RESEARCH PAPER

In Vitro–In Vivo Correlation Studies of Promethazine Theoclate Orodispersible Liquisolid Compact Tablets Prepared by Direct Compression

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Abstract
The study aimed to formulate promethazine theoclate orodispersible liquisolid compact tablets to enhance dissolution rate, improve oral absorption, and establish an *in vitro–in vivo* relationship for rapid therapeutic effect. Liquisolid compacts containing 10 mg of drug were prepared by direct compression using PEG 400 as the liquid vehicle, microcrystalline cellulose as carrier, and Aerosil 200 as coating material. Six formulations (F1–F6) were developed with excipient ratios of 5 and 10 and loading factors of 0.82 and 0.56. Dissolution studies were performed in 900 mL phosphate buffer (pH 6.8) at 37 ± 0.5 °C and 50 rpm. All formulations showed rapid release, with 5.5–6.8% drug liberated at 1 min and 91.7–98.9% within 20 min. F4 exhibited the highest release (98.9% at 20 min). The optimized formulation F4 was evaluated in rabbits and compared with a marketed tablet. *In-vivo*, F4 achieved Cmax of 2.34 µg/mL at Tmax of 2 hrs, with $AUC_{(0–12)}$ of 15.7 µg·hr/mL and half-life of 2.47hrs. The formulation produced faster and higher early plasma levels than the marketed product. The optimized formulation exhibited a relative bioavailability of 307.6%, indicating approximately a 3.08-fold increase in systemic exposure compared with the marketed formulation after correction for dose. The *in-vitro–in-vivo* correlation analysis demonstrated a strong positive relationship between the *in- vitro* drug release profile of the optimized formulation and the corresponding *in-vivo* absorption profile. Orodispersible liquisolid technology markedly enhanced dissolution and promoted rapid absorption of promethazine theoclate. Formulation F4 was identified as optimal, delivering near-complete release within 20 min and providing quick systemic availability suitable for conditions requiring immediate action.

Keywords: Promethazine theoclate; Orodispersible tablets; Liquisolid compact; *In vitro–in vivo* correlation
How to cite this article: Babu N, Nair SS, Mathews MM., In Vitro–In Vivo Correlation Studies of Promethazine Theoclate Orodispersible Liquisolid Compact Tablets Prepared by Direct Compression. Int J Drug Deliv Technol. 2026;16(76s): 1760-1768; DOI: 10.25258/ijddt.16.76s.166.

Introduction

Oral drug delivery remains the most preferred route of administration because of its convenience, patient compliance, and cost effectiveness [1, 2]. Many drugs administered orally suffer from delayed onset of action due to slow dissolution and limited bioavailability, particularly when the drug possesses poor aqueous solubility [3]. Promethazine theoclate, an antihistaminic agent widely used for the management of allergic conditions, nausea, and vomiting, requires rapid therapeutic availability to achieve prompt symptom relief [4]. Conventional tablet formulations may not always provide the desired onset, especially in paediatric, geriatric, or dysphagic patients who experience difficulty swallowing solid dosage forms. These limitations have prompted the development of patient-friendly dosage systems capable of disintegrating quickly in the oral cavity while enhancing dissolution characteristics.

Orodispersible tablets (ODTs) have emerged as an attractive alternative to conventional oral dosage forms [5]. They are designed to disintegrate or dissolve rapidly in saliva without the need for water, thereby improving compliance and convenience. The rapid breakup of the tablet increases the surface area available for dissolution and may promote faster absorption and earlier pharmacological response [6]. Despite these advantages, formulating ODTs for poorly soluble drugs remains challenging, as disintegration alone does not guarantee improved dissolution [7]. Therefore, strategies that simultaneously enhance wettability, surface exposure, and solubilization are essential for achieving optimal performance.

