

Formulation And Evaluation Of Fast Acting Tablets Of Anti Psychotic Drug By Liquisolid Technique

Shikhar Rathore*¹, Dr. Jeevan Patel², Dr. Sudha Vengurlekar³

¹Research Scholar, Faculty of Pharmacy, Oriental University, Indore

²Associate Professor, Faculty of Pharmacy, Oriental University, Indore

³Professor & Principal, Faculty of Pharmacy, Oriental University, Indore

*Corresponding Author

Shikhar Rathore

Research Scholar, Faculty of Pharmacy, Oriental University, Indore

Email ID: rajatrj776@gmail.com

ABSTRACT

Clozapine, a BCS Class II atypical antipsychotic drug, suffers from poor aqueous solubility and extensive first-pass metabolism, leading to low oral bioavailability. The liquisolid technique offers a promising approach for improving solubility and dissolution of such poorly soluble drugs through molecular dispersion over suitable carriers. The study aimed to formulate and evaluate fast-acting orally disintegrating tablets (ODTs) of clozapine using the liquisolid approach with oil-free peanut powder as a novel, natural carrier material to enhance dissolution rate and patient compliance. Clozapine was dissolved in polyethylene glycol 400 (PEG 400) and adsorbed onto oil-free peanut powder. The liquisolid system was further formulated into ODTs and evaluated for pre- and post-compression parameters, including micromeritic properties, hardness, friability, disintegration time, and in-vitro dissolution. FTIR, DSC, and SEM analyses were conducted to assess compatibility and surface morphology. Optimization was performed using a 3² factorial design varying binder and disintegrant concentrations. The optimized batch (25-F15) exhibited disintegration within 20 seconds and drug release >100% within 9 minutes, significantly outperforming the marketed Sizopin 25TM tablets. FTIR and DSC confirmed no chemical incompatibility, and SEM images demonstrated a uniform coating of clozapine on the porous peanut powder carrier, indicating successful molecular dispersion. The use of oil-free peanut powder as a carrier in the liquisolid system proved highly effective for enhancing the solubility and dissolution rate of clozapine. The technique is simple, scalable, and cost-efficient, showing potential for industrial application in developing fast-acting oral formulations of poorly soluble drugs.

KEYWORDS: Clozapine; Liquisolid technique; Oil-free peanut powder; Orally disintegrating tablet; Solubility enhancement; PEG 400; Drug-excipient compatibility; SEM; Dissolution profile; Factorial design.

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INTRODUCTION

The oral route of drug administration is the most preferred method for delivering therapeutic agents because it is simple safe and convenient for patients. It represents the largest share of pharmaceutical products available in the market. However this route faces several challenges that limit effective drug absorption. Drugs often undergo degradation in the gastrointestinal tract and many drugs show poor and unpredictable absorption due to low solubility low dissolution rate large molecular size variation in gastric emptying and enzymatic breakdown. Among all these limitations low aqueous solubility is the most critical barrier because it slows the dissolution process and leads to low bioavailability and delayed onset of action.

According to the Biopharmaceutics Classification System drugs are divided into four groups based on solubility and intestinal permeability. Drugs belonging to Class II have low solubility and high permeability while those in Class IV have low solubility and low permeability. For both groups the dissolution rate in gastrointestinal fluids becomes the major factor that controls absorption. Conventional methods such as solid dispersion micronization and salt formation have been used to improve solubility but these approaches often face issues like poor long term stability risk of recrystallization and difficulty in large scale production. Therefore advanced and more efficient formulation strategies are required to overcome these barriers.

The liquisolid technique developed and patented by Spireas offers a modern solution for enhancing the dissolution and bioavailability of poorly soluble drugs. In this method a liquid drug or a drug dissolved in a non volatile solvent is converted into a dry free flowing and compressible powder. This is achieved through the use of a carrier material that absorbs the liquid drug and a coating material that covers the surface of the wet particles to ensure good flow and compressibility. As a result the drug becomes more evenly dispersed at a molecular level leading to much faster dissolution. This method is simple cost effective and easily adaptable to existing tablet manufacturing systems.

