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# Formulation and *in vitro* evaluation of fast dissolving tablet of Lurasidone: A study on the effect of Cross Carmellose and Sodium starch glycolate on release profile of drug

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## ABSTRACT

The atypical antipsychotic medication lurasidone is used to treat schizophrenia and other psychotic (mental) disorder symptoms. that completely inhibits serotonin 5-HT2A and 5-HT7 receptors as well as dopamine D2 receptors. The BCS classification of lurasidone places it in class II, and it has a very low water solubility. With the goal of achieving rapid disintegration in gastric pH and quick action for acute conditions for therapeutic benefits to patients, studies were conducted on the formulation and design of fast dissolving tablets of lurasidone using super disintegrants like cross carmellose and sodium starch glycolate. Six different fast-dissolving tablet formulations of Luracedone are made using the wet granulation process. To make sure there is no interaction between the drug and the various excipients used in the formulation, FTIR experiments were conducted on the pure drug Lurasidone as well as on physical mixtures of the drug and excipients. Different pre- and post-compression characterizations of the tablet were conducted, and the results complied with pharmacopoeia requirements. For several formulations, *in vitro* release tests were performed using a USP II paddle type dissolve equipment; the formulation (LFDT) containing 3% sodium starch glycolate provided the best release profile. For the zero order and first order kinetic models, as well as the zero-order kinetic model incorporating drug release mechanism, in vitro release kinetic investigations were conducted. Studies on accelerated stability were conducted, and they verified the stability of dose formulations.

**Keywords:** Lurasidone, Fast Dissolving tablets, Cross Carmellose, Sodium starch glycolate, Schizophrenia, Antipsychotics.

## INTRODUCTION

Due to its ongoing evolution and adoption of novel concepts to get beyond the fundamental flaws of the current formulations, tablets are still the most widely used and acceptable dosage form. The new idea of a fast-dissolving medicine delivery system was created to address the fundamental problems with traditional tablets. Fast dissolving tablets have no particular rate-controlling elements, such as special coatings or other approaches, and are created to dissolve and release their medicine. When a medicine has a longer half-life and fewer doses are required, fast-dissolving dosage forms are most frequently created. Additionally, it improves patient compliance. Rapid reaction is another factor in the formulation of fast-dissolving dose forms. The crucial ingredient in the manufacturing of fast-dissolving tablets, along with a variety of widely used excipients such diluents, binder, lubricants, glidants, etc., is superdisintegrant. For quick and simple tablet disintegration, a variety of superdisintegrants such as sodium starch glycolate, crosscarmellose, and various grades of crosspovidone are typically used in the preparation of fast-dissolving tablets. [1] The mental illness known as psychosis alters how your brain functions. Atypical antipsychotics are a class of drugs that includes lurasidone. It functions by altering the way that a few organic brain chemicals behave. Serotonin 5-HT2A and 5-HT7 receptors, as well as dopamine D2 receptors, are completely blocked by lurasidone. It partially agonists the 5-HT1A serotonin receptor. Lurasidone has the greatest affinity for the 5-HT7 receptor when compared to other atypical antipsychotics. Lurasidone is chemically designated as

(3aR,4S,7R,7aS)-2-{(1R,2R)-2-[4-(1,2-benzisothiazol-3-yl) piperazin-1ylmethyl] cyclohexylmethyl} hexahydro-4,7-methano-2H-isoindole-1,3-dione hydrochloride. Lurasidone metabolism is primarily via the cytochrome P450 enzyme, CYP3A4. As a result, it is advised to cut the lurasidone dosage in half when used concurrently with mild CYP3A4 inhibitors, with a beginning dose of 20 mg and a maximum dose of 80 mg/day. A 40 mg dose produces peak plasma concentrations in adult healthy individuals in 1-3 hours, a mean elimination half-life of 18 hours (mainly removed in the stool), and an apparent volume of distribution of 6173 L; it is roughly 99% bound to serum plasma proteins. The BCS categorization of lurasidone places it in class II, and oral absorption is good. Lurasidone has a poor bioavailability, a sluggish onset of action, and is essentially insoluble in water. The active ingredient, lurasidone HCl, is a white to off-white powder. It has a pKa of 7.6, is practically insoluble or insoluble in 0.1 N HCl, practically insoluble or insoluble in toluene, barely soluble in acetone, hardly soluble in ethanol, sparingly soluble in methanol, and very faintly soluble in acetone. [2] The primary goal of the current research was to develop and conduct in vitro evaluation studies of fast-dissolving lurasidone tablets using super disintegrants like crosscarmellose and sodium starch glycolate in order to achieve rapid disintegration when taken orally and enable a rapid onset of action during acute psychosis conditions. [3]

## MATERIALS AND METHODS

### *Materials*

A gift sample of lurasidone was obtained from Dr. Reddy's Laboratories in Hyderabad, India. Additionally, we received a gift sample of the superdisintegrant crosscarmellose and sodium starch glycolate from Dr. Reddy's laboratories Pvt. Ltd. Otto Manufacturers provided the Micro crystalline cellulose, the diluent. In Mumbai, India, we bought PVP K30, aspartame, Talc, and magnesium Stearate from S.D. fine chemicals Pvt. Ltd. Every component was of laboratory-grade quality. The distilled water utilised in the research was created in the lab using a double distillation technique.