The liquisolid compact technique represents one such promising approach. In this system, a drug is dispersed or dissolved in a non-volatile liquid vehicle and subsequently converted into a dry, free-flowing, and compressible powder by blending with suitable carrier and coating materials [8]. This transformation enhances the drug's apparent solubility and improves wetting properties, leading to faster dissolution rates [9]. Moreover, the liquisolid method allows uniform drug distribution at the molecular level, which can contribute to improved release reproducibility. When combined with the orodispersible concept, liquisolid systems can provide both rapid tablet disintegration and enhanced drug availability, making them particularly useful for drugs requiring quick onset of action [10].

Several formulation variables influence the performance of liquisolid ODTs, including the excipient ratio between carrier and coating materials, the loading factor, and the concentration of superdisintegrants [11 12]. Optimization of these parameters is critical to obtaining tablets with adequate mechanical strength, acceptable flow properties, and rapid dissolution behaviour [8].

Establishing an *in vitro–in vivo* relationship helps to predict biological performance from laboratory data. The present study was therefore undertaken to develop and evaluate promethazine theoclate orodispersible liquisolid compact tablets prepared by direct compression. The work focused on assessing the *in-vitro* drug release characteristics, *in-vivo* pharmacokinetic behaviour in comparison with a marketed formulation. Through this approach, an optimized system capable of delivering rapid and efficient therapeutic action was sought.

Material and Methods

Formulation of orodispersible liquisolid compact tablets

Formulations of orodispersible liquisolid compacts were prepared, each delivering 10 mg of promethazine theoclate with PEG 400 employed as the non-volatile liquid vehicle. Binary blends composed of microcrystalline cellulose as the carrier and Aerosil 200 as the coating material were prepared at predetermined ratios. 5:1 carrier-to-coat ratio was applied for batches F1–F3 (R = 5), whereas 10:1 ratio was selected for batches F4–F6 (R = 10). The drug was first dissolved or uniformly distributed in the liquid vehicle. The carrier material was then incorporated, and the system was triturated thoroughly to facilitate complete uptake of the liquid medication (Table 1). After allowing the mixture to stand for approximately 10 minutes to reach equilibrium, the coating agent was added and blending was continued for an additional 15 minutes to promote proper adsorption onto the powder surface. Co-processed superdisintegrants along with other formulation components mannitol, aspartame, magnesium stearate, talc, and an appropriate flavoring agent were introduced and mixed for 10–20 minutes to obtain a homogeneous final blend. Before compression, each batch was assessed for drug-excipient compatibility using infrared spectroscopy and subjected to pre-compression flow and packing evaluations, including angle of repose, bulk and tapped densities, Carr's index, and Hausner's ratio. Compression was carried out using a twelve-station rotary tablet machine fitted with an 8 mm flat punch bearing a score line. The formulation design varied according to superdisintegrant proportions (1:1, 1:2, and 1:3) and the selected excipient ratio (R). Batches F1–F3 were prepared with a loading factor of 0.82, while F4–F6 employed a loading factor of 0.56. The finished tablets were examined for post-compression quality attributes such as hardness, friability, thickness, weight variation, wetting time, water uptake, *in-vitro* dispersion, drug content uniformity, disintegration behaviour, and dissolution performance [15].

Table 1. Formulation of orodispersible Promethazine theoclate liquisolid compact tablets

Ingredients	F1	F2	F3	F4	F5	F6
Promethazine theoclate(mg)	10	10	10	10	10	10
PEG 400 (mg)	100	100	100	92.05	92.05	92.05
Excipient ratio, R	5	5	5	10	10	10
Loading factor, Lf	0.82	0.82	0.82	0.56	0.56	0.56
Microcrystalline cellulose (mg)	134.15	134.15	134.15	182.23	182.23	182.23
Aerosil 200 (mg)	26.83	26.83	26.83	18.22	18.22	18.22
Superdisintegrants (mg)						
1:1	10	-	-	10	-	-
1:2	-	10	-	-	10	-
1:3	-	-	10	-	-	10
Magnesium stearate(mg)	2	2	2	2	2	2
Sodium saccharine(mg)	1	1	1	1	1	1
Aspartame(mg)	2	2	2	2	2	2
Lactose(mg)	20	20	20	20	20	20
Talc(mg)	2	2	2	2	2	2
Flavour(mg)	0.5	0.5	0.5	0.5	0.5	0.5
Mannitol up to	350	350	350	350	350	350

