Formulation and Evaluation of Lurasidone Hydrochloride Fast Dissolving Tablets

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Abstract:
Antipsychotic medication lurasidone is used to treat schizophrenia and bipolar disorder. In this study, a new effort was made to improve the solubility, rate of dissolution, and oral bioavailability of the poorly soluble drug lurasidone by manufacturing it as solid dispersions utilising a variety of methods and a carrier called polyethylene glycol (PEG) 6000. The prepared solid dispersions were used to prepare fast dissolving tablets by using super disintegrants. A novel super disintegrant called Microcrystalline Cellulose-Polyethylene Glycol (MCC-PEG) Conjugate was also created as part of the project. PEGylation of Microcrystalline Cellulose (MCC) was done since PEG has the ability to increase the water absorption capacity and MCC acts as a disintegrant. Super disintegrants such as sodium starch glycolate, croscarmellose sodium, crospovidone, and microcrystalline cellulose (MCC)-polyethylene glycol (PEG) conjugate were used to create Lurasidone tablets that dissolve quickly. Tablets were tested for physical parameters and drug release by *in vitro* dissolution studies. Through SEM examination, DSC, and XRD tests, optimised solid dispersions surface properties, drug-excipient interactions, and crystal morphology have all been assessed. All the tablet preparations containing superdisintegrants were formed to release the drug in the order MCC-PEG Conjugate>Crospovidone> Croscarmellose sodium > Sodium starch glycolate. The dissolution rate of such tablet formulations were found to release the drug at a faster rate than the tablets prepared with plain drug.

Key Words: Lurasidone Hydrochloride, PEG 6000, Sodium starch glycolate, Croscarmellose sodium, Crospovidone, Microcrystalline Cellulose (MCC) - Polyethylene Glycol (PEG) Conjugate.

Introduction:

Poor water solubility and/or poor membrane permeability of the drug molecule are the most important contributors to inadequate medication absorption from the gastrointestinal (GI) tract. When an active substance is administered orally, it must first dissolve in the stomach and/or intestines before it can pass through the gastrointestinal tract's membranes and enter the bloodstream[1]. As a result, a medicine with poor water solubility often exhibits restricted absorption by dissolving rate, while a drug with poor membrane permeability typically exhibits limited absorption by permeation rate. Therefore, improving the solubility and rate of dissolution of medications that are insufficiently water-soluble and increasing the permeability of drugs that are insufficiently permeable are two fields of pharmaceutical research that concentrate on optimising the oral bioavailability of active agents[2]. Therefore, a solid dispersion method is utilised to enhance the oral bioavailability of weakly water-soluble medicines by improving their dissolving properties. The drug lurasidone hydrochloride was chosen for the current study to improve its solubility and bioavailability by increasing its dissolution rate by making it in solid dispersion form[3].

Adults and adolescents who are at least 13 years old who have schizophrenia are treated with the antipsychotic drug lurasidone. It works primarily by inhibiting the neurotransmitter receptors for dopamine, 5-hydroxyltryptamine (also known as serotonin), and noradrenaline. Since these neurotransmitters are involved in schizophrenia, lurasidone works to normalise brain activity by inhibiting their receptors, which lessens symptoms. Lurasidone hydrochloride is a white to off white powder that is very slightly soluble in water, practically insoluble in 0.1 N HCl, slightly soluble in ethanol, sparingly soluble in methanol and very slightly soluble in acetone. After a 40 mg oral dose, lurasidone takes 1 to 3 hours to reach its maximal concentration. Its elimination half-life is 18 hours, and 99.8% of the active ingredient, lurasidone hydrochloride, has a propensity to bind to proteins.

Lurasidone hydrochloride was chosen to develop solid dispersions formulations for enhancing its solubility and dissolution rate based on the aforementioned physicochemical and biological properties[4, 5].

Materials:
Lurasidone hydrochloride was a gift sample from Hetero Labs Ltd., Hyderabad and sodium starch glycolate, microcrystalline cellulose, sodium saccharin were procured from Loba Chemicals Laboratories Reagent Chemicals, Mumbai. Croscarmellose sodium, crospovidone, polyethylene glycol 200, mannitol, talc were procured from Sisco Research Laboratories, Maharashtra. Polyethylene glycol 6000, potassium dihydrogen phosphate, sodium hydroxide, magnesium stearate were procured from SD FineChemicals Ltd., Mumbai and methanol was obtained from High-Pure Fine Chem.,Chennai. All other components were of pharmacopoeial quality.

Saturated solubility studies: Several conical flasks were filled with 100 mg of lurasidone hydrochloride after it had been weighed. Individual conical flasks were filled with 50 ml of various dissolution media, then the flasks were securely closed. The KEMI orbital shaker incubatorwas filled with all of the conical flasks[6]. A 24 hour period of 50 rpm operation at 37°C ± 1°C was given to the shaker. Following the removal of the conical flasks from the incubator shaker, whatman filter paper was used to filter the samples. The clear solution obtained by filtration was appropriately diluted with suitable dissolution medium, and the absorbance values at 235 nm were recorded using corresponding dissolution media as blank solutions.

Preparation of solid dispersions: Lurasidone, which is poorly soluble, was incorporated into the polymer polyethylene glycol 6000 using three distinct methods, including (1) physical mixing (2) fusion (3) solvent evaporation.

