DESIGN AND CHARACTERIZATION OF LURASIDONE-LOADED NIOSOMES FOR IMPROVED ORAL BIOAVAILABILITY AND TARGETED BRAIN DELIVERY

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Abstract

The present study aimed to develop and characterize lurasidone-loaded niosomes to improve oral bioavailability and targeted brain delivery. Lurasidone-loaded niosomes were prepared by the thin film hydration method using Span surfactants and cholesterol. Preformulation studies confirmed the poor aqueous solubility and lipophilic nature of lurasidone, supporting the need for a vesicular delivery system. The prepared formulations were evaluated for particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, drug content, in-vitro drug release, and stability. Among all formulations, F10 showed optimized characteristics with nanosized vesicles, high entrapment efficiency, good stability, and sustained drug release over 24 hours. Stability studies performed according to ICH guidelines demonstrated minimal changes in formulation parameters during storage. The study concluded that lurasidone-loaded niosomes are a promising approach for enhancing solubility, bioavailability, and brain-targeted delivery of lurasidone.

Keywords: *Lurasidone, Niosomes, Thin Film Hydration Method, Oral Bioavailability, Brain Targeting, Nanovesicular Drug Delivery*

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1. Introduction

Lurasidone is a second-generation atypical antipsychotic drug commonly used in the treatment of schizophrenia and bipolar depression due to its antagonistic action on dopamine D2 and serotonin 5-HT2A receptors (Shah et al., 2020). Although clinically effective, lurasidone exhibits poor aqueous solubility and low oral bioavailability because of extensive first-pass metabolism and dissolution-limited absorption (Junghanns and Müller, 2008). These limitations reduce its therapeutic efficiency and create a need for advanced drug delivery systems to improve its solubility and absorption.

Brain drug delivery remains challenging because of the blood–brain barrier (BBB), which restricts the entry of many therapeutic agents into the central nervous system (Pardridge, 2005). Nanocarrier-based systems have gained significant attention for improving the bioavailability and brain targeting of CNS-active drugs (Allen and Cullis, 2004). Among these carriers, niosomes are promising vesicular systems composed of non-ionic surfactants and cholesterol that can encapsulate both hydrophilic and lipophilic drugs (Uchegbu and Florence, 1995).

Niosomes offer several advantages, including enhanced drug stability, sustained drug release, improved membrane permeation, low toxicity, and better bioavailability (Moghassemi and Hadjizadeh, 2014). Their performance depends on factors such as surfactant type, cholesterol concentration, and preparation method (Yadav et al., 2012). The thin film hydration method is widely used for niosome preparation because of its simplicity and ability to produce stable vesicles with high drug entrapment (Kaur et al., 2004).

Therefore, the present study was aimed at developing and characterizing lurasidone-loaded niosomes for improved oral bioavailability and targeted brain delivery. The prepared formulations were evaluated for particle size, polydispersity index, zeta potential, entrapment efficiency, drug content, in-vitro drug release, and stability to identify an optimized and stable formulation.

2. Collection, Procurement, and Authentication of Materials

2.1 Collection and Procurement of Drug and Excipients

The active pharmaceutical ingredient in this study is lurasidone, obtained as a gift sample from a reputable pharmaceutical manufacturer. Non-ionic surfactants of the Span series (Span 20, Span 40, and Span 60) were selected for niosome preparation due to their suitable HLB values and vesicle-forming ability. Cholesterol was used to enhance bilayer rigidity

and stability. Analytical-grade solvents and reagents, including methanol and chloroform, were procured from standard suppliers and used without further purification. All materials were of analytical grade to ensure reproducibility and reliability of results.

2.2 Authentication of Materials

The drug sample was confirmed for purity and suitability using standard characterization techniques. The melting point of lurasidone was determined using the capillary method with a digital melting point apparatus and compared with literature values for identification. FTIR spectroscopy was performed to verify characteristic functional groups against reference spectra. Physical properties such as color, texture, and appearance were also visually examined and matched with reported descriptions. In addition, the Certificate of Analysis (CoA) from the supplier was used to confirm the quality and purity of lurasidone and excipients in accordance with pharmaceutical standards.

2.3 Storage and Handling of Materials

All materials were stored under appropriate conditions to maintain stability and integrity throughout the study. Lurasidone and other sensitive compounds were kept in tightly sealed, light-protected containers to avoid exposure to moisture, heat, and light. Surfactants and cholesterol were stored at controlled room temperature, while organic solvents were kept in cool, well-ventilated areas away from sunlight and ignition sources. All materials were properly labeled with relevant details, and standard laboratory procedures with proper documentation were followed to ensure GLP compliance, traceability, and reproducibility.

3. Preformulation Studies

3.1 Organoleptic Properties

As an initial step in preformulation studies, the organoleptic properties of lurasidone were evaluated under normal laboratory conditions. The drug was examined for color, appearance, texture, odor, and physical form (crystalline or amorphous). Texture was assessed by gentle handling, while odor was evaluated by cautious wafting. The observations were recorded and compared with available literature and pharmacopoeial standards to confirm drug identity, purity, and suitability for niosomal formulation development.

3.2 Solubility Analysis

As part of the preformulation studies, the solubility of lurasidone was determined using the shaking flask method. Excess drug was added to distilled water, methanol, ethanol, and

buffer solutions of pH 1.2, 6.8, and 7.4, followed by continuous shaking for 24 hours at 25 ± 2°C to achieve equilibrium. The samples were then filtered, suitably diluted, and analyzed using a UV-visible spectrophotometer at the λmax of lurasidone. The solubility profile obtained helped in selecting suitable solvents and dissolution media for the formulation and evaluation of niosomes.

