Formulation And Evaluation Pantoprazole Oral Disintegration Tablet for Pediatric Use

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***Abstract*—Pantoprazole is a widely used proton pump inhibitor (PPI) for managing Gastroesophageal Reflux Disease (GERD), which is a common condition in pediatric patients. The creation of Oral Disintegrating Tablets (ODT) for use in children provides a convenient and patient-friendly form of medication that addresses the issues associated with traditional tablets, including swallowing difficulties and low adherence. In this evaluation, we will examine the formulation approaches, assessment criteria, and real-world effectiveness of Pantoprazole ODT in pediatric patients. Detailed discussion is provided on the challenges related to taste masking, rapid disintegration, and stability of Pantoprazole, an acid-labile drug. The use of super disintegrates and sweeteners in excipient selection are highlight as an advancement to ensure patient acceptability while maintaining therapeutic efficacy. Regulatory considerations specific to pediatric formulations and the impact of ODT on treatment outcomes are also explored in the review. Pantoprazole ODT are seen as a promising alternative for effective GERD management in children as the demand for pediatric-friendly formulations increases, offering enhanced patient compliance and ease of administration. Future prospects include optimizing the formulation for even faster onset of action, improving taste masking techniques, and the potential for personalized ODT using emerging technologies.**

***Index Terms*—Pantoprazole, Oral Disintegrating Tablets, GERD, Pediatric Formulation, Proton Pump Inhibitors, Taste Masking.**

I. INTRODUCTION

Oral drug delivery system is the most convenient and widely accepted route of administration for various therapeutic agents. Other than other conventional dosage forms like capsules oral disintegrating tablets are defined as one of the sophisticated novel drug delivery systems that have medicinal substances that dissolve or disintegrate rapidly in the mouth without water or chewing. The pharmacology and treatment of children with peptic acid disorders (PPIs) should be optimized. The parietal cell acid pump is inactive without activation through ligand binding, and H+, k+, -ATPase must be activated to secrete gastric acid. PPIs' pharmacokinetics, including absorption rate and tmax, must be considered in the dosing schedule to be present when the proton pump is active. For children older than 1 year, the pharmacodynamics of PPIs for treating peptic acid disorders are similar to adults. This study found a wide range of perspectives and suggestions about Pediatric dose forms, especially with the perception of ODT among medical professionals. Second, the study found that HCP thought ODT had appropriate organoleptic qualities (such disintegration time), which affected Pediatric patients' acceptability. Further research is necessary to produce a broader range of ODT for usage in the Pediatric population, according to this study. Other synonyms for oral disintegrating tablets are or dispersible tablets, mouth dissolving tablets, quick dissolving tablets, and fast melt tablets.

Superdisintegrants are used to improve the efficacy of solid dosage forms. This is achieving by decreasing the disintegration time, which in turn enhances drug dissolution rate. Disintegrate are substances, mixture of substances added the drug formulation that facilitates the breakup or disintegration of tablet, or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrates. Superdisintegrants are generally used at a low level in the solid dosage form, typically 1- 10 % by weight relative to the total weight of the dosage unit. The present study comprises the various kinds of superdisintegrants, which are being used in the formulation to provide the safer, effective drug delivery with patient's compliance. The disintegration

with the help of super disintegrates occurs by five steps of mechanism processes like swelling, wicking, deformation, particle repulsive forces and enzymatic reaction. Some of the superdisintegrants used in this study are cross Carmel lose sodium, sodium starch glycol ate, microcrystalline cellulose and crospovidone.

Criteria for development of oral disintegrating tablets:

I. . Oral disintegrating tablets should dissolve or disintegrate in the mouth in matter of seconds without water.
II. Oral disintegrating tablets should leave minimal or no residue in mouth after administration.
III. Properties of drug and excipients should not affect the nature of the drug delivery system.
IV. Exhibit low sensitivity to environmental conditions such as humidity and temperature.
V. Should be compatible with pleasant mouth feel.

Advantages of oral disintegrating tablets:

- ✓ It may produce rapid onset of action by rapid dissolution of drug and absorption.
- ✓ Good mouth feel property of oral disintegrating tablets helps to change the psychology of medication as bitter pill particularly in paediatric patients.
- ✓ Convenience of administration and actuate dose as compared to liquids. 4. Ease of administration to patients who refuse to swallow a tablet such as paediatric, geriatric, mentally ill, disabled and uncooperative patients.