Physical mixing method: Separately weighed samples of the medication and the polyethylene glycol-6000 were run through screen no. 80. The substances that made it through sieve No. 80 were gathered and put into a dry, spotless glass mortar. PEG-6000 and lurasidone hydrochloride were triturated collectively before being screened once more via sieve No. 100. The combination that made it past sieve No. 100 was collected, packed, and hermetically sealed in a wide mouthed amber coloured glass container[7].

Fusion method: Specified amount of PEG-6000 was placed in a china dish, and it was heated on a mantle until a molten mass was created. A prescribed amount of medication was added to the molten material and forcefully triturated at room temperature. The resulting mixture was carefully triturated in a glass mortar before being screened through sieve No. 100. The mixture was then gathered, placed in a glass container with a wide opening that was amber in colour, and hermetically sealed[8].

Solvent evaporation method:A predetermined amount of the drug was placed in a china dish and dissolved in a little amount of methanol. After obtaining a clear solution, the carrier was added to it until a thick slurry was created. This thick slurry was then transferred to a petri plate, where the solvent was allowed to evaporate and the material was dried[9]. The resulting mixture was carefully triturated in a glass mortar before being screened through sieve No. 100. The mixture was then gathered, placed in a glass container with a wide mouth that was amber in colour, and hermetically sealed. The powder is then kept in an airtight container (a desiccator) for additional studies.

Table No-1: Composition of various Lurasidone Hydrochloride Solid Dispersions

Method	Solid Dispersion Code	Composition	Ratio(Drug* : Carrier)
Physical Mixing Method	LP1	L + PEG - 6000	1:1
	LP2	L + PEG - 6000	1:2
	LP3	L + PEG - 6000	1:3
Fusion Method	LF4	L + PEG - 6000	1:1
	LF5	L + PEG - 6000	1:2
	LF6	L + PEG - 6000	1:3
Solvent Evaporation Method	LS7	L + PEG - 6000	1:1
	LS8	L + PEG - 6000	1:2
	LS9	L + PEG - 6000	1:3

L – Lurasidone Hydrochloride (* one part = 40 mg)

Table No-2: Physical Parameters of Lurasidone Hydrochloride Solid Dispersions

Solid Dispersion	Angle of repose (°)	Carr's Index (%)	Particle Size (µm)	Drug Content (%)
LHD (Pure Drug)	28.22±0.39	18.42±0.52	158±2	100±0.3
LP1	25.66±0.36	14.74±0.34	148±3	98.53±0.4
LP2	24.38±0.58	14.34±0.28	145±3	99.02±0.6
LP3	22.90±0.24	14.12±0.14	146±2	99.45±0.3
LF4	23.56±0.45	13.34±0.35	146±3	98.49±0.5
LF5	22.89±0.34	13.12±0.42	149±3	98.42±0.3
LF6	22.86±0.29	12.83±0.25	145±2	99.52±0.4
LS7	21.20±0.68	13.12±0.49	146±2	98.44±0.4

LS8	20.99±0.56	12.87±0.36	148±3	99.41±0.6
LS9	20.67±0.45	12.63±0.27	146±3	99.53±0.5

Characterization and evaluation of solid dispersions: Measurements of particle size and flow characteristics, such as angle of repose and Carr's index, were used to describe the solid dispersions made using different techniques. The surface properties, drug-excipient interactions and crystal shape of optimised solid dispersions were assessed by SEM analysis, DSC, and XRD analysis, respectively[10–12].

Estimation of Lurasidone in solid dispersions: Randomly selected solid Lurasidone dispersions from a batch were put into a 100 ml volumetric flask, and 70 ml of methanol was then added. For 0.5 hours, it was occasionally shaken, and then methanol was added to get the volume up to 100 ml. The volumetric flask's solution was taken out, and 10 ml of it was centrifuged. The centrifuge tube's supernatant solution was removed, collected, and filtered once more using whatman filter paper. After that, the filtrate was diluted with phosphate buffer with a 6.8 pH, and the absorbance measured at 235 nm.

Dissolution rate studies on Lurasidone solid dispersions and Lurasidone tablets: In a calibrated 8 station dissolution test apparatus (LABINDIA) with paddles (USP apparatus II method), dissolution tests on solid dispersions and Lurasidone tablets were carried out. The medium used was 900 ml of 6.8 pH phosphate buffer. Throughout the experiment, the temperature was held constant at 37±1°C while the paddles were rotating at 50 rpm. To maintain a constant volume throughout the experiment, 5 ml samples were removed up to 90 minutes after being dissolved and replaced with an equivalent volume of the same dissolution medium[12]. The amount of the drug dissolved was determined by an LABINDIA double beam UV spectrophotometer at 235 nm after samples taken at various time intervals were properly diluted with the same dissolution media. Each formulation's dissolution tests were carried out three times.

Synthesis of Microcrystalline Cellulose (MCC) – Polyethylene Glycol (PEG) Conjugate:
Microcrystalline cellulose (MCC) was PEGylated in the current study because of MCC's extensive use as a disintegrant and PEG's propensity to increase water intake[13]. Lurasidone hydrochloride tablets were made using conjugates of Microcrystalline Cellulose (MCC) and Polyethylene Glycol (PEG). The PEGylated conjugate of microcrystalline cellulose (MCC) was produced by heating MCC with polyethylene glycol (PEG) 200 in the presence of catalyst.