### *Methods*

#### *Determination of λmax of pure Lurasidone and preparation of calibration curve*

Utilizing an HCl buffer with a pH of 1.2, a primary stock solution of lurasidone with a concentration of 1000 g/ml was created. Using the same HCl buffer pH, a secondary stock solution with a concentration of 10 g/ml was created from the first stock solution following the appropriate dilution. The generated secondary stock solution was then scanned using an Analytical Technologies Ltd. Spectro 2080 UV spectrophotometer at wavelengths ranging from 400 nm to 200 nm to determine the solution's maximum wavelength, which was discovered to be 230 nm. After that, the secondary stock solution was diluted with the same HCl buffer pH 1.2 to create a series of concentrations of 2, 4, 6, 8, and 10 g/ml, and the associated absorbance was measured at the maximum wavelength of 230 nm. For obtaining the calibration curve of pure Lurasidone, the measured absorbence were plotted against corresponding concentrations. [4]

#### *Drug excipients compatibility studies*

Drug excipients compatibility studies were done by FTIR.

#### *Fourier Transform Infrared (FTIR) spectroscopy*

To confirm any physical or chemical interactions between the pure medication and the excipients employed, a Fourier transform infrared (FTIR) research was conducted. Studies on the FTIR of the excipients utilised in formulations as well as the pure medication Lurasidone, MCC, PVP K30, croscarmellose, and sodium starch glycolate were conducted. The procedure used the pellet method with potassium bromide (KBr). The materials were triturated with KBr, and a pellet was created by applying 100 kg/cm2 of pressure for two minutes. The obtained pellet was examined in the Shimadzu, Japan, FTIR 8400S. Prior to the analysis of the test samples, the KBr background was first acquired. The same steps were performed for the analysis of the drug, each excipient, and the physical mixing of the excipients and the drug. [5]

#### *Formulation of Lurasidone fast dissolving tablets*

Wet granulation technology was used to create Lurasidone pills that dissolve quickly. Before being used in formulations, all materials were weighed precisely and put through filter #80. Specific and precise amounts of powder, such as lurasidone, mcc, crosscarmellose sodium, PVP K30, and aspartame, were combined equally and passed through #20 for each formulation. Binder utilised was PVP K30. To lower the moisture content and prevent sticking to the sieve, the aggregates created after the addition of the binder were first dried for five to ten minutes. To obtain granules, the aggregates were sent through filter #20. To lower the moisture content of the granules by up to 2-5%, they are dried at 40° C for 20 minutes. Talc and magnesium stearate were utilised as lubricants, and dried granules were combined with the necessary amounts for 2–3 minutes. Prior to compression, the formulations' angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio were assessed after lubrication. On a 10-station rotary punching machine (Saimach Pharmaceutical Pvt. Ltd.), using 8 mm concave punches, the evaluated granules were compressed into tablets. There are 40 milligrammes of lurasidone in each pill. **Table 1** contains the recipes for many formulations, and the same process was used for each formulation. Then, several post-compression characteristics were assessed for the generated tablet formulations, including average thickness, weight variation, hardness, friability, drug content, wetting time, water absorption ratio, disintegration study, and in vitro dissolution experiments. [6]

**Table 1: Compositions of different excipients used for Lurasidone fast dissolving tablets**

| F. No. ⇨ / Ingredient ⇩ | LFDT$_1$ | LFDT$_2$ | LFDT$_3$ | LFDT$_4$ | LFDT$_5$ | LFDT$_6$ |
|---|---|---|---|---|---|---|
| **Lurasidone (mg)** | 40 | 40 | 40 | 40 | 40 | 40 |
| **Cross Carmellose (mg)** | 4 | 6 | - | - | 2 | 3 |
| **Sodium Starch Glycolate (mg)** | - | - | 4 | 6 | 2 | 3 |
| **PVP K30 (mg)** | 20 | 20 | 20 | 20 | 20 | 20 |
| **MCC (mg)** | 129 | 127 | 129 | 127 | 129 | 127 |
| **Aspartame (mg)** | 2 | 2 | 2 | 2 | 2 | 2 |
| **Magnesium Stearate (mg)** | 3 | 3 | 3 | 3 | 3 | 3 |
| **Talc (mg)** | 2 | 2 | 2 | 2 | 2 | 2 |
| **Total Weight (mg)** | 200 | 200 | 200 | 200 | 200 | 200 |

## *Evaluation of pre-compression parameters of Lurasidone fast dissolving granules*

### *Angle of Repose (θ)*

Angle of repose is an important parameter that is used to find out the flow properties of granule and it is indicated as maximum angle possible between the surface of a pile of granules and the horizontal plane. The granules were allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

$$\theta = \tan^{-1}\left(\frac{h}{r}\right)$$

Where θ is called as angle of repose, h and r were height and radius of the granule heap respectably. According to the specifications the angle of repose value less than $25^0$ indicates excellent flow whereas angle "between" $25^0$-$30^0$ indicates good flow. The angle "between" $30^0$-$40^0$ indicates passable flow whereas angle greater than $40^0$ indicates very poor flow. [7]