***In-Vitro* Dissolution Studies**

In-vitro dissolution studies were performed to evaluate the drug release behaviour of the prepared Orodispersible

liquisolid compact tablets. The study was carried out using a USP dissolution apparatus type II (paddle method). The dissolution medium consisted of 900 mL of phosphate buffer (pH 6.8), maintained at 37 ± 0.5°C to simulate physiological conditions. The paddle rotation speed was set at 50 rpm. At predetermined time intervals of 0, 1, 2, 5, 10, 15, and 20 minutes, 10 mL samples were withdrawn from the dissolution medium. An equal volume of fresh dissolution medium, maintained at the same temperature, was immediately added to maintain constant volume and sink conditions. The withdrawn samples were filtered to remove undissolved particles and analyzed using a UV–Visible spectrophotometer at 249 nm, corresponding to the λmax of promethazine theoclate. The cumulative percentage of drug released at each time point was calculated using a previously established calibration curve [4, 13, 14].

In-Vivo Pharmacokinetic Study of Orodispersible Tablets in Rabbits

Male New Zealand white rabbits weighing 2.0–2.5 kg were used for the *in-vivo* pharmacokinetic evaluation. The animals were housed under standard laboratory conditions and fasted for 12 hrs prior to dosing, with free access to water throughout the study. All experimental procedures were carried out in accordance with the guidelines approved by the Institutional Animal Ethics Committee. The rabbits were randomly divided into two groups, wherein the test group received promethazine theoclate orodispersible liquisolid compact (10mg) and the reference group received marketed formulation (25mg) administered at an equivalent calculated Promethazine Theoclate dose expressed as mg/kg body weight. Each rabbit was weighed immediately before dosing. The drug quantity was adjusted to the actual body weight so that the target dose for marketed formulation remained 1.283 mg/kg and optimized formulation, F4 was 0.513 mg/kg. The freshly prepared suspension of marketed formulation was administered orally by oral-gavage. The weighed liquisolid compact was placed onto the dorsal tongue surface, rinsing with a small measured volume of water. After the compact had visibly dispersed, allowed the rabbit to swallow naturally. Blood samples were collected from the marginal ear vein at 0 (pre-dose), 0.02, 0.03, 0.06, 0.08, 0.17, 0.25, 0.33, 0.50, 1, 2, 4, 6, 8 and 12hrs after oral administration and transferred into heparinized tubes to prevent coagulation. The collected blood samples were centrifuged at 1900 × g for 10 minutes to separate plasma, which was then carefully transferred into labelled polypropylene tubes and stored at −80 °C. Promethazine Theoclate in plasma was quantified and the measured concentrations were used to construct plasma concentration-time profiles and calculate pharmacokinetic parameters. [16, 17, 18, 19].

Pharmacokinetic Analysis

The plasma concentration–time data obtained from individual animals were analysed using a non-compartmental approach. The maximum plasma concentration (Cmax) and the corresponding time to reach maximum concentration (Tmax) were obtained directly from the experimental observations. The area under the plasma concentration–time curve from zero to the last measurable concentration ($AUC_{(0-t)}$) was calculated using the linear trapezoidal method. Since the optimized formulation and the marketed formulation were administered at different rabbit-equivalent doses, dose-normalized pharmacokinetic parameters were calculated to facilitate comparison of systemic exposure. Relative bioavailability was calculated using the dose-corrected AUC values.

Statistical Analysis

Linear regression analysis was performed for the optimized F4 formulation and the marketed tablet to evaluate the relationship between the respective variables.

***In vitro–in vivo* correlation (IVIVC)**

The cumulative fraction of drug absorbed was estimated using the Wagner–Nelson method, and *in vitro–in vivo* correlation (IVIVC) was established to investigate the relationship between *in vitro* drug release and *in vivo* absorption. Wagner–Nelson method is widely employed for drugs exhibiting one-compartment pharmacokinetics with first-order absorption and elimination and enables estimation of the extent of drug absorption directly from plasma concentration–time data [20, 22]. Linear regression analysis was performed to establish the relationship between *in-vitro* drug release (%) and estimated *in-vivo* fraction absorbed (%) for the optimized F4 formulation.

