Formulation and Evaluation of Mouth Dissolving Tablets of Promethazine Theoclate for Enhanced Patient Compliance

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***Abstract*—The demand for Mouth Dissolving Tablets (MDTs) has significantly increased over the past decade, particularly among geriatric and pediatric populations and individuals with dysphagia (difficulty swallowing). MDTs rapidly disintegrate and dissolve in the mouth without the need for water, offering an effective solution for enhanced patient compliance. The aim of the present study was to formulate and evaluate mouth dissolving tablets of Promethazine theoclate using superdisintegrants to improve patient convenience and therapeutic efficacy. Promethazine theoclate is an antiemetic agent widely used in the management of nausea and vomiting, especially conditions associated with impaired gastric emptying and gastrointestinal disturbances. Traditional oral delivery of Promethazine theoclate is limited by extensive degradation in the acidic environment of the stomach and substantial first-pass metabolism, resulting in reduced bioavailability. This leads to challenges in achieving rapid therapeutic effects, particularly when drug loss occurs due to vomiting. The development of MDTs for Promethazine theoclate aims to bypass these obstacles by facilitating rapid disintegration and absorption through the oral mucosa, minimizing first-pass metabolism and promoting faster onset of action. The formulation was optimized using different superdisintegrants to achieve ideal tablet characteristics including hardness, disintegration time, and dissolution profile. The outcomes of this study suggest that MDTs provide a promising approach for improving patient adherence, reducing onset time, and enhancing therapeutic performance for antiemetic therapy.**

***Index Terms*—Promethazine theoclate, Direct compression method, Patient compliance, Evaluation parameters,**

I. INTRODUCTION

Mouth Dissolving Tablets (MDTs) are solid dosage forms that rapidly disintegrate and dissolve in the saliva within the oral cavity, forming a solution without the need for water during administration. [1] The primary technique for formulating mouth-dissolving tablets involves the use of superdisintegrants. These agents enable the tablet to break down rapidly on the tongue upon contact, facilitating the immediate release of the medication into the saliva.Oral drug delivery is considered the gold standard in the pharmaceutical industry due to its flexibility in dosage form design. It is regarded as the safest, most convenient, and often painless method of administration. Additionally, it does not require the medication to be sterile and offers the highest level of patient compliance.The European Pharmacopoeia defines an oro-dispersible tablet as a tablet that disperses and disintegrates in the mouth within three minutes before swallowing. "These tablets quickly break into small parts and become soft, making them easy to swallow." An effective mouth-dissolving tablet typically has a disintegration time ranging from a few seconds to about 2–4 minutes. [2-4]

Promethazine theoclate, a phenothiazine derivative, is an H1-receptor antagonist widely used for the prevention and treatment of nausea and vomiting. Its chemical name is N,N-dimethyl-1-(10H-phenothiazin-10-yl)propan-2-amine, and it exhibits both central and peripheral antihistaminic effects. According to the Biopharmaceutics Classification System (BCS), promethazine theoclate falls under Class II, characterized by low solubility and high permeability. Due to its poor aqueous solubility and extensive first-pass metabolism, the drug suffers from low oral bioavailability, which limits its therapeutic efficacy. These challenges make it a suitable candidate for formulation into mouth dissolving tablets (MDTs), which can enhance onset of action and potentially

bypass first-pass metabolism through buccal absorption.[5,6]

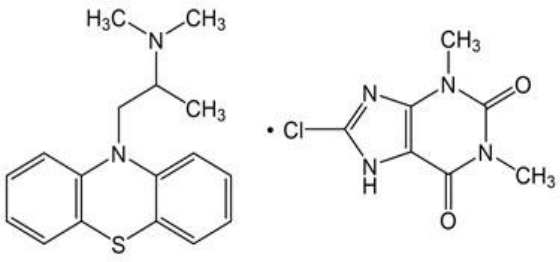

Figure 1: Structure of Promethazine theoclate

Aim

The present study focused on formulating mouth dissolving tablets of promethazine theoclate using a superdisintegrant to improve patient compliance.