### *Bulk density*

Both the loose bulk density (LBD) and tapped bulk density (TBD) of prepared Lurasidone fast dissolving granules of all the formulations were determined. The quantity of 2 gm of granules from each formula, previously lightly shaken to break any agglomerates formed; were introduced into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second interval. The tappings were continued until no further changes in volume were noted. LBD and TBD of prepared granules were calculated using the following formulas. [8]

$$LBD = \frac{\text{Weight of granules}}{\text{Volume of granules before tapping}}$$

$$TBD = \frac{\text{Weight of granules}}{\text{Volume of granules after tapping}}$$

### *Compressibility Index (Carr's index)*

The flow ability of granules can be evaluated by comparing the loose bulk density (LBD) and tapped bulk density (TBD) of granules and the rate at which it packed down. Compressibility index (Carr's index) of prepared Lurasidone fast dissolving granules were calculated by following formula

$$\text{Carr's index (\%)} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \times 100$$

According to the specification the Carr's index values "between" 5-15 indicates excellent flow whereas between 12-16 indicates good flow. Values "between" 18-21 indicate fare-passable whereas between 23-25 indicates poor flow. Between 33-38 indicates very poor and greater than 40 indicates extremely poor flow. [9]

### *Hausner's ratio*

The Hausner's ratios of prepared Lurasidone fast dissolving granules were determined by following formula.

$$\text{Hausner's ratio} = \frac{\text{TBD}}{\text{LBD}}$$

According to specifications values less than 1.25 indicate good flow (=20% of Carr's index), where as greater than 1.25 indicates poor flow (=33% of Carr's index). Between 1.25 and 1.5, added glidant normally improves flow. [10]

## *Evaluation of postcompression parameters of Lurasidone fast dissolving tablets*

### *Thickness*

Ten Lurasidone fast dissolving tablets from each formulation were randomly selected and used for thickness determination. Thickness of each tablet was measured by using digital Vernier Callipers (Mitutoyo dial Thickness Gauge, Mitutoyo, Japan) and the results were expressed as mean values of ten readings, with standard deviations. According to specification tablet thickness should be controlled within a ± 5% variation of standard value. [11]

### Tablet Hardness

All the formulations of Lurasidone fast dissolving tablets hardness were measured by using Monsanto hardness tester (Cad Mach). From each formulation the crushing strength of ten fast dissolving tablets with known weights were recorded in kg/cm$^2$ and average were calculated and presented with standard deviation. According to specifications of USP hardness values of 3-3.5 Kg for fast dissolving tablets is considered as acceptable limit. [12]

### Friability

Previously weighed ten Lurasidone fast dissolving tablets from each batch were taken in Roche friabilator (Roche friabilator, Secor India, Delhi, India). After hundred revolutions of friabilator tablets were recovered. The tablets were then made free from dust and the total remaining weight was recorded. Friability was calculated from the following formula.

$$\%F = \frac{(\square\square - \square\square)}{\square\square} \times 100$$

Where $W_i$ and $W_f$ were the initial and final weight of the tablets before and after friability test. For compress tablet that lose less than 0.1 to 0.5 % and maximum upto 1% of the tablet weigh are consider acceptable. [13]

### Weight variation test

All formulated Lurasidone fast dissolving tablets were evaluated for weight variation as per USP monograph. Twenty tablets were weighed collectively and individually using an electronic balance. The average weight was calculated and percent variation of each tablet was calculated. According to USP monograph, the weight variation tolerance limit for the uncoated tablet having average weight 130mg or less is 10% whereas for average weight between 130-324mg is 7.5% and for average weight more than 324mg is 5%. For the tablet to be accepted, the weight of not more than two tablets deviates from the average weight by not more than 7.5% and no tablet deviates by more than 15%.[14]

### Content uniformity

Twenty Lurasidone fast dissolving tablets were taken and triturated to form powder and powder equivalent to one tablet was taken and dissolved in 100 ml of HCl buffer pH 1.2 and heated at 37 $^0$C for 15 to 20 minutes with stirring. The solution was filtered, suitably diluted and the Lurasidone content was measured by using UV Spectrophotometer (Analytical Technologies Ltd. Spectro 2080) at 230 nm. Each measurement was carried out in triplicate and the average drug content in the Lurasidone fast dissolving tablets was calculated. [15]

### Wetting time and water absorption ratio

Twice folded tissue paper was placed in a petri dish having an internal diameter of 6.5 cm containing 10 ml of HCl buffer pH 1.2 containing methylene blue (0.1% w/v). A tablet from each formulation of Lurasidone fast dissolving tablets was carefully placed on the surface of the tissue paper in the petri dish. The time required for the dye to reach the upper surface of the tablet was recorded as wetting time. Measurements were carried out in triplicate and standard deviations were also determined.