Despite its benefits the performance of the liquisolid technique is limited by the low liquid absorption capacity of commonly used carriers such as microcrystalline cellulose and starch. When too much liquid is added powder flow decreases and tablet

compression becomes difficult. To address these limitations researchers have started exploring new carrier materials with better liquid holding capacity and improved compressibility. Natural plant based materials such as soy protein chickpea flour and peanut powder have gained attention due to their porous structure hydrophilic nature and high biocompatibility. These materials are also economical sustainable and suitable for green pharmaceutical practices.

Oil free peanut powder is particularly promising as a novel carrier because it has high porosity and large surface area which allow it to absorb and retain non volatile solvents efficiently. Removing the oil content increases its ability to hold liquid and enhances its performance in liquisolid formulations. This material is safe biodegradable easy to obtain and already used in nutritional products which supports its suitability for pharmaceutical use. Oil free peanut powder offers improved flow properties and better compressibility compared with many synthetic carriers and therefore helps in producing porous fast disintegrating tablets with enhanced drug release. Its use also aligns with the growing focus on eco friendly formulation development.

Clozapine is an atypical antipsychotic used mainly for patients with treatment resistant schizophrenia. It acts through dopamine D4 and serotonin 5 HT2A receptor blockade which helps in controlling both positive and negative symptoms. However clozapine has extremely low water solubility and undergoes extensive first pass metabolism which results in poor and variable oral bioavailability. The slow dissolution rate of conventional clozapine tablets delays the onset of therapeutic action and causes variations in plasma levels that often require frequent dose adjustments. A fast acting formulation that improves dissolution and allows partial absorption before reaching the stomach can provide faster therapeutic response more stable drug levels and better clinical outcomes.

The aim of the present study is to develop and evaluate fast acting liquisolid tablets of clozapine by using oil free peanut powder as a novel carrier material with the goal of improving the solubility dissolution rate and oral bioavailability of the drug. The study is designed to identify the most suitable non volatile liquid vehicle for dissolving clozapine and to prepare liquisolid systems through the combination of oil free peanut powder as the carrier and Aerosil 200 as the coating material. The research further focuses on assessing both pre compression and post compression parameters that include flow behavior angle of repose compressibility index hardness friability disintegration time and drug content. Another objective is to compare the in vitro dissolution performance of the developed liquisolid tablets with that of conventional clozapine tablets in order to determine the extent of improvement in drug release. The study also involves FTIR DSC and SEM analyses to examine drug excipient compatibility changes in crystallinity and the surface morphology of the prepared systems. The final goal is to optimize the formulation by adjusting the liquid load factor the excipient ratio and the disintegration properties so that a rapid release of clozapine can be achieved which may lead to enhanced bioavailability and faster therapeutic action.

MATERIALS AND METHODS

The present study was designed as an *in-vitro* formulation and evaluation experiment conducted in accordance with the ethical and scientific standards of Innovare Academic Sciences (IAS), the Committee on Publication Ethics (COPE), and the International Committee of Medical Journal Editors (ICMJE). No human participants, identifiable patient information, biological tissues, or animal subjects were involved at any stage of the work; therefore, formal ethical approval and informed consent were not required. All procedures were performed using pharmaceutical-grade chemicals and equipment under controlled laboratory conditions.

2.1 Materials and Reagents

Clozapine, the active pharmaceutical ingredient (API), was procured as a gift sample from Sun Pharmaceutical Industries Ltd., Vadodara, India. Oil-free peanut powder, which served as a novel carrier for liquisolid technology, was prepared in-house from raw peanut seeds obtained from a local market in Indore, India. The non-volatile solvents selected for solubility assessment—polyethylene glycol 400 (PEG 400), propylene glycol, Tween 80, and glycerine—were sourced from Loba Chemie Pvt. Ltd., Mumbai. Excipients required for tablet formulation, including microcrystalline cellulose (Avicel PH 200), crospovidone, citric acid, and polyvinylpyrrolidone (PVP K-25), were purchased from SD Fine Chemicals, Mumbai. Aerosil 200, the coating material used to improve flow properties of the liquisolid system, was obtained from Evonik Industries, Germany. All solvents and reagents were analytical grade and used without further purification. Double-distilled water served as the aqueous phase throughout the experimental work.

