IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

# Formulation And Evaluation Of Solid Dispersion Incorporated Fast Dissolving Tablet Of Promethazine Theoclate

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**Abstract:**

In the present research work, the aim was to successfully formulate solid dispersion and incorporate it into a fast-dissolving tablet of promethazine theoclate, which were reduce or prevent nausea and vomiting. The main objective of research work was to increase the solubility of poorly water-soluble promethazine theoclate by preparing solid dispersions and subsequently formulating them into fast dissolving tablets (FDTs) to improve patient compliance and convenience. Solid dispersions were prepared by the fusion method and solvent evaporation method using appropriate excipients. Among various formulations, batch B6 was selected as the best formulation because it showed excellent performance with a percentage yield of 95%, drug content of 98%, and dissolution drug release of 94% at 30 minutes. The selected batch B6 was further formulated into fast dissolving tablets, which exhibited a disintegration time of 12 seconds, and a drug release of 99% within 30 minutes. These results confirm that solid dispersion technologywas an effective approach to enhance the solubility and dissolution rate of promethazine theoclate, thereby providing better therapeutic efficiency and patient compliance.

**Keywords:** Solubility, Solid dispersion, Fast dissolving tablet, Promethazine theoclate.

## Introduction

Solubility is a significant physicochemical factor affecting the absorption of a drug and its therapeutic effectiveness. The rate and extent of dissolution of the drug from any solid dosage form determine the rate and extent of absorption of the drug [1]. In the case of poorly water-soluble drugs, dissolution is the rate-limiting step in the process of drug absorption. Solid dispersion (SD) is the method that involves the dispersion of one or more active ingredients in an inert carrier or matrix in solid-state prepared by melting, dissolution insolvent, or melting-solvent method [2]. Conventional oral drug delivery systems, including solutions, suspension, tablets, and capsules are difficult to administer to patients with dysphagia. Swallowing problems can also appear often in specific populations, including pediatric, elderly, nauseated patients, and developmentally disabled patients [3]. In addition to these difficulties, convenience is also a notable concern associated with oral antiemetics like the patients taking tablet formulations to require water to ease swallowing, which is not always available [4]. Fast dissolving tablets (FDTs) have been designed to allow a solid dose to be rapidly dissolved in the oral cavity without the need for water [5]. Several approaches have been used to formulate FDTs like freeze-drying, tablet molding, sublimation, direct compression, etc. Out of this direct compression has become the most popular used technique [6].

## MATERIALS:

Promethazine theoclate was obtained as a gift sample from Harika drugs private limited, Hyderabad, Telangana, India, Sodium Starch glycolate, Polyethylene glycol 6000, Microcrystalline cellulose, Magnesium Stearate, Mannitol, Talc, Croscarmellose Sodium were purchased from LOBA Chemie Pvt. Ltd

## METHODS:

## PREPARATION OF SOLID DISPERSION:

Solid dispersions of Promethazine theoclate were prepared by the fusion method and solvent evaporation method. For the formulation of solid dispersion with drug and Polymer ratio, with the different polymers in the ratio of 1:1, 1.3, and 1:5 three polymers were taken for screening of polymer for solid dispersion. They were PEG 6000 and sodium starch glycolate. F1-F3 Batch was prepared with the Fusion method and the F4-F6 Batches were Prepared with solvent evaporation method [7].

**Table No.01 Formulation of Solid dispersion**

## FORMULATION OF SOLID DISPERSION

| S.No. | Formulation No. | Drug(mg) | PEG6000 | Sodium starch glycolate |
|---|---|---|---|---|
| 1. | F1 | 10mg | 10mg | - |
| 2. | F2 | 10mg | 30mg | - |
| 3. | F3 | 10mg | 50mg | - |
| 4. | F4 | 10mg | - | 10mg |
| 5. | F5 | 10mg | - | 30mg |
| 6. | F6 | 10mg | - | 50mg |

**Fusion Method**

Weight accurately 10 mg polymer and placed it into a china dish and heat it on a water bath with continuous stirring until the polymer is dissolved. Add 10 mg Promethazine theoclate (drug) in dissolved polymer solution with continuous stirring to form a homogenous mixer. After complete mixing of drug and polymer rapidly transfer into the ice bath to solidified with vigorous stirring. Then, the final solid mass is crushed, pulverized, and sieved. Different optimized combinations of solid dispersion with different polymers were prepared and evaluated for different evaluation parameters [8].