Water absorption ratio (R), can be estimated by simple procedure include weighing ($W_b$) of the tablet prior to the placement on the petri dish, then after recording the wetting time. The wetted tablet was removed and reweighed ($W_a$), the water absorption ratio (R) was determined according to the following equation. [16]

$$R = \frac{(\square\square - \square\square)}{\square\square} \times 100$$

### In vitro disintegration time ($D_t$)

According to USP disintegration test for fast dissolving tablets, the disintegration apparatus is used without the covering plastic disks and 2 min is specified as the acceptable time limit for tablet disintegration fulfilling the official requirements (<2 min) for fast dissolving dosage form. The test was carried out using tablet disintegration apparatus (model EI D-16, Electrolab, Mumbai, India). *In vitro* disintegration test was carried out using a modified disintegration method (n = 6) using disintegration tester maintained at 37°C ± 0.5°C in HCl buffer pH 1.2. The tablets were kept in the basket and noted the time taken for the tablet to disintegrate completely into smaller particles. [17]

### In vitro drug release study

The *in vitro* dissolution study was conducted for all the formulations using an eight station USP dissolution rate test apparatus type-II (LABINDIA DS 8000, Mumbai, India). A total volume of 900 ml of HCl buffer pH 1.2 was taken as dissolution medium, which was maintain at 37°C ± 0.5°C at 50 rpm. 5ml of aliquots were periodically withdrawn and the sample volume was replaced with an equal volume of fresh dissolution medium. Samples were collected at 5 min intervals and filtered by Whatmann filter paper. Samples were analyzed spectrophotometrically at 230 nm for determination of Lurasidone that were released from fast dissolving tablets. [18]

### Characterization of the in vitro drug release profile

The rate and mechanism of release of Lurasidone from prepared fast dissolving tablets were analyzed by fitting the dissolution data into following exponential equations.

Zero order release equation:

$$\square = \square_0 t$$

Where Q is the amount of drug released at time t and $K_0$ is the zero-order release rate constant.

The first order equation:

$$\log(100 - \square) = \square\square\square 100 - \square_1 \square$$

Where, $K_1$ is the first order release rate constant. [19]

### *Stability studies of best formulation*

The stability studies of best formulation of Lurasidone fast dissolving tablet were carried out according to ICH guidelines. The best formulation was subjected to accelerated stress condition at 40 ºC ± 2 ºC/ 75% ± 5% RH for 90 days. After that period the product was evaluated for friability, hardness, weight variation, thickness, drug content and *in vitro* drug release study. [20]

## RESULTS AND DISCUSSION

### *Compatibility studies by FTIR*

By comparing the spectra of Lurasidone and spectra obtained from physical mixture, the sharp peaks that appear in spectra of Lurasidone at~ 3429.55 $cm^{-1}$ also appears in physical mixture (drug and excipients) at ~ 3377.47 $cm^{-1}$ due to presence of C-H stretching. The characteristic IR absorption peaks of Lurasidone at ~ 1761.07 $cm^{-1}$ (C=O stretch), at ~ 1681.96 $cm^{-1}$ (C=C stretch), at ~ 2256.79 $cm^{-1}$ (S-H stretching), and at ~1263.42 $cm^{-1}$ (N-H stretching) were also present in the physical mixture (drug and excipients) at ~ 1760.08 $cm^{-1}$ (C=O stretch), at ~1685.84 $cm^{-1}$ (C=C stretch), at ~2254.86 $cm^{-1}$ (S-H stretching) and at ~1026.16 $cm^{-1}$ (N-H stretching). From the results of it indicated that there was no interaction between drug and excipients. The frequencies of functional groups of drug remained intact in physical mixture containing different excipients. Hence, it was concluded that there were no major interactions occurred between the Lurasidone and excipients used in the preparation of different fast dissolving formulations under study. The FTIR spectra of pure drug Lurasidone and physical mixture all excipients used for formulations were shown in **figure 1 and 2**.