3.3 Partition Coefficient Determination

The lipophilicity of lurasidone was evaluated by determining its partition coefficient (log P) using the shake flask method with an n-octanol/water system. After mutual saturation of both phases, the drug was shaken with the solvent system at 25 ± 2°C for 24 hours. Following phase separation, the aqueous phase was analyzed by UV spectroscopy at the λmax of lurasidone, and the partition coefficient was calculated from the drug distribution between the two phases. The obtained log P value indicated the drug's lipophilic nature and its suitability for niosomal formulation and membrane permeability.

3.4 Melting Point Determination

The melting point of lurasidone was determined using the capillary method with a digital melting point apparatus to assess its purity and identity. A small quantity of finely powdered drug was filled into a capillary tube and heated gradually until melting occurred. The melting range was recorded from the onset of melting to complete liquefaction and compared with reported literature values. A sharp melting range indicated purity, while deviations suggested possible impurities. The study also aided in selecting suitable processing conditions for niosomal formulation development.

3.5 Determination of λmax (UV Spectroscopy)

UV–Visible spectroscopy was employed to determine the λmax of lurasidone based on Beer–Lambert's law. A standard stock solution of the drug was prepared in methanol and suitably diluted with phosphate buffer (pH 7.4). The solution was scanned in the range of 200–400 nm using a UV spectrophotometer to identify the wavelength of maximum absorbance. The experiment was performed in triplicate, and the average λmax value was recorded. This study was essential for accurate quantification of lurasidone in subsequent analytical and formulation evaluations.

3.6 Drug–Excipient Compatibility Studies (FTIR Analysis)

FTIR spectroscopy was performed to study the compatibility between lurasidone and selected excipients. Pure drug, individual excipients, and their physical mixtures were mixed with potassium bromide (KBr) and compressed into pellets for analysis. The samples were scanned in the range of 4000–400 cm^{-1} using an FTIR spectrophotometer. The spectra of the pure drug and mixtures were compared to identify any significant changes in characteristic peaks. The absence of major spectral alterations indicated compatibility between lurasidone and the excipients, supporting their suitability for niosomal formulation development.

4. Formulation Development of Niosomes

4.1 Selection of Method (Thin Film Hydration Method)

Lurasidone-loaded niosomes were prepared by the thin film hydration method. Accurately weighed amounts of surfactant, cholesterol, and lurasidone were dissolved in a chloroform–methanol mixture in a round-bottom flask. The organic solvent was evaporated using a rotary evaporator at 45°C to form a thin lipid film, which was further dried to remove residual solvent. The dried film was then hydrated with an aqueous phase to produce niosomal vesicles, followed by sonication to obtain a uniform dispersion with reduced particle size. This method was chosen due to its simplicity, reproducibility, and ability to produce stable vesicles with high drug entrapment efficiency.

4.2 Preparation of Lurasidone-Loaded Niosomes

Lurasidone-loaded niosomes were prepared by the thin film hydration method using Span surfactants (Span 20/40/60) and cholesterol. The components were dissolved in a chloroform–methanol (2:1 v/v) mixture, and the solvent was evaporated under reduced pressure at 45°C using a rotary evaporator to form a thin lipid film. The film was further dried and hydrated with distilled water or phosphate buffer (pH 7.4) at 60°C to produce vesicles, followed by sonication to obtain a uniform nanosized dispersion. This method was chosen for its simplicity, reproducibility, and ability to produce stable niosomes with high drug entrapment and enhanced bioavailability potential.

4.3 Optimization of Formulation Variables

Formulation variables were optimized to obtain niosomes with suitable particle size, uniform distribution, high entrapment efficiency, and good stability. Parameters such as the type and concentration of Span surfactants (Span 20, Span 40, and Span 60), cholesterol ratio, and

hydration conditions were systematically varied. Different surfactant-to-cholesterol ratios (1:1, 2:1, and 3:1) were evaluated to study their effect on vesicle characteristics and stability. Hydration temperature, time, and aqueous phase volume were also optimized. A series of formulations (F1–F10) were prepared by varying one parameter at a time, and the optimized formulation was selected based on particle size, polydispersity index, entrapment efficiency, and stability results.

Table 1: Composition of Lurasidone-Loaded Niosomal Formulations (F1–F10)

Formulation Code	Lurasidone (mg)	Span Type	Surfactant : Cholesterol Ratio	Chloroform (mL)	Methanol (mL)	Hydration Medium (mL)
F1	10	Span 20	1:1	10	5	20
F2	10	Span 20	2:1	10	5	20
F3	10	Span 20	3:1	10	5	20
F4	10	Span 40	1:1	10	5	20
F5	10	Span 40	2:1	10	5	20
F6	10	Span 40	3:1	10	5	20
F7	10	Span 60	1:1	10	5	20
F8	10	Span 60	2:1	10	5	20
F9	10	Span 60	3:1	10	5	20
F10	10	Span 60	2:1 (optimized)	10	5	20

5. Characterization of Niosomes

5.1 Particle Size

Particle size analysis of the optimized lurasidone-loaded niosomes was performed using Dynamic Light Scattering (DLS) with a Malvern Zetasizer. The formulation was suitably

diluted with distilled water and transferred into a clean, bubble-free cuvette for analysis at 25°C. The average particle size was determined based on light scattering patterns, and measurements were carried out in triplicate with the mean value recorded. Particle size evaluation is important as smaller vesicles enhance drug release, stability, and bioavailability, thereby improving the potential for brain-targeted delivery.

5.2 Polydispersity Index (PDI)

The Polydispersity Index (PDI) of the optimized lurasidone-loaded niosomal formulation was determined using Dynamic Light Scattering (DLS) with a Malvern Zetasizer. The formulation was diluted with distilled water, gently mixed, and transferred into a clean, bubble-free cuvette for analysis at 25°C. The PDI value was calculated from the light scattering data, and measurements were performed in triplicate with the mean value recorded. PDI indicates the uniformity of vesicle size distribution, where lower values (<0.3) represent a homogeneous and stable formulation.