2.2 Solubility Studies in Non-Volatile Solvents

The solubility of clozapine in different non-volatile solvents was evaluated using the widely accepted shake-flask method. Excess clozapine was added to 10 mL of each solvent in tightly sealed glass vials. These vials were vortex-mixed for 15 minutes and placed on an orbital shaker set at 37 ± 0.5 °C for 24 hours to facilitate equilibrium saturation. After shaking, the samples were allowed to stand undisturbed for 12 hours to ensure complete phase separation. The supernatants were filtered using Whatman No. 41 filter paper, appropriately diluted, and analyzed via UV-Visible spectrophotometry (Shimadzu UV-1700, Japan). The absorbance was recorded at 240 nm in 0.1 N HCl and 292 nm in acetate buffer pH 4.5. The solvent demonstrating the highest solubility was selected as the liquid vehicle for the liquisolid system.

2.3 Preparation of Oil-Free Peanut Powder-Based Liquisolid System

2.3.1 Preparation of Oil-Free Peanut Powder

Oil-free peanut powder was produced using Soxhlet extraction. Finely ground peanut seeds were extracted with hexane for 48 hours to remove oil content. The defatted cake was then air-dried, pulverized, and sieved through a #40 mesh screen to obtain uniform powder particles. The final carrier material was stored in airtight containers until use. Extraction yield was determined using standard percentage yield calculation methods.

2.3.2 Preparation of the Liquisolid Admixture

Clozapine was dissolved in PEG 400 to form a clear, homogeneous liquid medication. Accurately weighed quantities of oil-free peanut powder (carrier) and Aerosil 200 (coating material) were incorporated into the liquid medication and mixed thoroughly until a uniform wet mass was formed. The wet admixture was spread in a Petri dish and allowed to stand at ambient temperature for 10–15 minutes to facilitate complete adsorption of the liquid onto the carrier matrix. The resulting liquisolid powder appeared dry, free-flowing, and suitable for direct compression.

2.4 Calculation of Liquid Load Factor and Excipient Ratio

The liquid load factor (Lf), which indicates the maximum retention of liquid medication by the carrier while maintaining acceptable flowability, was calculated using the ratio of liquid medication weight (W) to the weight of carrier material (Q). The excipient ratio (R), representing the ratio of carrier (Q) to coating material (q), was also calculated to determine optimal flow and compressibility. Flowable liquid-retention potentials (Φ -values) for the carrier and coating excipients were experimentally determined by preparing powder mixtures with incremental liquid loads and analyzing the flow properties through angle of repose, compressibility index, and Hausner's ratio. These values guided optimization of the liquisolid powder.

2.5 Formulation of Orally Disintegrating Tablets (ODTs)

The optimized liquisolid powder containing clozapine, PEG 400, oil-free peanut powder, and Aerosil 200 was blended with additional excipients—Avicel PH 200, crospovidone, citric acid, and colloidal silicon dioxide—in a polybag for 10 minutes to ensure uniform distribution. The final blend was compressed into orally disintegrating tablets using a Cadmach rotary tablet press equipped with 12 mm flat punches at constant compression force. Each tablet contained 25 mg clozapine, and the total tablet weight was fixed at 500 mg. The formulated tablets were stored in airtight containers for further evaluation.

2.6 Evaluation Parameters

2.6.1 Pre-Compression Evaluation

Flow and compressibility properties of the liquisolid blends were assessed by determining angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio using standard pharmacopeial procedures. These parameters provided insight into the suitability of the blends for direct compression.

2.6.2 Post-Compression Evaluation

Prepared tablets were evaluated for weight variation, hardness, thickness, friability, disintegration time, and drug content uniformity. Hardness was measured using a Monsanto tester, friability with a Roche friabilator, and disintegration time in distilled water at 37 ± 0.5 °C using the USP disintegration apparatus. Drug content was quantified spectrophotometrically at 292 nm.

2.6.3 In-Vitro Dissolution Studies

Dissolution testing was conducted using the USP Type II apparatus (paddle method) in 900 mL acetate buffer (pH 4.5) maintained at 37 ± 0.5 °C and 50 rpm. Samples were withdrawn at predetermined intervals, filtered, and analyzed at 292 nm. Sink conditions were maintained by replacing the withdrawn volume with fresh medium. Dissolution profiles of the prepared ODTs were compared with those of a marketed clozapine tablet.