To develop a fast-acting, patient-friendly dosage form that enhances the onset of action and improves patient compliance, especially for those who have difficulty swallowing conventional tablets, such as pediatric and geriatric patients.[7]

II. MATERIALS AND METHODS

Materials

Promethazine theoclate (API) – Gift sample purchased from the Mehta Pharmaceutical Pvt. Ltd., Mumbai, Sodium Starch Glycolate (Superdisintegrant), β-cyclodextrin (Solubility enhancer), Mannitol (Diluent), Talc (Glident), Magnesium Stearate (Lubricant), Microcrystalline cellulose (Binder), Sucralose (Sweetener), Orange (Flavouring agent)., "all the excipients purchased from Solanki Enterprises, Pune "

Method of Preparation

Formulation of MDTs by Direct Compression Method

Promethazine theoclate, a BCS Class II drug with low water solubility, was formulated into mouth dissolving tablets using β-cyclodextrin to improve solubility. Sodium starch glycolate was used as a superdisintegrant, while mannitol acted as a diluent to improve mouthfeel. Microcrystalline cellulose served as both a binder and a diluent. Sucralose was added as a sweetener to enhance taste. To improve powder flow and tablet formation, talc was used as a glidant and magnesium stearate as a lubricant.

All ingredients were passed through a #60 mesh sieve to ensure uniform particle size. The powders were thoroughly mixed and then compressed into tablets using an automated tablet punching machine.

Tablets were prepared with an average weight of 150 mg, a thickness of 2.85 mm, and a diameter of 9 mm. Each batch produced a minimum of 50 tablets.[8-10]

Composition of Mouth dissolving Tablet (MDT)

Ingredients	**F_1 mg**	**F_2 mg**
Promethazine theoclate (API)	25 mg	25 mg
Sodium Starch Glycolate	10 mg	15 mg
Mannitol	80 mg	75 mg
Talc	2 mg	2 mg
Magnesium Stearate	2.5 mg	2.5 mg
Microcrystalline cellulose	15 mg	10 mg
β-cyclodextrin	5 mg	5 mg
Sucralose	2 mg	2.5 mg
Flavouring agent	Q.S	Q.S

Evaluation of post-compression process

Thickness

3 tablets of each batch were selected randomly, and thickness and diameter of tablets were measured in mm by vernier calliper. [11-12]

Hardness

The hardness of the tablet from each formulation was determined using Pfizer hardness tester

The hardness of tablets, also known as crushing strength, was determined using a tablet hardness tester (e.g., Monsanto or Pfizer type). This test measures the force required to break the tablet by compression. Individual tablets were placed between the anvils of the tester, and pressure was gradually applied until the tablet broke.

The force required to break the tablet was recorded in kilograms or Newtons. A minimum of three tablets were tested, and the average hardness value was calculated. [13-15]

Friability Test

The friability of tablets was assessed using a Roche Friabilator, which evaluates the mechanical strength of tablets by exposing them to abrasion and shock. A pre-weighed sample of tablets was placed in the friabilator, which operates at a speed of 25 revolutions per minute (rpm). During the test, tablets were dropped from a height of 6 inches with each revolution. The procedure was carried out for a total of 100 revolutions. [16-17]

After completion, the tablets were removed, dedusted using a soft muslin cloth, and reweighed. The percentage friability was calculated using the formula:

% friability = [(Initial Weight-Final Weight)/Initial Weight]*100

Where,

W0= Initial weight of the tablets before the test

W= Final weight of the tablets after the test

Weight Variation

20 tablets of each batch were selected randomly and weighed after that single tablet weighed and calculated % deviation with respect to average weight of 20 tablets by using this formula [18]

% deviation = [(Individual Wg.-Avg. Wg)/Avg. Wg.] X 100

Average weight of tablets (mg)	Maximum percent difference allowed
130 or less	10
130-324	7.5
More than 324	5

In Vitro Disintegration Test

The in vitro disintegration time of the tablets was evaluated using the USP disintegration test apparatus. One tablet was placed in each of the six tubes of the apparatus, and a disc was added to each tube. The test was conducted using a suitable medium maintained at 37 ± 2°C.

The time taken for each tablet to disintegrate completely,until no visible residue remained. [19-20]

Dissolution test

The dissolution studies were carried out using USP 2 paddle apparatus. Paddles were allowed to rotate at 50 rpm and 900 ml of phosphate buffer pH 6.8 were used as a dissolution medium. The temperature of dissolution medium was 37±0.5 °C. The duration of dissolution studies were for 24 min and samples (10 ml) were withdrawn at 4 min time intervals (subsequently 10 ml dissolution medium was replaced) and filtered through 0.45 µm Whatman membrane filter paper. The concentration of dissolving drug from tablets was determined by the Uv spectrophotometer at a wavelength, 300.60 nm. The dissolution study for each batch was carried out with three randomly selected tablets.[21]

III. RESULT AND DISCUSSION

The bulk drug sample containing Promethazine theoclate as the active pharmaceutical ingredient, prepared for molding into tablets, underwent pre-compression evaluations to ensure optimal product quality. The results of these evaluations are summarized below.

