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DEVELOPMENT AND *IN VITRO* ASSESSMENT OF MELT IN MOUTH TABLETS OF LURASIDONE HYDROCHLORIDE

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ABSTRACT

Objective: The present research work was to provide fast dissolving oral tablets of Lurasidone hydrochloride to enhance the solubility and thereby increase its onset of action. **Method:** Melt in mouth tablets of Lurasidone Hydrochloride were prepared by Direct compression method using Superdisintegrants; Crospovidone, Croscarmellose sodium, Sodium starch glycolate and disintegrant Pregelatinized starch in three different concentrations of 3%, 4%, 5% respectively and combination of superdisintegrants in 1:1 ratio with microcrystalline cellulose along with directly compressible mannitol to enhance mouth feel. The drug and drug with polymers after being subjected to FT-IR Studies were found to be interaction free. Pre-compression parameters of the blend and Post-compression parameters of the prepared batches were evaluated and found to be satisfactory. **Results:** Formulation containing Croscarmellose sodium as superdisintegrant was fulfilling all the parameters satisfactorily. It was observed that disintegration time decreases with increase in the concentration of superdisintergrant from 3% to 5% w/w. The formulation F9 and CF2 exhibited satisfactory release profile at each time point. All the formulations showed a disintegration time of less than 50 seconds. Among all, F9 containing 5% croscarmellose sodium showed a least disintegration time of 25 seconds with a drug release of 99.92% within 10 minutes and CF2 containing 1:1 ratio of croscarmellose sodium and crospovidone showed a least disintegration time of 28 seconds with a drug release of 99.84% within 10 minutes. Hence, F9 and CF2 were considered as the best formulations. Stability studies were conducted for formulations for 3 months.

Conclusion: It was concluded that melt in mouth tablets of Lurasidone Hydrochloride can be successfully formulated with increase onset of action.

INTRODUCTION:

Betterment of the dosage forms with a rapid and better efficacy, melt in mouth tablet is one of the best examples that can be justified. Tablet is the most widely used dosage form, because of its convenience in terms of self-administration, compactness, and unit dose. However, this form of dosage has some limitation like motion sickness (kinetosis), sudden episodes of allergic attacks or coughing and unavailability of water, but an imperative hitch is 'Dysphagia' or difficulty in swallowing. This is seen to afflict nearly 45% of the general population. Particularly, the difficulty is experienced by pediatric and geriatric patients[1]. To overcome this limitation, an innovative drug delivery system known as "Melt in mouth" or "Mouth Dissolving (MD)" tablets are introduced. *"Melt in mouth tablet" is defined as a tablet to be placed in mouth*

where it disappears rapidly before swallowing and which disintegrates in less than 3 minutes[2]. Mouth dissolving tablets disintegrate or dissolve in saliva and are swallowed without water. As tablets disintegrate in mouth this could enhance the clinical effect of drug through pre gastric absorption from the mouth, pharynx and esophagus[3].

Schizophrenia is a mental disorder characterized by a disintegration of the process of thinking and of emotional responsiveness[4]. It most commonly manifests as auditory hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking, and is accompanied by significant social or occupational dysfunction. The onset of symptoms typically occurs in young adulthood, with a global lifetime prevalence of around 1.5%. Diagnosis is based on the patient's self-reported experiences and observed behavior.

Lurasidone is an atypical antipsychotic belonging to the benzisothiazole derivative class used for the treatment of acute symptoms of schizophrenia. It is reported that the efficacy of Lurasidone in schizophrenia is mediated through a combination of central dopamine Type 2 (D2) and serotonin Type 2 (5-HT2A) receptor antagonism. Lurasidone showed relatively potent 5-HT2A receptor blocking actions and significantly enhanced the 5-HT1A receptor mediated behaviour[5]. Administration of conventional tablets of Lurasidone Hydrochloride has been reported to exhibit fluctuations in the plasma drug levels resulting in either manifestation of side effects or a reduction in drug concentration at the receptor site. More over the conventional tablets take time to show their effect. To overcome this problem a plan was made to prepare MMTs of Lurasidone Hydrochloride which had faster disintegration and to enhance the onset action of the drug. Mouth dissolving tablets of Lurasidone Hydrochloride were prepared using various superdisintegrants and combination of superdisintegrants[6].