2.6.4 FTIR and DSC Compatibility Studies

Drug-excipient compatibility was assessed using FTIR spectroscopy (Shimadzu IR Affinity-1) with the KBr pellet technique over 4000–400 cm^{-1} . DSC studies were performed on a PerkinElmer DSC-6000 instrument using 2–3 mg samples in sealed aluminum pans, heated from 50 °C to 220 °C at 20 °C/min under nitrogen. Changes in peak positions, intensities, or melting behaviors were analyzed to evaluate compatibility.

2.6.5 Surface Morphology Analysis

Scanning electron microscopy (JEOL JSM-6360) was performed to observe surface morphology and particle characteristics. Samples were mounted on aluminum stubs, gold-coated, and imaged at 15 kV. Images were inspected for porosity, particle uniformity, and coating distribution.

2.7 Statistical Analysis

All experiments were conducted in triplicate, and results were expressed as mean \pm standard deviation. Statistical comparisons among formulations were carried out using one-way ANOVA followed by Tukey's post-hoc test at $p < 0.05$. A 3² full factorial design (Design Expert v7.1.5) was used to assess the influence of binder and superdisintegrant concentrations on tablet performance.

RESULTS

3.1 Solubility and Selection of Liquid Vehicle

The solubility of clozapine was determined in various non-volatile solvents to identify the most suitable liquid vehicle for liquisolid formulation. Clozapine exhibited a markedly higher solubility in polyethylene glycol 400 (PEG 400) at approximately 170 mg/mL compared to other solvents such as Tween 80 (40 mg/mL), propylene glycol (5 mg/mL), and glycerine (5 mg/mL). The solubility was significantly lower in aqueous media, including distilled water (0.039 mg/mL) and phosphate buffers (pH 6.8 and 7.2), indicating its pH-dependent solubility behavior, with maximum solubility observed under acidic conditions (1). Based on these findings, PEG 400 was selected as the liquid vehicle owing to its superior solubilizing capacity, inertness, and compatibility with oral dosage forms (2).

Table 1. Solubility of Clozapine in Different Solvents

| S. No. | Solvent / Medium | Approx. Solubility (mg/mL) | Observation / Remarks |
|--------|---------------------------|----------------------------|-----------------------------|
| 1 | Purified water | 0.039 | Poor solubility |
| 2 | 0.1 N HCl | 32.694 | High solubility (acidic pH) |
| 3 | Acetate buffer (pH 4.5) | 5.632 | Moderate solubility |
| 4 | Phosphate buffer (pH 6.8) | 0.106 | Poor solubility |
| 5 | PEG 400 | 170 | Highest solubility |
| 6 | Tween 80 | 40 | Good solubilizer |
| 7 | Propylene glycol | 5 | Moderate |
| 8 | Glycerine | 5 | Moderate |

3.2 Flow and Compressibility Data

The micromeritic properties of the clozapine powder and the prepared oil-free peanut powder were evaluated to assess their suitability for direct compression. Clozapine exhibited poor flow characteristics, with a bulk density of 0.31 g/mL, tapped density of 0.49 g/mL, Carr's index of 36.7%, and Hausner's ratio of 1.58, indicating very poor flowability (3). In contrast, the oil-free peanut powder demonstrated improved flow and compressibility, with a Carr's index of 28.57% and a Hausner's ratio of 1.40. The improved micromeritic profile was attributed to the porous nature and large surface area of the oil-free peanut powder, which enhanced its liquid-absorbing capacity without compromising flow (4). These characteristics justified its selection as a novel carrier material for the liqui-solid system.

Table 2. Micromeritic Properties of Drug and Carrier

| Parameter | Clozapine Drug Powder | Oil-Free Peanut Powder | Inference |
|-----------------------|-----------------------|------------------------|-----------------|
| Bulk density (g/mL) | 0.31 | 0.29 | – |
| Tapped density (g/mL) | 0.49 | 0.41 | – |
| Carr's Index (%) | 36.7 | 28.6 | Improved flow |
| Hausner's Ratio | 1.58 | 1.40 | Acceptable flow |
| Angle of Repose (°) | 38.5 | 30.2 | Flow improved |