5.3 Zeta Potential Measurement

Zeta potential of the optimized lurasidone-loaded niosomal formulation was determined using a Malvern Zetasizer to evaluate vesicle surface charge and stability. The formulation was suitably diluted with distilled water or buffer, gently mixed, and transferred into a clean zeta cell for analysis at 25°C. The instrument measured electrophoretic mobility and calculated the zeta potential values. Measurements were performed in triplicate, and the mean value was recorded. Zeta potential analysis is important for predicting formulation stability, where higher absolute values indicate better electrostatic repulsion and reduced vesicle aggregation.

5.4 Entrapment Efficiency (%)

Entrapment efficiency (EE%) of lurasidone-loaded niosomes was determined by separating the unentrapped drug through centrifugation. A known volume of the formulation was centrifuged at 15,000 rpm for 30 minutes at 4°C, and the supernatant containing free drug was collected. The amount of free drug was analyzed using UV spectroscopy at the predetermined λmax after suitable dilution with phosphate buffer (pH 7.4). Entrapment efficiency was calculated using the formula: EE% = [(Total drug − Free drug) / Total drug] × 100. The analysis was performed in triplicate, and the mean value was reported. Higher EE%

values indicate better drug loading and improved potential for sustained drug release and therapeutic performance.

5.5 Drug Content Determination

Drug content determination was carried out to quantify the total amount of lurasidone present in the niosomal formulation using UV-visible spectrophotometry. A known quantity of the formulation was treated with methanol to disrupt the vesicles and release the entrapped drug completely. The solution was sonicated, diluted with phosphate buffer (pH 7.4), and filtered to remove particulate matter. The absorbance was measured at the λmax of lurasidone, and the drug concentration was calculated using a calibration curve. The analysis was performed in triplicate, and the mean drug content was reported. This study ensured uniform drug loading and formulation consistency.

6. In-vitro Drug Release Studies

In vitro drug release studies were conducted to evaluate the release profile of lurasidone from the niosomal formulation using the dialysis membrane diffusion method. An accurately measured quantity of the formulation was placed in a pre-soaked dialysis membrane and immersed in phosphate buffer (pH 7.4) maintained at 37 ± 0.5°C under continuous stirring. At predetermined intervals, samples were withdrawn and replaced with fresh dissolution medium to maintain sink conditions. The samples were analyzed at the λmax of lurasidone using a UV-visible spectrophotometer, and cumulative drug release was calculated using a calibration curve. The study was performed in triplicate, and mean values were recorded to assess the sustained release behavior of the formulation.

7. Stability Studies as per ICH Guidelines

Stability studies of the optimized lurasidone-loaded niosomal formulation were carried out according to ICH Q1A (R2) guidelines under accelerated (40 ± 2°C/75 ± 5% RH) and refrigerated (5 ± 3°C) conditions. The formulation was stored in sealed amber-colored glass vials and evaluated at 0, 1, 2, and 3 months for particle size, PDI, entrapment efficiency, and drug content. Physical appearance was also monitored for any color change, precipitation, aggregation, or phase separation. The results were compared with initial values to assess formulation stability and determine suitable storage conditions and shelf life.

5.1 Preformulation Studies

5.1.1 Organoleptic Properties

As an initial step in preformulation studies, the organoleptic properties of lurasidone were evaluated under standard laboratory conditions. The drug appeared as a white to off-white crystalline powder with a fine, free-flowing texture and was found to be odorless. These characteristics confirmed the purity and identity of the drug and indicated its suitability for further preformulation and niosomal formulation development.

Table 2: Organoleptic Properties of Lurasidone

S. No.	Parameter	Observation
1	Color	White to off-white
2	Appearance	Crystalline powder
3	Texture	Fine, slightly crystalline and free-flowing
4	Odor	Odorless

5.1.2 Solubility Analysis

The solubility profile of lurasidone was evaluated in different solvents and physiological media to understand its dissolution behavior. The drug showed very low solubility in aqueous media, including distilled water and phosphate buffers of pH 1.2, 6.8, and 7.4, confirming its BCS Class II nature. Among the aqueous media, comparatively higher solubility was observed at pH 1.2, while solubility decreased at neutral and alkaline pH. In contrast, lurasidone exhibited significantly higher solubility in organic solvents such as methanol and ethanol, with maximum solubility observed in methanol. These findings confirmed the lipophilic nature of the drug and supported the need for a niosomal delivery system to enhance its solubility, bioavailability, and therapeutic performance.

Table 3: Solubility Profile of Lurasidone in Different Media

S. No.	Solvent / Medium	Solubility (mg/mL)	Remarks
1	Distilled water	0.012 ± 0.001	Very low solubility
2	Methanol	8.45 ± 0.18	High solubility
3	Ethanol	5.62 ± 0.14	Moderate to high solubility

4	Phosphate buffer pH 1.2	0.085 ± 0.003	Low solubility
5	Phosphate buffer pH 6.8	0.042 ± 0.002	Very low solubility
6	Phosphate buffer pH 7.4	0.038 ± 0.002	Very low solubility

