Iranian Journal of Pharmaceutical Sciences
2013: 9 (1): 1-12
www.ijps.ir

Original Article

Formulation and Evaluation of Oral Disintegrating Tablets of Lamotrigine Solid Dispersions

P.K.Lakshmi*, Swetha Reddy, C. Kishore, B. Satish Reddy

G. Pulla Reddy College of Pharmacy, Hyderabad-500028, Andhra Pradesh, India.

Abstract

Lamotrigine is used in the treatment of CNS disorders, particularly epilepsy; pain; oedema; multiple sclerosis and psychiatric indications including bipolar disorder. Lamotrigine belongs to biopharmaceutical classification systems; BCS class II (Low solubility & High permeability). In addition, it requires immediate therapeutic action. Hence, the main objective of this study is to improve the solubility by solid dispersion technique and formulate it as oral disintegrating tablets (ODT) to avert the problems of swallowing and to provide rapid onset of action. Lamotrigine solid dispersion was prepared by using Tween 80 and Gelucire 44/14 as solubility enhancers and formulated it into ODT by direct compression technique using different concentrations of Kyron T-314, Kyron T-154, and Kyron T-104 as cross linked polymers. The tablets were evaluated for various parameters and the results were found to be satisfactory. The batches of $LMTK_{314\ (2)}$, $LMGK_{314\ (2)}$ were selected as optimized batch containing Kyron T-314 as super disintegrant in 2% concentration, as they showed 100% drug release in 8 minutes and 6 minutes with a disintegration time of 11 and 9 seconds respectively. Upon comparison of dissolution profiles of optimized formulae LMTK314 (2), LMGK314 (2) with a marketed product, it proved that the optimized formulae had shown better dissolution. The optimized formulations were subjected to stability studies for three months as per ICH guidelines and showed physical stability with insignificant change in the hardness, disintegration time, drug content and *in vitro* drug release.

Keywords : Fast dissolving tablets, Gelucire 44/14, Kyron, Lamotrigine, ODT, Solid dispersion technique, Solubility enhancers, Super disintegrant, Tween 80.

1. **Introduction**

The oral route is the most preferred route of drug administration due to its good patient compliance, convenience and is economical [1]. For a drug to be absorbed into the systemic circulation following oral administration, first the drug must be dissolved in the gastric fluids and cross G. I membrane. For hydrophobic drugs, dissolution process is the rate controlling step which determines the rate and degree of absorption. Dissolution of these drugs can be enhanced by decreasing the particle size and increasing hydrophilic character of the drug. Based on this criterion the technique called as Solid Dispersion was developed. The term solid dispersion refers to the dispersion of one or more active ingredients in an inert hydrophilic carrier or matrix at solid state [2].

The drug selected for the present work is lamotrigine. It is used in the treatment of CNS disorders, particularly epilepsy; pain; oedema; multiple sclerosis and psychiatric

Corresponding Author*: Dr. P. K. Lakshmi, M. Pharm, PhD, Department of Pharmaceutics, G. Pulla Reddy College of Pharmacy, Hyderabad, Andhra Pradesh, India Postal code 500028
Email:drlakshmisuresh@gmail.com
Tel:09000044452
Cite this article as: Lakshmi PK, Reddy S, Kishore C, Satish Reddy B.Formulation & Evaluation of Oral Disintegrating Tablets of La motrigine Solid Dispersions motrigine Solid Dispersions. *Iranian Journal of Pharmaceutical Sciences*. 2013, 9 (1): 1-12.

indications including bipolar disorder. The exact mechanism of lamotrigine is not precisely known. One of the proposed mechanism of action is that lamotrigine inhibits voltage-sensitive sodium channels and/or calcium channels, thereby stabilizing neuronal membranes and consequently modulating presynaptic transmitter release of excitatory amino acids (e.g., Glutamate and aspartate) [3].

Lamotrigine belongs to biopharmaceutical classification systems, BCS class II (Low solubility & High permeability) [4], in addition it requires immediate action. Hence, in this study solubility of lamotrigine is increased by preparing solid dispersion and formulated it as Orally Disintegrating tablets (ODT). USFDA defines ODT as a solid dosage form containing medicinal substances which disintegrate rapidly when placed on the tongue where they get dispersed in saliva, resulting in a solution or suspension without the need of water or chewing. The benefits in terms of patient compliance, increased bioavailability, avert the problems of swallowing in patients with psychiatric disorders, pediatrics or geriatrics patients and to provide rapid onset of action make these tablets popular as the choice of dosage form in the current market [5].

In this study, Tween 80, Gelucire 44/14 were used as solubility enhancers and Kyron T-314, Kyron T-104, Kyron T-154 were used as cross linked polymers. These polymers are believed to impart their disintegrating action through swelling and capillary action [6]. Kyron T-314 is derived from acrylate base polymer ("Polacrillin Potassium") as per USP/NF. It is an effective super disintegrant as well as dissolution enhancer in solid dosage forms like tablets, capsules, pellets etc. Kyron T-104 is derived from cross linked polymers of methacrylic acid with carboxylic acid functionality which enables its use as a taste masking agent. Kyron T-154 is derived from cross linked polymers of styrene and divinylbenzene and has sulphonic acid functionality which enables its use as a taste masking agent. Gelucire 44/14 is non-ionic water dispersible surfactant composed of well characterized PEG-esters, a small glyceride fraction and free PEG. Tween 80 is a polyoxyethylene sorbitan monooleate. It is widely used as solubilizing agents.

