Solubility enhancement of Lurasidone hydrochloride by solid dispersion technique

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***Abstract*- Solid dispersion was most widely and successfully applied to improve the solubility, dissolution rates, and consequently the bioavailability of poorly soluble drugs. Lurasidone hydrochloride (LH) is a poorly water-soluble drug. It belongs to BCS class II. It is prescribed as an antipsychotic drug for the treatment of symptoms of mental disorders such as schizophrenia and bipolar disorder. The present study was planned to prepare and evaluate the solid dispersion (SD) of Lurasidone hydrochloride. Solid dispersion of Lurasidone hydrochloride (LH SD) was prepared using Vitamin E TPGS and Polyethylene glycol (PEG) 6000 as a carrier by Fusion method and using Cyclodextrin-B (CD-B) by the solvent evaporation method. The prepared SD was characterized and filled into hard gelatin capsules. The filled hard gelatin capsules were evaluated for weight variation, drug content, and disintegration time, and *in-vitro* dissolution study. The cumulative amount of drug release of LH: vitamin ETPGS in 1:3 ratio showed 99.31% at the end of 1 hour. Therefore, it can be concluded that the dissolution rate of the poorly soluble drug Lurasidone hydrochloride can be enhanced by formulating it into solid dispersion using water soluble carrier vitamin E TPGS.**

***Keywords:* Solid dispersion, Lurasidone hydrochloride Vitamin E TPGS, Cyclodextrin-B, PEG-6000, solubility.**

I.INTRODUCTION

One of the most challenging parts of formulation creation continues to be the solubility behavior of medications. Combinatorial chemistry and high throughput screening have greatly expanded the availability of poorly water-soluble molecules. About 40–45% of all newly discovered chemical entities fail to make it to market as medications because of poor solubility in water. Because of the solubility issue, the drug's bioavailability is impacted, necessitating the need for solubility improvement [1]. There are various methods available to improve the solubility of the drug. One of these techniques, solid dispersion, has been used most frequently and successfully to enhance the solubility, dissolution rates, and ultimately the bioavailability of poorly soluble drugs. One of the most effective and widely used methods for accelerating the dissolution of water-insoluble drugs is solid dispersion technology. Solid dispersion has several benefits over other methods, including ease of scaling; its conversion to solid dosage forms such as capsules, tablets, taste-masking strips, and implants [2].

Lurasidone Hydrochloride is a poorly water-soluble drug and it belongs to Class II in the Biopharmaceutics Classification System and is prescribed as an antipsychotic drug for the treatment of symptoms of mental disorders such as Schizophrenia and Bipolar depression. Lurasidone hydrochloride acts mainly by blocking the receptors for the neurotransmitters dopamine, 5-hydroxytryptamine (also called serotonin), and nor-adrenaline. Solid dispersions of Lurasidone Hydrochloride would increase the solubility and bioavailability of the drug and improve drug efficiency. [3, 4]

In this study, an attempt was made to develop a solid dispersion of Lurasidone Hydrochloride using different carriers like vitamin E TPGS, cyclodextrin B and PEG 6000 with three different ratios in order to improve the solubility and hence the bioavailability of the drug. The developed solid dispersion of Lurasidone hydrochloride was filled into a capsule and subjected to evaluation studies.

Hence the main objective of the present study was to carry out the solubility enhancement technique for the BCS class II drug Lurasidone hydrochloride by using the solid dispersion technique.

II.MATERIALS AND METHODS

Lurasidone Hydrochloride was received as a gift sample from Dr.Reddy's Laboratories; Vitamin E- tocopheryl polyethylene glycol succinate was obtained from Bioplus Life Science as a gift sample Hosur, Cyclodextrin B and Polyethylene glycol 6000 were supplied from SD chemicals. All other materials used were of pharmaceutical grade.

FT-IR spectroscopy:

The compatibility study of the drug with the excipients was determined by FTIR Spectroscopy using Shimadzu spectrometer. The sample KBr ratio is 1:100, and the pellets were made under high compaction pressure. The KBr pellet technique was used to record the FT-IR spectra. The spectra of pure drugs, physical mixtures of drugs, and polymers were recorded. The spectra were captured over the 4000-400 cm^{-1} wavenumber range. [5, 6]

Solubility:

The solubility of lurasidone hydrochloride was tested by adding 10 mg of lurasidone hydrochloride to each of the following solvents: water, methanol, ethanol, 0.1N sodium hydroxide, 0.1N HCl, and phosphate buffer 7.4 separately. The mixture was then vigorously shaken for 5 minutes, and the mixture was then placed in a bath of constant temperature for 15 minutes. [7]

PREPARATION OF CALIBRATION CURVE OF LURASIDONE HYDROCHLORIDE IN METHANOL: [8]

10 mg of Lurasidone hydrochloride was taken in a 10ml standard flask and then it was made up to 10ml volume with methanol to a concentration of 1000µg/ml. From this stock solution, 1 ml was taken in a 10 ml standard flask and made up to 10 ml volume with methanol to a concentration of 100µg/ml. A serial dilution of 1, 2, 3, 4, and 5 ml was pipetted out and diluted to 10 ml with methanol to get the concentration of 10, 20, 30, 40, 50µg/ml and the absorbance was measured at 230nm. A standard graph was plotted by keeping the known concentration on X-axis and obtained absorbance on Y axis.

Preparation of physical mixture: [9]

The physical mixtures of Lurasidone hydrochloride were prepared by mixing Lurasidone hydrochloride and selected carriers vitamin E-TPGS, cyclodextrin B and PEG 6000 in the ratio of 1:1, 1:2, and 1:3 in individual formulations. The mixtures were thoroughly mixed in a mortar until a homogeneous mixture was obtained. The resulting mixture was sieved through#60.

Preparation of solid dispersion: [10, 11]

Solid dispersions were prepared with the drug Lurasidone hydrochloride and carriers (Vitamin E-TPGS, cyclodextrin B and PEG 6000) using 1:1,1:2 and 1:3 weight ratios by means of fusion method (for Vitamin E TPGS and PEG 6000) and solvent evaporation method (for cyclodextrin carrier).

Fusion Method:

Solid dispersions were prepared with the drug Lurasidone hydrochloride and the carrier-Vitamin E-TPGS and PEG 6000 using 1:1, 1:2, and 1:3 weight ratios by the fusion method. An accurately weighed quantity of drug and carrier was mixed using a mortar and pestle. Then, it was directly heated at or above the melting point of all the components to achieve a homogenous dispersion. The molten mixture was then cooled and solidified rapidly in an ice bath. The resulting solid mass was then crushed, pulverized, and sieved.