Results and Discussion

***In-Vitro* Drug Release Profile of Promethazine Theoclate Liquisolid Compacts**

The *in-vitro* dissolution profiles of promethazine theoclate from liquisolid compact formulations (F1–F6) were evaluated using phosphate buffer (pH 6.8), and the cumulative percentage drug release at different time intervals is presented in Table 2. All formulations exhibited a rapid and progressive drug release pattern, characteristic of Orodispersible liquisolid systems. At the initial time points (1–2 min), all formulations showed measurable drug release, indicating prompt wetting and early drug dissolution. At 1 min, drug release ranged from approximately 5.5% to 6.8%, while at 2 min it increased to 9.5–14.8%, with F4 and F6 showing comparatively higher early release, suggesting enhanced drug availability due to efficient liquid adsorption and rapid dispersion. At 5 min, a notable increase in drug release was observed across all formulations. F4 demonstrated the highest release (~31.6%), followed by F6 and F5, whereas F1 and F2 showed relatively lower release, indicating formulation-dependent differences in dissolution behaviour. This trend became more pronounced at 10 min, where F5 exhibited the highest release (~63.5%), followed by F6 (58.4%) and F4 (56.9%), while F1–F3 showed comparatively slower release. By 15 min, all formulations released more than 69% of the drug, confirming rapid dissolution

performance. Formulations F4, F5, and F6 showed superior release (>80%), whereas F1 and F2 exhibited slightly lower but still substantial release. At the final time point (20 min), near-complete drug release was achieved for all formulations, ranging from 91.7% to 98.9%. Formulation F4 showed the highest cumulative drug release (~98.9%), followed by F5 (96.8%) and F6 (95.8%), indicating the most efficient dissolution behaviour. Overall, the rank order of drug release efficiency at 20 min can be summarized as F4 > F5 ≈ F6 > F1 ≈ F2 ≈ F3.

Table 2: *In-vitro* Drug Release Data of Promethazine theoclate orodispersible Liquisolid Compacts (F1-F6)

Time (min)	F1	F2	F3	F4	F5	F6
0	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
1	6.20 ± 0.22	6.10 ± 0.25	6.80 ± 0.20	5.50 ± 0.22	6.00 ± 0.21	6.20 ± 0.25
2	9.50 ± 0.23	10.10 ± 0.25	12.00 ± 0.32	14.80 ± 0.25	13.20 ± 0.25	14.50 ± 0.28
5	24.30 ± 0.41	23.80 ± 0.34	25.20 ± 0.44	31.60 ± 0.32	29.40 ± 0.34	30.80 ± 0.36
10	45.80 ± 0.32	41.30 ± 0.44	43.70 ± 0.44	56.90 ± 0.41	63.50 ± 0.45	58.40 ± 0.45
15	69.40 ± 0.32	70.80 ± 0.32	76.10 ± 0.52	82.30 ± 0.54	80.00 ± 0.50	81.80 ± 0.52
20	92.50 ± 0.42	91.80 ± 0.42	91.70 ± 0.41	98.90 ± 0.44	96.80 ± 0.45	95.80 ± 0.56

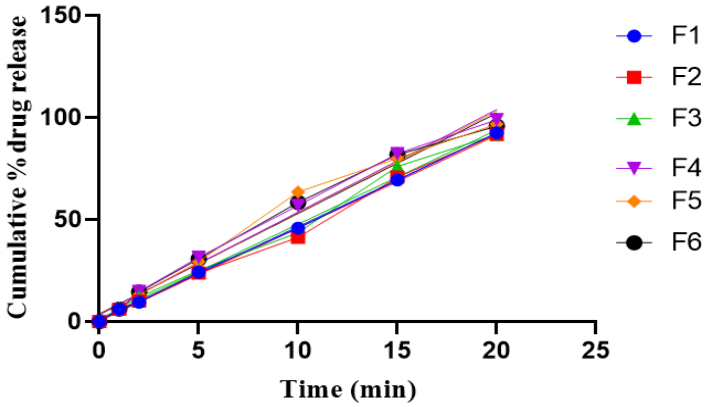

Figure 1: *In-vitro* drug release behaviour of Promethazine theoclate liquisolid compact formulations (F1–F6)