The current pharmaceutical market for oral disintegrating tablets is on the rise due to availability of few technologies and patient demand. Hence, an attempt has been made in the development of a less laborious and economic method which could be industrially applicable for the delivery of lamotrigine for fast disintegration.

2. Materials and Methods

2.1. Materials

Lamotrigine was obtained from RA Chem Pharma Ltd (Hyd) as a gift sample, Gelucire 44/14 from RA Chem Pharma Ltd (Hyd), Kyron T-314, Kyron T-154, Kyron T-104 from Corel Pharma chem, Ahmedabad. Magnesium stearate, spray dried lactose, aspartame from SD Fine –Chem Pvt, Mumbai. All other materials used were of analytical grade.

2.2. Methods

2.2.1. Analytical Methodology

The standard curve of lamotrigine, compendia media of 0.1N hydrochloric acid and water was performed to quantify the samples. All the solutions were prepared with fresh before use.

2.2.2. Preparation of Standard Graph

Standard solutions in the range of 2 to 35 mcg/ml were prepared and absorbance values were recorded at 245nm (in water) and 244nm (in 0.1N HCl) against the respective blank. From this data, the standard curve of lamotrigine was obtained by plotting absorbance on Y-axis against concentration on X-axis.

2.2.3. Preparation of Solid Dispersions of Lamotrigine

Kneading method: 25mg of lamotrigine and carrier (Tween 80 and Gelucire 44/14) weighing 0.5mg, 1mg, 1.5mg and 2mg were taken. Each of this specified quantities of the carrier were mixed with water separately, and then the drug is added. It is followed by drying in an oven at 40ºc for 2 hours which

is then cooled and pulverized.

2.2.4. Evaluation of Solid Dispersion

2.2.4.1. In Vitro Dissolution Studies

In vitro dissolution studies for pure lamotrigine (LM) and solid dispersions were carried out in a USP II paddle apparatus. Samples equivalent to 25mg of LM were added to 900ml of distilled water and maintained at 37ºC ± 0.5ºC at 50 rpm. 5 ml samples were withdrawn at regular time intervals and same volume was replaced with fresh media. Absorbance of the solution was checked by a UV spectrophotometer at a wavelength of 245 nm and drug release was determined from the standard curve.

2.2.4.2. Solubility Studies

Saturation solubility was determined by the shake flask method. Pure drug and solid dispersion in excess quantity was placed in separate flasks containing 10ml distilled water. The samples were placed in orbital shaker at 37ºC and rotated at 100 rpm until equilibrium was achieved. The aliquots were filtered and analyzed spectrophotometrically at 245nm.

2.2.4.3. Preformulation Studies

2.2.4.3.1. Drug-Excipients Compatibility with FTIR

Identification of pure drug and the polymer were performed using infrared spectroscopy. FT-IR spectroscopy (Shimadzu Corporation, Tokyo, Japan) by KBr pellet method was carried out on drug and polymer. The pellet was compressed under 10 tons pressure in a hydraulic press to form a transparent pellet. The pellet was scanned from 4000 to 400 cm^{-1}. The resultant spectrum was compared for any spectral changes. They were observed in the presence of characteristic peaks for the respective functional group in the compound.

2.2.4.4. Flow Property Related Studies

2.2.4.4.1. Preparation of Mixed Blend of Drug and Excipients

All the ingredients were passed through mesh no 60. Required quantity of each ingredient was taken for each specified formulation and all the ingredients were subjected to grinding to a required degree of fineness. The powder blend was evaluated for pre compression parameters.

2.2.4.4.2. Angle of Repose

The frictional forces in powder can be measured by the angle of repose (q). The angle of repose of the prepared powder was evaluated by using the fixed funnel method. Specified quantity of the powder was taken and poured into the funnel, which automatically forms the heap. The formed heap's diameter and height were measured. Then the angle of repose of the powder was measured by using below mentioned formula,

$$q = Tan^{-1} (h/r)$$

Where h and r are the height and radius of the powder heap

2.2.4.4.2.1. Determination of Bulk Density and Tap Density

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

$$\rho b = M/Vb$$

The measuring cylinder containing a known mass of powder was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the powder was measured. The tapped density (ρt) was

$$\rho t = M/Vt$$

2.2.4.4.2.2. Compressibility Index

The simplest way for the measurement of free flow of powder is compressibility. It is an indication of the ease with which a material can be induced to flow and is given by compressibility index (I), which is calculated as:

$I = (\rho t - \rho o/\rho t) \acute{}100$

ρt = tapped density
ρo = initial bulk density

Hausner ratio is an indirect assessment of ease of powder flow. It is calculated by the following formula

Hausner ratio = $\rho t / \rho d$

ρt = tapped density
ρo = bulk density

2.*2.5. Preparation of Lamotrigine Oral Disintegrating Tablets*

The two formulations of lamotrigine (25mg) solid dispersion with Tween 80 (1.5mg) and Gelucire 44/14 (1.5mg) were selected based on dissolution studies for the preparation of lamotrigine ODT.