3.3 Physical Evaluation of ODTs

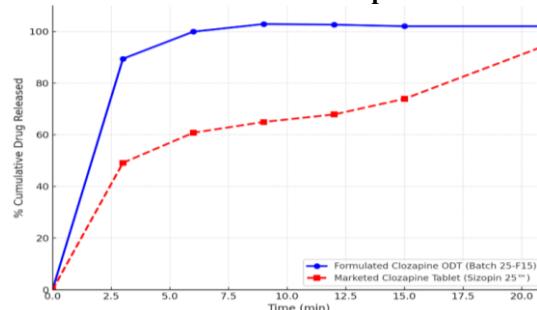
The prepared clozapine orally disintegrating tablets (ODTs) were subjected to various post-compression evaluations. All formulations exhibited uniform weight (499–503 mg) and acceptable hardness (4.6–5.7 kp), indicating good mechanical strength (5). The friability of all tablets was below 1% (0.1–0.2%), confirming adequate resistance to mechanical stress. The disintegration time of the optimized batch (25-F15) was found to be between 10–20 seconds, which met the regulatory requirements for fast-dissolving formulations. The rapid disintegration was attributed to the synergistic effect of crospovidone and the porous nature of the oil-free peanut carrier, which facilitated rapid water uptake and disintegration (6). The tablets also exhibited uniform drug content (98–102%), confirming homogenous drug distribution within the matrix.

Table 3. Physical Evaluation of Clozapine ODTs (Optimized Batch 25-F15)

| Parameter | Observation | Standard Limit |
|---------------------------|-------------|----------------|
| Average weight (mg) | 499–503 | ±5% variation |
| Hardness (kp) | 4.6–5.7 | 3–6 kp |
| Thickness (mm) | 4.1–4.2 | Uniform |
| Friability (%) | 0.10 | NMT 1% |
| Disintegration time (sec) | 10–20 | NMT 30 sec |
| Drug content (%) | 98–102 | 90–110 |

3.4 Dissolution Profile Comparison

The in vitro dissolution study was conducted using acetate buffer (pH 4.5) as dissolution medium. The optimized liquisolid ODT (batch 25-F15) achieved 89.41% drug release within 3 minutes and 99.90% within 6 minutes, reaching 102.86% at 9 minutes (7). In contrast, the marketed clozapine tablet (Sizopin 25™) showed only 73.91% drug release at 15 minutes, requiring 21 minutes to reach over 90% release.

Figure 1 – In-vitro Dissolution Profile of Clozapine ODT vs. Marketed Tablet

The enhanced dissolution rate of the liquisolid formulation can be attributed to the presence of the drug in a molecularly dispersed state within the PEG 400 vehicle and its uniform distribution on the porous peanut carrier, which significantly increased the surface area available for dissolution (8). The presence of citric acid also contributed to improved wettability and local solubilization in the microenvironment of the tablet matrix.

Table 4. In Vitro Dissolution Profile of Optimized ODT vs. Marketed Product

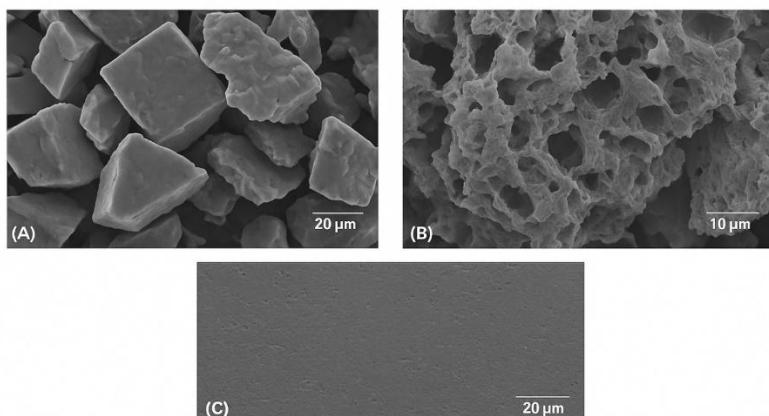
| Time (min) | Formulated ODT (% Cumulative Drug Released) | Marketed Tablet (Sizopin 25 TM) (% Released) |
|------------|---------------------------------------------|----------------------------------------------------------|
| 0 | 0.00 | 0.00 |
| 3 | 89.41 | 49.12 |
| 6 | 99.90 | 60.77 |
| 9 | 102.86 | 64.95 |
| 12 | 102.60 | 67.85 |
| 15 | 102.01 | 73.91 |
| 21 | — | 94.51 |