Solvent Evaporation Method:

A weighed amount of carrier (cyclodextrin) was dissolved in a glazed porcelain evaporating dish in a quantity of methanol sufficient to dissolve it completely. The drug was then added to this solution and mixed thoroughly until the methanol used was volatilized. It was allowed to air dry at room temperature for 48 hrs. The resulting solid mass was then pulverized and sieved.

Composition of solid dispersion of lurasidone hydrochloride

Table 1 Composition of solid dispersion of lurasidone hydrochloride

FORMULATION CODE	DRUG WITH CARRIER	DRUG: CARRIER
F1	Lurasidone hydrochloride: Vitamin E TPGS	1:1
F2		1:2
F3		1:3
F4	Lurasidone hydrochloride: Cyclodextrin B	1:1
F5		1:2
F6		1:3
F7	Lurasidone hydrochloride: PEG 6000	1:1
F8		1:2
F9		1:3

Characterization of the prepared solid dispersion: [12]

1. Angle of Repose:

The Angle of repose was calculated using the funnel method.

The mixture was poured through a funnel that could be raised vertically to a maximum cone height.

$\tan \theta = h/r$

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

Where, θ= angle of repose; h=height of pile; r= radius

2. Bulk Density:

Apparent bulk density was determined by placing the presieved drug excipients blend into a graduated cylinder and measuring the volume and weight.

$D_b = M/V_0$

Where, D_b= Bulk density; M= mass of powder (g); V_0=bulk volume of powder (cc)

3. Tapped Density:

The measuring cylinder containing a known mass of blend was tapped for a fixed number of taps. The minimum volume occupied in the cylinder and the weight of the blend was measured. The tapped density was calculated using the following formula:

Tapped density = mass of powder (g) / tapped volume of powder (cc)

4. Hausner's Ratio:

Hausner's ratio is an index of ease of powder flow; it is calculated by following the formula,

$$\text{Hausner's ratio} = \frac{\text{Tapped density of the powder}}{\text{Bulk density of the powder}}$$

5. Carr's Index:

The simplest way of measuring of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility

It is calculated as follows:

$$\text{Carr's Index} = \frac{\text{Tapped density} - \text{bulk density}}{\text{Tapped density}} \times 100$$

6. Percentage yield: [13]

Thoroughly dried solid dispersion was collected and weighed accurately. The percentage yield was then calculated using the formulae given below,

$$\text{Percentage Yield} = \frac{\text{Mass of solid dispersion obtained}}{\text{Total weight of drug and polymer}} \text{ x } 100$$

Capsule filling method:

The prepared solid dispersion was filled in the Hard-Gelatin Capsule by the manual hand filling method using microcrystalline cellulose as diluent. The capsules were evaluated for disintegration time and *in vitro* dissolution study for Cumulative drug release characteristics respectively.

III. EVALUATION OF HARD GELATIN CAPSULE FILLED WITH SOLID DISPERSION:

1. Weight variation: [14]

20 capsules are selected and weighed individually; the average weight was taken and compared each capsule's weight with the average weight.

2. *In-vitro* dissolution study: [15, 16]

For *in vitro* dissolution study, prepared solid dispersion equivalent to 10mg of Lurasidone Hydrochloride was filled in hard gelatin capsules. It was carried out using USP dissolution Apparatus-type I (Basket) using phosphate buffer pH 7.4 as dissolution medium to check the release pattern. The temperature was maintained at 37 ºC±0.5 ºC and the basket speed was set at 50 rpm. 5 ml aliquots were withdrawn at 5, 10, 15, 20, 25, 30, 45, and 60 min intervals. At the same time, 5 ml of fresh media was replaced in the vessel to maintain the sink condition. The samples were analyzed for drug content by spectrophotometric method at λ max 230 nm using a UV visible double beam spectrophotometer.

The prepared physical mixture was also filled into a hard gelatin capsule and subjected to an *in-vitro* dissolution study in the same manner.

3. Disintegration time: [17]

The disintegration of capsules was measured using a disintegration apparatus supporting six cylindrical glass tubes. Water at 37° ± 2°C was used as a medium and a disk was added to keep the capsules in the media. For each test, the basket and the disk were dried prior to use in the disintegration test. The endpoint was determined visually by the operator and by an automated endpoint detection system using a disintegration apparatus equipped with automated detection of the endpoint. The endpoint of the automatic detection system is defined as the time by which the dosage form is disintegrated and the disk gets in contact with the stainless-steel wire cloth at the bottom of the disintegration tube**.**

4. Drug content uniformity: [18]

About 10mg of prepared solid dispersion was transferred to a 100ml volumetric flask. To this, a small quantity of methanol was added to dissolve and the volume was made with phosphate buffer pH 7.4. The solution was filtered using the Whatman filter paper. The filtrate was subsequently diluted with phosphate buffer pH 7.4 and the absorbance was measured at 230nm using phosphate buffer pH 7.4 as blank.

5. Stability studies: [19]

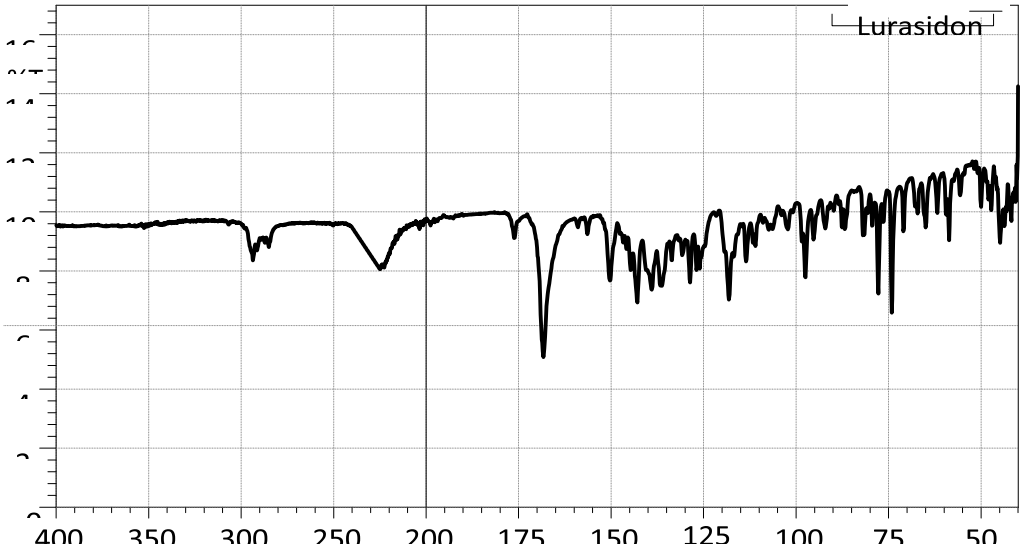
The capsules were subjected to a stability study for the period of 1 month at 40±20ºC & 75±5%RH. After that period, the capsules were evaluated for various parameters like weight variation, drug content, disintegration time, and *invitro* dissolution study.