**Solvent Evaporation Method**

Weight accurately 10mg of polymer and 10mg Promethazine theoclate (drug) placed into china dish. Add a sufficient volume of methanol to dissolve completely with continuous stirring. Allow mixture to evaporate completely on a water bath at 45 °C with continuous stirring to obtain dry mass. The dried mass was pulverized and passed through 44 mesh sizes. Different optimized combinations of solid dispersion with different polymers were prepared and evaluated for different evaluation parameters [9].

## 3.CHARACTERIZATION OF SOLID DISPERSION

**1.Determination Of Percent Drug Content of Solid Dispersion.**

Determination Percent drug content, accurately weighed solid dispersion equivalent to 10 mg of Promethazine theoclate was transferred to100 ml of volumetric flask and diluted to 100 ml with methanol and sonicated for 30 min for complete solubilization of the drug. The solution was filtered through a 0.45 µ filter and measured at 245nm in a double beam UV spectrophotometer (UV 1800, Shimadzu, Kyoto, Japan). The concentration of Aprepitant was determined using the calibration curve of the drug in methanol[9].

**2. Solubility Studies of Solid Dispersion.**

Saturation solubility studies were conducted as per the method described by Higuchi. The saturation solubility was performed by adding an excess amount of solid dispersion in 10 ml 6.8 PH phosphate buffer in a glass vial. Mixed vigorously for 30 mins and shaken mechanically for 72 h at 37°C ± 0.5°C. then vials are centrifuged for 10 mins at 2500 RPM.The saturated solutions were filtered through a 0.45-µm membrane filter. And filtrates were suitably diluted, analyzed using Shimadzu UV-1800, (UV-1800 Shimadzu, Kyoto, Japan) UV-1800 spectrophotometer at 255 nm[10].

**3.Percentage Yield of Solid Dispersion[11].**

Thoroughly dried solid dispersion was collected and weighed accurately. The percentage yield was then calculated using formulae given below

$$\text{Percentage yield} = \frac{\text{Mass of Solid dispersion obtained}}{\text{Total weight of drug and polymer}} \times 100$$

**4. Dsc Analysis Differential Scanning Colorimetry (Dsc) Analysis**

The thermal properties of the pure drug and sodium starch glycolate mixtures were evaluated using a differential scanning calorimeter. The analysis was performed with a heating range of 48-50oC and a rate of 10° C min-1 in an inert nitrogen atmosphere [12].

## 4. FORMULATION FAST DISSOLVING TABLET WITH SOLID DISPERSION.

**Method of Preparation of Fast Dissolving Tablets:**

- ✓ All the ingredients were passed through an 80# sieve.
- ✓ Solid dispersion (150mg is equivalent to 25 mg Promethazine theoclate) was mixed with super disintegrant Croscarmellose sodium, mannitol, and directly compressible microcrystalline cellulose as diluents and other excipients such as magnesium stearate and talc [13].
- ✓ The powder blend was directly compressed using flat punches on a double rotary tablet compression machine [14].

**Table No.02 Formulation Fast Dissolving Tablet**

| S. No. | Ingredients | B1 | B2 | B3 | B4 | B5 | B6 | B7 | B8 | B9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. | Solid Dispersion (F6) equivalent to 25mg | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 |
| 2. | Croscarmellose Sodium | 10 | 13 | 17 | 20 | 23 | 26 | 29 | 32 | 35 |
| 3. | Microcrystalline Cellulose | 68 | 65 | 61 | 58 | 55 | 52 | 49 | 46 | 46 |
| 4. | Mannitol | 0.95 | 95 | 95 | 95 | 95 | 95 | 95 | 95 | 95 |
| 5. | Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 6. | Magnesium Stearate | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| | Total | 330mg | 330mg | 330mg | 330mg | 330mg | 330mg | 330mg | 330mg | 330mg |

## 5. EVALUATION OF TABLET

### 1. PRE-COMPRESSION STUDIES

### 1) Angle Of Repose [15]

The angle of repose is defining as the maximum angle possible between the surface of the pile of the horizontal plate and powder. For determining the angle of repose of powder a funnel was kept on a stand in a vertical position and about 10 gm of the drug was filled in that funnel. Then the powder was release on the paper to form a conical heap. Then that heap was measured in different directions like height was measured by the scale. And the angle of repose was calculated by using the following formulae