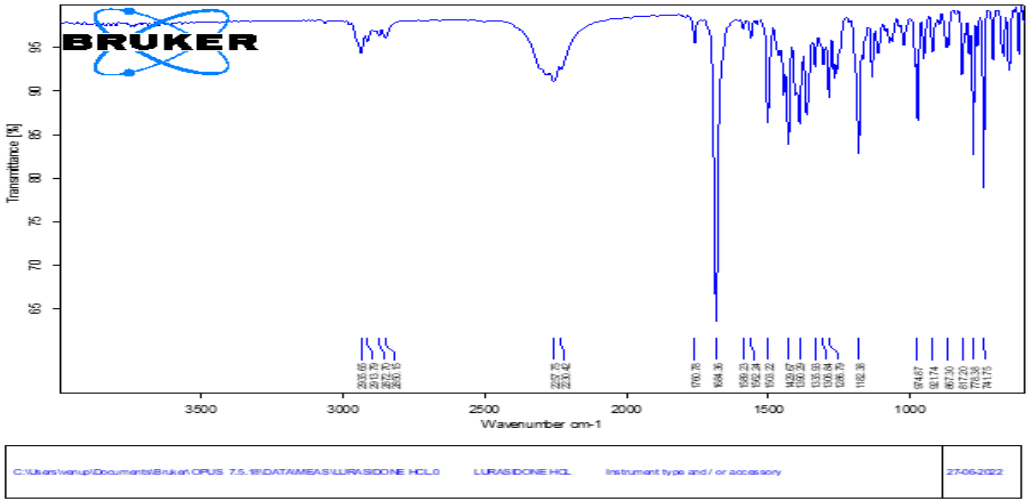


**Fig 1: FT-IR spectra of Lurasidone pure drug**

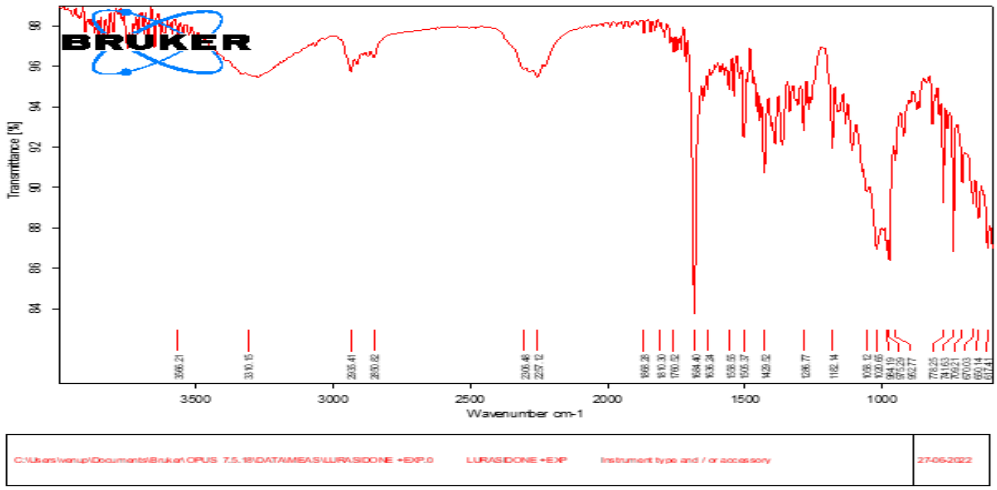


**Fig 2: FT-IR spectra of Lurasidone and excipients used for the formulations**

The loose bulk densities of Lurasidone fast dissolving granules of all formulations were found to be in the range of 0.351±0.04 to 0.390±0.06 g/$cm^3$ and the tapped densities were found to be in between 0.411±0.03 to 0.462±0.05 g/$cm^3$. This indicates good packing capacity of granules. Bulk density and tapped density measurements found that density

of granules depends on particle packing and that density changes as the granules consolidates. Values of Carr's index for all the formulations were found below 16% that usually indicates good flow characteristics except the formulations $LFDT_1$ and $LFDT_4$ which may indicate lake of uniformity in granule sizes and presences of more fine particles in those formulations. Hausner's ratio is simple method to evaluate stability of power and granule column and to estimate flow properties. Low range was observed of Hausner's ratio that indicates good flow ability. In all formulations the Hausner's ratios values were found "between" 1.11 to 1.21 that indicates good flow characteristics. Angle of repose is suited for particle > 150µm.Values of angle of repose ≤ 25 generally indicates the free-flowing material and angle of repose ≥ 40 suggest a poor flowing material. The angle of repose is indicative of the flowability of the material. The angle of repose of all formulations fell within the range of 22.14±0.11 to 26.84±0.16 *i.e.* dry granules of Lurasidone fast dissolving layer showed good flow properties. The results of precompression parameters for all the formulations were given in **table 2**.

**Table 2: Evaluation of precompression parameters of Lurasidone fast dissolving Granules ($LFDT_1$ – $LFDT_6$)**

| F. No. | Bulk density (gm/ml) | Tapped density (gm/ml) | Angle of repose (θ) | Carr's Index (%) | Hausner's ratio |
|---|---|---|---|---|---|
| **$LFDT_1$** | 0.381±0.02 | 0.460±0.03 | 26.25±0.15 | 17.17 | 1.21 |
| **$LFDT_2$** | 0.372±0.05 | 0.441±0.06 | 25.41±0.14 | 15.64 | 1.18 |
| **$LFDT_3$** | 0.390±0.06 | 0.462±0.05 | 22.73±0.13 | 15.58 | 1.18 |
| **$LFDT_4$** | 0.351±0.04 | 0.423±0.04 | 24.76±0.12 | 17.02 | 1.21 |
| **$LFDT_5$** | 0.370±0.05 | 0.411±0.03 | 22.14±0.11 | 09.98 | 1.11 |
| **$LFDT_6$** | 0.381±0.04 | 0.450±0.02 | 26.84±0.16 | 15.33 | 1.18 |

***All values are expressed as average± SD; (n=3)***

The physical parameters such as average hardness, average weight variation, average friability and average thickness of the all the formulations of Lurasidone fast dissolving tablets were found to be satisfactory. Typical tablet defects, such as capping, chipping and picking, were not observed. The physicochemical characterizations of different batches of Lurasidone fast dissolving tablets are given in table 3. The thickness of the tablets were ranged between 3.24±0.12 to 3.51±0.11mm. All the batches showed uniform thickness. Weight variations for different formulations were found to be 3.26±0.36 to 4.56±0.35%. The acceptable average percentage variation for tablet formulations having weight 200mg is 5% and all the formulations fall within the limit, and hence passed the test for uniformity of weight as per official requirement. The average hardness of all the Lurasidone fast dissolving tablet formulations was ranged from 2.8±0.4 to 3.9±0.4 $kg/cm^2$. By increasing the concentration of superdisintegrant concentration the hardness usually decreased that noticed in case of formulation $LFDT_2$ and $LFDT_6$. The percentage friability of all the formulations were ranged from 0.34±0.04% to 0.59±0.06% and also the % friability were found more by increased concentration of superdisintegrant concentration. In the present study, the percentage friability for all for formulations was within the prescribed limits. The percentages of drug content for $LFDT_1$ to $LFDT_6$ were found to be in between 98.34±1.3% to 101.43±1.4% of Lurasidone fast dissolving tablet formulations which were within the acceptable limits. Disintegration time were determined for all the formulations and it was found that by increasing concentration of superdisintegrant, the disintegration time decreases; but increase in concentration above 6% the hardness value didn't fall in the acceptable range. The wetting time of all the formulations were found between 85±0.71 sec to 124±0.35 sec. For the case of wetting time by increasing the concentration of superdisintegrant the wetting time decreases those were noticed in case of formulations of $LFDT_2$, $LFDT_4$, $LFDT_5$ and $LFDT_6$. Between cross carmellose and Sodium Starch Glycolate the later having less wetting time than former at equal concentrations. The water absorption ratio of formulations $LFDT_1$ to $LFDT_6$ was found in the range of 11.25±0.31 to 22.72±0.30. By increasing the concentration of superdisintegrant the water absorption ratio increases that might be due to increase in the porosity of the formulation with increase in superdisintegrant concentration.