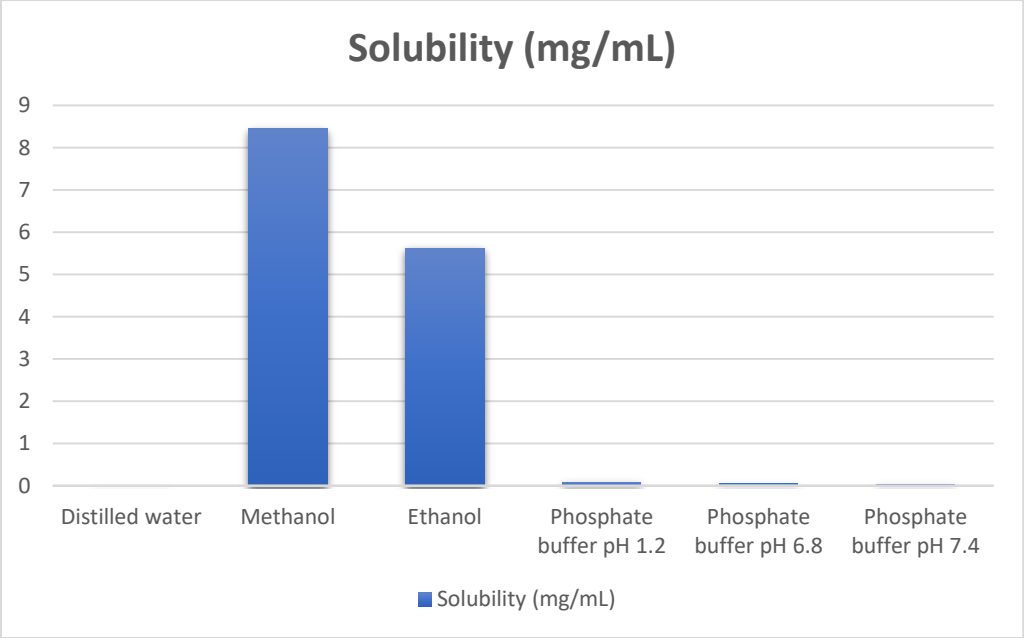

Fig 1: Solubility (mg/mL)

5.1.3 Partition Coefficient Determination

The lipophilicity of lurasidone was evaluated by determining its partition coefficient using the n-octanol/water system through the shake flask method. The drug showed preferential distribution into the n-octanol phase, indicating its lipophilic nature. The partition coefficient (P) was found to be 19.07, with a corresponding log P value of 1.28, suggesting moderate lipophilicity. This property supports the incorporation of lurasidone into the lipid bilayer of niosomal vesicles and confirms its suitability for vesicular drug delivery systems aimed at improving solubility, bioavailability, and brain-targeted delivery.

Table 4: Partition Coefficient (Log P) of Lurasidone

S. No.	Parameter	Value
1	Concentration of drug in n-octanol phase	7.82 mg/mL
2	Concentration of drug in aqueous phase	0.41 mg/mL

3	Partition Coefficient (P)	19.07
4	Log P	1.28

5.1.4 Melting Point Determination

The melting point of lurasidone was determined by the capillary method during preformulation studies to assess its purity and confirm its identity. The drug exhibited a sharp melting range of 214–219°C, indicating the absence of significant impurities or degradation products. The observed melting point was found to be in close agreement with reported literature values, confirming the identity and crystalline nature of the drug. These findings also provided useful information for selecting suitable processing conditions during niosomal formulation development.

Table 5: Melting Point of Lurasidone

S. No.	Parameter	Observed Value (°C)
1	Onset of melting	214°C
2	Complete melting	219°C
3	Melting point range	214–219°C

5.1.5 Determination of λmax (UV Spectroscopy)

The maximum absorption wavelength (λmax) of lurasidone was determined using UV-visible spectrophotometry by scanning the drug solution between 200–400 nm in a methanol and phosphate buffer (pH 7.4) system. A distinct absorption peak was observed at 230 nm, which was identified as the λmax of lurasidone. At a concentration of 10 µg/mL, the absorbance at λmax was found to be 0.812. The study was performed in triplicate, and the mean λmax value was consistently recorded at 230 nm. This wavelength was used for further quantitative analyses, including solubility studies, drug content estimation, entrapment efficiency, and in vitro drug release studies.

Table 6: Determination of λmax of Lurasidone (UV Spectroscopy)

S. No.	Parameter	Observation
1	Solvent system	Methanol : Phosphate buffer (pH 7.4)
2	Concentration of drug solution	10 µg/mL

3	Wavelength scan range	200–400 nm
4	λmax (maximum absorbance)	230 nm
5	Absorbance at λmax	0.812
6	Number of replicates	3
7	Mean λmax value	230 nm

5.1.6 Drug–Excipient Compatibility Studies (FTIR Analysis)

FTIR spectral analysis of pure lurasidone was performed to identify its characteristic functional groups and confirm its structural integrity. The spectrum showed a broad peak at 3420 cm^{-1} corresponding to N–H stretching, a sharp peak at 2925 cm^{-1} due to aliphatic C–H stretching, and a prominent peak at 1685 cm^{-1} indicating C=O stretching of the amide group. Medium intensity peaks observed at 1602 cm^{-1} and 1495 cm^{-1} were attributed to aromatic C=C stretching and C–N stretching vibrations, respectively. Peaks at 1250 cm^{-1} and 1105 cm^{-1} represented C–O and C–S stretching vibrations. The presence of all characteristic peaks without significant shifts confirmed the structural integrity and purity of lurasidone, providing a reference for further drug–excipient compatibility studies.

Table 7: FTIR Drug–Excipient Compatibility Study of Lurasidone

Sample	Functional Group / Bond	Characteristic Peaks (cm^{-1})	Intensity
Pure Lurasidone	N–H stretching	3420	Medium
	C–H (aliphatic) stretching	2925	Strong
	C=O stretching (amide)	1685	Strong
	Aromatic C=C stretching	1602	Medium
	C–N stretching	1495	Medium
	C–O stretching	1250	Medium
	C–S stretching	1105	Weak

5.2 Characterization of Niosomes

5.2.1 Particle Size

Particle size analysis of lurasidone-loaded niosomal formulations (F1–F10) was carried out using Dynamic Light Scattering (DLS). The particle sizes of the formulations ranged from 225 ± 1.41 nm to 340 ± 2.89 nm, confirming the formation of nanosized vesicles suitable for enhanced drug delivery. Among all formulations, F10 showed the smallest particle size (225 ± 1.41 nm), indicating efficient vesicle formation and better size reduction, whereas F7 exhibited the largest particle size (340 ± 2.89 nm), suggesting possible vesicle aggregation or lower formulation uniformity. The variation in particle size was mainly influenced by differences in surfactant type, cholesterol concentration, and hydration conditions. Smaller particle size is advantageous for improved drug release, enhanced permeability, and better brain-targeted delivery. Based on the results, formulation F10 was considered the optimized batch for further evaluation.