MATERIALS AND METHODS:

Lurasidone Hydrochloride was obtained as gift sample from Gland Pharma Pvt. Ltd Crospovidone, Sodium starch glycolate, Cross carmellose sodium were procured from S D fine chemical Ltd. Pregelatinised starch, DC-Mannitol, Microcrystalline Cellulose, Aspartame, Magnesium stearate, Talc were procured from Shreeji Chemicals, Mumbai.

Formulation Design of Melt in Mouth Tablets of Lurasidone Hydrochloride.

Lurasidone Hydrochloride Tablets were prepared by means of two approaches using Direct Compression method.

Approach 1: Superdisintegrant addition method

Approach 2: Mixture of Different Superdisintegrants addition method

Preparation of Lurasidone Hydrochloride Tablets using Superdisintegrant addition method[7]:

Lurasidone Hydrochloride MMT was prepared by direct compression method. A blend was prepared by passing all ingredients through 60-mesh sieve separately and collected. The drug and microcrystalline cellulose were mixed in small portion of both at each time and blended to get a uniform mixture and kept aside. Then the other ingredients were weighed and mixed in geometrical order and the tablets were compressed using flat face 8 mm size punch to get a tablets of 200 mg weight using ten station Rimek tablet compression machine (Karnavati Engineering Ltd. Ahmadabad, India).

Preparation of Lurasidone Hydrochloride Tablets using mixture of Different Superdisintegrants by addition method[6]:

Melt in mouth tablets of Lurasidone Hydrochloride was prepared by direct compression method. In this approach two different superdisintegrants were mixed in 1:1 proportion. A Blend was prepared by first passing all the ingredients through 60-mesh sieve separately and collected. The drug and microcrystalline celullose were mixed in small portion of both each time and

blended to get a uniform mixture and kept aside. Then the other ingredients were weighed and mixed in geometrical order and the tablets were compressed using flat face 8 mm size punch to get a tablets of 200 mg weight using 10-station Rimek tablet compression machine (Karnavati Engineering Ltd. Ahmadabad, India).

Pre-Compression Parameters:

Drug Excipient Compatibility Studies: Compatibility of the drug with excipients were determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combining it with the excipients. The samples were taken for FT-IR study.

Angle of Repose (θ) [8]:

The frictional force in a loose powder or granules can be measured by angle of repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane.

$$\tan \theta = h / r$$

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

Where, θ is the angle of repose
h is height of pile,
r is radius of the base of pile.

Bulk Density (D_b) [9]:

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed amount of powder, in to a measuring cylinder and the initial volume was noted. From this, the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by,

$$D_b = M / V_o$$

Where, M is the mass of powder
V_o is the bulk volume of the powder.

Tapped Density (D_t) [9]:

It is the ratio of total mass of powder to the tapped volume of powder. The volume was measured by tapping the powder for 500 times. Then the tapping was done for 750 times and the tapped volume was noted, if the difference between the two volumes is less than 2%. And if it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by,

$$D_t = M / V_t$$

Where, M is the mass of powder
V_t is the tapped volume of the powder.

Compressibility Index (Carr's Consolidation Index) [10]:

One of the methods of measurement of free flowing powder is compressibility, as computed from density of a powder. It was calculated by using the formula,

% Compressibility = [Tapped density-bulk density/tapped density] x 100

Hausner's Ratio[10]:

Hausner's ratio is an indirect index of ease of powder flow. If the hausner's ratio of powder is near to 1.18, it indicates better powder flow. It is calculated by the formula

$$\text{Hausner's Ratio} = D_t / D_b$$

Where, D_b = Bulk density of the powder
D_t = Tapped density of the powder

POST-COMPRESSION PARAMETERS:

Weight Variation Test[11]

From each batch 20 tablets were selected at a random and average weight was determined. Then individual tablets were weighed was expressed in terms of %deviation.

Uniformity of Thickness

The crown thickness of individual tablet may be measured with a vernier caliper, which permits accurate measurements and provides information on the variation between tablets. Other technique employed in production control involves placing 5 or 10 tablets in a holding tray, where their total crown thickness may be measured with a sliding caliper scale. The tablet thickness was measured using vernier calipers[12].

Tablet Hardness Test[13]

Hardness indicates the ability of a tablet to withstand mechanical shocks while packaging, handling and transportation. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and analyzed for hardness. The mean and standard deviation values were calculated.58

Friability Test[13]

The friability of tablets was determined by using Roche friabilator. It is

expressed in percentage (%). Ten Tablets were initially weighed ($W_{initial}$) and transferred in to friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions and dropping the tablets at a height of 6 inches in each revolution. The tablets were weighed again (W_{final}). Tablets were then de-dusted using a soft muslin cloth and reweighed[14].