**Table 3: Evaluation of Post-compression parameters of Lurasidone fast dissolving tablets**

| F. code | Average hardness ($kg/cm^2$) | Average Weight Variation (%) | Average friability (% w/w) | Average thickness (mm) | Drug content uniformity (%) | $D_t$ (Sec) | Wetting time (Sec) | Water absorption ratio |
|---|---|---|---|---|---|---|---|---|
| **$LFDT_1$** | 3.9±0.4 | 3.26±0.36 | 0.59±0.06 | 3.24±0.12 | 98.34±1.3 | 211±1.05 | 124±0.35 | 11.25±0.31 |
| **$LFDT_2$** | 2.8±0.4 | 3.41±0.51 | 0.49±0.03 | 3.31±0.13 | 98.52±1.2 | 133±1.12 | 85±0.71 | 14.38±0.36 |
| **$LFDT_3$** | 3.6±0.5 | 4.52±0.38 | 0.34±0.04 | 3.42±0.12 | 99.36±1.7 | 202±1.10 | 112±0.46 | 12.47±0.21 |
| **$LFDT_4$** | 3.4±0.6 | 4.56±0.35 | 0.48±0.03 | 3.51±0.11 | 101.43±1.4 | 84±1.22 | 88±0.47 | 21.56±0.28 |
| **$LFDT_5$** | 3.2±0.4 | 3.95±0.42 | 0.39±0.02 | 3.43±0.14 | 99.52±1.3 | 97±0.95 | 106±0.38 | 22.72±0.30 |
| **$LFDT_6$** | 3.1±0.3 | 4.52±0.48 | 0.36±0.05 | 3.35±0.12 | 98.61±1.4 | 92±0.95 | 103±0.52 | 20.64±0.35 |

***All values are expressed as average± SD; (n=3)***

The *in vitro* drug release characteristics of Lurasidone fast dissolving tablets were studied in HCl buffer pH 1.2 dissolution medium for a period of 30 minutes using USP type-II paddle type dissolution apparatus. The rate of dissolution increased by increasing the concentration of superdisintegrant upto an best concentration of 3%. The formulation $LFDT_4$ having 6% of Sodium Starch Glycolate released 99.72% of the drug in 25 minute whereas formulation $LFDT_2$ having 3% of cross carmellose released

96.66% of the drug in 25 minute and cumulative percentage release 99.78% in 30 minute. When both the superdisintegrants were used ($LFDT_5$) in combination in total concentration of 2% it shows some better dissolution profile and release almost all the drug (99.85%) within 30 minutes. Formulation $LFDT_6$ having superdisintegrant concentration of 6% (1.5% cross carmellose and 1.5% Sodium Starch Glycolate) release the drug upto 99.25% within 30 minutes. MCC worked good as diluents for better dissolution properties, so it was used in all the formulations. The dissolution profiles of all the formulations ($LFDT_1$ to $LFDT_6$) were shown in figure 3.