IV.RESULTS AND DISCUSSION

Compatibility study (Fourier transform infrared spectroscopic studies)

The characteristic peak in the FTIR spectrum of the LH was found at 2935 of Ar-H stretch, 1686 of C=O stretch (Aryl ketone), 1503 of Ar C=C stretch, 1400 of C-H bending, 2259 of CN stretch, 1200 of C-N stretch (tertiary amine) and 750 of C-Cl stretch. Each peak falls within the specified range, confirming LH purity. The physical mixture also exhibits all of the major LH peaks. Consequently, no drug-excipient interactions occurred. Hence, it may be concluded that there was no interaction of the drug with excipients. Fig.1, 2, 3, and 4 represent the FT-IR spectra

Figure 1 FTIR spectrum of Lurasidone Hydrochloride



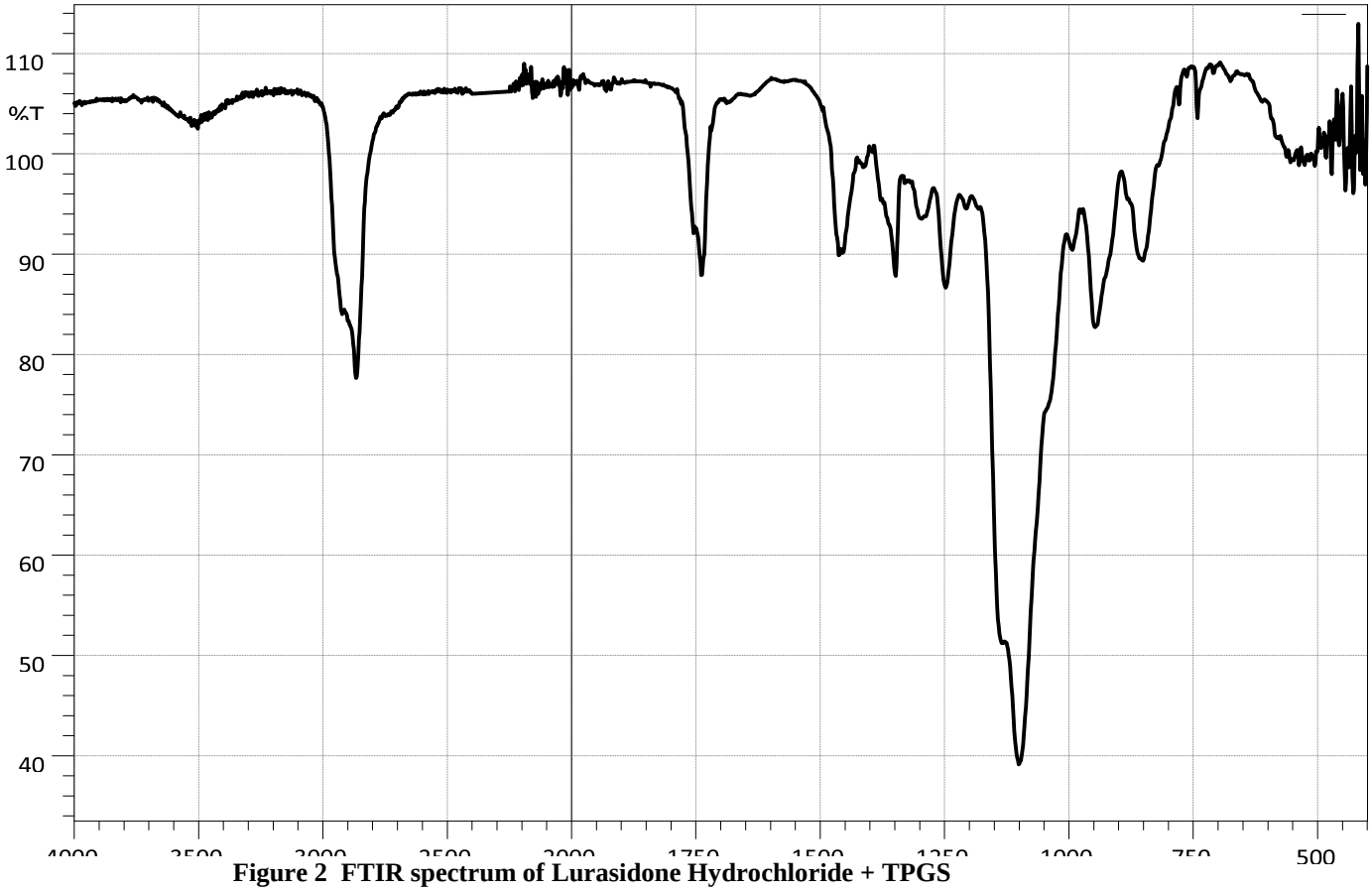


Figure 2 FTIR spectrum of Lurasidone Hydrochloride + TPGS

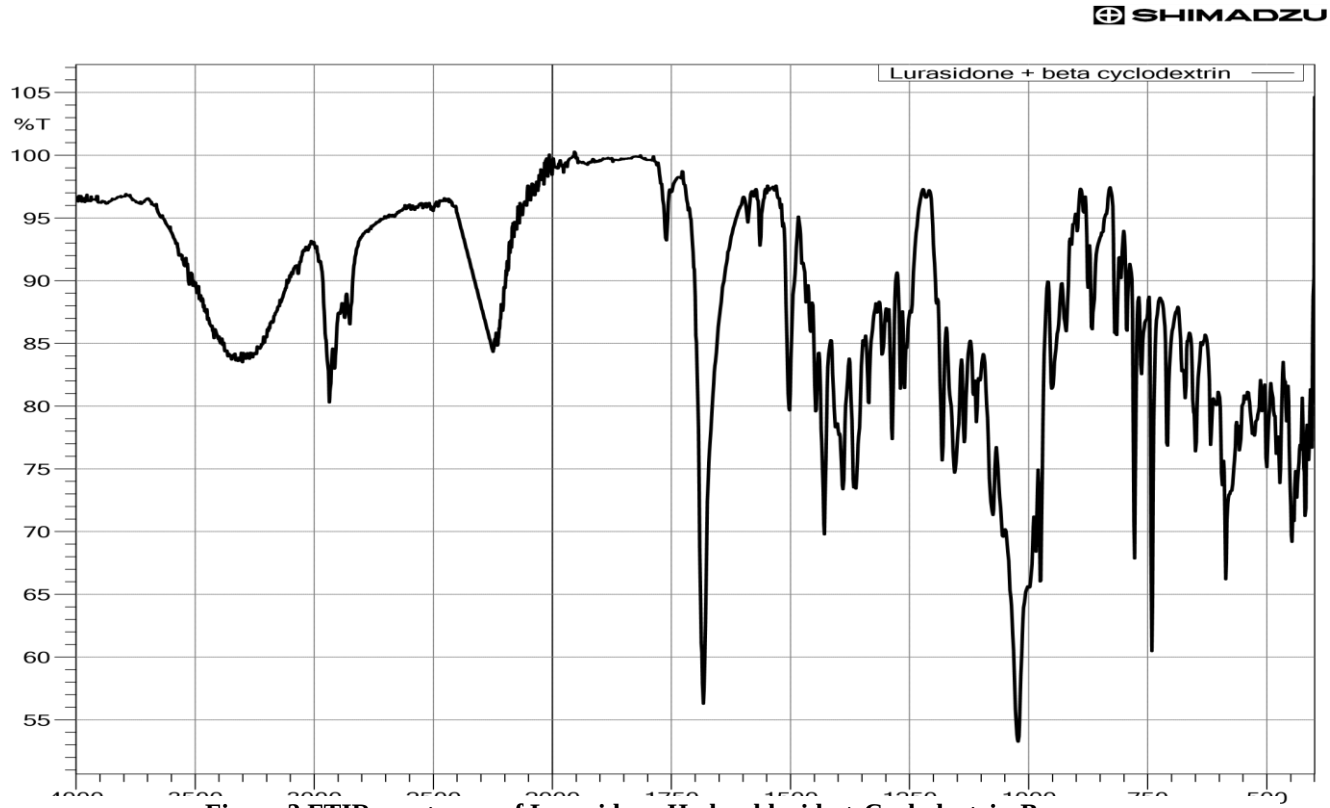


Figure 3 FTIR spectrums of Lurasidone Hydrochloride + Cyclodextrin-B

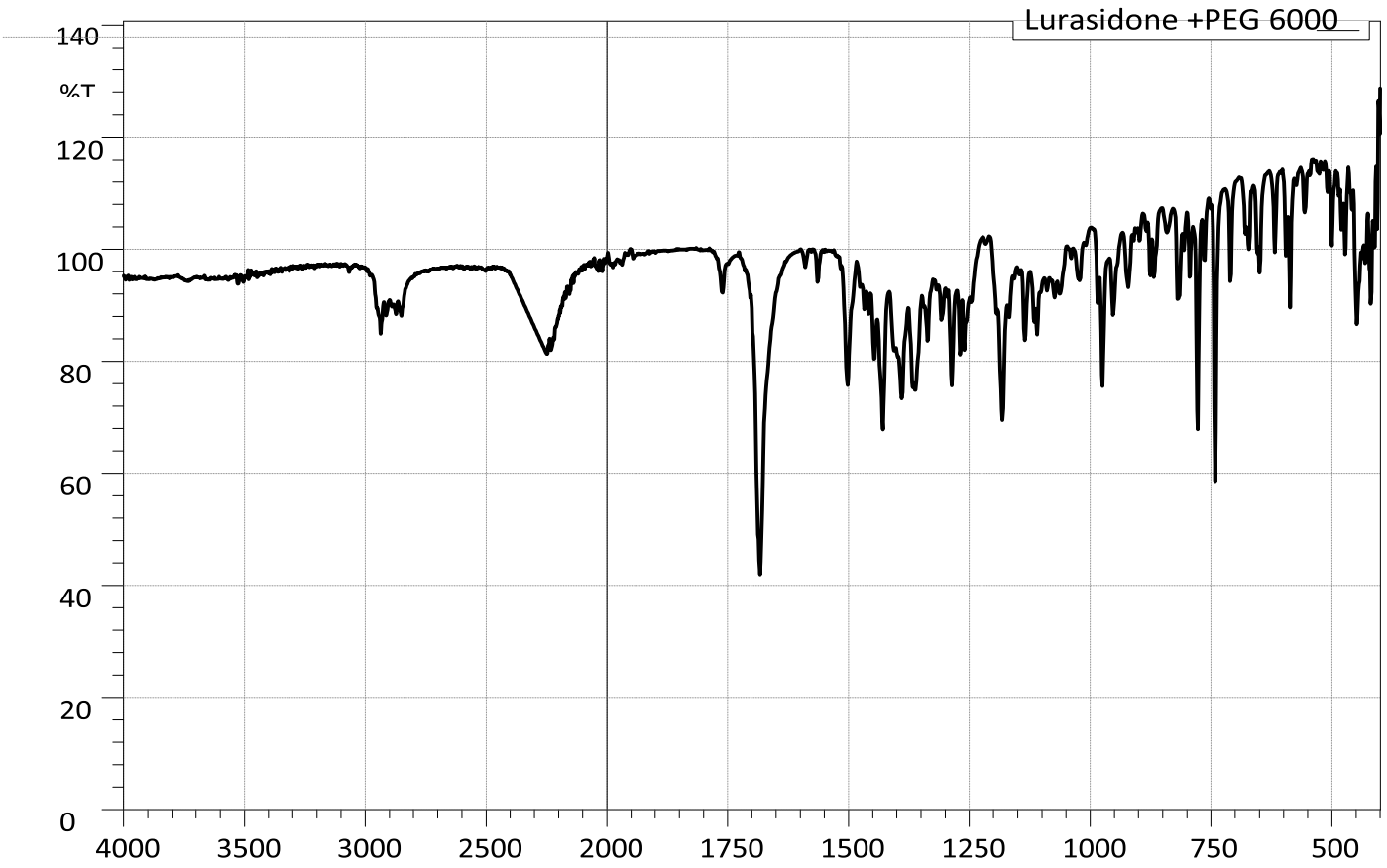


Figure 4 FTIR spectrum of Lurasidone Hydrochloride + PEG 6000

Solubility test:

Solubility was done by dissolving Lurasidone hydrochloride with various solvents as shown in Table 2. Lurasidone hydrochloride was freely soluble in Methanol and insoluble in water.