The percentage friability was then calculated by,

$$\% Friability = \frac{W\ initial - W\ final}{W\ initial} \times 100$$

% Friability of tablets less than 1% is considered acceptable.

EVALUATION PARAMETERS

Uniformity of Drug Content[11]

Five uncoated tablets were selected randomly and average weight was calculated. Tablets were crushed in a mortar and accurately weighed and the amount of average tablet was taken from the crushed blend. Then, the samples were transferred to three 100 ml volumetric flasks and were diluted up to the mark with phosphate buffer (pH 6.8) solution. The content was shaken periodically and kept for 24 hours for dissolution of drug completely. The mixtures were then filtered and appropriate dilutions were made. The drug content in each tablet was estimated at λ_{max} 230 nm against blank reference and reported.

Wetting time[15]: Wetting time of dosage form is related with the contact angle. Two circular tissue papers of 10 cm diameter are placed in a petri dish having the same inner diameter. 10 ml of phosphate buffer solution, 6.8 pH containing Eosin, a water soluble dye, is added to petri dish. A tablet is carefully placed on the surface of the tissue paper so that complete tablet was not immersed in the solution. Then, the time required for buffer to reach upper surface of the tablet is noted as wetting time[16].

Water Absorption Ratio[11]: A piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of distilled water. A tablet was put on the paper and time required for complete wetting was measured[17]. The wetted tablet was then weighed. Water absorption ratio R, was determined using equation

$$R = W_b - W_a / W_a * 100$$

Where,

W_a = weight of tablet before water absorption

W_b = weight of tablet after water absorption.

***In vitro* Dispersion Time[18]**

In vitro dispersion time was measured by dropping a tablet into a petri dish containing 10 ml of phosphate buffer pH 6.8 solution (simulated saliva fluid). Three tablets from each formulation were randomly selected and tested. In vitro dispersion time was found and expressed in seconds.

***In vitro* Disintegration Time[11]**

The *in-vitro* disintegration time of a tablet was determined using disintegration test apparatus as per I.P specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using phosphate buffer pH 6.8 (simulated saliva fluid) maintained at 37 ± 2^0C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the phosphate buffer pH 6.8 maintained at 37 ± 2^0C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

***In vitro* Drug Release Studies[11]**

The studies were carried out by using USP XXIII Dissolution Apparatus II (Paddle Type) at 50 rpm. The drug release profile was studied in 900 ml of phosphate buffer (pH 6.8) solution maintained at 37 ± 0.5°C. Aliquots of 5 ml of dissolution medium were withdrawn at specific time intervals (2, 4, 6, 8, 10 minutes) were filtered and the amount of drug released was determined by UV-Visible Spectrophotometer at 230 nm. 5 ml of fresh buffer sample was replaced as soon as the drug samples were withdrawn. Two objectives in the development of in-vitro dissolution tests was to show that,

a. Release of the drug from the tablet is as close as possible upto 100% and

b. Rate of drug release is uniform from batch to batch and is the same as the release rate from those proven to be bioavailable and clinically effective.

Table 1: Different Formulations of Lurasidone Hydrochloride using Superdisintegrant addition method

Ingredients (mg)	Formulation codes											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Lurasidone HCl	40	40	40	40	40	40	40	40	40	40	40	40
Crospovidone	6	8	10	--	--	--	--	-	--	--	--	--
Croscarmellose sodium	--	--	-	6	8	10	--	--	--	--	--	--
Sodium Starch Glycolate	--	--	--	--	--	--	6	8	10	--	--	--
pregelatinised starch	--	--	--	--	--	--	--	--	--	6	8	10
DC Mannitol	96	94	92	96	94	92	96	94	92	96	94	92
MCC	50	50	50	50	50	50	50	50	50	50	50	50
Aspartame	4	4	4	4	4	4	4	4	4	4	4	4
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Total wt (mg)	200	200	200	200	200	200	200	200	200	200	200	200

Table2: Different Formulations of Lurasidone Hydrochloride using Combination of Superdisintegrants