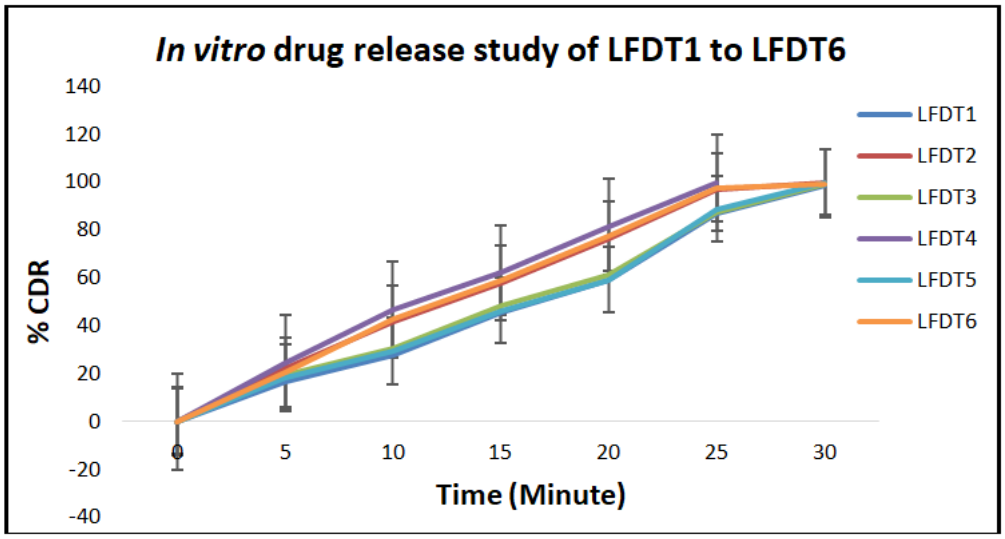


**Fig 3: *In vitro* drug release study of Lurasidone fast dissolving formulations**

On the basis of highest dissolution profile, the formulation $LFDT_4$ was chosen for drug release kinetic. The *in vitro* dissolution data of Lurasidone fast dissolving tablets ($LFDT_4$) were fitted in different kinetic models viz. zero order and first order graphs were plotted figure 4 and 5. The zero order kinetic plots were found to be fairly linear as indicated by their highest regression values (0.999) for $LFDT_4$ formulation. So in present study *in vitro* drug release kinetic of Lurasidone fast dissolving tablet followed zero order release kinetic model. The regression values were represented **table 4**.

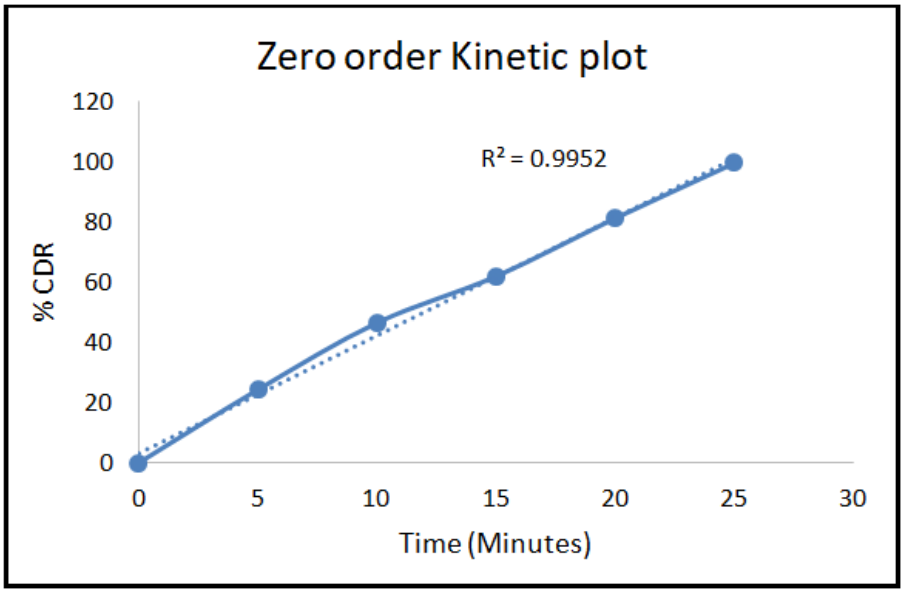


**Fig 4: Zero order release kinetic study of best formulation $LFDT_4$**

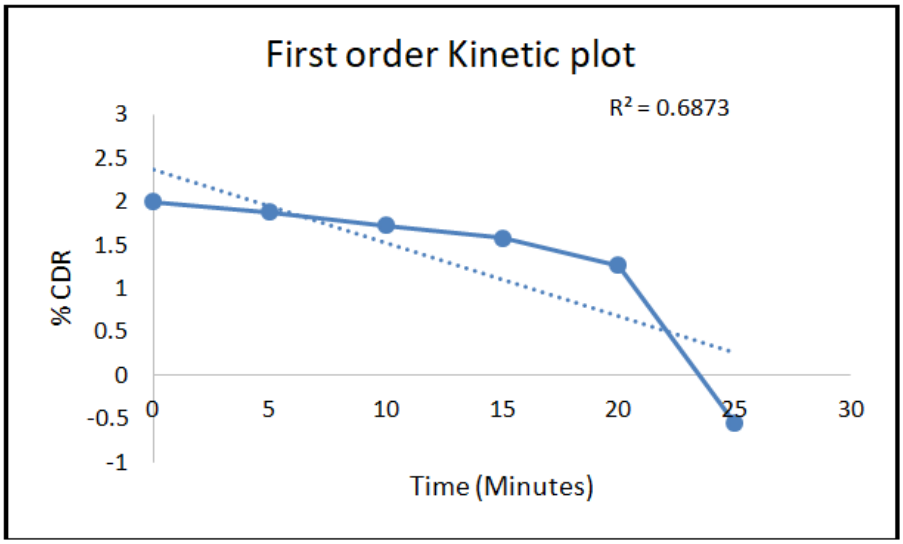


**Fig 5: First order release kinetic study of best formulation LFDT$_4$**

**Table 4: Regression values of *in vitro* release kinetic study best formulation (LFDT$_4$)**

| Formulation code | $R^2$value of Zero order | $R^2$ value of 1st order | Remarks |
|---|---|---|---|
| **LFDT$_4$** | 0.9952 | 0.6873 | Follows Zero order kinetic as it is having highest regression value |

The best formulation (LFDT$_4$) of Lurasidone fast dissolving tablets was selected for accelerated stability studies. The best formulation (LFDT$_4$) Lurasidone fast dissolving tablets did not show any significant changes in physicochemical parameters and *in vitro* drug release characteristics. More than 90% of the drug had been retained in the *in vitro* dissolution studies after 90days of exposure to accelerated stress condition. Thus, it was found that the fast dissolving tablets of Lurasidone (LFDT$_4$) were stable under short term accelerated storage conditions for at least 3 months.