Table 2 Solubility profile of Lurasidone hydrochloride

Raw material (API)	**Solubility**
Lurasidone hydrochloride	Freely soluble in methanol
	Soluble in Ethanol, acetonitrile
	Insoluble in water, 0.1N NaOH, pH buffer 7.4

Preparation of calibration curve of lurasidone hydrochloride:

UV absorption of Lurasidone hydrochloride in Methanol shows λmax at 230 nm. Absorbance obtained for various concentrations of Lurasidone hydrochloride in Methanol. The graph of absorbance vs. concentration for Lurasidone hydrochloride was shown in Fig 5. The regression coefficient was found to be 0.9999 which indicates a linearity with an equation of y = 0.016x + 0.0026. Hence Beer- Lambert's law was obeyed.

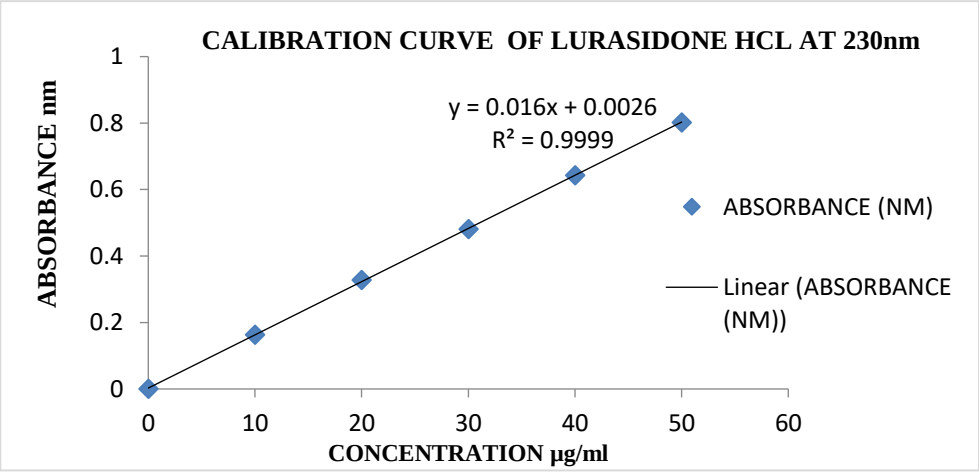


Figure 5 Calibration curve of Lurasidone hydrochloride at 230nm

Preparation of solid dispersion of lurasidone hydrochloride (LH SD)

Solid dispersion of lurasidone hydrochloride was prepared by fusion method (Vitamin E TPGS, PEG-6000) and solvent evaporation method (beta-Cyclodextrin) and evaluated. The physical mixture was also prepared and evaluated for an *in-vitro* dissolution study.

Characterization of prepared solid dispersion

For each formulation blend of drugs and excipients was prepared and evaluated for various pre-formulation parameters described earlier in the methodology.

Table 3 characterization of solid dispersion of Lurasidone Hydrochloride

Formulation Code	Angle of repose	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Hausner's Ratio	Compressibility Index (%)	Yield (%)
F-1	27.82º	0.487	0.529	1.09	7.94	95
F-2	31.09º	0.627	0.700	1.117	10.50	96.33
F-3	26.33º	0.742	0.823	1.109	9.84	97.25
F-4	28.14º	0.485	0.557	1.14	12.92	94.5
F-5	30.15º	0.652	0.715	1.09	8.81	95.6
F-6	27.17º	0.729	0.815	1.11	10.55	96.8
F-7	30.17º	0.454	0.495	1.09	8.28	85
F-8	26.06º	0.633	0.707	1.12	10.61	88.33
F-9	27.01º	0.742	0.814	1.09	8.84	95

1. The bulk density of all formulations was found in the range of (0.4 - 0.9) g/ cm^3 and tapped density was in the range of (0.4 - 0.9) g/ cm^3
2. The Carr's index and Hausner's ratio were calculated from tapped density and bulk density was found to be within the limit.
3. The Angle of repose values were between 25°- 32° which shows good flow property in most formulations.
4. The Percentage yield of different formulations was determined by weighing the solid dispersion after drying. The percentage yield of different formulations was in the range of 85% - 97.25% as shown in Table 3. The maximum percentage yield was found in F3.

Capsule filling method:

The prepared solid dispersion was filled in the Hard-Gelatin Capsule by the Manual Hand Filling Method using microcrystalline cellulose as a diluent and evaluated. The prepared physical mixture was also filled in the capsule. Each capsule contains solid dispersion equivalent to 50mg of Lurasidone hydrochloride. Hence capsule size 3 was selected and filled.

Evaluation of filled hard gelatin capsule

Table 4 Evaluation of filled hard gelatin capsule containing solid dispersion of LH HCl

Formulation code	Weight variation (g)	% drug content	Disintegration time (mins)
F1	0.367	95.47	20.15
F2	0.356	95.19	20.57
F3	0.401	96.60	16.48
F4	0.447	96.3	20.28
F5	0.391	95.45	18.17
F6	0.475	95.12	17
F7	0.433	96	20.46
F8	0.393	96.09	19.32
F9	0.388	95.6	21.36

Weight variation:

All the filled capsules were evaluated for uniformity of weight using electronic weighing balance and the results are shown in Table 4. The average capsule weight of all the formulations was noted down. It was about 0.35 to 0.48 g.

Drug content:

All the filled capsules were evaluated for drug content according to the procedure prescribed in the methodology. The assay values for all the formulations were found to be in the range of (95%- 97%) indicating the applications of the present method for the preparation of solid dispersion with high content uniformity. The results were shown in Table 4.

Disintegration time:

The *in vitro* disintegration time was measured by the time taken by the LH hard gelatin capsules to undergo complete disintegration. The LH SDs prepared with Vitamin E TPGS disintegrated in 20.15, 20.57, and 16.48 minutes, respectively. The LH SDs prepared with Cyclodextrin-B, disintegrated in 20.28, 18.17, and 17 minutes, respectively, whereas LH SDs with PEG-6000 disintegrated in 20.46, 19.32, and 21.36 minutes. Formulation F3 showed rapid disintegration compared to other formulations. The faster disintegration of the capsule with Vitamin E TPGS was due to easy wettability. The results were shown in Table 4.

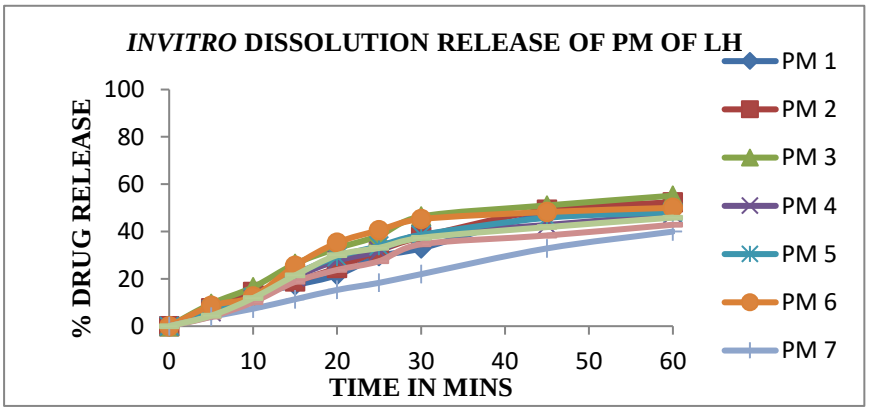
***In-vitro* dissolution study**:

The results of the percentage drug release profile of capsules filled with physical mixture were shown in Table 5 and the graphical representation of all the capsules of physical mixtures were shown in Figure 6.