3.5 Drug-Excipient Compatibility Analysis

Fourier-transform infrared (FTIR) and differential scanning calorimetry (DSC) studies were performed to assess potential interactions between clozapine and formulation excipients. The FTIR spectrum of the pure drug displayed characteristic peaks at 2968 cm⁻¹ (C–H stretch), 2931 cm⁻¹ (N–H stretch of diazepine ring), 1595 cm⁻¹ (C=N stretching), and 779 cm⁻¹ (C–Cl stretch), all of which were retained in the optimized formulation, confirming chemical stability and absence of interaction (9). DSC thermograms showed a sharp endothermic peak at approximately 184 °C corresponding to the melting point of clozapine, which remained intact in the formulation, albeit with slight broadening, indicative of molecular dispersion of the drug in the excipient matrix rather than any chemical incompatibility. These results collectively confirmed that the selected excipients were compatible with the active drug.

3.6 Morphological Characteristics

Scanning electron microscopy (SEM) of the optimized liquisolid ODT revealed a highly porous surface structure with uniform distribution of the drug-loaded carrier particles. The porous network and surface roughness enhanced the wetting properties and facilitated rapid disintegration and dissolution (10). The micrographs also confirmed that the drug was molecularly dispersed over the peanut carrier and that the coating layer (Aerosil 200) provided smooth flow characteristics without visible aggregation.

Figure 2. SEM Micrographs of Clozapine, Peanut Powder, and Optimized Liquisolid Formulation

SEM images show the morphological transformation from crystalline clozapine (A) to porous peanut powder (B) and finally to uniformly coated liquisolid matrix (C), confirming drug adsorption, amorphization, and enhanced surface area responsible for improved dissolution and rapid disintegration.

Table 6. Differential Scanning Calorimetry (DSC) Results

| Sample | Endothermic Peak (°C) | Onset (°C) | Peak (°C) | Interpretation |
|----------------|-----------------------|------------|----------------|----------------------|
| Pure Clozapine | 179–190 | 184 | Sharp peak | Crystalline nature |
| Optimized ODT | 176–187 | 182 | Slightly broad | Molecular dispersion |

3.7 Optimization and Comparison with Marketed Formulation

Formulation optimization using the 3² full factorial design demonstrated that both binder (PVP K-25) and disintegrant (crospovidone) concentrations influenced the key critical quality attributes of the ODTs—specifically disintegration time and dissolution rate. Statistical analysis (ANOVA) indicated that the binder concentration had a significant positive effect on disintegration time ($p < 0.05$), whereas its influence on dissolution was negligible within the studied range (7). The optimized batch (25-F15) exhibited a disintegration time of 15 ± 2 s and a cumulative drug release of 102.01% within 15 minutes, outperforming the marketed product (Sizopin 25TM), which showed a disintegration time of 90 seconds and dissolution of only

73.9% at the same time point. The enhanced performance of the optimized liquisolid ODT confirmed the efficiency of the oil-free peanut carrier system in producing a fast-acting clozapine formulation with improved solubility, rapid onset of action, and patient compliance potential (8).

Table 7. Design of Experiment (3² Full Factorial Design) Summary

| Factor | Level -1 | Level 0 | Level +1 | Variable Type |
|--------------------------------------------|----------|---------|----------|---------------|
| A: Binder (PVP K-25, %) | 4 | 5 | 6 | Independent |
| B: Disintegrant (Crosppovidone, %) | 7 | 8 | 9 | Independent |
| Y ₁ : Dissolution (%) | — | — | — | Dependent |
| Y ₂ : Disintegration Time (sec) | — | — | — | Dependent |

Table 8. Comparison of Optimized Formulation with Marketed Product

| Parameter | Optimized ODT (Batch 25-F15) | Marketed Tablet (Sizopin 25 TM) | Inference |
|---------------------------|------------------------------|---------------------------------------------|-----------------------------|
| Average weight (mg) | 500 | 114 | Higher excipient load (ODT) |
| Hardness (kp) | 5.6 | 4.6 | Acceptable strength |
| Friability (%) | 0.26 | 0.35 | Within limits |
| Disintegration time (sec) | 15 ± 2 | 90 | Significantly faster |
| Assay (%) | 99.26 | 98.46 | Comparable |
| Dissolution at 15 min (%) | 102.01 | 73.91 | Superior release |