Preparation of Microcrystalline Cellulose (MCC) – Polyethylene Glycol (PEG) Conjugate:
Step 1:
8 g of polyethylene glycol 200 (PEG 200), equivalent moles of strong hydrochloric acid, and a minor amount of zinc chloride as a catalyst were added to a glass reactor. On a water bath set at 70°C, the mixture was heated for two hours. The amount of taken PEG 200 in the reactor is half that of the microcrystalline cellulose.

Step 2:
Preparation of 30% w/v aqueous sodium hydroxide solution:
30 grams of the sodium hydroxide was added to water, stirred well and made up to100 ml of the solution.

Step 3:
Separately, 16 g of microcrystalline cellulose were put to a 30% w/v aqueous sodium hydroxide solution and allowed to swell for a whole night to attain their maximum size.

Step 4:
A magnetic stirrer assembly with a heater was used to slowly mix the products of stages 1 and 3 for 10 hours while it was continually heated to 70°C. To 100 cc of hot water kept at 70°C, the obtained product was added. Then it was neutralized to pH 7 by using glacial acetic acid solution. Glacial acetic acid solution was then used to neutralize it to pH 7. For the purpose of getting rid of any surplus acid, the product was thoroughly washed in hot water (70°C). Finally, the product was dried in an oven set at 80°C for two hours.

Preparation of Lurasidone tablets with solid dispersions:
Based on the results of the dissolution investigations conducted and among the created solid dispersions, the optimised dispersion (LF 6) was chosen for further tablet manufacturing. The solid dispersion created using the fusion procedure (LF 6) with a 1:3 drug to polymer ratio was then further compressed into tablets. The direct compression procedure was used to create the tablets. While varying the superdisintegrant concentration, the drug to polymer ratio remained constant. Using microcrystalline cellulose as a diluent enabled to maintain uniform weights across all of the tablet formulations. The drug was put through sieve #60 along with the diluent, sweetener, and super disintegrant. The aforementioned ingredients were well combined in a plastic bag. Talc and Magnesium stearate were added to the initial mixture in a polybag after being passed through mesh #60. Using 8 mm circular punches and a 10-station rotary punch

tableting equipment, the powder mixture was compressed into tablets[14]. Table 3 lists the ingredients of several tablet formulations.

TableNo-3:Formulation of Lurasidone Hydrochloride Fast Dissolving Tablets

S.No.	Ingredients	LT 1 (mg)	LT 2 (mg)	LT 3 (mg)	LT 4 (mg)	LT 5 (mg)	LT 6 (mg)	LT 7 (mg)	LT 8 (mg)	LT 9 (mg)	LT 10 (mg)	LT 11 (mg)	LT 12 (mg)	LT 13 (mg)
1	Lurasidone Hydrochloride Solid dispersion (1:3)	160	160	160	160	160	160	160	160	160	160	160	160	160
2	Sodium Starch Glycolate	---	3.125	6.25	12.5	---	---	---	---	---	---	---	---	---
3	Croscarmellose Sodium	---	---	---	---	3.125	6.25	12.5	---	---	---	---	---	---
4	Crospovidone	---	---	---	---	---	---	---	3.125	6.25	12.5	---	---	---
5	Conjugate (MCC-PEG)	---	---	---	---	---	---	---	---	---	---	3.125	6.25	12.5
6	Sodium saccharin	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
7	Mannitol	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5
8	Microcrystalline cellulose PH -101	47.5	44.375	41.25	35	44.375	41.25	35	44.375	41.25	35	44.375	41.25	35
9	Talc	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
10	Magnesium Stearate	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Total Weight		250	250	250	250	250	250	250	250	250	250	250	250	250

Estimation of physical parameters of Lurasidone tablets: The physical parameters such as weight uniformity,hardness, friability, wetting time, dispersion time and drugcontent were evaluated for the prepared tablets as per the Indian Pharmacopoeial standards[15-18].

Results and Discussion:

According to study results on saturated solubility, 6.8 pH phosphate buffer was the medium in which lurasidone dissolved the most easily out of all the others. So, for subsequent research, phosphate buffer with a 6.8 pH was chosen as the dissolving medium. The dissolution media was evaluated for drug concentration at 235 nm using a UV spectrophotometer. By physical mixing, fusion, and solvent evaporation procedures, solid dispersions were created by adding poorly soluble Lurasidone into PEG 6000 in accordance with the composition provided in Table 1. To prevent variations from batch to batch, all dispersions were made under the same conditions. In terms of their characteristics, the dispersions were found to be uniform. The size range of all the solid dispersions was 145 to 149 μm. All of the prepared dispersions had good and free-flowing characteristics, according to the angle of repose and Carr's index values (Table 2). All of the solid dispersion's estimated drug content ranged from 98.44% to 99.53% (Table 2). Amorphous form of lurasidone hydrochloride solid dispersions generated by fusion was seen in the SEM photomicrograph. The SEM photomicrograph of a solid dispersion made using the fusion process revealed that the dispersion was low dense, friable, and extremely porous. Figures 1 and 2 display SEM photomicrographs of pure lurasidone hydrochloride and lurasidone hydrochloride solid dispersion respectively (LF 6).

