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Formulation and evaluation of orally disintegrating tablet containing a high concentration of micronized Lurasidone

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ABSTRACT

This study presents the formulation and evaluation of orally disintegrating tablets (ODTs) containing high concentrations of micronized lurasidone hydrochloride, an atypical antipsychotic agent. The research focuses on optimizing two key material attributes: particle size distribution (PSD) and specific surface area (SSA). These optimizations enhance granulation performance and tablet quality. Fluidized-bed granulation was employed alongside dry coating techniques and various glidants to improve powder flowability and reduce cohesion. Comprehensive characterization included pre- and post-compression parameters such as visual evaluation, sieve analysis, weight variation, hardness, tensile strength, friability, disintegration, and dissolution testing. The results demonstrated that API batches with D50 > 3.5 μm achieved 85% drug release within 15 minutes. No significant differences were observed between formulations containing different glidants, indicating flexibility in excipient selection. These results underscore the importance of controlling PSD and SSA and employing effective dry coating and fluidization strategies to produce robust and reproducible ODTs. The developed tablets improve patient compliance and therapeutic efficacy for psychotic disorders and provide valuable insights for the future development of patient-friendly dosage forms.

INTRODUCTION

Lurasidone hydrochloride is an atypical antipsychotic medication used to treat psychiatric disorders. It is classified as a dopamine-serotonin receptor antagonist, and as a benzothiazoline derivative, both pharmacologically and chemically [1,2].

According to the Biopharmaceutics Classification System (BCS), lurasidone hydrochloride is classified as a class II compound. It is characterized by low aqueous solubility and high membrane permeability. Consequently, the drug substance is usually formulated as a micronized powder to improve its dissolution characteristics. Lurasidone hydrochloride is commercially available as an immediate-release oral tablet in strengths ranging from 20 to 120 milligrams (mg) [4].

Orally disintegrating tablets (ODTs) are a patient-centric dosage form that is particularly advantageous for individuals with dysphagia or impaired swallowing ability. These tablets rapidly disintegrate in the mouth without the need for water, facilitating administration and potentially improving treatment adherence in patients with psychotic disorders [5-7].

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Fluidized bed granulation is a widely used manufacturing technique for producing ODTs. During this process, solid particles are suspended in an air stream flowing upward, which enables a binder solution to be sprayed onto the fluidized particles. This results in particle adhesion, granule formation, and simultaneous drying. This technique improves the flowability of powders, promotes uniform particle size distribution, and enhances the compressibility of the resulting granules [8-10].

The effectiveness of fluidized bed granulation depends heavily on achieving and maintaining optimal bed fluidization throughout the process. Adequate fluidization ensures homogeneous particle movement and uniform binder distribution, both of which are critical for producing granules of consistent size and composition. This parameter directly affects the quality attributes of the granules and final tablets. Insufficient fluidization can result in agglomeration, uneven drying, and the formation of oversized particles. This compromises granulation efficiency, reducing process efficiency and impairing tablet performance [8,11]. Additionally, effective fluidization promotes uniform and efficient drying, minimizing the risk of incomplete drying or excessive moisture content [11].

Two key material attributes, specific surface area (SSA) and particle size distribution (PSD), play a crucial role in granulation behavior, particularly in formulations with a high active pharmaceutical ingredient (API) load. Powders with high SSA have increased interparticle cohesive forces due to their elevated surface energy. This can result in poor powder flowability and unstable fluidization. In extreme cases, highly cohesive powders, particularly those in Geldart group C, may exhibit channeling, agglomeration, or bed collapse due to insufficient particle mobility [12].

Conversely, powders with a well-controlled, moderately broad PSD, particularly those with an optimized median particle size (D50), generally promote stable fluidization and uniform granule growth. The interplay between SSA and PSD directly influences critical process parameters, including binder distribution, granule nucleation, and growth mechanisms. While a larger surface area provides more sites for binder adsorption, it also increases the risk of over-wetting if not balanced properly with the binder spray rate and airflow conditions [13].