Invitro dissolution for the physical mixture containing drug and Vitamin E TPGS (1:1, 1:2, and 1:3) were found to be 50.34%, 52.35%, and 55.15% respectively at the end of 1 hour. *Invitro* dissolution for a physical mixture containing drug and beta Cyclodextrin (1:1, 1:2, and 1:3) was found to be 47.25%, 48.13%, and 50.01% at the end of 1 hour. The release profile for the physical mixture containing the drug and PEG 6000 (1:1, 1:2, and 1:3) was found to be 39.97%, 42.87%, and 45.87% at the end of 1 hour. The dissolution data of the physical mixture were shown in Table 5 and the Graphical representation was in Fig 6

Table 5 *Invitro* dissolution profile of physical mixture of Lurasidone hydrochloride and carriers.

Figure 6 Graphical representation of *invitro* dissolution profile of physical mixture of Lurasidone hydrochloride and carriers



TIME (MINS)	% DRUG RELEASE								
	LH: TPGS			*LH: CD-B*			*LH: PEG 6000*		
	PM 1	*PM 2*	*PM 3*	*PM 4*	*PM 5*	*PM 6*	*PM 7*	*PM 8*	*PM 9*
0	0	0	0	0	0	0	0	0	0
5	6.57	7.54	9.47	6	7.02	8.595	3.97	4.01	4.44
10	13.43	14.44	16.47	11.37	12.1	12.5	7.38	10.16	11.89
15	17.35	18.93	26.34	20.76	21.9	25.59	11.38	18.73	21.46
20	21.6	24.65	32.88	27.67	29.33	35.25	15.33	23.766	29.99
25	29.54	31.93	38.23	31.76	33.88	40.54	18.31	27.46	33.08
30	32.88	37.65	46.34	38.67	38.56	45.23	21.99	34.61	37.34
45	47.26	49.25	51.03	42.76	45.78	48.25	32.87	38.32	41.86
60	50.34	52.35	55.15	47.25	48.13	50.01	39.97	42.87	45.87

Table 6 *Invitro* dissolution profile of solid dispersion of Lurasidone hydrochloride and carriers and pure drug

TIME (MINS)	% DRUG RELEASE									
	LH: TPGS			*LH: CD*			*LH: PEG 6000*			*PURE DRUG*
	F1	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*	
0	0	0	0	0	0	0	0	0	0	0
5	16.81	12.31	20.41	13.43	11.74	8.59	10.73	5.33	12.76	1.96
10	31.28	25.04	23.67	27.53	27.06	17.91	13.1	11.92	18.75	7.38
15	42.65	36.35	43.17	39.65	40.52	42.3	25.73	27.46	36.73	8.92
20	52.12	47.32	55.91	49.87	54.13	50.87	40.3	36.65	50.97	11.38
25	58.42	61.56	67.2	62.11	60.35	64.36	53.79	57.41	61.32	15.33
30	73.45	78.54	77.27	75.95	71.47	76.42	61.24	75.71	72.78	18.31
45	89.09	86.37	89.13	83.97	85.51	85.69	77.88	85.75	82.79	22
60	98.83	99.11	99.31	94.55	94.75	95.16	90.31	92.19	93.25	27.52