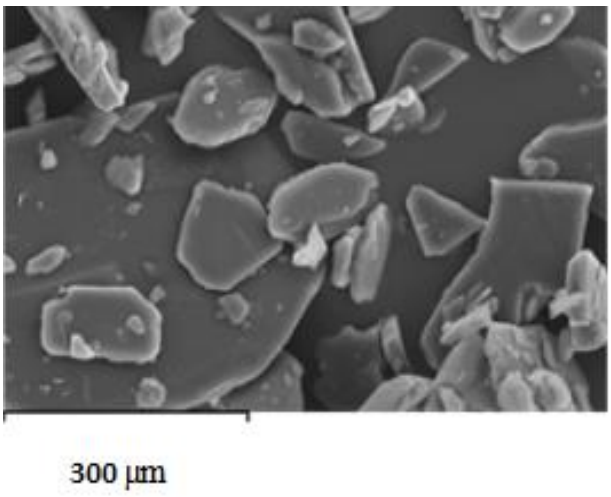

Figure No-1: SEM Photograph of Pure Lurasidone Hydrochloride

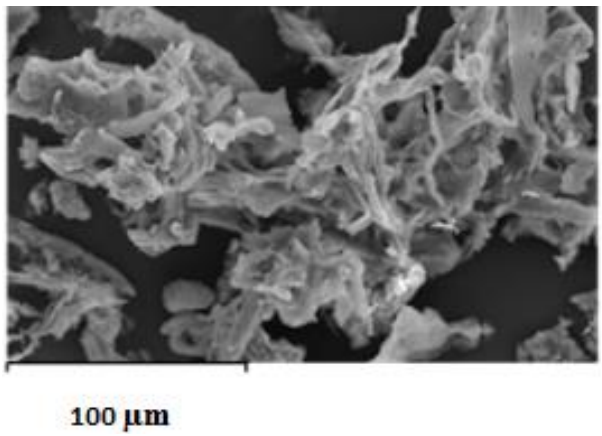

Figure No-2: SEM Photograph of Lurasidone Hydrochloride Solid Dispersion (LF 6)

The Lurasidone Hydrochloride DSC thermogram shows a clear peak at 269.2°C. Polyethylene glycol-6000 has a melting point endotherm in the 66.8°C range. Endothermic peak was seen at 257.13°C in the DSC thermogram of lurasidone hydrochloride solid dispersion (LF 6). It was noted from the spectra that the melting isotherm had slightly changed, which may have been caused by a partial change in crystallinity. It is indicated that the drug was incorporated in the polymer and there was no interaction between the two. Figures 3 to 5 display the DSC thermograms of solid dispersions of pure lurasidone hydrochloride, polyethylene glycol-6000, and lurasidone hydrochloride. The development of the drug-carrier complex was shown by the DSC thermogram of the solid dispersion of lurasidone hydrochloride.