Ingredients	Formulation codes		
	CF1	CF2	CF3
Lurasidone HCl	40	40	40
Crospovidone	5	5	--
Croscarmellose sodium	5	--	5
Sodium Starch Glycolate	--	5	5
DC Mannitol	92	92	92
MCC	50	50	50
Aspartame	4	4	4
Mg.stearate	2	2	2
Talc	2	2	2
Total wt	200	200	200

Fig 1: FTIR Spectrum of Lurasidone Hydrochloride

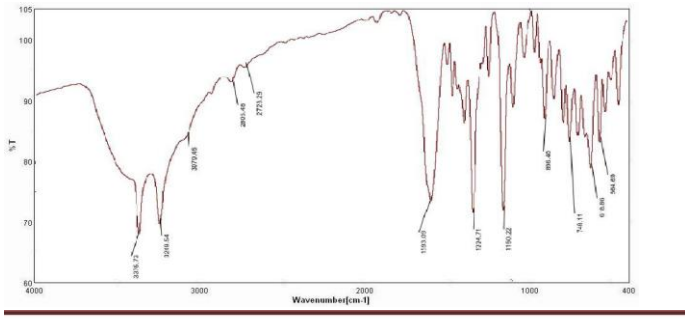

Fig 2: FTIR Spectrum of Lurasidone Hydrochloride +Crospovidone

Table 3: FTIR Spectral details of ingredients

Functional Groups	Lurasidone HCL	Crospovidone	Croscarmellose sodium	Sodium starch glycolate	Pregelatiniged starch
	Wavelength cm^{-1}				
C-N	1150.22	1080.2	1032.45	1032.95	1083.83
N-H	3316.73	3382.03	3402.37	3384.35	3326.14
C=C	1593	1597	1598	1598	1597
Aromatic	3079.45	2928.91	2920.62	2915.15	2932.17

Table 4: Evaluation of Different Formulations of Lurasidone Hydrochloride Tablets using Superdisintegrant addition method

Formulation code	***Angle of Repose(θ)**	***Bulk Density(g/cc)**	***Tapped Density(g/cc)**	***Carr's Index**	**Hausner's ratio**
F1	25.43±0.202	0.65±0.005	0.754±0.001	13.79±0.01	1.16±0.024
F2	26.55±0.476	0.64±0.002	0.745±0.006	14.09±0.06	1.16±0.041
F3	28.30±0.561	0.66±0.021	0.755±0.031	12.58±0.05	1.14±0.031
F4	25.29±0.206	0.65±0.001	0.747±0.007	12.98±0.07	1.15±0.052
F5	27.43±0.109	0.63±0.005	0.742±0.025	15.09±0.07	1.18±0.071
F6	28.82±0.117	0.64±0.015	0.753±0.017	15.01±0.51	1.18±0.032
F7	29.45±0.220	0.65±0.005	0.744±0.007	12.63±0.56	1.14±0.065
F8	26.45±0.476	0.64±0.011	0.744±0.005	13.98±0.22	1.16±0.076
F9	25.67±0.502	0.66±0.051	0.755±0.035	12.58±0.07	1.13±0.025
F10	27.84±0.782	0.64±0.006	0.744±0.005	13.97±0.02	1.16±0.035
F11	29.25±0.543	0.65±0.054	0.742±0.075	12.34±0.01	1.14±0.035
F12	27.27±0.473	0.65±0.091	0.754±0.085	13.79±0.08	1.16±0.051

* Mean ± SD, n = 3 (All values are the average of three determinations)

Table 5: Evaluation of Different Formulations of Lurasidone Hydrochloride Tablets using Combination of Superdisintegrants addition method

Formulation code	*Angle of Repose	*Bulk Density(g/cc)	*Tapped Density(g/cc)	*Carr's Index	Hausner's ratio
CF1	26.22±0.245	0.64±0.041	0.745±0.016	14.09±0.09	1.16±0.071
CF2	25.12±0.125	0.650±0.028	0.744±0.025	12.63±0.18	1.14±0.086
CF3	27.32±0.145	0.64±0.068	0.744±0.069	13.97±0.61	1.16±0.051

* Mean ± SD, n = 3 (All values are the average of three determinations

Table 7: Evaluation of tablets from CF1 to CF3 prepared by Direct compression method

Formulation Code	*Thickness (mm)	*Diameter (mm)	*Hardness (kg/cm2)	Friability (%)	*Weight Variation(mg)
CF1	3.44±0.51	7.95±0.09	3.50±0.35	0.55	200.19±0.25
CF2	3.39±0.66	8.04±0.12	3.42±0.51	0.546	199.41±0.96
CF3	3.47±0.23	8.10±0.54	3.52±0.24	0.668	199.61±0.58

* Mean ± SD, n = 3 (All values are the average of three determinations)

Table 6: Evaluation of tablets from F-1 to F-12 prepared by direct compression method.