2.2.6. Preparation of ODT

The composition of different formulations lamotrigine ODT is shown in table1. All ingredients were triturated individually in a mortar and passed through #60 sieve. Then required quantity of all ingredients was weighed for a batch size of 50 tablets and mixed uniformly in a mortar except talc and magnesium stearate. Finally magnesium stearate and talc were added as a lubricant. This uniformly mixed blend was compressed into tablets containing 25mg drug using 6mm flat face surface punches on a Rimek-1 rotary tablet machine by the direct compression method. Total weight of the tablet was kept 100mg.

2.2.7. Evaluation of Oral Dispersible Tablets

2.2.7.1. Weight Variation Test

Twenty tablets were selected at random, individually weighed in a single pan electronic balance and the average weight was calculated. The uniformity of weight was determined according to I.P. Specifications. As per I.P not more than two of individual weights should deviate from the average weight by more than 5% and none deviate more than twice that percentage.

2.2.7.2. Thickness and Diameter

The thickness and diameter of the tablets were measured using vernier caliper. Ten tablets were selected from each batch and results were expressed as mean values ±SD.

2.2.7.3. Hardness Test

Tablet requires a certain amount of strength or hardness and resistance of friability to withstand mechanical shocks of handling during manufacture, packing and shipping. The Monsanto hardness tester was used for the measurement of hardness of the prepared ODT. Three tablets were selected from each batch for testing and results were expressed in Kg/cm^2.

2.2.7.4. Friability Test

It was done in a Roche friabilator apparatus where the tablets were subjected to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of six inches with each revolution. Pre weighed samples of 20 tablets were placed in the friabilator, which was operated for 100 revolutions. The tablets were reweighed. Conventional compressed tablets lose less than 0.5 to 1.0% of their weight which is generally considered acceptable.

$$\text{Friability} = \frac{\text{Weight loss}}{\text{Weight of tablets before operatio}} \times 100$$

2.2.7.5. Drug Content Uniformity

Twenty tablets were individually weighed and crushed using mortar and pestle. A quantity equivalent to the mass of 25mg of drug is weighed and extracted with 100 ml of 0.1 N HCl. The solution was filtered through watt mans filter paper. The drug content was determined by UV visible-spectroscopy (Shimadzu Corporation, Tokyo, Japan) at a wavelength 244 nm after suitable dilution with 0.1 N HCl. The amount of drug was calculated using standard graph.

Table 1. Formulations of Lamotrigine with Tween 80 and Gelucire 44/14 tablets containing different cross linked polymers.

Formulations of lamotrigine and Tween 80 (1.5mg) tablets containing different cross linked polymers								
Formulation	**Lamotrigine (mg)**	**KyronT-314 (mg)**	**Kyron T-154 (mg)**	**Kyron T- 104 (mg)**	**Spray dried lactose (mg)**	**Mannitol (mg)**	**Aspartame (mg)**	**Total (mg)**
$LMTK_{314(1)}$	25	1	-	-	42	25	4	100
$LMTK_{314(2)}$	25	2	-	-	41	25	4	100
$LMTK_{154(1)}$	25	-	1	-	42	25	4	100
$LMTK_{154(2)}$	25	-	2	-	41	25	4	100
$LMTK_{104(1)}$	25	-	-	1	42	25	4	100
$LMTK_{104(2)}$	25	-	-	2	41	25	4	100
Formulations of lamotrigine and Gelucire 44/14(1.5mg) tablets containing different cross linked polymers.								
Formulation	**Lamotrigine (mg)**	**KyronT-314 (mg)**	**Kyron T-154 (mg)**	**Kyron T- 104 (mg)**	**Spray dried lactose (mg)**	**Mannitol (mg)**	**Aspartame (mg)**	**Total (mg)**
$LMGK_{314(1)}$	25	1	-	-	42	25	4	100
$LMGK_{314(2)}$	25	2	-	-	41	25	4	100
$LMGK_{154(1)}$	25	-	1	-	42	25	4	100
$LMGK_{154(2)}$	25	-	2	-	41	25	4	100
$LMGK_{104(1)}$	25	-	-	1	42	25	4	100
$LMGK_{104(2)}$	25	-	-	2	41	25	4	100

LMT=Formulations of Lamotrigine solid dispersion (SD) with Tween 80;
LMG=Formulations of Lamotrigine SD with Gelucire 44/14.
LMTK314, LMGK314 = Formulations of Kyron T-314 with its corresponding SD;
LMTK154, LMGK154 = Formulations of Kyron T-154 with its corresponding SD;
LMTK104, LMGK104 = Formulations of Kyron T-104 with its corresponding SD.
Note: 1 mg of talc, magnesium stearate, and vanillin LR flavor were used in all formulations.

2.2.7.6. Wetting Time

Five circular tissue papers of 10-cm diameter were placed in a petri dish with 10-cm diameter. 10 ml of water at 37ºC+0.5ºC containing eosin, a water-soluble dye, was added to the petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time. Six tablets from each formulation batch were tested randomly and the average reading was noted [7].

2.2.7.7. Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed.

Water absorption ratio R, was determined using the following equation

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

W_a = weight of the tablet after absorption

W_b = weight of the tablet before absorption

2.2.7.8. Content Uniformity

20 tablets were randomly selected and average weight was calculated. Tablets were powdered in a glass mortar. Powder equivalent to 4mg was weighed and dissolved in 100 ml of 0.1N Hydrochloric acid, filtered and drug content were analyzed spectrophotometrically at 244 nm.