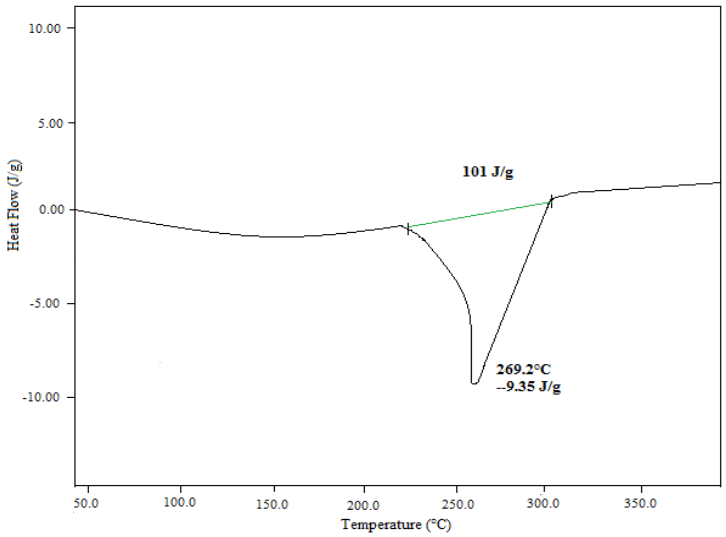

Figure No-3: DSC Thermogram of Pure Lurasidone Hydrochloride

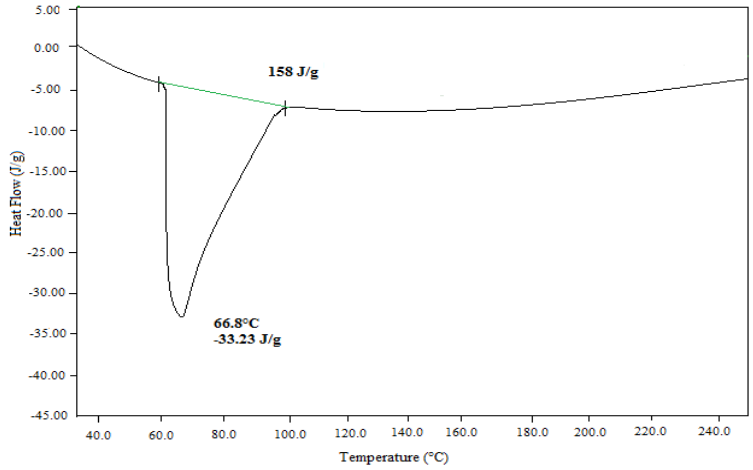

Figure No-4: DSC Thermogram of Pure PEG-6000

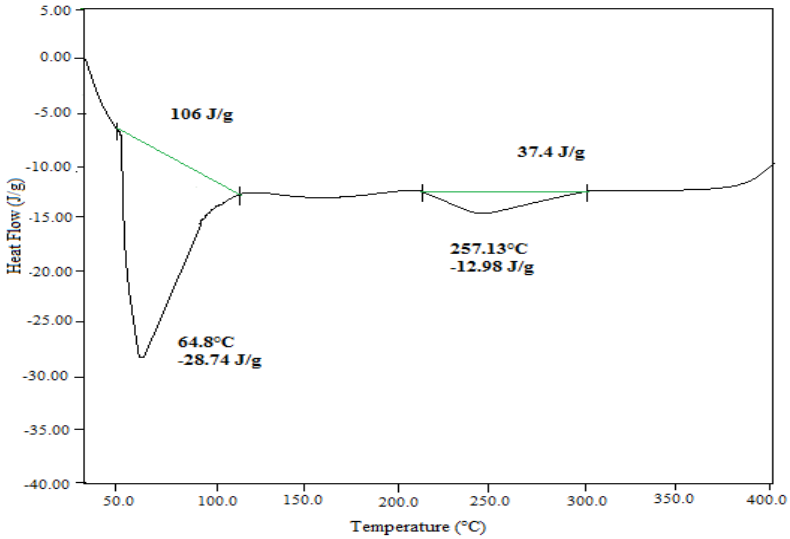

Figure No-5: DSC Thermogram of Lurasidone Hydrochloride Solid Dispersion (LF6)

Using an X-ray diffractometer (Bruker AXS), the PXRD patterns of lurasidone hydrochloride and lurasidone hydrochloride solid dispersion (LF 6) were traced. The highly crystalline form of the pure medication Lurasidone Hydrochloride is evident in the diffraction pattern, which displays a number of distinctive peaks at a diffraction angle of 2ɵ throughout the scan range. A significant decline in crystallinity may be seen in the PXRD pattern of solid dispersions of lurasidone hydrochloride due to the absence of sharp distinctive peaks. The amorphous form of lurasidone hydrochloride complexed in the carrier polyethylene glycol-6000 was thus shown by the PXRD of lurasidone hydrochloride solid dispersions (LF 6).

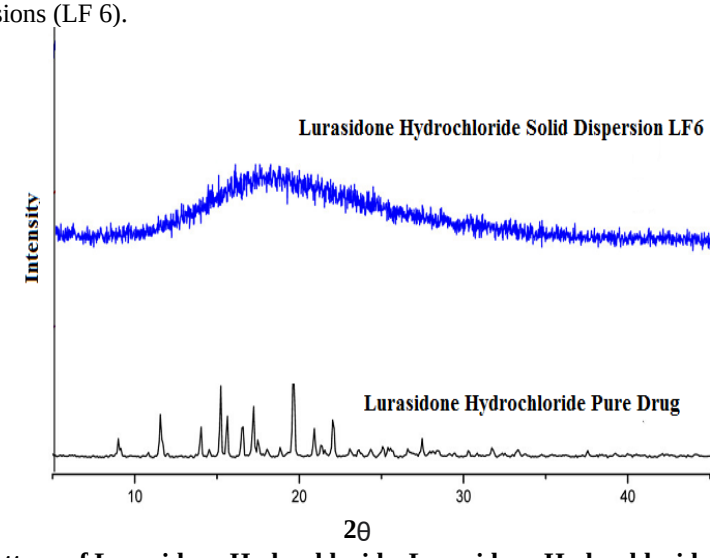

Figure No-6: PXRD Pattern of Lurasidone Hydrochloride, Lurasidone Hydrochloride Solid Dispersion (LF 6)

In 6.8 pH phosphate buffer, the paddle method was used to conduct investigations on the dissolution of lurasidone in both its pure drug form and in solid dispersions. When compared to the drug's pure form, lurasidone, it was discovered that all solid dispersions dissolved more quickly. Each dispersion's drug release kinetics followed the first order law. When compared to other solid dispersions made by physical mixing and solvent evaporation, formulation LF 6 prepared by fusion method released the drug more quickly, with a drug to polymer ratio of 1:3. Drug release has been found to increase with increasing polymer content.

Table No-4: Physical Parameters of Lurasidone Hydrochloride Fast Dissolving Tablets

Formulation	Weight Uniformity (mg)	Hardness (Kg/cm^2)	Friability (%)	Wetting time (sec)	Dispersion time (Sec)	Drug Content (mg/tablet)
LT 1	248±2.0	3.5±0.52	0.23	82±0.57	180±1.00	39.45±0.45
LT 2	249±3.0	3.4±0.24	0.21	72±1.00	85±0.54	39.25±0.52
LT 3	248±2.0	3.3±0.34	0.25	65±1.15	72±0.24	39.26±0.23
LT 4	249±3.0	3.3±0.26	0.24	62±0.57	64±0.36	40.10±0.24
LT 5	250±2.0	3.5±0.35	0.16	68±1.00	72±0.23	39.25±0.32
LT 6	248±2.0	3.4±0.42	0.29	59±1.00	64±0.54	39.65±0.44
LT 7	250±2.0	3.4±0.53	0.26	56±1.15	59±0.56	39.43±0.52
LT 8	249±2.0	3.5±0.65	0.16	64±0.57	68±1.00	39.25±0.23
LT 9	251±3.0	3.4±0.24	0.31	53±1.00	56±0.21	39.62±0.42
LT 10	248±2.0	3.4±0.26	0.34	50±1.15	54±0.33	39.41±0.15
LT 11	249±2.0	3.4±0.26	0.26	58±0.57	61±0.41	40.01±0.16
LT 12	249±1.0	3.3±0.14	0.28	50±1.00	54±0.16	39.89±0.17
LT 13	250±2.0	3.3±0.09	0.19	46±0.57	48±0.17	39.98±0.16