Various formulation strategies can be employed to mitigate the challenges associated with high SSA and narrow PSD. These strategies include incorporating glidants and functional excipients to reduce powder cohesion by modifying surface properties. The pre-treatment of cohesive powders by blending them with flow-enhancing agents has been shown to greatly improve fluidization stability, even in systems containing highly cohesive materials [14].

Dry coating is an advanced particle engineering approach that modifies powder surface properties without using liquid media. This technique involves depositing a thin layer of a flow-enhancing agent onto the surface of powder particles. The primary goal is to reduce inter-particle friction and cohesion, thereby improving the powder's overall flow properties [14,15].

Advanced dry coating techniques, including magnetic-assisted impaction coating (MAIC) and hybridization, enable uniform coverage and substantially enhance the flowability of cohesive powders. For instance, applying nanoscale silica as a coating agent has been shown to greatly improve the flow behavior of model powders, such as corn starch [14,16].

In pharmaceutical manufacturing, dry coating has been shown to improve blend homogeneity, dosing precision, and tablet compression performance. This ultimately contributes to better product quality and reduced manufacturing costs [17].

This study systematically evaluates how specific surface area and particle size distribution influence powder cohesiveness and bed behavior during fluidized bed granulation of formulations with a high micronized API load. Additionally, the study examines the impact of API pre-treatment through dry coating with different glidants to improve granulation performance and tablet compressibility. The overarching objective is to develop robust, reproducible, orally disintegrating tablets containing lurasidone hydrochloride.

MATERIALS AND METHODS

Particle size distribution

The particle size distribution of lurasidone hydrochloride was determined using a Mastersizer 3000 laser diffraction analyzer (Malvern, UK) equipped with an Aero S dry dispersion unit. Prior to the measurement, the sample was gently homogenized to prevent agglomeration and ensure consistent feeding. Approximately 0.5 g of the active pharmaceutical ingredient (API) was introduced into the dispersion unit. Compressed air at 2.5 bar was applied via a Venturi system to disperse the sample without breaking the particles. The obscuration level was maintained within the range of 0.5%-5% to ensure accurate, reproducible results. Measurements were performed in triplicate, and the data were averaged. The instrument software, based on volume distribution analysis, provided the following key parameters: D10, D50, and D90. These parameters represent the particle diameters below which 10%, 50%, and 90% of the sample volume are present, respectively.

Specific surface area

The specific surface area of lurasidone hydrochloride was determined using an automated surface area analyzer (Gemini VII, Micromeritics, UK) according to Method II of the European Pharmacopoeia (Ph. Eur.) monograph 2.9.26. Prior to analysis, the samples were degassed for two hours at 40°C to remove residual moisture. Approximately 0.5 ± 0.05 g of active pharmaceutical ingredient (API) was used for each measurement.

Nitrogen adsorption isotherms were recorded at a temperature of 77 K (liquid nitrogen) over a relative pressure range (P/Po) of 0.05-0.20. The SSA was calculated using the multi-point Brunauer-Emmett-Teller (BET) equation.

Formulation table for tablets

Table 1. Different formulations of 40 mg Lurasidone hydrochloride based ODT tablets

Ingredients [mg]	Amounts [mg]					
Intragranular phase						
Granulate batch no.	F0	F0	F1	F1	F2	F2
Lurasidone hydrochloride	40.00	40.00	40.00	40.00	40.00	40.00
Mannitol	80.00	80.00	80.00	80.00	80.00	80.00
Hydroxypropyl methyl cellulose (HPMC)	5.00	5.00	5.00	5.00	5.00	5.00
Tricafos 200-7 (tricalcium phosphate)	1.25	1.25	-	-	-	-
Aerosil 200 (hydrophilic colloidal silica)	-	-	1.25	1.25	-	-
Aerosil R972 (hydrophobic colloidal silica)	-	-	-	-	1.25	1.25
Extragranular phase						
Final product batch no.	F0A	F0B	F1A	F1B	F2A	F2B
Croscarmellose sodium	17.00	-	17.00	-	17.00	-
Low-substituted hydroxypropyl cellulose	-	17.00	-	17.00	-	17.00
Cellulose microcrystalline	16.55	-	16.55	-	16.55	-
Xylitol	-	16.55	-	16.55	-	16.55
Colloidal hydrophilic silica	0.34	0.34	0.34	0.34	0.34	0.34
Sodium Stearyl Fumarate	3.40	3.40	3.40	3.40	3.40	3.40
Aroma_1	1.36	1.36	1.36	1.36	1.36	1.36
Aroma_2	1.70	1.70	1.70	1.70	1.70	1.70
Sucralose	3.40	3.40	3.40	3.40	3.40	3.40