**Table 5: Comparative physicochemical properties of LFDT$_4$ at accelerated conditions (40 ° C ± 2 ° C/ 75% ± 5% RH)**

| Sl. No. | Physicochemical characteristics | Initial | After 30 days | After 60 days | After 90 days |
|---|---|---|---|---|---|
| 1 | **Physical appearance** | Pale white, circular, concave smooth surface without any cracks | No change | No change | No change |
| 2 | **Weight variation** | 4.56±0.35 | 4.35±0.42 | 4.23±0.42 | 4.09±0.21 |
| 3 | **Hardness** | 3.4±0.6 | 3.2±0.3 | 3.1±0.4 | 3.0±0.4 |
| 4 | **Friability** | 0.52±0.04 | 0.54±0.02 | 0.57±0.04 | 0.59±0.04 |
| 5 | **Wetting time (Sec)** | 88±0.47 | 92±0.33 | 96±0.51 | 99±0.25 |
| 6 | **Drug content** | 101.43±1.4 | 98.73±1.2 | 96.55±1.2 | 93.26±1.5 |
| **7** | **$D_t$ (Sec)** | 84±1.22 | 95±1.31 | 101±1.42 | 105±1.36 |

**All values are expressed as mean± SD; (n=3)**

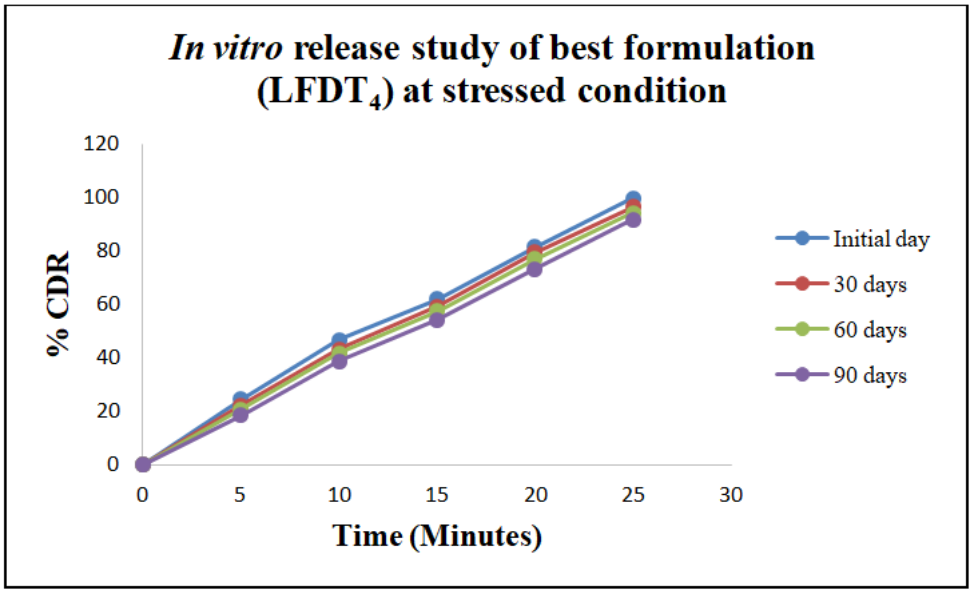


**Fig 6: *In vitro* release study of best formulation ($LFDT_4$) at stressed condition**

## CONCLUSION

Lurasidone fast-dissolving tablets were successfully created in the current work. Studying the impact of cross-carmellose and sodium starch glycolate on the in vitro release rate of a fast-dissolving tablet of lurasidone presented the most hurdle in this work. A promising method for achieving rapid drug release and helping to cure the symptoms of psychotic (mental) disorders like schizophrenia was the fast-dissolving drug delivery system. The medication and excipients were compatible, according to FTIR analyses. For the creation of Lurasidone fast-dissolving granules, wet granulation techniques were used, and the evaluation of all precompression parameters fulfilled the approval standards, demonstrating the granules' good flow characteristics. The average thickness, hardness, friability, weight fluctuation, wetting time, water absorption ratio, and disintegration are all within acceptable limits for postcompression characteristics. The best formulation was LFDT4, which contained 3% sodium starch glycolate and released 99.72% of the medication in 25 minutes. Combining both superdisintegrants did not result in a superior drug release profile than LFDT4. The drug release profile was accelerated by an increase in superdisintegrant concentration, although the formulation's hardness and friability were negatively impacted. The optimal formulation's in vitro drug release kinetics The zero order kinetic model with the highest R2 value was discovered to be LFDT4. According to ICH guidelines, stability experiments were conducted, and a chosen LFDT4 formulation was stable at 40°C/75% RH for up to 3 months with only a minor change in the formulations' physicochemical and drug release properties. The Lurasidone rapid dissolving tablets drug delivery method therefore has a promising future and can be used as an alternative to the traditional dose form since it releases the medication quickly and is effective for the acute condition of psychotic (mental) illnesses, such as schizophrenia. To determine the effectiveness of this technique for patients with psychotic (mental) illnesses like schizophrenia, more clinical research is required.

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