Overall, the dissolution study confirmed that all liquisolid compact formulations significantly enhanced the dissolution rate of promethazine theoclate. Among them, formulation F4 shows the most rapid and complete drug release, which may be attributed to its optimized excipient ratio, efficient liquid load factor, and favourable dispersion and disintegration characteristics. These results indicate F4 as the optimized formulation for improved oral drug delivery.

***In-Vivo* Evaluation of Drug Release Behaviour of Promethazine Theoclate Orodispersible Liquisolid Compact (F4) and marketed tablet.**

The *in-vivo* pharmacokinetic profile of the F4 promethazine theoclate orodispersible liquisolid compact and marketed tablet, following oral administration in rabbits is presented in Table 3. The plasma concentration demonstrated a rapid increase in drug concentration shortly after administration, indicating fast absorption of the drug from the orodispersible formulation. Measurable plasma levels were observed as early as 0.02 hrs, confirming the prompt onset of drug absorption. The rapid rise in plasma concentration may be attributed to the fast disintegration and enhanced dissolution of the liquisolid orodispersible tablet, which improves drug availability for absorption in the gastrointestinal tract. The presence of superdisintegrants and the liquisolid system likely contributed to improved wettability and increased surface area, facilitating faster absorption. The plasma concentration increased progressively with time and reached a maximum concentration, Cmax of 2.34 µg/mL at 2.00 hrs (Tmax), suggesting efficient dissolution and absorption of the drug from the liquisolid compact whereas the marketed formulation achieved a lower peak concentration of 1.800 µg/mL at 4 hrs (Figure 2). The optimized formulation maintained comparatively higher plasma concentrations during the absorption phase, indicating improved oral drug availability. The rapid attainment of peak plasma concentration is

consistent with the intended performance of orodispersible formulations designed for quick drug release and early therapeutic action. Following attainment of peak concentration, plasma drug levels declined in both formulations indicating systemic distribution and elimination of promethazine theoclate.

The calculated pharmacokinetic parameters, including maximum plasma concentration (Cmax), time to attain maximum plasma concentration (Tmax), area under the plasma concentration–time curve $AUC_{(0–12)}$, elimination rate constant (Kel), and elimination half-life (t½) are summarized in Table 4. The dose-normalized pharmacokinetic parameters were calculated to compare the intrinsic bioavailability of both formulations. The calculated values are presented in Table 5.

Table 3: Plasma drug concentration–time data of Promethazine Theoclate following oral administration of optimized F4 and marketed tablet

Time (h)	Cp (µg/mL) Optimized F4	Cp (µg/mL) Marketed tablet
0.00	0.000	0.000
0.02	0.111	0.012
0.03	0.195	0.026
0.06	0.390	0.053
0.08	0.431	0.062
0.17	0.585	0.080
0.25	0.910	0.106
0.33	1.230	0.133
0.50	1.560	0.266
1.00	1.670	0.400
2.00	2.340	1.200
4.00	2.000	1.800
6.00	1.450	1.270
8.00	0.920	1.120
12.00	0.220	0.520