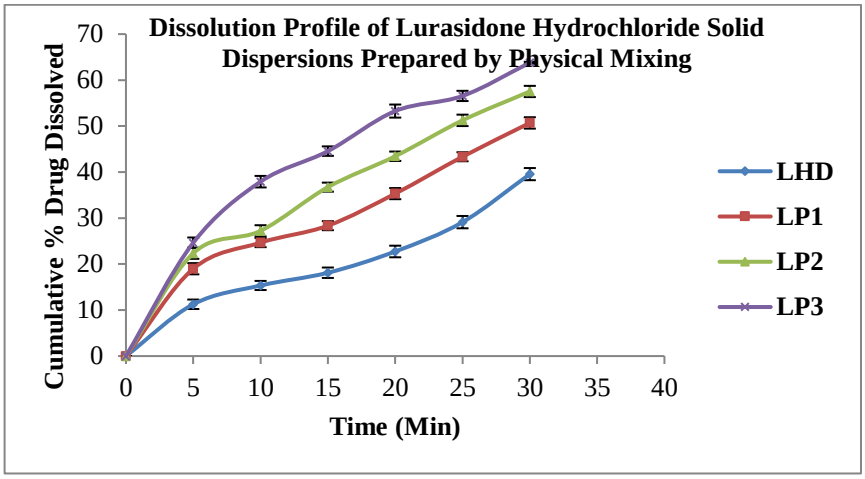

Figure No-7:Dissolution Profile of Lurasidone Hydrochloride Solid Dispersions Prepared by Physical Mixing

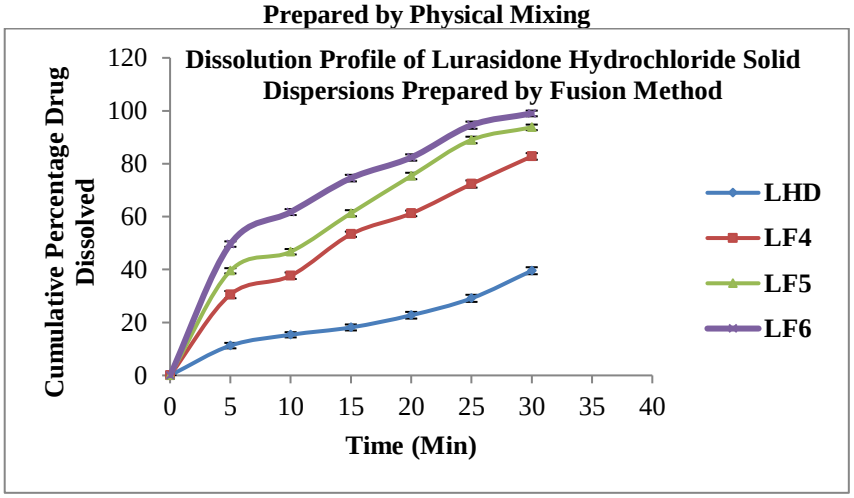

Figure No-8: Dissolution Profile of Lurasidone Hydrochloride Solid Dispersions Prepared by Fusion Method

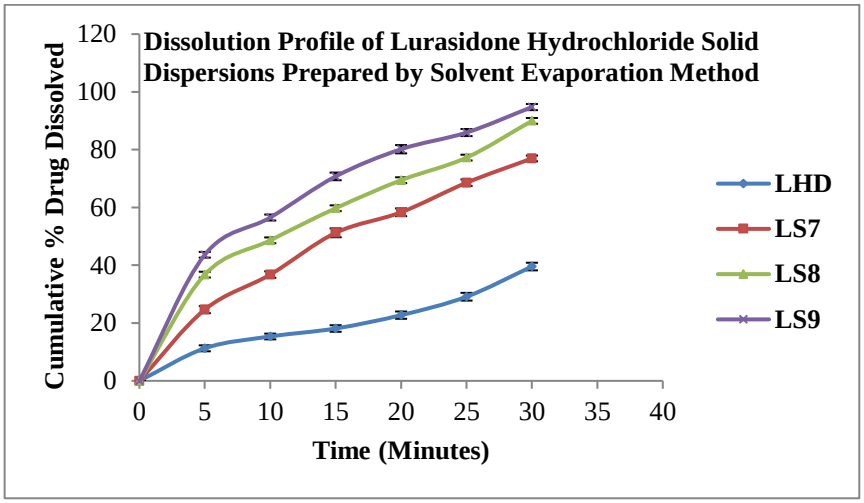

Figure No-9: Dissolution Profile of Lurasidone Hydrochloride Solid Dispersions Prepared by Solvent Evaporation Method

Table No-5: Dissolution Parameters of Lurasidone Solid Dispersions

Formulation	T_{50} (Minutes)	T_{90} (Minutes)	DE_{20}%	First order K (min^{-1})	First order R^2
LHD	>30	>30	61.21	0.015	0.947
LP1	30	>30	67.01	0.021	0.973
LP2	24	>30	68.34	0.027	0.985
LP3	18	>30	69.45	0.031	0.974
LF4	14	>30	68.21	0.054	0.974
LF5	11	26	71.56	0.089	0.955
LF6	5	23	73.85	0.136	0.896
LS7	14.5	>30	67.92	0.047	0.993
LS8	11	30	70.35	0.068	0.950
LS9	7.5	27.5	72.24	0.089	0.965

The direct compression of the solid dispersions into tablets was done next. In order to eliminate processing variations, each tablet was compressed under the same circumstances. While varying the superdisintegrant concentration, the drug to polymer ratio remained constant. According to the guidelines of the official compendium, produced tablet's physical characteristics, including weight uniformity, hardness, friability, drug content, dispersion time, and wetting time, were assessed (Table 4).