2.2.7.9. In Vitro Disintegration Time

Disintegration time was measured using a modified disintegration method. For this purpose, a petri dish was filled with 10 ml of water at 37ºC±0. 5ºC. The tablet was carefully put in the center of the petri dish and the

time for the tablet to completely disintegrate into fine particles was noted [8].

2.2.7.10. Swelling Index

Swelling index is the volume in milliliters that is occupied by 1 g of the drug after it has swollen in an aqueous liquid for 4 h. The methods of studying swelling index for Kyron T-314, Kyron T-154 and Kyron T-104 were carried out. Swelling index was calculated from mean readings of three determinations [9].

2.2.7.11. In-vitro Drug Release Studies

Drug release studies of prepared ODT were performed in a triplicate, in a USP dissolution test apparatus, type-II (paddle method) at 37±0.5°C. The paddles rotated were at a speed of 50 rpm. The tablets were placed in 900 ml of 0.1 N HCl solution (pH 1.2). Aliquots of 5 ml were withdrawn at regular time interval from the dissolution medium and filtered through watts man filter paper. The drug content was determined spectrophotometrically at a wave length of 244 nm, as mentioned before. After each withdrawal, 5ml of fresh medium was replaced into the dissolution vessel. The cumulative percentage drug release was calculated using an equation obtained from the standard graph.

2.2.7.12. Similarity and Difference Factors

A model independent approach was used to estimate the dissimilarity factor (f1) and similarity factor (f2) to compare the dissolution profile of optimized formulations with marketed formulation [10].
The following equations were used for calculating f1 and f2.

$$f_1 = \{[\Sigma_{t=1}^{n} |R_t - T_t|] / [\Sigma_{t=1}^{n} R_t]\} \times 100$$

The similarity factor (f2) is given by the following equation:

$$f_2 = 50 \times \log \{[1 + (1/n) \Sigma_{t=1}^{n} (R_t - T_t)\ 2] - 0.5 \times 100\}$$

Where n = no of time points, the R_t = dissolution value of the reference batch at time t, the T_t=dissolution value of the test batch at the same time point.

2.2.7.13. Accelerated Stability Studies

Stability studies were carried out for optimized formulations, according to an international conference on Harmonization (ICH) guidelines. The best formulae LMTK314 (2) and LMGK314 (2) were wrapped in aluminum foil and placed in an amber colored bottle and kept at 40°C /75% RH in stability chamber (Oswald, Mumbai) for 3 months. At an interval of 30 days, the tablets were withdrawn and evaluated for physical properties, *in vitro* drug release.

2.2.7.14. Statistical Analysis of Data

Disintegration time, wetting time, water absorption ratio and swelling index of tablets containing 2% of Kyron T-314, Kyron T-154 and Kyron T-104 were taken as parameters for ANOVA (Turkey's multiple comparison test) analysis at 5% significance levels using GraphPad software.

3. Results and Discussion

The present investigation was undertaken to improve the solubility of lamotrigine by using solubility enhancers like Gelucrie 44/14 and Tween 80, and to formulate oral disintegrating tablets by using cross linked polymers. For this study different polymer like Kyron T-314, Kyron T-154 and Kyron T-104 were selected to formulate the tablets as these polymers are believed to impart their rapid disintegrating action through swelling and capillary action.

3.1. In Vitro Dissolution Studies of Solid Dispersions

From the reports, the cumulative percentage drug release was found to be 100% in 6mins for LMT (1.5mg) and 4mins for LMG (1.5mg) and these formulations were optimized for the preparation of oral disintegrating tablets. 30 fold increase in drug release was obtained by preparing solid dispersions when compared to pure drug. This infers that as the concentration of Tween 80 and Gelucire 44/14 increases the micellar concentration increases, which in turn increase the rate of drug release [11].

3.2. Solubility Studies

Pure lamotrigine showed 0.163mg/ml of saturation solubility, whereas solid dispersions showed 15 fold increase in saturation solubility as compared to pure lamotrigine. This might be attributed to an improvement of wetting of drug particles and localized solubilization by hydrophilic polymers [12].

3.3. Flow Property Related Studies

Results of flow properties are found to be Angle of repose (θ) = 24.47±0.92 to 27.54±0.81 ; Bulk density (gm/cm3) = 0.606±0.005 to 0.661±0.009;Tapped density (gm/cm3) = 0.661±0.001 to 0.746±0.012; Compressibility index (I) =1.126±0.004 to 1.134±0.021;Hausners ratio = 8.24±0.947 to 11.89±0.562. These values indicate that the prepared powder blend exhibited good flow properties.

All the formulations were evaluated for various parameters like hardness, friability, drug content, wetting time, water absorption ratio, disintegration time and *in vitro* drug release studies.

The hardness of the tablets was found to be 3.2 + 0.61 to 3.5 + 0.56 kg/cm2 and friability was found to be below 1% indicating good mechanical resistance.

The thickness of the tablets was found to be 2.44± 0.07 to 2.58± 0.04. All the tablets passed weight variation test, as percentage weight variation was within the pharmacopoeial limits i.e. ±10%.

The drug content was found to be 98.64 to 101.12 %, indicating the uniform distribution of drugs in the tablets.

3.4. Swelling Index

Kyron T-314 showed higher percentage of swelling index (79±2.3%) than other polymers like Kyron T-154 (69±2.7 %) and Kyron T-104 (63±1.9 %).