ODT mechanism:

1. Tablet containing rapidly disintegrating agents when come in contact with saliva of oral cavity causes disintegrating agents to swell and create channels/pores for saliva to enter inside the tablet creating swelling and pressure.
2. Tablet disintegrates rapidly in mouth. Resins and other sweeteners mask the presence of bitter taste.
3. Physicochemical and biopharmaceutical properties of drug substance aids in solubilisation and its absorption across gastro intestinal tract.

II. PHARMACOLOGY

MECHANISM OF ACTION

There are two types of PPIs: Benz imidazole and imidazopyridine. Pantoprazole is classified as a Benz imidazole PPI. The distinction between these two groups is that benzimidazoles have a faster rate of metabolism, resulting in a shorter plasma presence. Pantoprazole irreversibly blocks the H+/K+ ATP pumps, which is its mode of action. With decreasing ambient pH, pantoprazole breakdown rates rise. As a result, it seems sense that this medicine would be most effective in the stomach, where the H+/K+ ATP pumps are found (particularly, within the parietal cells of the stomach lining). This is the most important stage in stomach acid generation. As a result, pantoprazole's binding to these pumps inhibits acid secretion for up to 24 hours. After 24 hours, additional pumps have formed, necessitating a subsequent dose of pantoprazole to suppress their activity. The beginning of action is quick, with the peak effect occurring between 2 and 6 hours after medication intake. Pantoprazole is also metabolized in the liver, mostly through CYP2C19 demethylation and sulfation. These metabolites are not known to have any significance.

Pharmacokinetics/Pharmacodynamics

A. Absorption
- ✓ Rapid, well absorbed

B. Distribution
- ✓ V_d: Children and Adolescents (Kearns 2008): IV (2 to 16 years of age): 0.22 ± 0.14 L/kg; Oral (5 to 16 years of age): 0.24 ± 0.09 L/kg
- ✓ Adults: 11 to 23.6 L

C. Metabolism
- ✓ Extensively hepatic; CYP2C19 (DE methylation), CYP3A4; no evidence that metabolites have pharmacologic activity

➢ Excretion
- ✓ Urine (71% as metabolites); faces (18%); pantoprazole clearance increased with weight and age

D. Onset of Action
- ✓ Onset of action: Acid secretion: Oral: 2.5 hours; IV: 15 to 30 minutes
- ✓ Maximum effect: IV: 2 hours

E. Time to Peak
- ✓ Children and Adolescents (Kearns 2008): IV (2 to 16 years of age): 0.34 ± 0.12 hours; Oral (5 to 16 years of age): 2.54 ± 0.72 hours
- ✓ Adults: Oral: 2.5 hours

F. Duration of Action
- ✓ Oral, IV: 24 hours

G. Half-Life Elimination

- ✓ Neonates (PMA: 37 to 44 weeks): ~3 hours (Ward 2010)
- ✓ Children and Adolescents (Kearns 2008): IV (2 to 16 years of age): 1.22 ± 0.68 hours; Oral (5 to 16 years of age): 1.27 ± 1.29 hours
- ✓ Adults: 1 hour; increased to 3.5 to 10 hours with CYP2C19 deficiency [22,23]

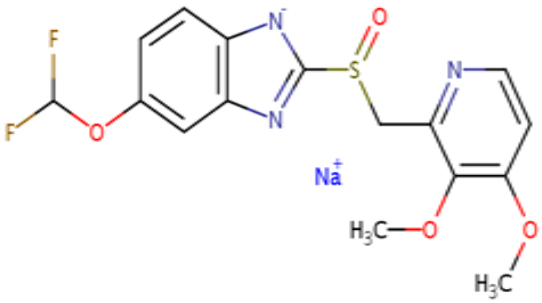
H. Protein Binding 98%, primarily to albumin

ADVERSE EVENTS

Pantoprazole's major adverse reactions are diarrhoea, headaches to occur, upper respiratory tract infections, and abdominal pain. Long-term complications of pantoprazole use include diarrhoea caused by Clostridium difficult or small colitis, small-intestinal bacterial overgrowth, and vitamin B12 deficiency, iron deficiency, calcium deficiency, magnesium deficiency, bone demineralization, interstitial nephritis, and reduced absorption of medications such as clopidogrel.[24]