Method of tablet preparation

The active pharmaceutical ingredient and one of the selected glidants were weighed and introduced into a shear mixer. The impeller speed was adjusted to ensure the powder bed moved uniformly, which promoted thorough mixing without overloading the central zone. This process allowed for the dry coating of micronized API particles with the glidant, thereby improving their flow properties. The resulting blend was transferred to a fluidized bed granulator where granulation was performed using an aqueous solution of hydroxypropyl methylcellulose (HPMC). The granules were dried to a loss on drying (LOD) of less than 1% and sieved through a 0.8 mm mesh.

Next, the external phase ingredients were incorporated into the granulate in a two-step mixing process.

Finally, the blend was compressed into 170-mg tablets using a STYL'One Evolution compression simulator (Medelpharm). A main compression force of 4 kN was applied, accompanied by a pre-compression force set to approximately 10% of the main compression force.

Pre-compression parameters of tablets

Visual evaluation

The powders were placed in an open metal container to minimize electrostatic effects and enable visual assessment of cohesion and granule behavior influenced by particle size and morphology.

Sieve analysis

Sieve analysis was chosen as the method to determine the particle size distribution of the granulates. This technique is routinely used in both laboratory technology development and IPC analyses performed during routine pharmaceutical manufacturing. It is a rapid, cost-effective procedure described in detail in European Pharmacopoeia 2.9.38.

The particle size distribution was determined using a vibratory sieve shaker (AS 200, Retsch). The samples were passed through calibrated sieves, and the mass of material retained on each sieve was determined. The data were analyzed using EasySieve software (Retsch).

Granule Size Metrics

Key parameters D10, D50, and D90 were used to characterize the particle size distribution:

- D10 is the particle size below which 10% of the particles are present (fine fraction).
- D50: median particle size.
- D90 is the particle size below which 90% of the particles are present (the coarse fraction).

A narrow particle size distribution is indicated by a small difference between the D10 and D90 values.

Post-compression parameters for tablets

Weight variation test

The weight variation test, as described in the European Pharmacopoeia, ensures the uniform mass of single-dose pharmaceutical preparations. The test involves weighing 20 tablets from a batch individually. The average tablet mass is calculated, and each individual tablet's mass is compared to this value. This test was performed using a SmartTest 50 instrument (Pharmatron).

Hardness

Tablet hardness was determined according to the European Pharmacopoeia, which defines it as the force required to fracture a tablet under standardized conditions. Each tablet was placed between two plates, and a compressive force was applied until breakage occurred. These measurements were taken using a SmartTest 50 tester (Pharmatron). For round tablets, tensile strength was used as a quantitative measure of mechanical resistance. It was calculated from the measured crushing force and the tablet's dimensions. This provided a size-independent assessment of tablet strength.

Friability test

The friability test was conducted in accordance with the European Pharmacopoeia using a FT2 friability apparatus (Pharmatron).

Thirty-eight tablets were placed in a standardized drum. The drum was rotated 100 times, after which the tablets were removed. The tablets were weighed before and after the test, and the percentage weight loss was calculated.

Disintegration test

The disintegration test was performed according to the European Pharmacopoeia to assess whether the tablets disintegrate within the specified time when placed in a liquid medium.

The tablets were placed in a basket-rack assembly consisting of six open-ended tubes that were immersed in water maintained at 37°C ± 2°C. The assembly was mechanically moved in a vertical direction. The tablets were considered disintegrated when no residue remained on the screens of the tubes. This test was performed using a DisiTest 50 apparatus (Pharmatron).

***In vitro* study**

Dissolution testing was performed in accordance with the European Pharmacopoeia using a Hanson Research SR8 Plus dissolution batch station equipped with an online UV-Vis detection system (Agilent 8453 UV-Visible Spectrophotometer with ChemStation Software).