Angle of repose (θ)
The angle of repose for Promethazine theoclate was found to be in the range of 25° to 30°, indicating that the drug possesses good flow properties.The results are presented in the below Table

Bulk density:
The bulk density was observed to be in the range of 0.47 to 0.48 g/ml. The results are presented in the below Table

Tapped density:
The tapped density was found to be in the range of 0.55 to 0.56 g/ml. The results are presented in the below Table

Hausner Ratio:
The Hausner ratio was found to be less than 1.24, indicating good flow properties of the powder blend. The results are presented in the below Table

Carr's Index
Carr's index was found to be in the range of 12% to 15%, indicating that the powdered drug exhibits good flow properties. The results are presented in the below Table

Drug	Angle of repose	Bulk density	Tapped density	Hausner Ratio	Carr's Index
Promethazine theoclate	28.36	0.47	0.55	1.17	14.54
	28.34	0.49	0.54	1.18	14.52
	28.38	0.46	0.57	1.19	14.55
	Avg= 28.36	Avg=0.47	Avg= 0.55	Avg=1.18	Avg=14.53

The pre-compression study of the sample indicated that the drug powder possessed good flow properties. All evaluated parameters of the bulk powder fell within the standard acceptable range, confirming its suitability as a freely flowing material. Therefore, it can be concluded that the powder exhibited excellent flow characteristics.

Post - compression parameters

Parameters	F_1 (mg)	F_2 (mg)
Thickness(mm) n=5	3.35 ± 0.25	3.40 ± 0.30
Weight Variation	151.2 ± 2.8	149.6 ± 3.1
Hardness (kg/cm²) n=5	3.0 ± 0.5	3.2 ± 0.6
Friability (%) n=10	0.42 ± 0.03	0.38 ± 0.02
Disintegration time	22.4±2.5	23.1±2.8

0 sec 8 sec

15 sec. 23 sec

Figure 2: Disintegration Test of Tablet

The post-compression evaluation of the formulated mouth dissolving tablets (F1 and F2) was carried out to assess their physical and mechanical properties. The thickness of the tablets was found to be 3.35 ± 0.25 mm for F1 and 3.40 ± 0.30 mm for F2 (n = 5), indicating uniformity in tablet dimensions. The weight variation was observed to be 151.2 ± 2.8 mg for F1 and 149.6 ± 3.1 mg for F2, which was within the acceptable pharmacopeial limits. The hardness of the tablets was measured to be 3.0 ± 0.5 kg/cm² for F1 and 3.2 ± 0.6 kg/cm² for F2 (n = 5), indicating satisfactory mechanical strength. Friability values were found to be 0.42 ± 0.03% for F1 and 0.38 ± 0.02% for F2 (n = 10), demonstrating that the tablets possessed good resistance to mechanical stress. The disintegration time of the formulations was 22.4 ± 2.5 seconds for F1 and 23.1 ± 2.8 seconds for F2, indicating rapid disintegration, which is essential for mouth dissolving tablets.

IV. CONCLUSION

The present study successfully developed mouth dissolving tablets (MDTs) of Promethazine Theoclate using various superdisintegrants to enhance patient compliance, especially in populations with

swallowing difficulties such as pediatrics and geriatrics. Among all formulations, batch F1 demonstrated superior performance in terms of rapid disintegration time, optimal drug release profile, and acceptable mechanical strength. The findings confirm that direct compression is an effective and simple technique for preparing MDTs of Promethazine Theoclate. This novel dosage form can potentially improve the onset of action and overall therapeutic efficacy of the drug, offering a promising alternative to conventional tablets.

V. FUTURE SCOPE

Mouth dissolving tablets (MDTs) of Promethazine Theoclate offer enhanced patient compliance, especially for children, the elderly, and mentally ill patients who have difficulty swallowing conventional tablets. Future research may focus on improving the formulation using advanced superdisintegrants, taste-masking agents, and natural excipients to enhance palatability and reduce disintegration time. Emerging technologies like 3D printing and nanotechnology can aid in personalizing dosage forms and controlling drug release. Clinical studies comparing MDTs with traditional tablets, along with research on stability and large-scale production, can further support their development as a preferred, fast-acting medication option.

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