Formulation Code	*Thickness (mm)	*Diameter (mm)	*Hardness (kg/cm2)	Friability (%)	*Weight Variation(mg)
F1	3.49±0.02	8.10±0.05	3.14±0.15	0.564	199.10±1.02
F2	3.48±0.62	8.11±0.06	3.69±0.25	0.647	201.09±0.65
F3	3.48±0.71	8.10±0.04	3.12±0.37	0.549	200.19±1.01
F4	3.46±0.54	7.98±0.08	3.20±0.25	0.543	200.33±1.04
F5	3.44±0.21	7.89±0.10	3.47±0.15	0.621	198.80±0.73
F6	3.38±0.58	8.13±0.04	3.51±0.23	0.762	200.33±1.12
F7	3.36±0.43	8.12±0.04	3.12±0.54	0.543	199.60±0.98
F8	3.45±0.87	7.90±0.08	3.20±0.67	0.675	200.43±0.85
F9	3.41±0.21	8.03±0.08	3.50±0.37	0.654	199.67±0.96
F10	3.48±0.33	7.92±0.05	3.34±0.24	0.589	199.26±1.10
F11	3.59±0.65	8.08±0.05	3.66±0.25	0.632	200.34±0.98
F12	3.63±0.45	8.10±0.07	3.20±0.45	0.674	199.67±1.04

* Mean ± SD, n = 3 (All values are the average of three determinations)

Table 8: Results of Wetting time, water absorption ratio, *In vitro* Dispersion time, *In vitro* Disintegration time and % Drug content of F1-F12 Lurasidone Hydrochloride Tablets

Formulation Code	*Wetting time (sec)	*Water Absorption Ratio	**In vitro* dispersion Time(sec)	**In vitro* disintegration time(sec	%Drug content
F1	40±1.52	68.06±0.60	35±1.50	42±0.65	98.21±0.39
F2	42±1.73	75.60±0.91	37±0.52	45±1.57	98.83±0.42
F3	32±1.00	56.38±0.49	28±0.55	35±1.52	99.23±0.41
F4	40±1.00	76.44±0.91	35±1.16	47±0.56	99.40±0.64
F5	36±1.52	64.20±0.03	30±1.00	40±1.45	98.61±o.42
F6	32±1.72	56.10±0.26	26±1.50	36±1.75	99.32±1.37
F7	40±0.52	68.07±0.86	36±1.55	44±1.25	98.01±0.85
F8	32±1.20	69.63±0.13	28±0.57	38±1.59	98.56±0.87
F9	23±0.46	56.13±0.31	20±0.57	25±0.75	99.87±0.67
F10	38±0.78	59.00±0.23	34±0.75	43±1.75	98.40±0.55
F11	42±1.50	68.00±0.54	38±1.25	45±1.27	98.52±0.43
F12	30±1.11	65.26±0.03	26±1.52	36±0.52	99.16±0.44

* Mean ± SD, n = 3 (All values are the average of three determinations)

Table 9: Results of Wetting time, water absorption ratio, *in vitro* Dispersion time, *in vitro* Disintegration time and % Drug content of CF1-CF3

Formulation Code	*Wetting time (sec)	*Water Absorption Ratio	**In vitro* dispersion Time(sec)	**In vitro* disintegration time(sec
CF1	42±1.56	68±0.91	38±1.25	46±1.55
CF2	24±1.21	58±0.51	20±0.95	28±1.25
CF3	38±0.95	62±0.68	34±1.12	43±1.32

* Mean ± SD, n = 3 (All values are the average of three determinations)

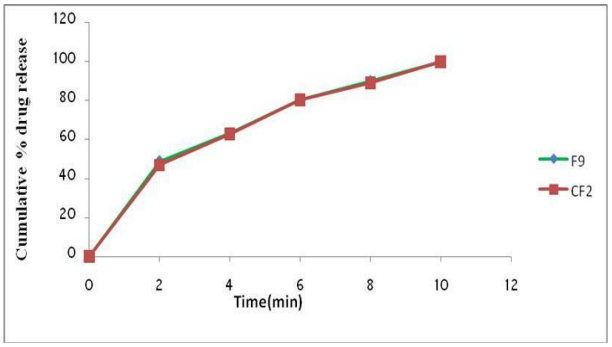

Fig 3: Cumulative % of drug release of F9 and CF2 Lurasidone Hydrochloride Tablets