The test conditions were as follows: Apparatus 2 (paddle method) with a paddle rotation speed of 50 rpm and a dissolution medium of 900 mL of 0.01 M hydrochloric acid maintained at 37°C ± 0.5°C.

Each tablet (n = 6) was placed in a dissolution batch vessel filled with the medium. Immediately after initiating paddle rotation, the samples were analyzed online at 2.5, 5, 7.5, 10, 15, 20, and 30 minutes. Absorbance was measured at a wavelength of 315 nm using a quartz cuvette with an optical path length of 5 mm.

RESULTS AND DISCUSSION

Pre-formulation study

The particle size distribution and specific surface area were identified as key factors that influence the processability of the active pharmaceutical ingredient (API) during the fluidized-bed granulation process. Of these parameters, median particle size (D50) was found to have a significant impact on granulation performance and process stability.

Batches of API characterized by D50 values exceeding 3.5 µm and SSA values below 2 m²/g consistently demonstrated favorable fluidization behavior, homogeneous granule growth, and minimal agglomeration. Conversely, batches containing finer particles with higher SSA values showed poor powder mixing, significant channeling, and, in some cases, granulation failure.

Table 2 Particle size distribution and specific surface area of lurasidone hydrochloride

API supplier	Batch	SSA (m^2/g)	PSD		
			D,v 10 (µm)	D,v 50 (µm)	D,v 90 (µm)
Supplier_1	2011108269	1.42	0.46	3.60	7.73
Supplier_1	2011100987	1.51	0.41	3.54	7.47
Supplier_1	1811130421	1.30	0.39	3.44	6.62
Supplier_1	1811130422	1.29	0.47	4.01	8.18
Supplier_1	1811131252	1.68	0.38	3.37	6.70
Supplier_1	1811131356	1.58	0.37	3.47	6.91
Supplier_1	1811131357	1.97	0.36	3.05	6.31
Supplier_1	1811131697	1.57	0.44	3.76	8.23
Supplier_1	1811131698	1.74	0.38	3.39	7.12
Supplier_2	LUR4O20001	3.19	0.36	1.99	5.83
Supplier_2	LUR4O20003	0.92	1.30	8.78	26.70
Supplier_2	LUR4P22005	1.86	0.40	3.01	8.66
Supplier_3	AFNH009009	3.49	0.39	1.75	4.32
Supplier_3	AFNH009779	3.57	0.41	1.77	4.01
Supplier_3	AFOH006765	2.83	0.42	3.34	9.75

A statistically significant correlation (Pearson r = 0.86) was observed between D50 and SSA (Figure 1), indicating that finer particles tend to exhibit higher surface areas, negatively affecting fluidization due to increased cohesion. Conversely, larger particles with correspondingly lower SSA values enhance powder flow and facilitate controlled granule formation.

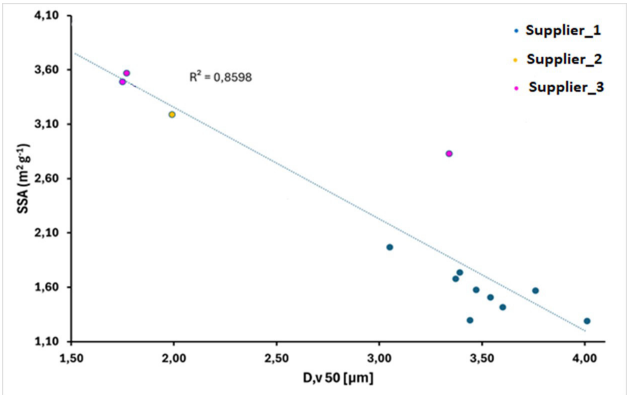

Figure 1. Correlation between D50 and SSA values

The experimental batches described below were manufactured using batch number 2011108269. The experiments showed that larger particle size and lower SSA improved granule formation and powder flowability [16-17]. Higher PSD is often associated with lower cohesion, resulting in improved powder flowability. Overall, the strong correlation between D50 and SSA underscores the importance of carefully controlling PSD and SSA to ensure robust granulation and downstream manufacturability.