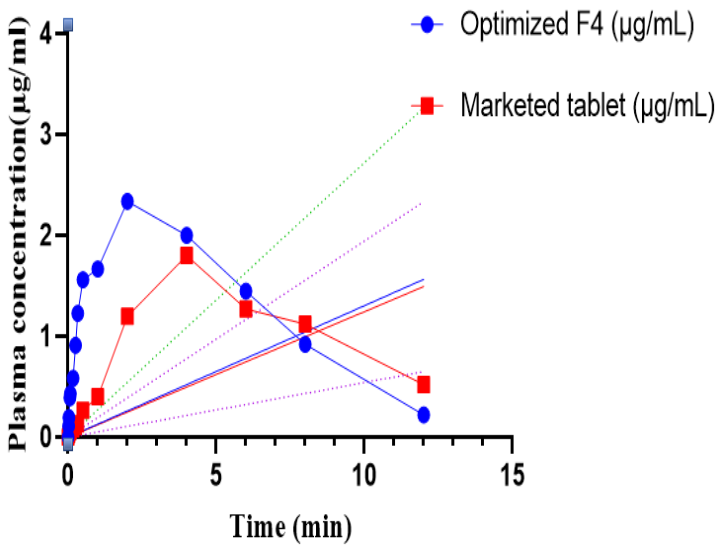

Figure 2: Plasma concentration–time profile of Promethazine Theoclate following oral administration of optimized formulation (F4) and marketed formulation.

Table 4: Pharmacokinetic parameters of Promethazine Theoclate following oral administration of optimized formulation (F4) and marketed formulation

Parameter	Optimized F4	Marketed formulation
Cmax (µg/mL)	2.340	1.800
Tmax (hrs)	2.00	4.00
$AUC_{(0–12)}$ (µg·hr/mL)	15.700	12.766

Kel (hr−1)	0.281	0.151
t½ (hrs)	2.47	4.57

Table 5: Dose-normalized pharmacokinetic parameters of Promethazine Theoclate

Parameter	Optimized Formulation F4	Marketed formulation
Dose (mg/kg)	0.513	1.283
Dose-normalized (Cmax) (µg/mL)	4.561	1.403
Dose-normalized $AUC_{(0–12)}$ (µg·hr/mL)	30.605	9.950

Table 6: Relative bioavailability of optimized formulation (F4) with respect to the marketed formulation

Parameter	Value
Dose-normalized $AUC_{(0–12)}$ of optimized F4	30.605
Dose-normalized $AUC_{(0–12)}$ of marketed formulation	9.950
Relative bioavailability (%)	307.6

Normalization of pharmacokinetic parameters clearly demonstrated the superior performance of the optimized formulation. The dose-normalized maximum plasma concentration of the optimized formulation was more than three times higher than that of the marketed formulation. Similarly, the dose-normalized $AUC_{(0–12)}$ indicated a marked increase in systemic drug exposure per unit dose. Overall, the *in-vivo* results showed that the F4 orodispersible liquisolid compact provides rapid drug release and absorption, achieving early peak plasma levels followed by elimination. Such a pharmacokinetic profile is advantageous for therapeutic indications requiring prompt onset of action, supporting the suitability of the optimized F4 formulation for conditions requiring immediate therapeutic response.

Relative Bioavailability

The relative bioavailability of the optimized formulation was calculated using dose-normalized AUC values to eliminate the influence of dose variation. The calculated relative bioavailability is presented in Table 6. The optimized formulation exhibited a relative bioavailability of 307.6%, indicating approximately a 3.08-fold increase in systemic exposure compared with the marketed formulation after correction for dose. The considerable enhancement in bioavailability can be attributed to the liquisolid technique, which improved drug wettability, increased the effective surface area available for dissolution, accelerated drug release, and promoted rapid gastrointestinal absorption.

Wagner–Nelson Analysis

To characterize the *in-vivo* absorption profile of Promethazine Theoclate following oral administration of the optimized orodispersible liquisolid compact (F4), the cumulative fraction of drug absorbed was estimated using the Wagner–Nelson method. The calculated fraction absorbed at each sampling interval is presented in Table 7, and the corresponding absorption profile is illustrated in Figure 3.