3.5. Disintegration Time

Disintegration time of all batches was found in the range of 9 ± 1.11 to 99 ± 1.76 sec fulfilling the official requirements (<3 min) for oral disintegrating tablets [13]. It was observed that the disintegration time of the tablets decreased with increasing concentration of Kyron T-314, Kyron T-154 and Kyron T-104. Figure 1 clearly shows that formulae LMTK314(2), LMGK314(2) containing Kyron T-314 as super disintegrant in 2% concentration has shortest disintegration time when compared with other formulations i.e.., 11 seconds and 9 seconds respectively.

Lesser disintegration time was observed when Kyron T-314 was used as super disintegrant. This could be due to swelling at a faster rate upon contact with water or G. I fluids and elimination of lump formation after disintegration when compared with Kyron T-154 and Kyron T-104 [14].

3.6. Wetting Time

Figure 2 depicts the relation between the concentrations of polymers and wetting time. Wetting time was used as a parameter to correlate with disintegration time in the oral cavity. This is an important criterion for understanding the capacity of disintegrants to swell in the presence of a little amount of water. Since the dissolution process of a tablet depends upon wetting followed by disintegration of the tablet, it could be assumed that wetting is the only cause of disintegration. This indicates that aqueous medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bonds and breaks the tablet into fine particles.

The wetting time of the formulated tablets were found in the range of 24±1.55 to 89 ±1.42 Sec.

3.7. Water Absorption Ratio

The water absorption ratio was performed to know the moisture sorption and water uptake properties of polymers.

The water absorption ratio was increased and disintegration time, wetting time was decreased with an increase in concentration of polymers. The water absorption ratio of the formulated tablets was found in the range of 198±1.54 to 233±1.65.

Figure 1 shows an inverse relationship between the oral disintegration time and water absorption ratio. It was also observed that formulae LMTK 314(2), LMGK 314(2) containing Kyron T-314 showed the highest water absorption ratio with the most rapid disintegration time. This implies that ODT

containing Kyron T-314 in 2% concentration have comparatively the highest swelling capacity and are the most porous tablets.

3.8. In-vitro Drug Release Studies

In-vitro drug release of all formulations showed above 90% release within 20 minutes. It was observed that the drug release was increased with increasing concentration of Kyron T-314, Kyron T-154 and Kyron T-104. Batch LMTK 314 (2), LMGK314 (2) was selected containing Kyron T-314 as super disintegrate in 2% concentration, it showed 100% drug release in 8 minutes and 6 minutes. Kyron T-314 used as super disintegrant increases the porosity of the tablets due to which the absorption of water takes place at a higher rate that results in breaking of tablets and therefore faster disintegration/ dissolution [15].

3.9. Statistical Analysis of Data

Upon comparison of disintegration time, wetting time, water absorption ratio and swelling index of all batches containing 2% of Kyron T-314, Kyron T-154 and Kyron T-104 by "one way ANOVA" (Turkey's multiple comparison test) it was found that there was a significant difference in the disintegration time, wetting time and water absorption ratio (p<0.0001) of Kyron T-314 when compared with Kyron-154 and Kyron 104. Results shown in table 2.

No significant difference was seen in swelling index between Kyron T-314 and Kyron T-154, Kyron T-104.Hence, based on results of disintegration studies, wetting time, water absorption ratio and dissolution studies it was found that LMTK 314 (2), LMGK 314 (2) to be optimized batch. And these optimized batches were compared with marketed formulation (LAMITOR DT 25mg).

3.10. Incompatibility Studies

FTIR spectra's of pure lamotrigine, blend of polymer with drug were studied. Lamotrigine and polymers showed their respective principle IR peaks.

Figure 3, figure 4 and figure 5 shows the FTIR spectra of pure lamotrigine, LMTK 314 (2) and LMGK 314 (2) respectively.

From the above IR graphs the peaks representing the pure drug were similar in all graphs suggesting that there is as such no interaction and pure drug is not altered functionally.

3.11. Comparison of Optimized Formulations with Marketed LAMITOR DT 25mg

The optimized formulations LMTK 314(2) and LMGK 314(2) were compared with the marketed tablet for disintegration time, wetting time, hardness, friability. The result showed that the formulated ODT disintegrated in 9 seconds as compared to 14 seconds for marketed lamotrigine tablet (LAMITOR DT).

In vitro dissolution of optimized formulations LMTK314 (2), LMGK314 (2) and marketed formulation were performed