Pre-compression parameters of tablets

Visual evaluation

Figures 2-5 illustrate the morphology of the powders at various stages of the process.

Figure 2. Pure API

Figure 3. Formulation F0 after high-shear mixing (dry-coating)

Figure 4. Formulation F1 after high-shear mixing (dry-coating)

Figure 5. Formulation F2 after high-shear mixing (dry-coating)

The dry-coating process altered the powder's physicochemical characteristics by reducing interparticle cohesion. As a result, the powder's flowability increased, leading to improved vessel-filling behavior. This observation aligns with the findings of studies [15,18], which reported that dry particle coating effectively reduces interparticle friction. Furthermore, the presence of silica nanoparticles on the API surface likely prevents the formation of large agglomerates during dissolution by acting as a spacer that improves wetting, a mechanism described in literature regarding cohesive micronized powders.

Sieve analysis

After the granulation step, sieve analysis was conducted using sieves with mesh sizes of 90, 125, 180, 250, 355 and 500 µm. The results are summarized in Tables 3 and 4.

Table 3 Sieve analysis of obtained granulates F0, F1 and F2

Sieve size [µm]	Sieve residue [%]		
	F0	F1	F2
Collector	4.8	9.6	11.2
90	14.0	12.4	13.9
125	24.8	19.3	19.5
180	28.8	26.5	27.1
250	23.2	28.9	25.1
355	4.0	2.8	2.8
500	0.4	0.4	0.4

Table 4 Particle size distribution of obtained granulates F0, F1 and F2

	F0	F1	F2
d10 [um]	103	91	81
d50 [um]	196	203	194
d90 [um]	330	330	326

Evaluation of the pre-compression characteristics revealed consistent behavior across all formulations tested. Each formulation exhibited superior granule formation properties, reflecting robust processability while maintaining formulation integrity. The choice of fluidized bed granulation over direct compression was validated by the poor flow properties of the pure micronized API (Fig. 2). Literature indicates that, for high-dose cohesive APIs, direct compression often results in weight variation and capping, unless very high ratios of flow aids are used [19]. Using fluid bed granulation with an initial dry coating step produced uniform granules (Table 4) that can be used for high-speed tableting. This consistency is often difficult to achieve with simple physical blends of micronized powders.

Post-compression parameters for tablets

Weight variation test

Table 5 summarizes the weight variation of all obtained formulations, providing an overview of batch-to-batch consistency.

Table 5 Weight variation of obtained formulations

	Individual weight of tablet [mg]					
	F0A	F0B	F1A	F1B	F2A	F2B
Min	168.6	171.7	169.4	170.9	170.2	168.9
Max	170.5	173.9	171.6	172.2	172.1	171.0
Max-Min	1.9	2.2	2.2	1.3	1.9	2.1
Mean	169.3	172.5	170.6	171.6	171.1	169.9
S	0.60	0.73	0.77	0.42	0.55	0.64
RSD	0.36%	0.42%	0.45%	0.25%	0.32%	0.38%
Variation	0.7%	0.8%	0.7%	0.4%	0.6%	0.6%

All batches exhibited very low variability, indicating negligible weight variation and compliance with Ph. Eur. specifications. These results suggest that the obtained granules possess excellent flow properties, resulting in highly uniform and well-controlled die filling during the tableting process [19].

Hardness and Tensile strength

The hardness values and corresponding tensile strengths of all formulations are presented in Tables 6 and 7, respectively. This allows for a comparison of the formulations' mechanical properties across batches.

Table 6. Hardness of obtained formulations

	Individual hardness of tablet [N]					
	F0A	F0B	F1A	F1B	F2A	F2B
Min	43	32	45	34	45	27
Max	46	34	48	36	48	29
Max-Min	3	2	3	2	3	2
Mean	45	33	47	35	47	28
S	1.1	0.8	1.1	0.9	0.8	0.7
RSD	2.4%	2.4%	2.3%	2.5%	1.8%	2.4%

Table 7. Tensile strength of obtained formulations

Tensile strength of tablets [MPa]					
F0A	F0B	F1A	F1B	F2A	F2B
1.1	0.8	1.2	0.8	1.2	0.7

Hardness was converted into a parameter known as tensile strength. Based on this metric, it can be concluded that all formulations have relatively low mechanical

robustness. However, the B batches demonstrate particularly poor performance. The expected tensile strength value was approximately 1.7 MPa.

