DRP= Disintegrant primellose, DRPX = Disintegrant polyplasdone XL



**Fig. 5: In vitro drug release profile of six formulations of lamotrigine ODTs, DRF= Disintegrant F-melt, DRP= Disintegrant primellose, DRPX = Disintegrant polyplasdone XL**



**Fig. 6: Comparison of drug release profile of formulations comprising optimized formulation 3 % of F-Melt (super disintegrant) marketed formulation and pure drug**

**Table 7: Moisture uptake study of (F1) optimized formulations of lamotrigine ODTs**

Formulation	Average weight of 10 tablets before exposed to moisture (mg)	Average weight of 10 tablets after exposed to moisture (mg)	% moisture uptake
F1	248.4±0.78	248.4±0.79	0.004

## FTIR results

The FTIR spectra of pure drug, inclusion complex F-Melt (super disintegrant) and optimized formulation (F1) are taken for the characterization studies.

As the shifts in the positions of major functional groups of the lamotrigine and eudragit E100 are observed in the infrared spectrum of inclusion complex, it suggests that there is strong physical interaction (peak intensities were smoothed and disappeared) between drug and polymer as shown in fig. 7.

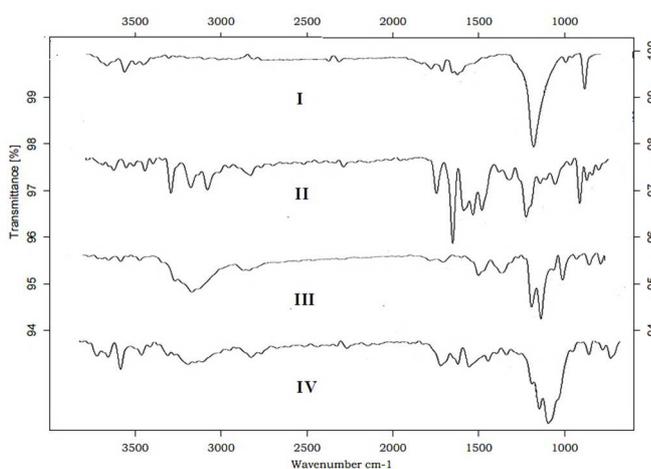


Fig. 7: FTIR spectrum of pure API and other formulations, drug (I), drug polymer complex (II), F-Melt (III) and optimized formulation F1 (IV)

## DISCUSSION

The flowability of all the powder blends was excellent due to their flow enhanced by the presence of aerosil which reduces inter particulate friction and moreover the formulation containing F-melt has good flow characteristics and good compressibility as it is a cospray dried excipient [25]. Compared to other formulations those containing F-melt showed better compressibility and also have shown better disintegration as the material is porous in nature thus making wicking effect increase making the tablet disintegrate faster which is also strengthened by the observation that the disintegration time and water absorption ratio are inversely proportional [26]. It was also observed that formula F1 which had the least wetting time also had the minimum disintegration time showing a strong correlation between disintegration times and wetting time [27]. The dispersion time of formulations (F1) containing F-Melt was lower than those containing primellose and polyplasdone XL-10, which might be attributed due to its rapid water absorbing nature and delayed dispersion time for other super disintegrants due to their tendency to gel more than F-melt [28]. Water absorption ratio is proportional to dissolution rate profile as higher the water absorption ratio faster the dissolution [29]. Optimized formulation F1 showed faster dissolution because of its high water absorption as well as less disintegration time when compared to marketed product [30]. Addition of inorganic silicates along with disintegrants will shorten the disintegration time which explains why tablets containing F-melt showed rapid disintegration time [31].

## CONCLUSION

Lamotrigine orodispersible tablets were prepared by direct compression technique by using 3% and 5% of three super disintegrants (F-Melt, primellose and polyplasdone XL-10). Precompression evaluation results showed that all formulations exhibited excellent flow properties compared to pure drug which has passable flow properties. Tablets of all six formulations (F1-F6) were evaluated for uniformity of weight, thickness, hardness and they were found to comply with the I. P standards. % friability was found to be less than one for all formulations which indicates that the tablets have good mechanical strength, which is a basic requirement for any orodispersible tablet. Disintegration time is less than 30 seconds for all formulation which clearly indicates that the formulated tablets are said to be orodispersible tablets. Disintegration time of F1 (3% F-Melt) formulation was found to be least (7 seconds). It might be due to its rapid water absorbing nature

involving both capillary and swelling mechanisms, building up the pressure internally leading to the faster disintegration. Correlation between water absorption ratio 'R' and disintegration time was observed and the results demonstrated that there is an inverse relationship between them.

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## AUTHORS CONTRIBUTIONS

All the author has contributed equally and Corresponding author guided the work and constructed the manuscript.

## CONFLICT OF INTERESTS

None

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