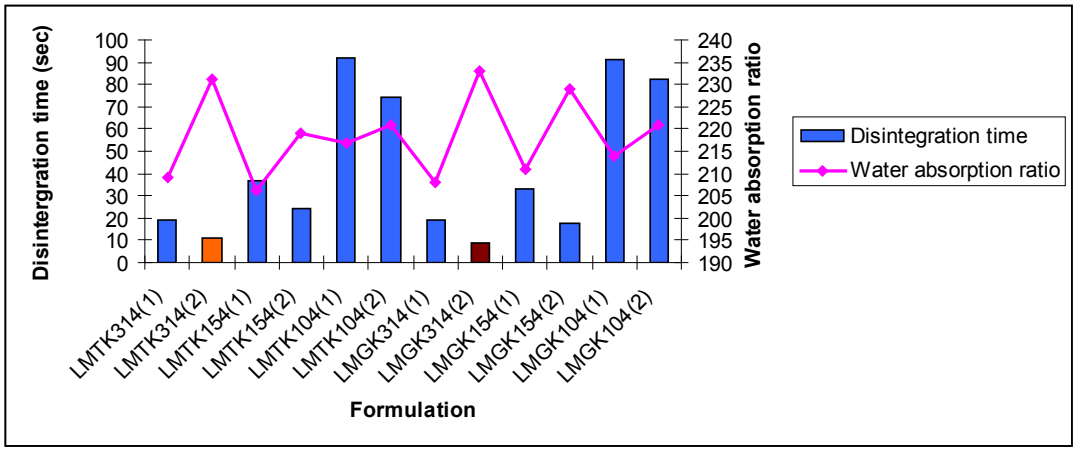

Figure 1. Disintegration time VS Water absorption ratio for all formulations.

Table 2. Comparison of disintegration time, wetting time, water absorption ratio and swelling index of tablets containing 2% of Kyron T-314, Kyron T-154 and Kyron T-104 using one way ANOVA(Tukey's multiple comparison test).

Parameters of ODT	**LMTKK104(2) VS LMTK154(2)**	**LMTK104(2) VS LMTK314(2)**	**LMTK154(2) VS LMTK314(2)**	**F Value**	**P value**
Disintegration time	***	***	**	1425	***=<0.0001
Wetting time	***	***	**	811.5	***=<0.0001
Water absorption ratio	**	***	**	211.2	***=0.0006
Swelling index	NS	**	NS	33.77	**= 0.0088
	LMGK104(2) VS LMGK154(2)	**LMGK104(2) VS LMGK314(2)**	**LMGK154(2) VS LMGK314(2)**	**F value**	**P value**
Disintegration time	***	***	*	2004	***=<0.0001
Wetting time	*	**	*	73.79	**=<0.0028
Water absorption ratio	**	**	NS	151.0	**=0.001
Swelling index	NS	**	NS	33.77	**=0.0088

NOTE: N=6; one way ANOVA (Turkey's multiple comparison test); *** (High significance) =p<0.0001; ** (Moderate significance) =p<0.001; * (Low significance) =p<0.01; NS= non-signicant.

and the percentage release was found to be 101.25% in 8minutes, 101.16% in 6 minutes and 99.36% in 10 minutes respectively. Figure 6 depicts the comparison *In vitro* dissolution of optimized formulations with marketed formulation.

f_1 and f_2 values were calculated and were found to be 0.125 and 37.98 for LMGK314 (2), 4.25 and 48.65 for LMT314 (2) .

Upon comparison of disintegration time, wetting time, *in vitro* dissolution and f1, f_2 values, it has been proved that the optimized formulations had shown better results than the marketed product.

3.12. Accelerated Stability Studies

The stability of this optimized formulation was estimated by performing stability studies for three months at accelerated conditions of 40±2ºC/75±2% RH. The formulation was found to be stable even at the end of three months with insignificant change (±1.5%) in the hardness, disintegration time, drug content and in-vitro

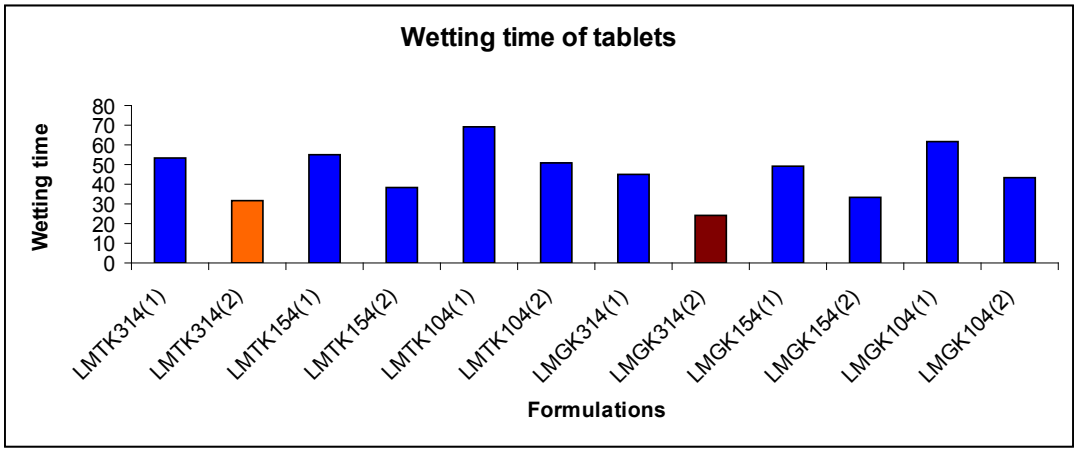

Figure 2. Wetting time for all formulations.