Mechanical strength in orodispersible tablets is often intentionally reduced to facilitate rapid disintegration and ensure compliance with pharmacopoeial requirements. Nevertheless, the formulation must maintain an appropriate balance between minimal disintegration time and adequate mechanical strength [21].

Friability

Table 8 provides insight into the mechanical integrity of the tablets under stress conditions by compiling the friability results for all formulations.

Table 8. Friability of obtained formulations

Friability of tablets [%]					
F0A	F0B	F1A	F1B	F2A	F2B
0.0904	0.1686	0.1076	0.1385	0.1535	2.7331

The friability results were highly satisfactory, with values approaching 0%. This indicates that the tablets' mechanical strength was sufficient to maintain the efficiency of the manufacturing process. Only the F2B series exceeded the pharmacopoeial limit. In this case, significant edge chipping of the tablets was observed during the friability test, resulting in notable mass loss and substantially impacting the test outcome.

Disintegration

The disintegration times of the obtained formulations are summarized in Table 9, which illustrates the tablets' suitability for rapid oral administration.

Table 9 Disintegration test results of obtained formulations

	Disintegration test results [min:sec]					
	F0A	F0B	F1A	F1B	F2A	F2B
Min	00:45	02:44	01:00	02:33	01:03	02:24
Max	01:11	04:00	01:39	02:39	01:47	02:41
Range	00:26	01:16	00:39	00:06	00:44	00:17
Average	00:58	03:16	01:17	02:36	01:33	02:33
S	9.1	29.5	17.7	2.3	19.9	7.4
RSD	15.7%	15.1%	23.0%	1.5%	21.4%	4.9%

All **A** formulation batches complied with the European Pharmacopoeia requirements for ODTs. The **B** batches approached the pharmacopoeial limit, with one batch exceeding it. This is considered unacceptable from both a regulatory and patient compliance perspective.

Assay and impurities

The assay results and impurity profiles are presented in Table 10, which allows for an assessment of the formulations' chemical quality and purity.

Table 10. Assay and impurities of obtained formulations.

Sample no.	F0A	F0B	F1A	F1B	F2A	F2B
Assay [%]	95.7	95.7	96.7	97.5	96.2	96.1
Total imp. [%]	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1

All formulations demonstrated assay values within the 95-105% range specified by the Ph. Eur., confirming that the formulations meet the standards necessary to ensure pharmacotherapeutic efficacy.

In vitro study

Based on preliminary physical evaluations, B formulations were deemed non-promising and excluded from further testing. Tables 11-13 summarize the dissolution profiles of the A formulations, and Figure 6 visually compares them, providing a comprehensive assessment of drug release characteristics.

Table 11. Batch F0A dissolution results [%]

Value\Time points [min]	2,5	5	7,5	10	15	20	30
Min	38.4	65.8	77.1	86.3	91.4	94.1	95.9
Max	55.2	76.5	90.2	94.6	96.6	97.8	98.2
Span	16.8	10.7	13.1	8.3	5.2	3.7	2.3
Average	47.2	72.7	84.1	90.3	95.0	96.2	96.8
SD	5.4	4.6	5.2	3.4	1.9	1.2	0.8
RSD	11.5	6.4	6.1	3.8	2.0	1.3	0.8

Table 12. Batch F1A dissolution results [%]

Value\Time points [min]	2,5	5	7,5	10	15	20	30
Min	41.1	73.9	81.7	88.9	94.5	94.8	95.2
Max	53.3	78.0	90.6	94.5	95.9	96.8	97.3
Span	12.2	4.1	8.9	5.6	1.4	2.0	2.1
Average	45.7	75.9	86.2	91.6	95.3	95.8	96.2
SD	4.2	1.6	3.7	2.1	0.6	0.7	0.7
RSD	9.3	2.1	4.2	2.2	0.6	0.7	0.7

Table 13 Batch F2A dissolution results [%]