Every tablet's rate of release adhered to first order kinetics (Table 5). Formulation LT 13 was developed using Microcrystalline cellulose-Polyethylene Glycol (MCC-PEG) as a superdisintegrant, and based on *in vitro* dissolution experiments of fast dissolving tablets, it was found to display a higher dissolution rate than the others. Fast-dissolving tablets with different superdisintergrants released the drug in the following order: MCC-PEG > CP > CCS > SSG.

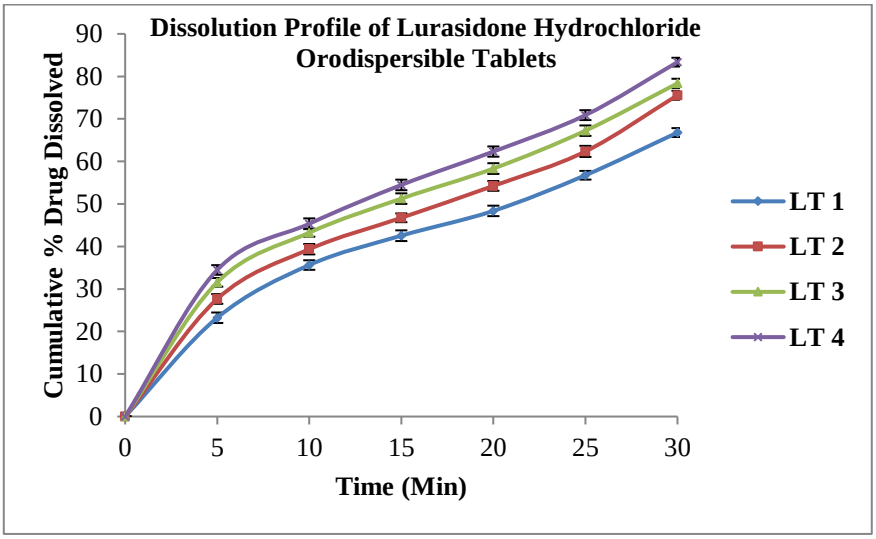

Figure No-10: Dissolution Profiles of Lurasidone Hydrochloride Tablet Formulations Containing Sodium starch glycolate as Superdisintegrant

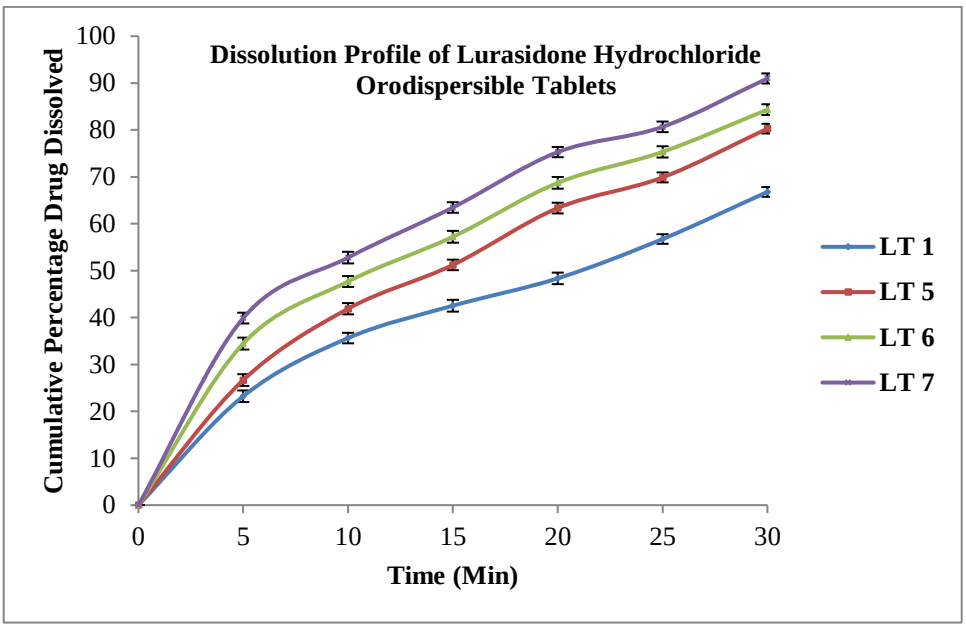

Figure No-11: Dissolution Profiles of Lurasidone Hydrochloride Tablet Formulations Containing Croscarmellose sodium as Superdisintegrant