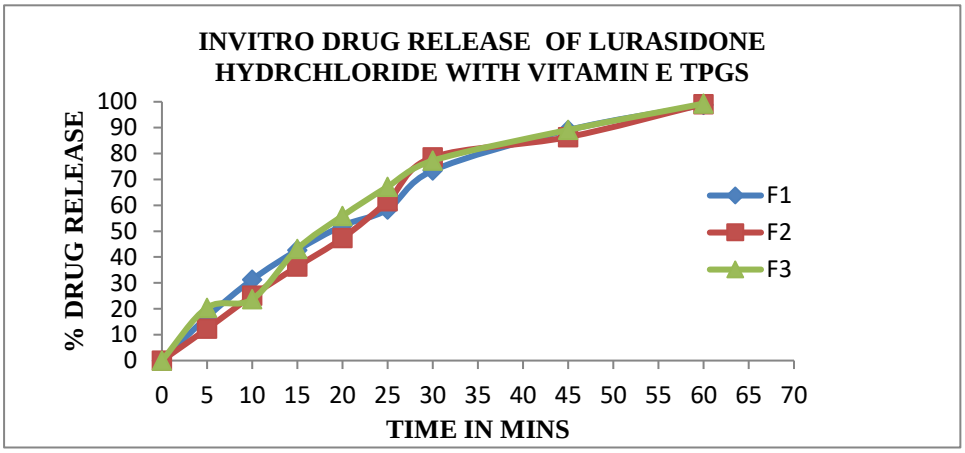


Figure 7 Graphical representation of *invitro* dissolution data of LH: TPGS

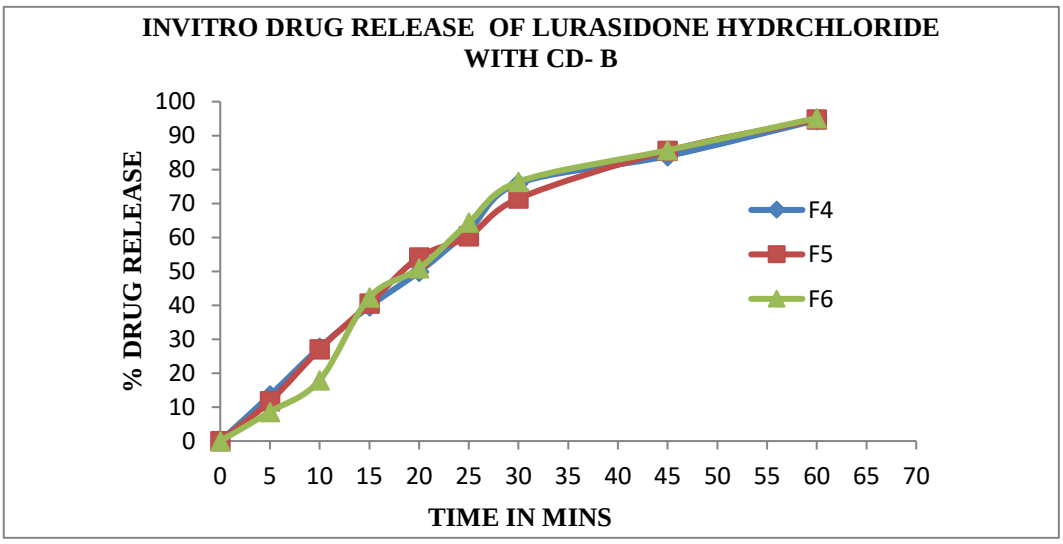


Figure 8 Graphical representation of *invitro* dissolution data of LH: CD- B

Figure 9 Graphical representation of *invitro* dissolution data of LH: PEG 6000

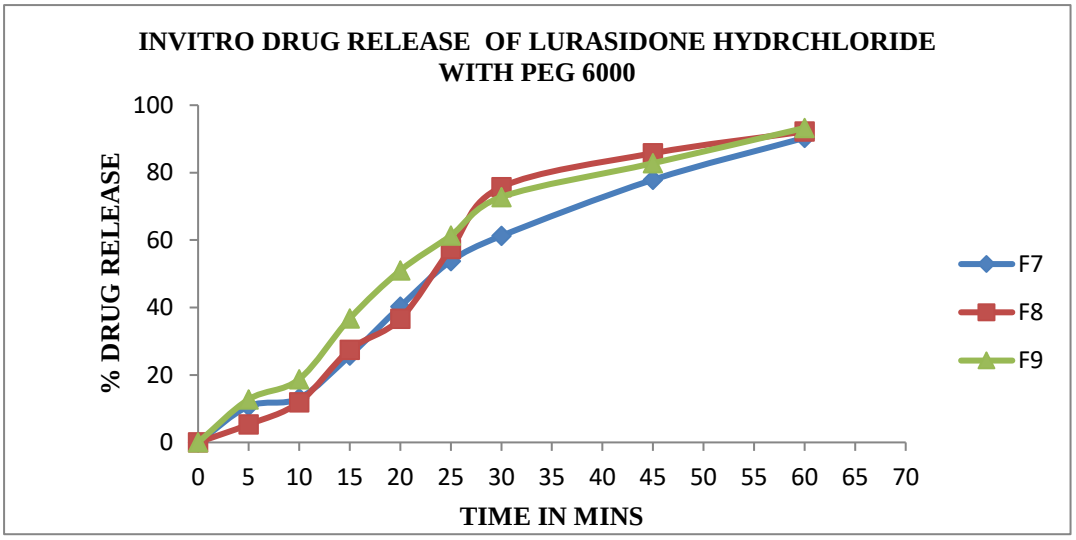
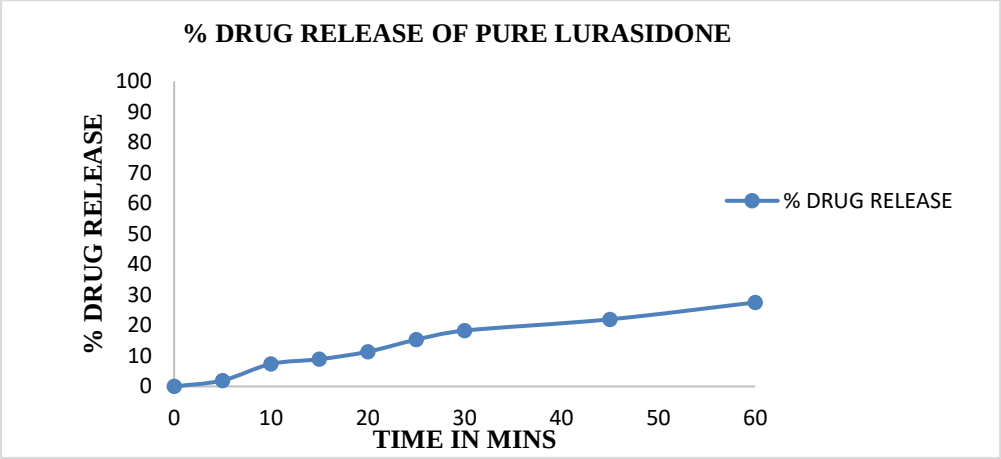


Figure 10 Graphical representation of *invitro* dissolution profile of Plain Lurasidone Hydrochloride



In vitro drug release for the capsule using vitamin E TPGS F1, F2, and F3 were found to be 98.83%, 99.11%, and 99.31% respectively at the end of 1 hour. As the concentration of the carrier increases the drug release were also increased. The drug release profile of the formulation F4, F5, and F6 prepared using cyclodextrin B was found to be 94.55%, 94.75%, and 95.16% at the end of 1 hour. The drug release profile of the formulation F7, F8, and F9 prepared using polyethylene glycol 6000 showed 90.31%, 92.19%, and 93.25% at the end of 1 hour. The *In-vitro* drug release of pure drug was found to be 27.52% at the end of 1 hour. The results were shown in Table 7 and a graphical representation of the release profile was shown in Fig. 6,7,8,9, and 10.

From the results, the formulation containing the physical mixtures of LH and vitamin E TPGS (PM3) showed a good release profile compared with pure drugs. The physical mixture of LH containing TPGS showed less drug release when compared with solid dispersion but showed higher release than the pure drug LH release.

In all the formulations, with an increase in carrier concentration, the drug release also increased. But compared to pure drugs, drug release was enhanced due to Vitamin E TPGS in solid dispersion.

In the case of Vitamin E TPGS, with the increase in the concentration of carrier, there was an increase in drug release because TPGS has an amphiphilic structure comprising a hydrophilic polar head portion and lipophilic alkyl tail and it exhibits excellent drug delivery capability based on this special amphiphilic structure and it provides enough wettability.

Among all the formulations F3 showed a maximum drug profile of 99.31% at the end of 1 hour which contains 1:3 ratios of Lurasidone hydrochloride and Vitamin E TPGS compared to other formulations containing Cyclodextrin-B and PEG 6000. The results indicated that increasing the carrier concentration will increase the dissolution of the drug.