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

$\theta$ = Angle of the repose

h = Height of the heap

r = Radius of the heap

### 2) Bulk Density [16]

It is obtained by measuring the volume of a mass of powder that passed through the screen. The ratio of the mass of powder to the volume of bulk. Bulk density mostly depends on the shape if the shape of the powder is spherical bulk density is increase. The powder sample equivalent to the 10 gm is weighed then that powder was filled in a 50ml of cylinder. And then the powder will be leveled and that volume was noted.

$$\rho i = m / Vi$$

ρi=Bulk density

m=mass of the blend

Vi = untapped volume

**3). Tapped Density**

It is the ratio of a mass of the powder which was occupied the volume after it has been tapped for a defined period.

$$\rho t = m/Vt$$

ρt = Tapped density

m = mass of the blend

Vt = tapped volume

**4). Powder Compressibility [17]**

The compressibility index measures the propensity of a powder to be compressed. As such, they are measuring the relative importance of inter particulate interactions. In a free-flowing powder, such interactions generally less, and tapped densities will be closer in value. And for the poorer flowing materials, there are frequently greater and larger inter particulate interactions and a greater difference between tapped and bulk density will be observed. These differences are reflected in the compressibility index calculated by the formula. One of the important measures that can be obtained from bulk and tapped density determinations is the percent compressibility or Carr's index (I), which is determined by the following equation.

$$I = \frac{\text{Tapped density - Tapped density}}{\text{Bulk density}} \times 100$$

**6. POST COMPRESSION STUDIES**

The prepared tablet of Aprepitant was evaluated on the various parameters according to the Indian Pharmacopeia e.g. appearance, dimensions (diameter and thickness), weight variation, hardness, friability, assay, and drug content[18].

**1. Weight Variation**

Randomly selected 20 tablets will be weighed individually and calculate average weight will be calculated. The individual weight is compared with the average weight. And the difference in weight variation should be within the standard limits according to the USP and IP. And the percent in deviation was calculated by formulating.[19]

$$\textbf{\% Weight Variation Difference} = \frac{\text{Individual Weight - Average Weight}}{\text{The Average Weight Of}} \times 100$$

| The Average Weight of the Tablet (As per IP) | Allowed Percentage Deviation (%) | Average Weight of The Tablet (According To USP) |
|---|---|---|
| 80 mg or less | 10 | 130mg or less |
| More than 80 mg but less than 250 mg | 7.5 | 130mg to 324 |
| 250 mg or more | 5 | More than 324 |

**Table No.03: - Allowed Percentage Deviation in Weight Variation**

**2.Friability Test**

This test is used for the determination of the physical strength of the tablets and mainly applies to the compressed tablet. De dust the 10 tablets and weigh accurately the required number of tablets. Keep the tablets in the friability and rotate them 100 times. Then after that remove the tablets. Remove its dust and then weigh them accurately [20].

$$\% F = I - F \times 100$$

I=initial weight

F=final weight

**3.Hardness**

Tablet hardness has been defined as the force required breaking a tablet in a diametric compression test. Several devices are used to test tablet hardness: the Monsanto tester, the strong- cobb tester, the Pfizer tester, the Erweka tester, and the Schleuniger tester Pfizer tester operates on the same mechanical principle as a pair of pliers. As the plier handles are squeezed, the tablet is compressed between a holding anvil, and a piston connected to a direct force reading gauge. The dial indicator remains at the reading where the tablet breaks and is returned to zero by depressing a reset button [21].

**4. Drug Content Uniformity**

Ten tablets will be finely powdered and an amount equivalent to 100 mg of powder will be accurately weighed and transferred to a 100 ml volumetric flask, then 100 ml of methanol will be added. The filtrate is further diluted with phosphate buffer 6.8 pH. Then analyzed with UV visible spectrophotometrically [22]. Drug content was calculated using a standard curve generated using various concentrations of Aprepitant in phosphate buffer (pH6.8) [23].

**5.Dissolution Test**

In vitro dissolution study is performed by using USP Type II Apparatus (Paddle type). The tablet is kept in 900 ml of dissolution fluid is generally gastric fluid for first 2 hr and intestinal fluid (for subsequent fluid) with a stirrer rotating at a specified r.p.m and maintaining the temperature at 37 ± 0.5 °C of dissolution media [24]. 5 ml of samples withdrawn at different time intervals were replaced with fresh medium and analyzed in UV Visible spectrophotometer for estimation of absorbance taking a suitable blank solution.Finally, the drug release rate is calculated using a suitable equation [25].