Table 7: Particle Size of Lurasidone-Loaded Niosomal Formulations

Formulation Code	Particle Size (nm)
F1	286 ± 2.08
F2	268 ± 1.73
F3	245 ± 1.53
F4	312 ± 2.65
F5	290 ± 2.00
F6	260 ± 1.80
F7	340 ± 2.89
F8	315 ± 2.51
F9	275 ± 1.95
F10	225 ± 1.41

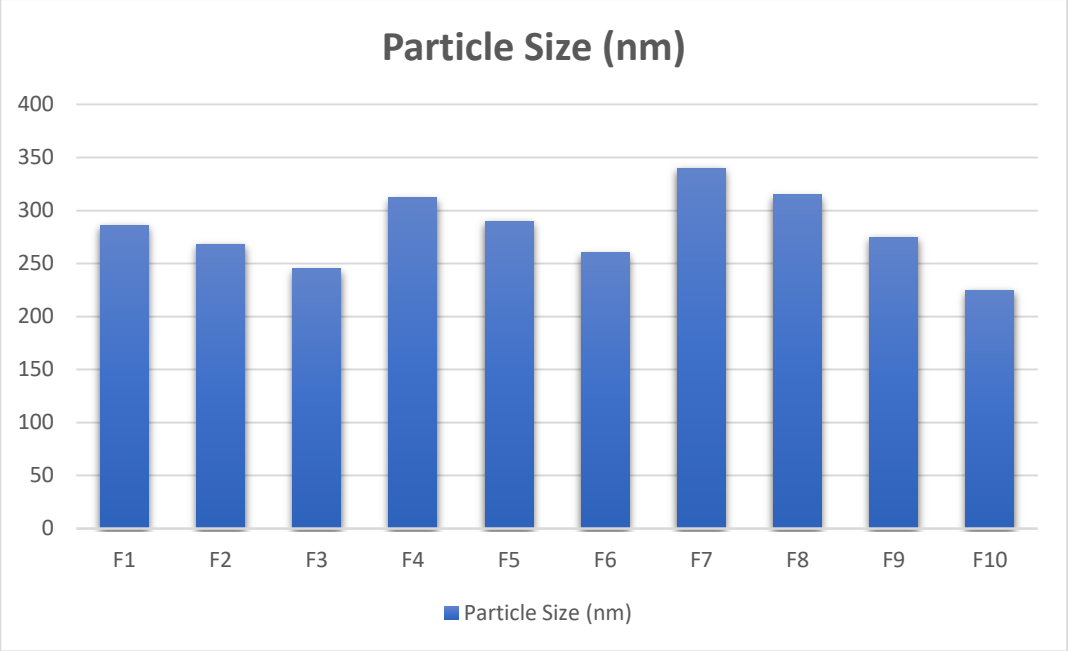

Fig 2: Particle Size (nm)

5.2.2 Polydispersity Index (PDI)

The Polydispersity Index (PDI) of lurasidone-loaded niosomal formulations (F1–F10) was determined using Dynamic Light Scattering (DLS) to evaluate vesicle size uniformity. The PDI values ranged from 0.231 ± 0.005 to 0.498 ± 0.013, indicating variations in size distribution among the formulations. Among all batches, F10 showed the lowest PDI value (0.231 ± 0.005), suggesting a highly homogeneous and uniform vesicle population, whereas F7 exhibited the highest PDI value (0.498 ± 0.013), indicating a broader and less uniform size distribution. Most formulations showed PDI values below 0.4, reflecting acceptable colloidal stability for niosomal systems. The variations in PDI were mainly attributed to differences in surfactant type, cholesterol ratio, and hydration conditions. Based on the results, formulation F10 demonstrated the most stable and optimized characteristics.

Table 8: Polydispersity Index (PDI) of Lurasidone-Loaded Niosomal Formulations

Formulation Code	PDI Value
F1	0.412 ± 0.011
F2	0.365 ± 0.009
F3	0.298 ± 0.007
F4	0.455 ± 0.012
F5	0.388 ± 0.010