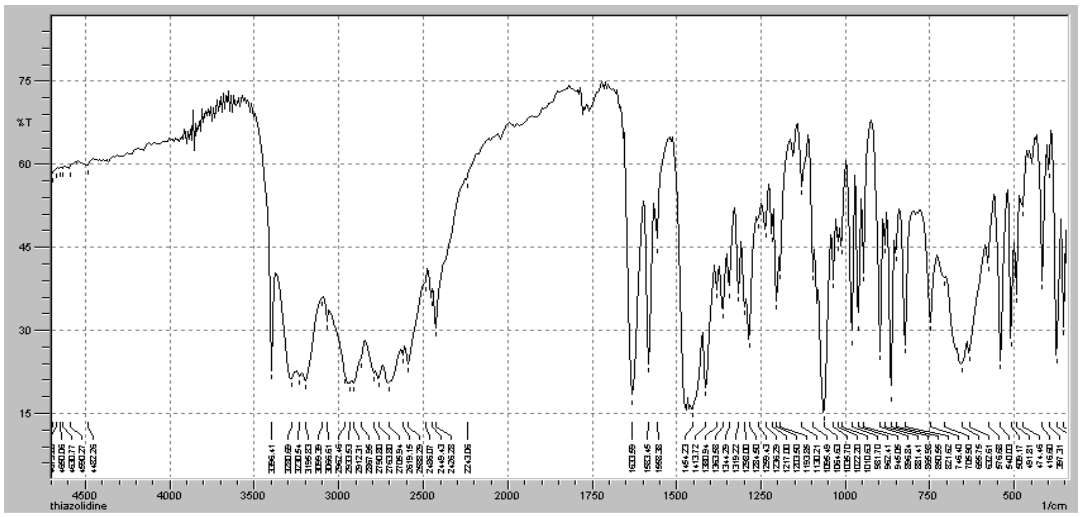

Figure 3. FTIR graph of lamotrigine.

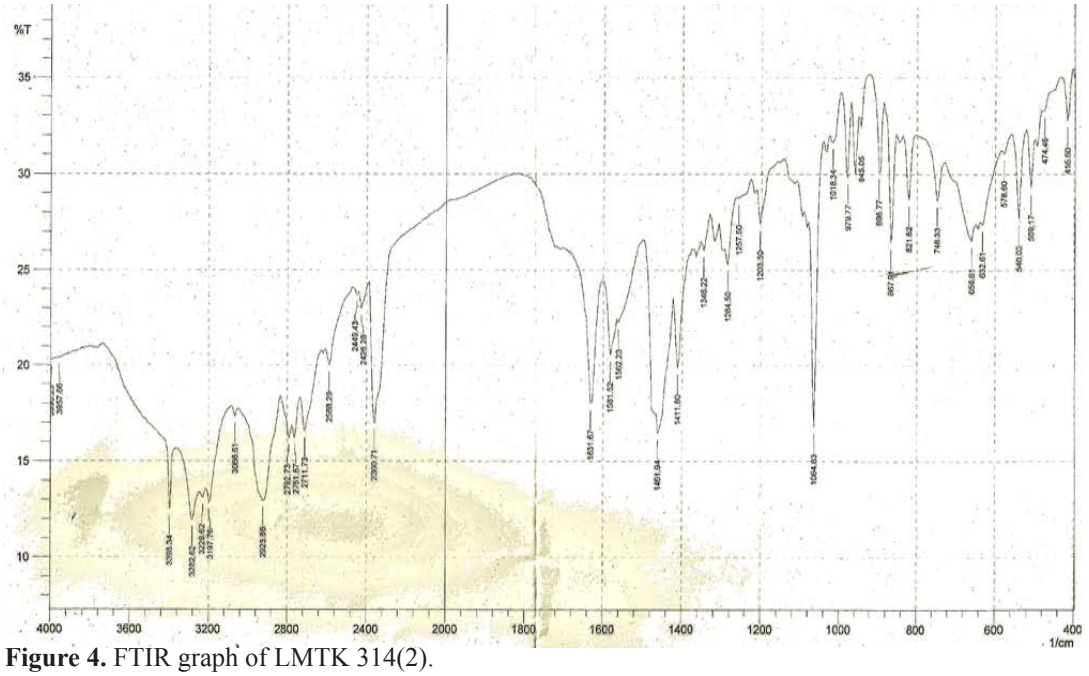

Figure 4. FTIR graph of LMTK 314(2).

drug release.

4. Conclusion

An easy and economical method was implemented for the preparation of oral disintegrating tablets of lamotrigine solid dispersion using Tween 80, Gelucire 44/14 as solubility enhancers and Kyron T-314, Kyron T-154, Kyron T-104 as super disintegrant. The formulae LMTK 314 (2), LMGK 314 (2) was optimized as they showed satisfactory results in terms of disintegration time, wetting time and *in vitro* drug release. These formulae had shown better results in comparison with a marketed product. Optimized formulations showed physical stability when stored at 40°C under 75% RH for 3 months.

Acknowledgements

The authors are thankful to RAchem. Pharma Ltd, AP for providing the gift sample of lamotrigine. The authors are also thankful to Corel Pharma Chem, Ahmedabad for providing the polymers as a gift sample such as Kyron T-314, Kyron T-154 and Kyron T-104. Also thankful to management of G. Pulla Reddy College of Pharmacy College of Pharmacy for providing all the facilities for carrying out this research work.