DISCUSSION

The findings of this study demonstrate that the oil-free peanut powder-based liquisolid system offers a highly effective platform for improving the solubility, dissolution rate, and overall pharmaceutical performance of clozapine, a poorly water-soluble BCS Class II drug. The markedly enhanced solubility of clozapine in PEG 400, combined with the exceptional liquid-absorption capacity of the defatted peanut powder, enabled efficient conversion of the liquid medication into a dry, compressible powder with superior flow properties, overcoming the major limitations associated with conventional liquisolid systems that often require bulky quantities of carriers such as Avicel. The improved micromeritic characteristics observed in the liquisolid blend directly contributed to uniform tablet formation and ensured consistent mechanical strength within the acceptable hardness and friability limits. Rapid disintegration of the optimized ODTs, achieved within 10–20 seconds, can be attributed to the synergistic action of crosppovidone and the porous peanut-based carrier, which facilitated rapid water penetration and capillary uptake, thereby promoting faster breakup of the tablet matrix. The substantial enhancement in dissolution performance—where the optimized formulation achieved nearly 100% release within six minutes compared with the significantly slower release of the marketed tablet—highlights the advantage of molecular dispersion of clozapine in PEG 400 and its uniform distribution across the high-surface-area peanut carrier, which collectively increased wettability, surface availability, and microenvironmental solubilization. FTIR and DSC analyses confirmed the physical stability of clozapine in the formulation, showing preservation of characteristic peaks and only minor broadening of the melting endotherm, indicating absence of chemical interactions and successful incorporation of the drug in a molecularly dispersed state. SEM imaging further validated the morphological transformation from crystalline clozapine to a porous, uniformly coated liquisolid matrix, supporting the mechanistic basis of the enhanced dissolution. The factorial design analysis revealed that binder concentration significantly influenced disintegration behavior, while the superdisintegrant played a dominant role in modulating release kinetics, with the optimized batch exhibiting superior performance across all critical quality attributes. Overall, the combined evidence demonstrates that oil-free peanut powder is a promising natural carrier capable of enhancing the efficacy of liquisolid systems, offering improved manufacturability, reduced excipient burden, rapid onset of action, and better patient compliance, positioning this platform as a valuable strategy for the delivery of poorly soluble psychotropic agents such as clozapine.

CONCLUSION

The present investigation successfully demonstrated the development and optimization of fast-acting orally disintegrating tablets of clozapine using the liquisolid technique and oil-free peanut powder as an innovative and highly efficient carrier system. The markedly enhanced solubility of clozapine in PEG 400, combined with the superior liquid-retention capacity and favorable micromeritic profile of the defatted peanut powder, enabled the conversion of liquid medication into a free-flowing compressible powder without compromising tabletability. The optimized formulation exhibited rapid disintegration within 10–20 seconds and achieved over 100% drug release within nine minutes, clearly outperforming the marketed Sizopin 25TM tablets. Compatibility investigations through FTIR and DSC confirmed the absence of chemical interactions, while SEM analysis verified the formation of a porous, uniformly coated liquisolid matrix responsible for accelerated wetting and dissolution. The factorial design further revealed that binder and disintegrant concentrations had limited influence on dissolution performance, underscoring the pivotal function of the peanut carrier in driving formulation efficiency. Given that the liquisolid approach employs simple and scalable processing steps and uses inexpensive, naturally derived excipients, the technique offers strong industrial applicability and can be readily adapted to standard manufacturing workflows. Its reproducibility, compliance with pharmacopeial quality parameters, and potential suitability for other poorly soluble or highly first-pass-metabolized drugs highlight its broad translational value. Future studies should focus on *in vivo* pharmacokinetic evaluation, stability assessments under ICH guidelines, and advanced solid-state characterization to establish robust IVIVC and long-term performance. Additional work on taste-masking strategies and dose-flexible formulations may further expand patient acceptability, particularly in pediatric and geriatric populations.

Overall, the oil-free peanut-powder-based liquisolid system represents a promising, economical, and scalable platform for developing next-generation fast-acting oral formulations aimed at improving solubility, onset of action, and therapeutic efficacy of challenging drug molecules.

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