STABILITY STUDIES:

The optimized formulation F3 was selected and stored at 40 ± 2° C/ 75% ± 5% RH for a period of 1 month. The capsules were evaluated for various parameters like weight variation, drug content, disintegration time, and In-vitro dissolution study. The results were found satisfactorily and that reveals that the selected best formulation was stable. The stability study of the optimized formulation was shown in Table 7. The dissolution profile of optimized formulation F3 was shown as a graphical representation in Fig.11

Table 7 Stability study of optimized formulation

S. No.	Evaluation Parameter	Observation
		Formulation – F3
1	Weight variation	0.401
2	Drug content (% w/w)	96.60
3	Disintegrate test (minutes)	16.48
4	Dissolution test (%)	99.31 %

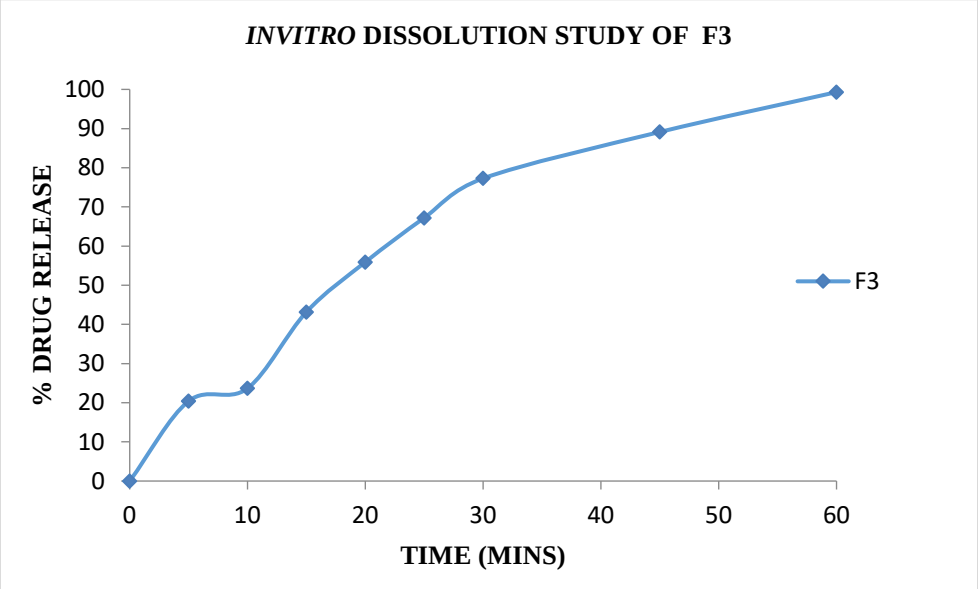


Figure 11 Graphical representation of *Invitro* dissolution profile of Optimized formulation

V. CONCLUSION:

In this study, an attempt was made to develop a solid dispersion of Lurasidone Hydrochloride using different carriers like vitamin E TPGS, cyclodextrin B and PEG 6000 with different ratios in order to improve the solubility and hence the bioavailability of the drug. The developed solid dispersion of Lurasidone hydrochloride was filled into a capsule and subjected to evaluation studies.

FTIR study proved that there was no interaction between LH and excipients. Construction of the calibration curve was done using methanol and it obeyed Beer-Lambert's law at a wavelength of 230 nm with a regression of 0.9999. Solid dispersion of Lurasidone Hydrochloride was prepared by fusion method and Solvent Evaporation Method using carriers like vitamin E TPGS, cyclodextrin B and PEG 6000 in the ratio of 1:1, 1:2 and 1:3 and it denoted as F1 to F9. The physical mixtures of drugs and carriers were prepared by simple mixing with mortar and pestle. The prepared solid dispersion was evaluated for various characterizations. The angle of repose values for formulations ranges from 26.06° to 31.09°. Bulk and tapped densities are used for the measurement of the compressibility index. The bulk and tapped values for formulations range from 0.454g/cm^3 to 0.742g/cm^3 and 0.495g/cm^3 to 823g/cm^3 respectively. The Carr's index and Hausner's ratio values for formulations range from 7.94 to 12.92 and 1.09 to 1.14 respectively. The percentage yield of all formulation contains 85% to 98%. Thus, all the values of formulation were found to be in the prescribed range.

Based on the Literature survey, Capsule size 3 was selected and filled. Microcrystalline cellulose was selected as a diluent to improve the flowability of solid dispersion. Solid dispersion was filled in hard gelatin capsules by hand filling method using prepared mixtures of solid dispersion. The prepared physical mixtures were also filled in capsules. The filled capsules containing solid dispersion of LH were then evaluated for various parameters like weight variation, drug content, and disintegration time, and *in-vitro* drug release. The filled hard gelatin capsules containing a physical mixture were also tested for drug release and compared. The weight variation in all formulations ranged from 0.35 to 0.48 g. The drug content of all the formulations was ranging from 95%- 97%. The average disintegration time of all formulations was found to be 16 - 22 minutes. Formulation F3 disintegrates within 16.48% mins. *In vitro* drug release study was carried out for formulations F1 to F9 containing different ratios of carriers like vitamin E TPGS, cyclodextrin B and PEG 6000. Among 9 formulations, F3 containing LH and vitamin E TPGS in 1: 3 ratio was selected as the best formulation based on *in vitro* drug release. The cumulative percentage of drug release of F3 was 99.31% at the end of 1 hour. From the *in vitro* dissolution studies, the order of dissolution was observed as follows,

Solid dispersion of LH > physical mixtures of LH and carrier > pure drug and this was the clear indication of dissolution enhancement in case of solid dispersion.

The performed *in vitro* drug release of solid dispersion of Lurasidone hydrochloride was compared with the release profile of physical mixtures. The formulation F3, which contains drug and Vitamin E TPGS (1:3) showed a better drug release profile of

99.31% than the physical mixture showed 51.03% and the pure drug showed 27.52%. The stability studies were carried out for F3 formulation at 40 ± 2º C/ 75% ± 5% RH for a period of 1 month. Data revealed that there were no significant changes before and after storage and the product was stable.

The research work concluded that solid dispersions of Lurasidone hydrochloride by using the water-soluble carrier vitamin E TPGS in the ratio 1:3 prepared by fusion method provide the best drug release (99.31% released in 60 mins) among all the selected 9 formulations. Further, it may be assumed that the bioavailability may be increased due to the incorporation of vitamin E TPGS as a novel carrier. Vitamin E TPGS is non-ionic and highly hydrophilic which is used for improving solubility and absorption of poorly water soluble drugs. TPGS can act as not only a carrier to improve drug dissolution rate but also as a P-gp inhibitor for enhancing the drug intestinal absorption.

Hence it was a prominent approach to enhance the dissolution rate and bioavailability of poorly water-soluble drugs Lurasidone hydrochloride. Thereby, increasing its bioavailability and patient compliance, by decreasing the frequency of drug intake with minimal doses and reducing the side effects. Formulation F3 may be selected for *In-vivo* studies followed by clinical studies in the future.

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