Table 10: Cumulative percent drug release of F1-F12 Lurasidone Hydrochloride MMTs

Time (min)	% cumulative drug release											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
2	38.86 ±0.76	41.67 ±1.28	48.23 ±0.78	37.28 ±1.40	42.67 ±0.40	48.86 ±0.54	38.28 ±1.34	39.17 ±1.42	48.86 ±0.74	37.16 ±1.10	46.67 ±1.34	0
4	56.87 ±1.50	61.12 ±0.78	65.45 ±1.34	49.32 ±1.84	62.12 ±1.30	64.45 ±0.74	47.22 ±1.20	56.87 ±0.63	63.12 ±1.24	49.32 ±0.94	59.12 ±1.14	44.86 ±1.12
6	68.40 ±0.57	70.54 ±0.57	76.32 ±0.34	60.22 ±0.94	71.54 ±0.94	74.32 ±1.40	60.22 ±1.07	68.40 ±1.10	80.43 ±1.10	62.22 ±0.39	75.54 ±1.04	55.45 ±1.32
8	76.65 ±0.87	80.78 ±0.98	87.42 ±0.94	71.73 ±1.24	81.78 ±1.24	86.42 ±1.10	73.73 ±0.84	76.65 ±1.40	89.90 ±1.50	75.73 ±0.65	89.78 ±0.56	72.32 ±1.30
10	88.51 ±1.20	91.75 ±1.56	98.02 ±1.04	80.27 ±1.14	92.15 ±0.84	98.62 ±1.20	83.30 ±1.40	89.51 ±0.94	99.92 ±0.74	86.75 ±1.32	90.15 ±0.86	84.42 ±0.75

Table 11: Cumulative percent drug release of CF1-CF3 Lurasidone Hydrochloride MMTs

S.no	Time (min)	% Cumulative drug release		
		CF1	CF2	CF3
1	0	0	0	0
2	2	37.28±1.34	46.76±1.52	39.21±1.25
3	4	46.52±0.64	62.72±1.25	58.62±0.92
4	6	58.32±0.58	80.21±0.69	69.54±0.98
5	8	72.21±0.65	88.91±0.95	78.45±1.21

Stability data in Table 10 of optimized formulations indicated that stable formulations can be developed using direct compression method.

Table 12: Stability data of optimized formulations

Formulation code	Evaluation parameters					
	Time (RH-humidity%)		Wetting time	%Drug content	*In vitro* Disintegration Time	% Drug release
F9	Initial	25oC ,60%	22±0.78	99.87±0.65	25±0.56	99.92±0.76
	1st month	25oC , 60%	23±0.54	99.80±0.58	26±0.74	99.91±0.76
		40oC, 75%	2`1±0.76	99.82±0.54	25±0.22	99.89±0.62
	2nd month	25oC ,60%	24±1.54	99.78±0.88	26±1.74	99.91±0.64
		40oC, 75%	22±0.64	99.84±0.95	26±0.42	99.86±0.21
	3rd month	25oC 60%	22±0.24	99.82±0.38	25±0.34	99.79±0.24
		40oC,75%	24±0.62	99.79±0.94	27±0.55	99.88±0.66
CF2	Initial	25ºC , 60%	23±0.52	99.81±0.21	28±1.24	99.84±0.32
	1st month	25oC , 60%	24±0.21	99.71±0.54	29±1.12	99.76±0.67
		40oC, 75%	24±0.22	99.54±0.21	28±0.65	99.75±0.84
	2nd month	25oC ,60%	26±0.54	99.75±0.58	30±1.24	99.74±0.54
		40oC, 75%	28±0.22	99.77±0.88	32±1.65	98.98±0.39
	3rd month	25oC 60%	22±0.35	99.69±1.25	24±0.32	99.79±0.35
		40oC,75%	52±0.64	99.72±0.45	29±0.44	99.80±1.32

STABILITY STUDIES

Stability study of melt in mouth Tablets containing Lurasidone Hydrochloride was performed at following temperatures for First month, Second month and Third month- Ambient temperature: 25oC ± 2oC/ 60% ± 5% RH and Accelerated testing: 40oC ± 2oC/ 75% ± 5% RH