## 7. RESULT AND DISCUSSION

### EVALUATION OF SOLID DISPERSION

1. **Drug Content**

| S. No. | Formulation | Drug Content (%) |
|---|---|---|
| 1 | F1 | 88.72±0.88 |
| 2 | F2 | 90.26±0.81 |
| 3 | F3 | 92.48±0.73 |
| 4 | F4 | 94.69±0.65 |
| 5 | F5 | 96.30±0.54 |
| 6 | F6 | 97.82±0.49 |

**Table No.04 Observation table of drug content**

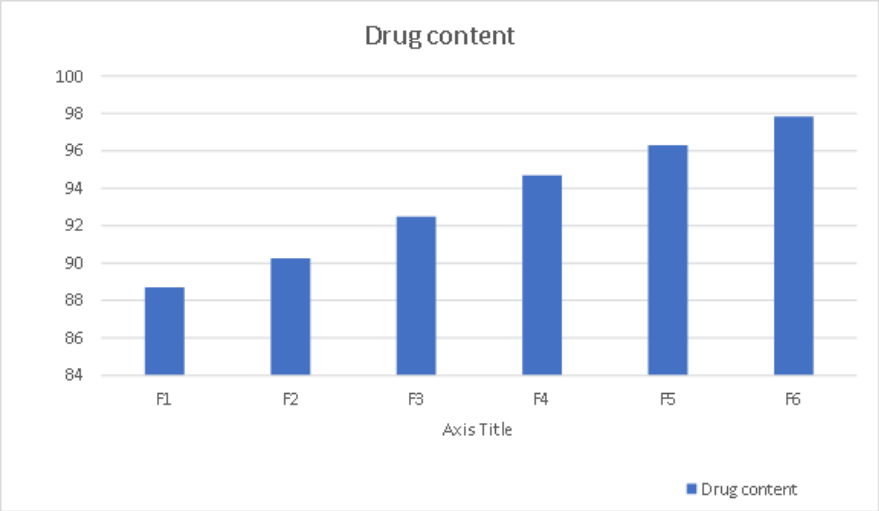


**Figure No.01 Graph of Drug Content**

1. Solubility Studies

| S. No. | Formulation Batch of Solid Dispersion | Saturation Solubility (Mg/Ml) |
|---|---|---|
| 1 | F1 | 0.1086±0.0006 |
| 2 | F2 | 0.0525±0.0006 |
| 3 | F3 | 0.2522±0.0010 |
| 4 | F4 | 0.0663±0.0006 |
| 5 | F5 | 0.3624±0.0006 |
| 6 | F6 | 0.3867±0.0006 |

**Table No. 02 Saturation Solubility Studies**

2. Percentage Yield

| S .No. | Formulation | Percentage yield (%) |
|---|---|---|
| 1 | F1 | 88.76±0.82 |
| 2 | F2 | 89.42±0.67 |
| 3 | F3 | 90.63±0.59 |
| 4 | F4 | 92.10±0.53 |
| 5 | F5 | 93.56±0.50 |
| 6 | F6 | 94.85±0.47 |