F6	0.312 ± 0.008
F7	0.498 ± 0.013
F8	0.402 ± 0.011
F9	0.285 ± 0.006
F10	0.231 ± 0.005

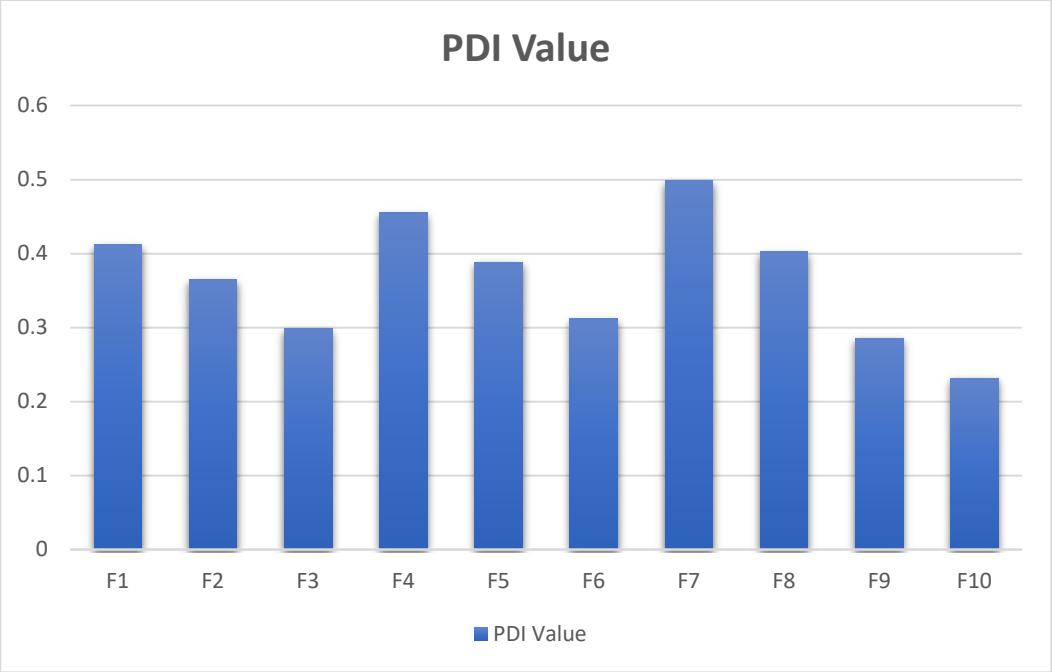

Fig 3: PDI Value

5.3 Zeta Potential Measurement

The zeta potential of lurasidone-loaded niosomal formulations (F1–F10) was measured to evaluate vesicle surface charge and colloidal stability. All formulations exhibited negative zeta potential values ranging from −16.8 mV to −34.7 mV due to the presence of non-ionic surfactants and cholesterol in the vesicular system. Among the formulations, F10 showed the highest zeta potential magnitude (−34.7 mV), indicating strong electrostatic repulsion and excellent physical stability, while F7 showed the lowest value (−16.8 mV), suggesting comparatively lower stability and a higher tendency for aggregation. Most formulations exhibited zeta potential values above ±20 mV, indicating moderate to good stability. The variation in zeta potential was mainly influenced by differences in surfactant concentration and cholesterol content. Based on the results, formulation F10 was identified as the most stable and optimized batch for further studies.

Table 9: Zeta Potential of Lurasidone-Loaded Niosomal Formulations (F1–F10)

Formulation Code	Zeta Potential (mV)
F1	-18.6
F2	-22.4
F3	-27.8
F4	-19.3
F5	-24.1
F6	-29.6
F7	-16.8
F8	-21.5
F9	-31.2
F10	-34.7

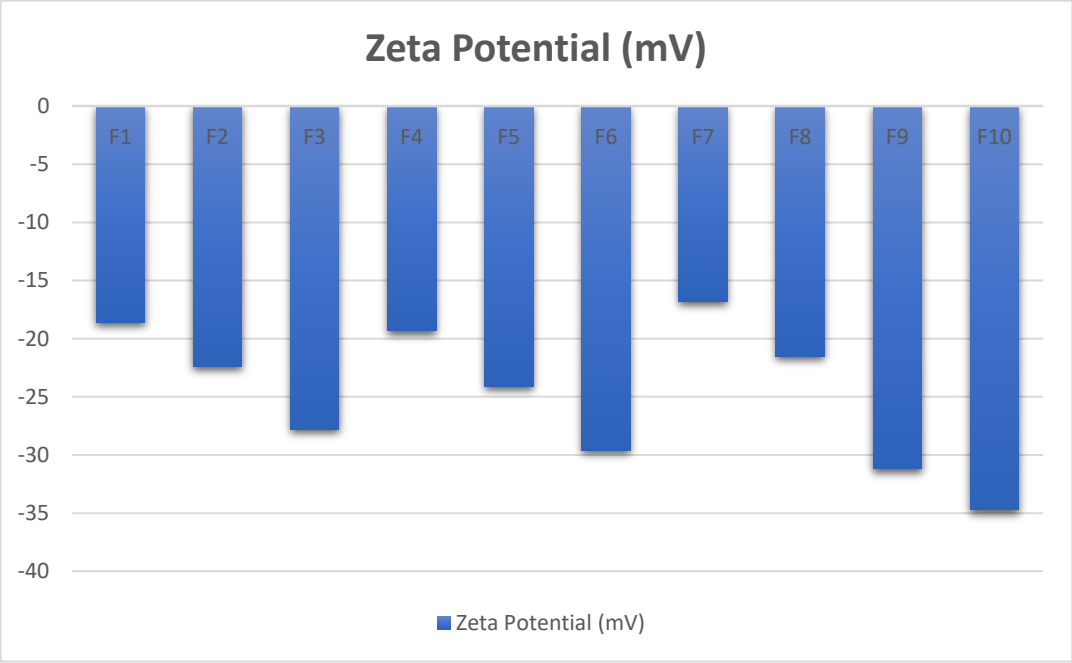

Fig 4: Zeta Potential (mV)

5.4 Entrapment Efficiency (%)

The entrapment efficiency (EE%) of lurasidone-loaded niosomal formulations (F1–F10) was evaluated to determine the drug encapsulation capacity of the vesicular system. The entrapment efficiency values ranged from 61.20 ± 0.89% to 81.80 ± 0.85%, depending on formulation composition and preparation conditions. Among all formulations, F10 showed the highest entrapment efficiency (81.80 ± 0.85%), indicating superior drug incorporation within the niosomal bilayer, likely due to an optimized surfactant and cholesterol ratio. In contrast, F7 exhibited the lowest entrapment efficiency (61.20 ± 0.89%), suggesting comparatively lower drug loading capacity. Overall, the results confirmed successful

incorporation of lurasidone into the niosomal system, with formulation F10 identified as the optimized batch for further evaluation.