RESULTS & DISCUSSION: FTIR of drug-polymers interaction studies are shown in Fig 1 and 2, the data are reported in Table 1. By observing spectra's we can say that there are no interactions between the Drug and Superdisintegrants. The range of angle of repose of all the powder blends was observed as 25.12º-29.45º. All the blends

have shown good flowing ability. Bulk density was found in the range of 0.63-0.66g/cm^3. Tapped density of all the formulation blend was found to be in between 0.742 and 0.755g/cm^3. The compressibility index was found between 12.34 and 15.09 % and the compressibility-flowabilty data indicated as good to excellent flow ability of all powder blends, the hausner's ratio for all the formulations lies within the range of 1.13 to 1.18, which indicates flow of powder is good to excellent. The percentage deviation in weight variation for all formulation batches was found to be between ±0.65% and ±1.12%. Hence, weight variation test for all batches of tablets comply USP specifications. Hardness for all formulation batches was found to be between 3.12 and 3.69 Kg/cm^2 , thickness for all formulation batches was found to be between 3.38 to 3.63 mm and the % friability found to be between 0.543 to 0.762%. These findings were observed due to constant tablet press setting across all batches, irrespective of weight variation. As the formulation batches F1 to F12 comprised four different types of superdisintegrants, wetting time was found between 24 and 42 seconds. Hence it was evident that selected superdisintegrants for study played vital role in wetting behavior. Better wetting time was found with croscarmellose sodium with respect to batches consisting of other superdisintegrants. Formulation batches CF1 to CF3 comprised of mixture of different superdisintegrants in 1:1 proportion; wetting time was found between 50 and 62 seconds. Hence, again there was better wetting time found with crospovidone with croscarmellose sodium and croscarmellose sodium with sodium starch glycolate than rest of the batch. Thus wetting time for all these formulation batches varied in the following decreasing order: Croscarmellose sodium > Crospovidone > Sodium starch glycolate > Pregelatinized starch.

In vitro disintegration time for all formulation batches showed wide variation in the range of 25 and 47 seconds. This wide variation range was observed due to developmental changes in formulation to attain preliminary objectives. Batches F1 to F12 comprised of four different types of superdisintegrants; *in vitro* disintegration time was found between 25 and 47 seconds. Hence it was evident that selected superdisintegrants for study played vital role in disintegration behavior, in that there was better *in vitro* disintegration time found with croscarmellose sodium than rest of batches consisting of other superdisintegrants viz. Crospovidone, sodium starch glycolate, and pregelatinized starch. Formulation batches CF1 to CF3 comprised of mixture of different superdisintegrants in 1:1 proportion; in vitro disintegration time was found between 28 and 46 seconds. Hence, again it was found that least in vitro disintegration time was obtained with mixture of Croscarmellose sodium with Crospovidone and Croscarmellose sodium with Sodium starch glycolate than rest of the batch. Drug percent dissolved at 10 minutes for all formulation batches showed wide variation in the range of 80.27and 99.92%.As the formulation batches F1 to F12 comprised of four different types of superdisintegrants, *in vitro* drug release at 10 minutes was found between of 80.27and 99.92%. Hence it was evident that selected superdisintegrants for study played vital role in dissolution behavior. Formulation prepared with Croscarmellose sodium gave the best *in vitro* drug release than rest of batches consisting of other superdisintegrants. Formulation batches CF1 to CF3 comprised of mixture of different superdisintegrant in 1:1 proportion, *in vitro* drug release at 10 minutes was found between 90.62 and 99.84 %. Formulation with a mixture of croscarmellose sodium with sodium starch glycolate and Crospovidone with croscarmellose sodium showed better results than the rest of batch.

CONCLUSION:

Melt in Mouth tablets of lurasidone hydrochloride formulated with direct compression method using mixture of croscarmellose sodium and crospovidone shown better disintegrating efficiency and release as compared with rest of the superdisintegrants and combination. Thus melt in mouth tablets aided in the faster

release of drug, and can improve the patient compliance. Present work was a satisfactory attempt in designing MMTs for Lurasidone Hydrochloride. Further the same work should be confirmed for its therapeutic efficacy with the experimental and clinical trials.

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CONFLICT OF INTEREST:

Authors declare no Conflict of interest.

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