**Table No.06 Observation of Percentage Yield**

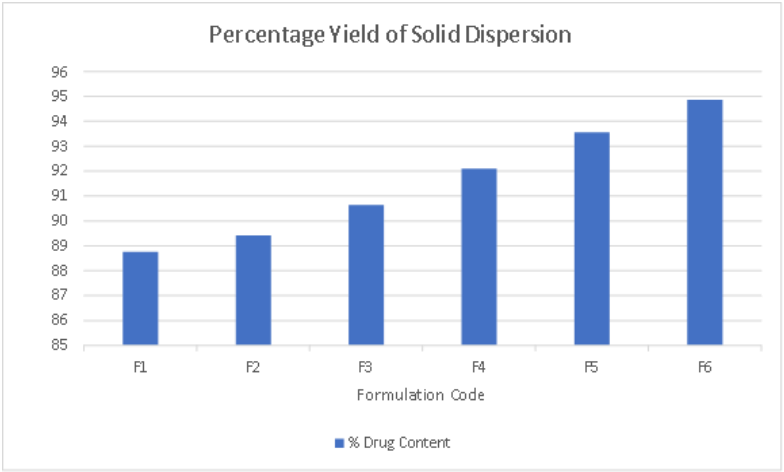


**Figure No.02 Graph of Percentage yield**

### 3. Differential Scanning Colorimetry Studies.

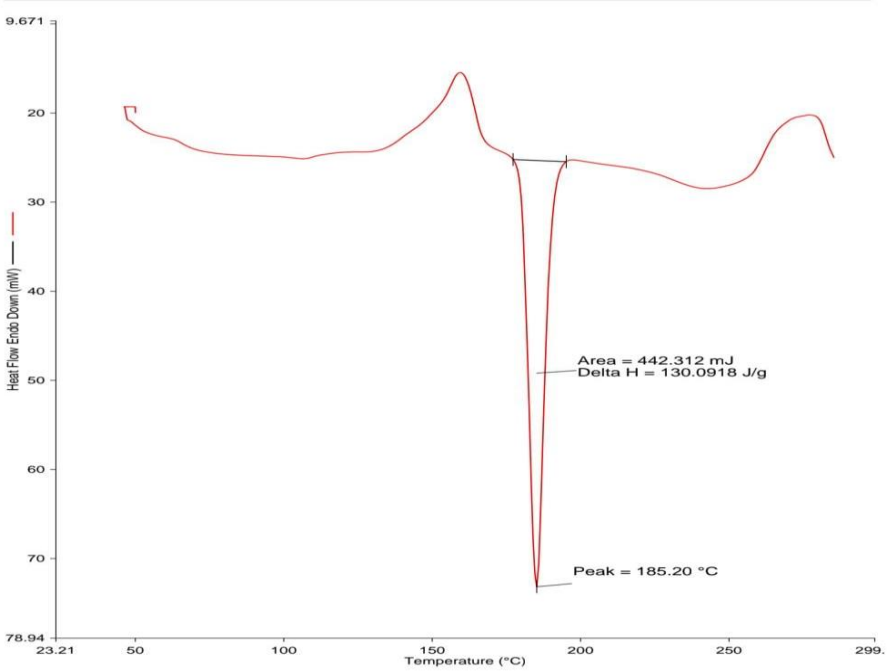


**Figure No.03 DSC of Pure drug Promethazine theoclate**

In the Present study, the DSC graph shows a sharp peak at 182.20$^0$C, which corresponds to the melting point of Promethazine theoclate. The presence of a single, well- defined peak indicates that the drug remained in its crystalline form and did not undergo any significant interaction or degradation during formulation. This confirms the thermal stability and compatibility of Promethazine theoclate with the other ingredients used in the formulation.