Value\Time points [min]	2,5	5	7,5	10	15	20	30
Min	39.4	67.2	82.0	88.4	92.1	93.0	93.7
Max	57.4	86.1	93.2	95.0	96.2	96.6	97.0
Span	18.0	18.9	11.2	6.6	4.1	3.6	3.3
Average	47.0	77.5	88.1	92.4	94.7	95.2	95.6
SD	6.4	8.2	4.8	2.4	1.6	1.4	1.3
RSD	13.6	10.6	5.5	2.6	1.7	1.5	1.4

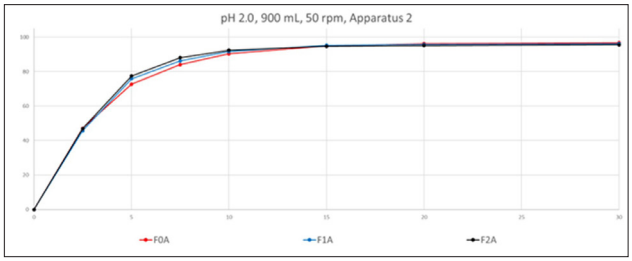

Figure 6. Comparison of dissolution profiles

Under the specified conditions (pH 2.0, 900 mL dissolution medium, 50 rpm, and Apparatus 2), all batches of A (F0A, F1A, and F2A) achieved over 85% drug release within the first 15 minutes. According to the criteria of the

European Pharmacopoeia (Ph. Eur.) monograph, formulations that release more than 85% of the drug within this timeframe are considered to exhibit comparable dissolution characteristics. Therefore, the dissolution profiles of the tested A formulations are similar and consistent with regulatory standards. While our study demonstrates the efficacy of fluidized bed granulation, other researchers have explored alternative techniques for lurasidone oral disintegrating tablets (ODTs). For instance, recent studies have investigated melt granulation and the preparation of micellar systems to enhance bioavailability [24]. Although these methods effectively improve dissolution rates, they often require complex processing. In contrast, our results indicate that dry coating the micronized API with a glidant followed by standard fluid bed granulation is sufficient to achieve rapid disintegration and high dissolution (>85% in 15 minutes), offering a more energy-efficient manufacturing pathway. Additionally, it is worth noting the positive impact of the glidant on the dissolution rate (Fig. 6), despite the potential hydrophobicity of silicon dioxide. This aligns with previous observations that nanosilica particles can improve the wettability of hydrophobic drugs by increasing the effective surface area available for the solvent and disrupting the hydrophobic agglomerates of the API. These findings suggest that the dry-coating step improves flowability and acts as a dissolution-enhancing mechanism for BCS Class II compounds.

CONCLUSIONS

This study successfully formulates and evaluates orally disintegrating tablets containing high concentrations of micronized lurasidone hydrochloride. These ODTs have great potential to improve patient compliance and the efficacy of treating psychotic disorders. Furthermore, the available literature provides limited information on ODT formulations containing lurasidone hydrochloride. Existing studies primarily focus on specific delivery platforms or micellar systems designed to enhance bioavailability, leaving the broader context insufficiently explored.

Key findings emphasize the importance of optimizing the particle size distribution and specific surface area of the active pharmaceutical ingredient (API) to ensure consistent tablet quality. The fluidized bed granulation process combined with formulation strategies using microcrystalline cellulose and croscarmellose sodium in the extragranular phase has proven effective in producing ODTs with desirable characteristics, such as rapid disintegration, uniform granule formation, and minimal weight variation.

Evaluating both pre-compression and post-compression parameters, including visual inspection, sieve analysis, weight variation, hardness, tensile strength, friability, and disintegration tests, confirmed the successful development of the ODT formulations. Furthermore, the study highlights the critical roles of dry coating and effective bed fluidization in achieving uniform mixing and coating, which directly affect the quality and performance of the final product. No significant differences were observed between formulations containing different glidants, indicating flexibility in excipient selection without compromising product quality.

These findings offer valuable insights into the formulation and manufacturing of lurasidone hydrochloride oral disintegrating tablets (ODTs), providing a promising approach to improving medication adherence by offering patients a convenient dosage form for managing psychotic disorders.

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