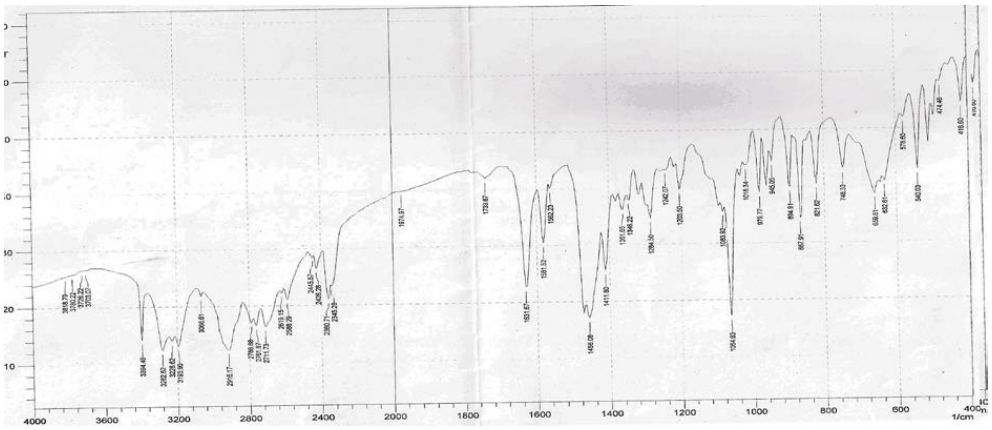

Figure 5. FTIR graph of LMGK 314(2).

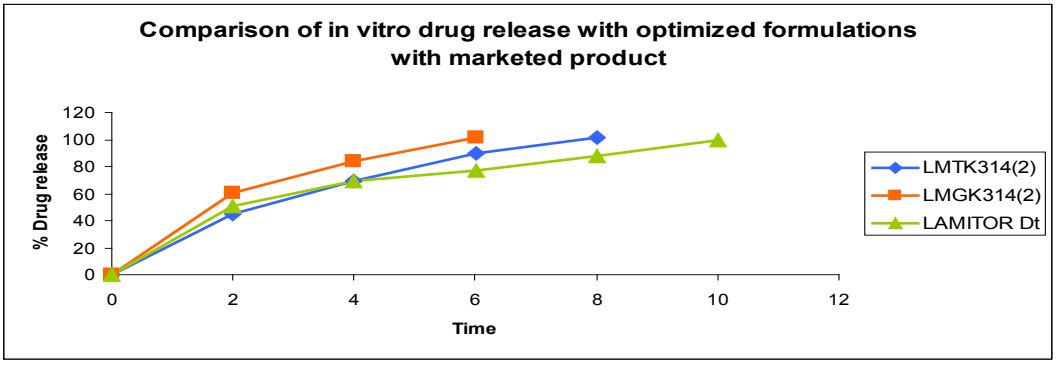

Figure 6. Comparison of *in vitro* release with optimized formulations with marketed product.

References

[1] Tejas B, Patel LD, Patel TB, Sunil H, Patel R. Enhancement of the dissolution rate and oral absorption of drug insoluble in gastric fluid by spray dried microparticles. *International Journal of ChemTech Research*, 2010, 2:185-193.

[2] Deveswaran R, Sravya S, Bharath, B, Madhavan V. Development of modified porous starch as a carrier to improve aqueous solubility. *Advances in Applied Science Research*, 2012, 3:162-170.

[3] Magda TM, Clésio SP, Martin S. Development of a dissolution test for lamotrigine in tablet form using an ultraviolet method. *Brazilian Journal of Pharmaceutical Sciences*, 2010, 46:180-186.

[4] Venkat BY, Adhikrao VY . Enhancement of solubility and dissolution rate of bcs class ii pharmaceuticals by nonaquious granulation technique. *International journal of pharma research and development-online*, 2010,1.

[5] Mudgal VK, Pooja S, Rajat K, Saraogi GK, Singhai A K. Orally disintegrating tablets: review. *Intenational journal of pharmacy*, 2011, 2:16-22.

[6] Chowdary KPR, Srinivasa R. Investigation of dissolution enhancement of itraconazole by solid dispersion in superdisintegrants. *Drug Dev. Ind. Pharm*, 2000, 26:1207-11.

[7] Gohel M, Patel M, Amin A, Agarwal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. *AAPS Pharm.Sci.Tech*, 2004, 5:1-6.

[8] United States Pharmacopoeia. Rockville: USP Convention, Inc; 2004 ; 2302.

[9] Magesh KM, Antaryami J, Ruckmani K, Rajen dran P. Formulation and evaluation of taste masked orally disintegrating ondansetron hydrochloride tab let. *Int. J. Res. Pharm. Sci*, 2010, 1:328-332.

[10] Dressman J and Kramer J, Eds., Pharmaceutical Dissolution Testing. USA,2005; 91-93.

[11] Kiran T, Nalini S, Ramakrishna S, Sadanandam M. Surface solid dispersion of glimepiride for enhancement of dissolution rate. *International Journal of PharmTech Research*, 2009, 1:822-31.

[12] Yang KY, Glemza R, Jarowski CI. Effects of amorphous silicon dioxides on drug dissolution. *J. Pharm. Sci*, 1979,68:560-5.

[13] European Pharmacopoeia.Strasbourg (France): European department for the quality of medicines. 2001;1666–9.

[14] Yusuke S, Makiko F, Hideko O, Shinobu N,Masuo K, Yoshiteru Watanabe. Evaluation of the compaction properties of a solid dispersion of indomethacin with crospovidone by tableting process analyzer. Chemical & pharmaceutical bulletin, 2005, 53:759.

[15] Raymond CR, Paul JS, Marian E Quinn, Eds., Handbook of pharmaceutical excipients,6th edition, 2009; London, Pharmaceutical Press. 206-210,424-428,404-407,185-188,48-50,129-133, 504-506.