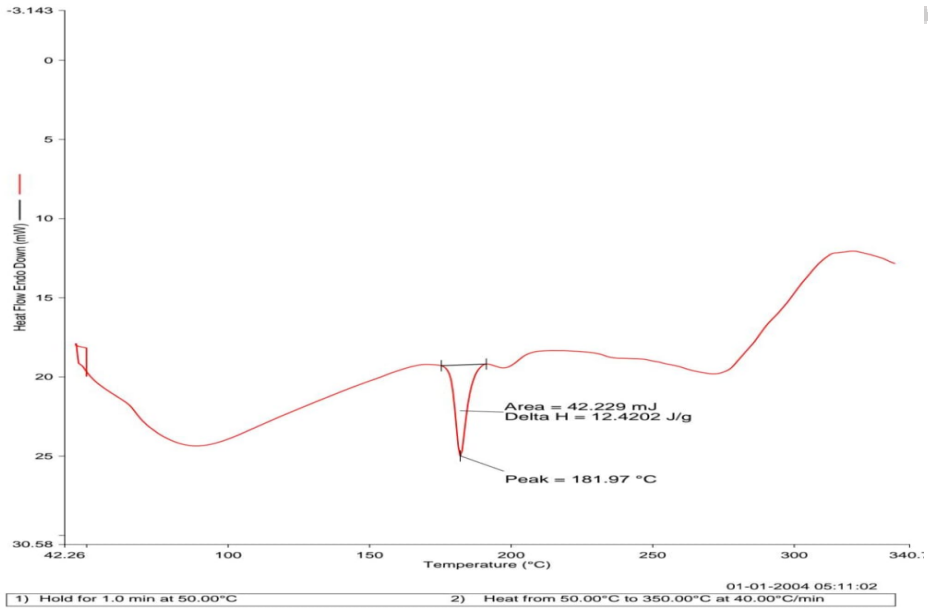


**Figure No. 04 DSC F6 Batch Solid Dispersion**

## EVALUATION of FAST DISSOLVING TABLET

### 1. PRE COMPRESSION EVALUATION

**Table No.07 Pre-Compression Evaluation Studies of Fast Dissolving Tablet**

| Formulations | Angle of Repose (θ) | Bulk Density (gm/ml) | Tapped density (gm/ml) |
|---|---|---|---|
| B1 | 30.5 | 0.42 | 0.55 |
| B2 | 29.8 | 0.44 | 0.57 |
| B3 | 28.9 | 0.41 | 0.54 |
| B4 | 27.6 | 0.43 | 0.56 |
| B5 | 26.8 | 0.40 | 0.54 |
| B6 | 26.2 | 0.39 | 0.53 |
| B7 | 25.4 | 0.41 | 0.55 |
| B8 | 24.8 | 0.42 | 0.56 |
| B9 | 23.9 | 0.45 | 0.55 |

### 2. POST COMPRESSION EVALUATION

**Table No.08 Post Compression Evaluation Studies of Fast Dissolving Tablet**

| Formulations | Weight Variation (mg) | Hardness (kg/cm2) | Friability (%) | Disintegration time (sec) | Drug Content (%) | Moisture Content |
|---|---|---|---|---|---|---|
| B1 | 283.82±3.95 | 2.93±0.15 | 0.92±0.06 | 20.26±2.22 | 90.72±1.05 | 3.45±0.12 |
| B2 | 302.05±3.87 | 3.10±0.10 | 0.56±0.08 | 17.34±3.55 | 91.18±0.92 | 3.38±0.11 |
| B3 | 323.80±3.82 | 3.43±0.15 | 0.32±0.06 | 13.80±1.92 | 91.64±0.84 | 3.29±0.10 |
| B4 | 326.45±3.60 | 3.50±0.12 | 0.30±0.04 | 12.52±1.85 | 92.31±0.78 | 3.20±0.09 |
| B5 | 328.90±3.58 | 3.58±0.14 | 0.28±0.05 | 11.34±1.63 | 92.89±0.71 | 3.12±0.08 |
| B6 | 331.20±3.50 | 3.65±0.13 | 0.25±0.03 | 10.45±1.40 | 93.34±0.68 | 3.05±0.07 |
| B7 | 333.45±3.46 | 3.72±0.15 | 0.23±0.04 | 9.85±1.12 | 93.89±0.74 | 2.94±0.06 |
| B8 | 335.70±3.40 | 3.80±0.13 | 0.21±0.03 | 9.15±0.94 | 94.35±0.65 | 2.85±0.06 |
| B9 | 337.90±3.35 | 3.88±0.12 | 0.20±0.02 | 8.62±0.82 | 94.92±0.57 | 2.72±0.05 |

**Table No.09 *In- vitro* Dissolution Studies:**

| S. No. | Formulations | % Drug released at 0 min | % Drug released at 5 min | % Drug released at 10 min | % Drug released at 15 min | % Drug released at 20 min | % Drug released at 25 min | % Drug released at 30 min |
|---|---|---|---|---|---|---|---|---|
| 1 | B1 | 0 | 58.2±0.9 | 68.4±0.8 | 74.6±0.7 | 81.2±0.6 | 86.5±0.5 | 88.2±0.4 |
| 2 | B2 | 0 | 60.5±0.8 | 70.1±0.9 | 76.8±0.7 | 83.0±0.6 | 87.8±0.5 | 89.5±0.4 |
| 3 | B3 | 0 | 62.8±0.7 | 72.3±0.8 | 78.5±0.7 | 84.6±0.5 | 88.9±0.5 | 90.2±0.4 |
| 4 | B4 | 0 | 64.5±0.6 | 74.1±0.7 | 80.2±0.6 | 85.8±0.5 | 89.6±0.5 | 91.0±0.4 |
| 5 | B5 | 0 | 66.2±0.6 | 75.8±0.7 | 82.1±0.6 | 86.9±0.5 | 90.5±0.5 | 91.8±0.4 |
| 6 | B6 | 0 | 67.9±0.6 | 77.4±0.7 | 83.5±0.6 | 87.8±0.5 | 91.2±0.5 | 92.4±0.4 |
| 7 | B7 | 0 | 69.1±0.5 | 78.9±0.6 | 84.8±0.5 | 88.6±0.5 | 91.8±0.4 | 93.0±0.4 |
| 8 | B8 | 0 | 70.3±0.5 | 80.1±0.6 | 86.0±0.5 | 89.5±0.4 | 92.4±0.4 | 93.6±0.3 |
| 9 | B9 | 0 | 72.5±0.5 | 82.0±0.6 | 87.5±0.5 | 91.0±0.4 | 93.8±0.3 | 94.9±0.3 |
| 10 | Marketed Preparation | 0 | 42.7±0.59 | 57.3±0.54 | 68.9±0.51 | 78.2±0.48 | 84.7±0.43 | 90.1±0.39 |