Statistical Analysis

Linear regression analysis was performed for the optimized F4 formulation and the marketed tablet to evaluate the relationship between the respective variables. For the optimized F4 formulation, the regression equation obtained was Y = 0.1304X + 0.000, with a slope of 0.1304 ± 0.06612. The regression analysis yielded an F-value of 3.892 with 1 and 14 degrees of freedom and a P-value of 0.0486. Since the P-value was less than 0.05, the slope was considered statistically significant at the 5% significance level, although the result was close to the significance threshold. For the marketed tablet, the regression equation was Y = 0.1245X + 0.000, with a slope of 0.1245 ± 0.03271. The analysis produced an F-value of 14.48 with 1 and 14 degrees of freedom and a P-value of 0.0019, indicating a statistically significant non-zero slope. The 95% confidence interval for the slope of the marketed tablet ranged from 0.05432 to 0.1947, which did not include zero, further supporting the statistical significance of the regression relationship. Both the optimized F4 formulation and marketed tablet demonstrated statistically significant positive regression slopes at the 5% significance level. The slope obtained for F4 (0.1304) was slightly higher than that of the marketed tablet (0.1245), indicating a comparable positive relationship between the variables in both formulations.

Table 7: Fraction of drug absorbed calculated by the Wagner–Nelson method for the optimized formulation (F4)

Time (h)	Plasma concentration (µg/mL)	$AUC_{0–t}$ (µg·hr/mL)	Fraction absorbed (%)
0.00	0.000	0.000	0.00
0.02	0.111	0.001	2.40
0.03	0.195	0.003	4.22
0.06	0.390	0.011	8.49

0.08	0.431	0.020	9.42
0.17	0.585	0.065	13.02
0.25	0.910	0.125	20.40
0.33	1.230	0.211	27.82
0.50	1.560	0.448	36.39
1.00	1.670	1.255	43.66
2.00	2.340	3.260	70.28
4.00	2.000	7.600	89.27
6.00	1.450	11.050	98.34
8.00	0.920	13.420	101.28
12.00	0.220	15.700	100.00

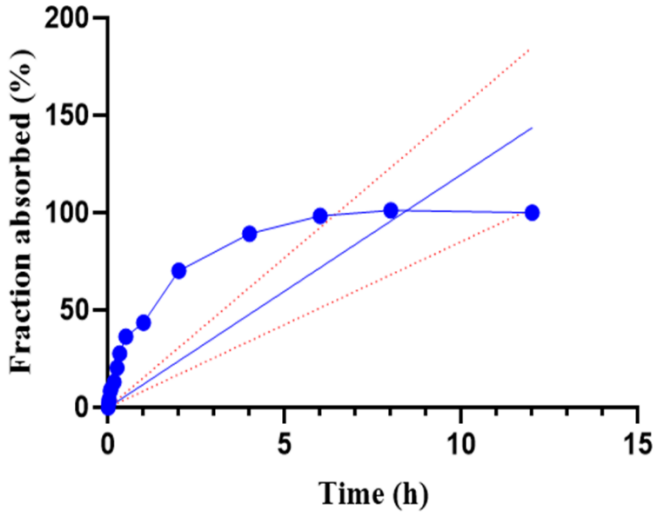

Figure 3. Wagner–Nelson plot showing the fraction of drug absorbed versus time for the optimized formulation (F4).

The Wagner–Nelson absorption profile demonstrated that the optimized formulation exhibited rapid and progressive absorption following oral administration. Detectable drug absorption was observed within the initial sampling interval, indicating prompt dissolution and gastrointestinal uptake of the drug. Approximately 36.39% of the administered dose was absorbed within 0.5 hrs, increasing to 43.66% at 1 hr and 70.28% by 2 hrs. The fraction of drug absorbed reached 89.27% at 4 hrs and approached complete absorption by 6–8 hrs, indicating that the majority of the administered dose had entered the systemic circulation within the early post-administration period. The rapid increase in the fraction absorbed during the initial phase is consistent with the enhanced dissolution characteristics of the liquisolid compact, which improves drug wetting, increases the effective surface area available for dissolution, and facilitates faster gastrointestinal absorption. The gradual plateau observed after 6 hrs suggests completion of the absorption process, with subsequent plasma concentration changes primarily governed by systemic elimination rather than continued drug uptake**.** To evaluate the absorption kinetics, linear regression analysis was performed on the Wagner–Nelson absorption data. The regression analysis demonstrated a statistically significant positive linear relationship ($F = 55.63$, $P < 0.0001$), confirming that the increase in cumulative drug absorption with time was highly significant.