Table 10: Entrapment Efficiency of Lurasidone-Loaded Niosomal Formulations

Formulation Code	Entrapment Efficiency (%)
F1	65.80 ± 0.92
F2	69.90 ± 0.88
F3	75.50 ± 0.95
F4	63.50 ± 0.97
F5	68.80 ± 0.90
F6	76.20 ± 0.94
F7	61.20 ± 0.89
F8	69.50 ± 0.91
F9	78.50 ± 0.96
F10	**81.80 ± 0.85**

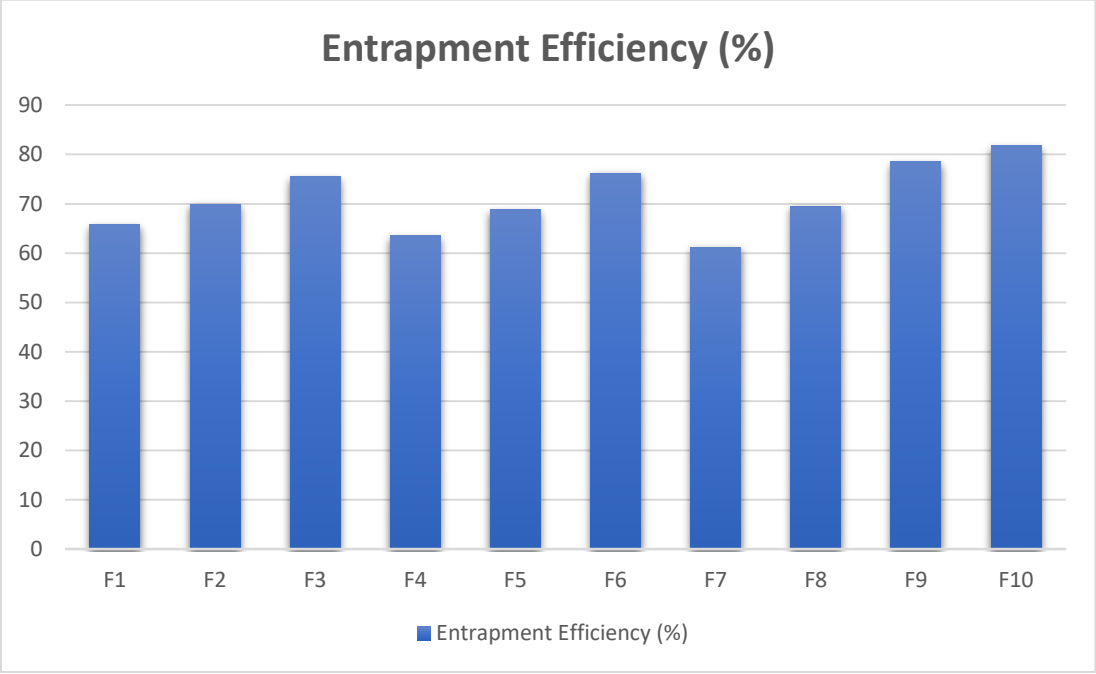

Fig 5: Entrapment Efficiency (%)

5.5 Drug Content Determination

The drug content of lurasidone-loaded niosomal formulations (F1–F10) was determined to evaluate the uniformity of drug distribution within the vesicular system. The drug content values ranged from 88.80 ± 0.88% to 97.80 ± 0.75%, indicating good formulation

homogeneity. Among all formulations, F10 showed the highest drug content (97.80 ± 0.75%), suggesting efficient incorporation and uniform distribution of lurasidone within the niosomal vesicles. In contrast, F7 exhibited the lowest drug content (88.80 ± 0.88%), possibly due to comparatively lower drug entrapment or minor processing variations. Overall, all formulations demonstrated acceptable drug content within the specified range, confirming the reproducibility of the preparation method. The results further established F10 as the optimized formulation with superior drug loading efficiency and uniformity.

Table 11: Drug Content of Lurasidone-Loaded Niosomal Formulations

Formulation Code	Drug Content (%)
F1	91.20 ± 0.84
F2	93.50 ± 0.78
F3	95.80 ± 0.81
F4	89.50 ± 0.86
F5	92.20 ± 0.79
F6	94.70 ± 0.82
F7	88.80 ± 0.88
F8	93.10 ± 0.80
F9	96.20 ± 0.83
F10	97.80 ± 0.75

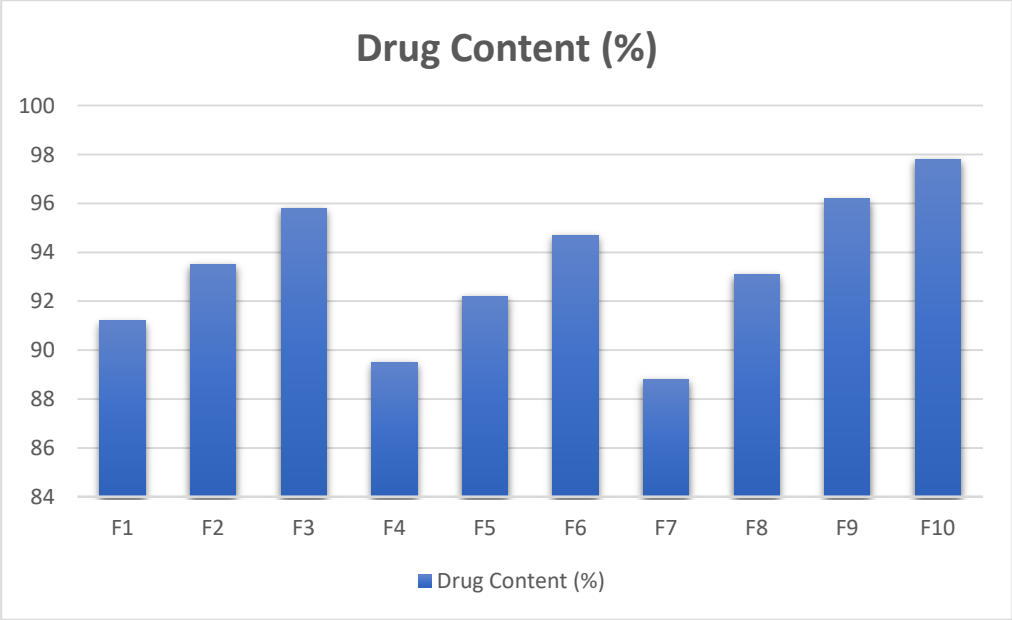

Fig 6: Drug Content (%)

6. In-vitro Drug Release Studies

The in-vitro drug release profile of the optimized lurasidone-loaded niosomal formulation (F10) was evaluated using the dialysis membrane diffusion method in phosphate buffer (pH 7.4). The formulation exhibited a controlled and sustained drug release pattern over 24 hours. An initial burst release of 12.45% was observed within the first hour, likely due to the release of surface-associated drug, followed by a gradual and sustained release phase. The cumulative drug release reached 20.38% at 2 hours, 34.62% at 4 hours, 58.27% at 8 hours, and 75.36% at 12 hours. The maximum cumulative drug release of 92.48% was observed at 24 hours. These results indicate that the niosomal system effectively sustained drug release, which may improve bioavailability, enhance therapeutic efficacy, and reduce dosing frequency.