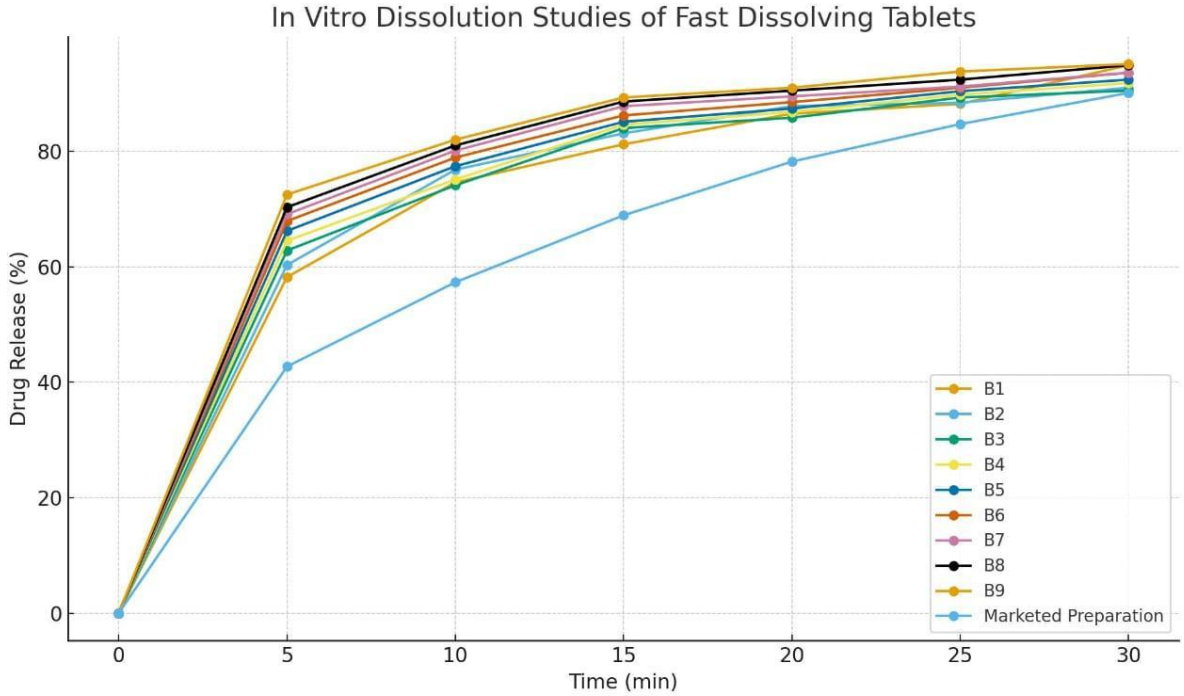


**Figure No. 05 *In vitro* Studies of fast dissolving tablets**

## Summary and Conclusion

1. The drug content of all formulations (B1–B9) was found in the acceptable range of 90.5% to 94.3%, with batch B9 showing the highest content (94.3%) ensuring uniform drug distribution.
2. The moisture content of formulations was found between 2.1% to 2.8%, which was within the permissible limits for fast dissolving tablets. B9 showed optimum stability with 2.8% moisture content.
3. The *in-vitro* dissolution study revealed that formulation B9 released 94.3% drug in 30 minutes and 99.1% in 45 minutes, which was significantly higher compared to the marketed preparation (85.1% in 30 minutes and 92.0% in 45 minutes). Hence, B9 was selected as the best formulation.
4. These results confirm that solid dispersion technology was incorporate in fast dissolving tablets preparation an effective approach to enhance the solubility and dissolution rate of promethazine theoclate, thereby providing better therapeutic efficiency and patient compliance.

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