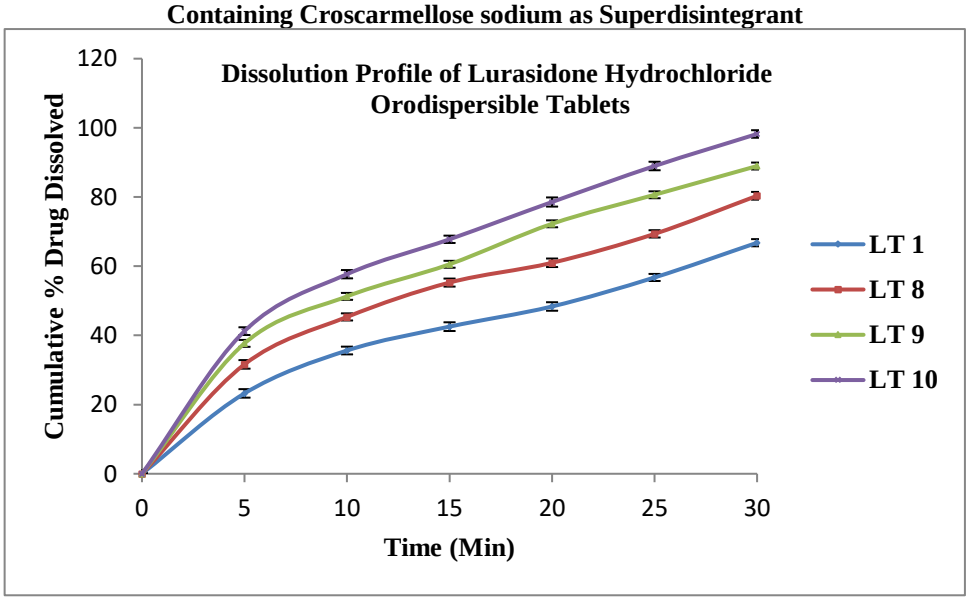

Figure No-12: Dissolution Profiles of Lurasidone Hydrochloride Tablet Formulation Containing Crospovidone as Superdisintegrant

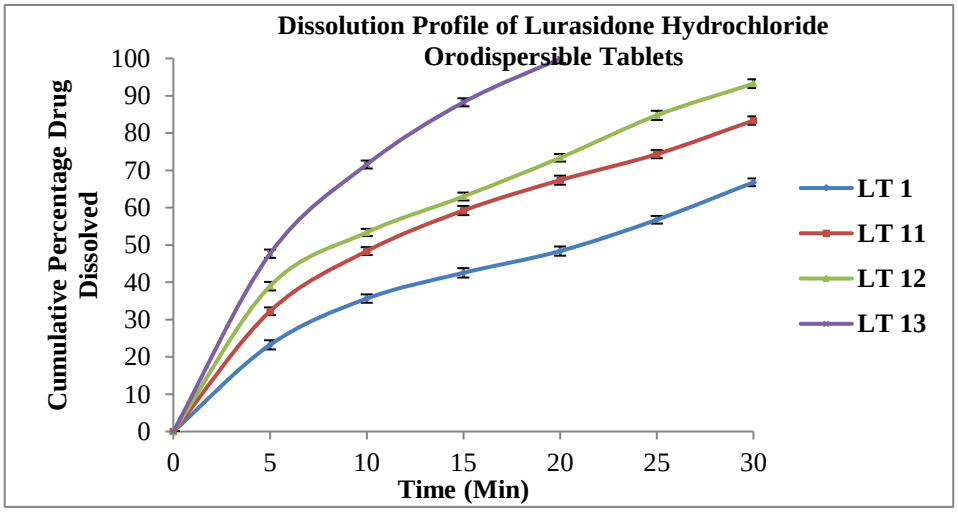

Figure No-13: Dissolution Profiles of Lurasidone Hydrochloride Tablet Formulations Containing Microcrystalline cellulose – Polyethylene glycol (MCC-PEG) as Superdisintegrant

Table No-5: Dissolution Parameters of Lurasidone Tablet Formulations

Formulation	T_{50} (Minutes)	T_{90} (Minutes)	DE_{20}%	First order K	First order R^2
LT 1	21.1	>30	64.57	0.033	0.980
LT 2	17.3	>30	65.30	0.041	0.965
LT 3	14.0	>30	66.34	0.044	0.972
LT 4	12.5	>30	67.63	0.053	0.962
LT 5	14.4	>30	67.00	0.051	0.989
LT 6	11.3	>30	68.62	0.057	0.988
LT 7	8.82	29.7	71.23	0.072	0.970
LT 8	12.5	>30	68.23	0.048	0.975
LT 9	9.7	>30	72.34	0.068	0.981
LT 10	7.6	25.6	73.35	0.082	0.980
LT 11	10.6	>30	69.67	0.056	0.989
LT 12	8.8	28	73.36	0.082	0.955
LT 13	5.5	8.2	75.27	0.141	0.993

Conclusion:

The present study has shown that it is possible to increase the dissolution rate of poorly water soluble drug Lurasidone by preparing solid dispersions with superdisintegrants like, sodium starch glycolate, croscarmellose sodium, crospovidone and Microcrystalline Cellulose - Polyethylene glycol conjugate (MCC-PEG). The solid dispersions exhibit faster dissolution characteristics as compared to plain drug. This was due to solubilizing effect of the carrier or entrapment of drug in molecular state by the carrier. Solid dispersions in the drug to polymer ratio 1:3 prepared by fusion (LF 6) released the drug rapidly than the pure drug and other dispersions. Based on the study it may be concluded that Lurasidone tablets (LT 13) prepared with 5% microcrystalline cellulose - Polyethylene glycol conjugate as superdisintegrant showed rapid drug release when compared to marketed andother tablet formulations. After comparing results obtained with MCC-PEG conjugate, with that of commercial super disintegrants, it can be concluded that MCC–PEG conjugate is an effective superdisintegrant. The drug release of tablet formulations in the presence of various superdisintegrants were in the order of MCC-PEG > CP > CCS > SSG.

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