***In Vitro–In Vivo* Correlation (IVIVC)**

In vitro–in vivo correlation (IVIVC) was established by correlating the cumulative percentage of drug released during the *in vitro* dissolution study with the fraction of drug absorbed estimated by the Wagner–Nelson method. The correlation dataset is presented in Table 8.

Table 8: Correlation between *in vitro* drug release and *in vivo* fraction absorbed

***In-vitro* drug release (%)**	***In-vivo* fraction absorbed (%)**
0.00	0.00
5.50	2.40
14.80	4.22
31.60	8.49
56.90	9.42
82.30	13.02
98.90	20.40

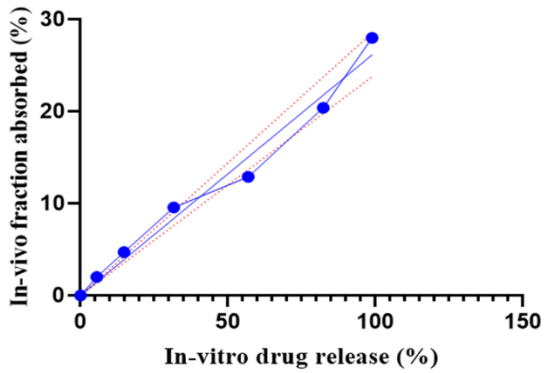

Figure 4: Level A *in vitro–in vivo* correlation plot between cumulative *in vitro* drug release and *in vivo* fraction absorbed.

The *in-vitro–in-vivo* correlation analysis demonstrated a strong positive relationship between the drug release profile of the optimized formulation and the corresponding *in-vivo* absorption profile. The obtained correlation coefficient ($r = 0.9904$) and coefficient of determination ($R^2 = 0.9808$) indicated a high degree of linear association between the fraction dissolved and fraction absorbed. The regression relationship was statistically significant ($p < 0.0001$), confirming that the observed association was unlikely to have occurred by chance. Overall, the findings support the presence of a strong Level A *in-vitro–in-vivo* relationship for the optimized formulation, suggesting that the *in-vitro* drug release behaviour was closely associated with the *in-vivo* absorption pattern.

Conclusion

The present study demonstrated that the liquisolid approach is an effective strategy to enhance the dissolution and absorption of promethazine theoclate from orodispersible tablets. All prepared formulations showed rapid disintegration and substantial drug release, with the optimized batch providing almost complete release within a short period. Optimized formulation significantly decreased the time to reach peak plasma concentration (Tmax) and increased the peak plasma concentration (Cmax) and exhibited superior onset and higher bioavailability compared to marketed product. The observed Level A *in-vitro–in-vivo* correlation further supported the relationship between enhanced dissolution behaviour and improved in-vivo performance. The outcomes of this work also provide a scientific foundation for further formulation development, scale-up studies, long-term stability evaluation, and future clinical investigations aimed at translating this technology into practical pharmaceutical applications. Overall, the developed system offers a promising option for achieving rapid therapeutic action and improved patient convenience.

Conflict Of Interest: Nil

Acknowledgement:

Data Availability: The data produced during this study are available from the corresponding author upon reasonable request.

Abbreviations

AUC – Area under the plasma concentration–time curve
$AUC_{(0-\infty)}$ – Area under the curve from time zero to infinity
$AUC_{(0-12)}$ – Area under the curve from time zero to 12 h
CDR – Cumulative drug release
Cmax – Maximum plasma concentration
DT – Disintegration time
IR – Infrared spectroscopy
Kel – Elimination rate constant
Lf – Loading factor
ODT – Orodispersible tablet
PEG – Polyethylene glycol
r^2 – Regression coefficient
rpm – Revolutions per minute
Tmax – Time to reach maximum plasma concentration
t½ – Elimination half-life
UV – Ultraviolet
USP – United States Pharmacopoeia
µg – Microgram
mg- Milligram
kg- Kilogram
min- Minutes
hr – Hour
mL- Millilitre
% - Percentage
°C - Degrees Celsius
pH - Potential of Hydrogen
λmax - lambda max/ Maximum wavelength

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