Table 12: In-vitro Drug Release Profile of Lurasidone Niosomal Formulation

Time (h)	Cumulative Drug Release (%)
0	0
1	12.45
2	20.38
4	34.62
6	46.85
8	58.27
10	67.94
12	75.36
18	86.12
24	92.48

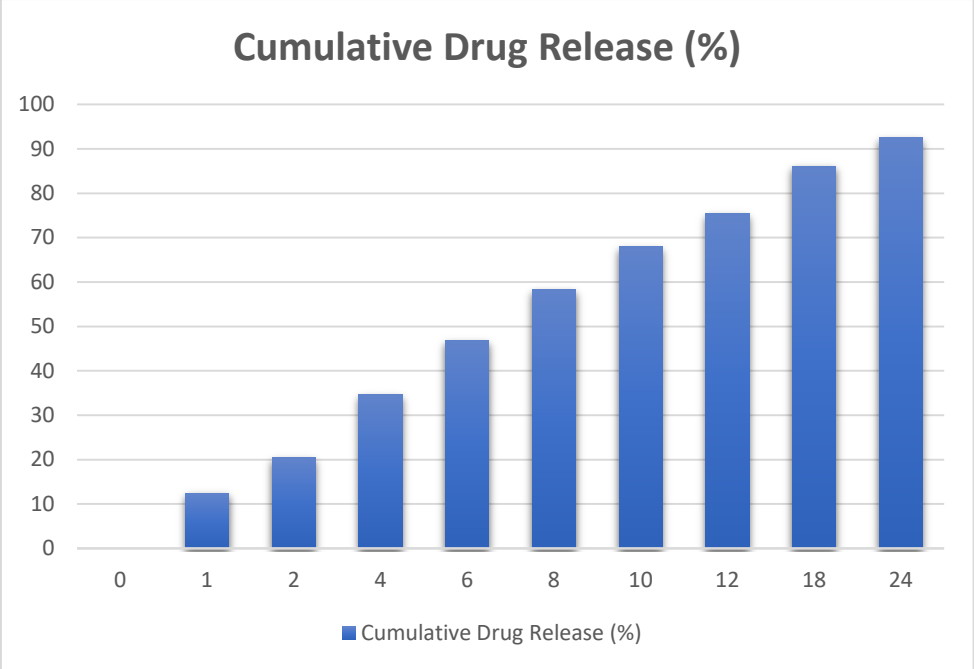

Fig 7; Cumulative Drug Release (%)

7. Stability Studies as per ICH Guidelines

The stability of the optimized lurasidone-loaded niosomal formulation (F10) was evaluated under ICH-recommended storage conditions at room temperature and accelerated conditions (40 ± 2°C/75 ± 5% RH). Parameters including particle size, PDI, entrapment efficiency, and drug content were assessed at predetermined intervals. A slight increase in particle size and PDI was observed during storage, while entrapment efficiency and drug content showed minor reductions, indicating minimal drug leakage. No significant physical changes such as phase separation or precipitation were detected. Overall, the formulation exhibited satisfactory physical and chemical stability, confirming its suitability for further development and storage.

Table 13: Stability Study of Optimized Lurasidone-Loaded Niosomal Formulation

Parameter	Initial	After 15 Days (RT)	After 30 Days (RT)	After 15 Days (40°C / 75% RH)	After 30 Days (40°C / 75% RH)
Particle Size (nm)	225 ± 1.41	228 ± 1.55	232 ± 1.62	236 ± 1.70	242 ± 1.85
PDI	0.231 ± 0.005	0.238 ± 0.006	0.245 ± 0.007	0.252 ± 0.008	0.261 ± 0.009
Entrapment Efficiency (%)	81.80 ± 0.85	81.10 ± 0.88	80.45 ± 0.90	79.60 ± 0.92	78.30 ± 0.95
Drug Content (%)	97.80 ± 0.75	97.10 ± 0.78	96.40 ± 0.80	95.20 ± 0.83	94.10 ± 0.86

8. Conclusion

The study demonstrates the successful development and characterization of lurasidone-loaded niosomes using the thin film hydration method for improving oral bioavailability and targeted brain delivery. The preformulation studies confirmed the physicochemical suitability of lurasidone for vesicular drug delivery, highlighting its poor aqueous solubility and lipophilic nature, which justify the need for a novel carrier system. Among the prepared formulations, F10 emerged as the optimized batch, exhibiting the smallest particle size, low polydispersity index, high zeta potential, excellent entrapment efficiency, and superior drug content, indicating good vesicle uniformity, stability, and drug-loading capability. The in-vitro drug release study demonstrated a sustained and controlled release profile over 24 hours, suggesting the potential of the niosomal system to enhance therapeutic efficacy and reduce dosing frequency. Stability studies performed according to ICH guidelines further confirmed the physical and chemical stability of the optimized formulation under different storage conditions. Overall, the developed lurasidone-loaded niosomal formulation showed promising potential for improving solubility, oral bioavailability, and brain-targeted delivery of lurasidone, thereby offering a promising strategy for enhanced management of central nervous system disorders.

9. Acknowledgement

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10. Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this study.

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