FORMULATION ASPECTS OF PANTOPRAZOLE: -

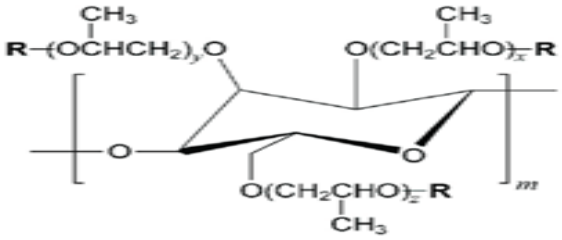
- ➢ ACTIVE INGREDIENTS
- ➢ Pantoprazole Sodium
- ✓ Drug Name: Pantoprazole Sodium
- ✓ Synonym: Pantoprazole Na
- ✓ Drug Category: Proton Pump Inhibitor (PPI)



1. Mannitol

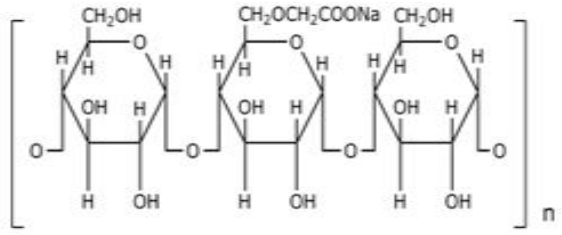
- ✓ Mannitol functions as an osmotic diuretic that remains metabolically inert in humans and is found naturally as a sugar or sugar alcohol in various fruits and vegetables.
- ✓ By increasing blood plasma osmolality, mannitol enhances the movement of water from tissues, including the brain and cerebrospinal fluid, into interstitial fluid and plasma.
- ✓ it can help lower cerebral enema, intracranial pressure, as well as the volume and pressure of cerebrospinal fluid.

2. Hydroxypropyl Methylcellulose (HPMC)



- ❑ HPMC is a non-ionic, water-soluble cellulose ether used as a binder, film former, and controlled-release agent in oral drug delivery systems.
- ❑ It offers excellent swelling, thickening, and stabilizing properties.
- ❑ HPMC is marketed under brand names like Methocel™, Benecel™, and Pharmacoat™.The manufacturing process involves treating purified cellulose with alkali, followed by reaction with methyl chloride and propylene oxide under controlled conditions.

3. Sodium Starch Glycolate



- ❑ Starch is a polysaccharide consisted of amylose and amylopectin, and can be extracted and processed for pharmaceutical use by several plants including maize, potato, rice, corn.
- ❑ Starch modification can be performed in order to improve its functionality as disintegrant. SSG is the sodium salt of the carboxymethyl ether of starch SSG derives from starch (from several sources) after two chemical modification processes: substitution to increase hydrophobicity and cross-linking to reduce solubility and gel formation upon contact with water.
- ❑ It is used in pharmaceutical manufacturing as a superdisintegrant as it acts through rapid swelling due to the adsorption of large amounts of water leading to fast disintegration

4. Sodium Bicarbonate

- Sodium bicarbonate ($NaHCO_3$), commonly known as baking soda, is an inorganic compound widely used in pharmaceutical formulations. It is naturally occurring or synthetically produced and exhibits mild alkalinity
- . It acts as an effervescent agent, alkalizing agent, and pH buffer in oral solid dosage forms. Upon contact with acid or moisture, it releases carbon dioxide, which helps in tablet disintegration and enhances drug dissolution.
- Sodium bicarbonate is particularly valuable in formulations requiring effervescence or pH modulation, such as antacids, buffered tablets, and certain fast-disintegrating oral dosage forms.

5. Sucrose

- Sucrose is a natural disaccharide composed of glucose and fructose. It is widely used in pharmaceuticals as a sweetening agent, tablet binder, and bulking agent.
- Derived primarily from sugarcane or sugar beet, sucrose improves palatability and helps in granule cohesion during tablet formation

. In oral formulations, sucrose masks bitter drug taste and contributes to patient compliance, especially in pediatric formulations.

6. Vanillin

- Vanillin is the primary component of vanilla bean extract and is used in pharmaceutical formulations as a flavoring agent to improve taste and aroma.
- It is used in small quantities to enhance the acceptability of oral liquid or chewable products and mask unpleasant odors or flavors

It is obtained synthetically or from natural sources like vanilla pods.

7. Sodium Lauryl Sulfate (SLS)

- SLS is an anionic surfactant commonly used in pharmaceutical formulations as a wetting agent, emulsifying agent, and solubilize
- .It enhances drug dissolution by reducing surface tension, especially in poorly soluble drugs, and is also used in tablet granulation to improve powder flow and mixing.
- It is synthetically derived from lauryl alcohol and has detergent-like properties

8. Magnesium stearate

- Magnesium stearate (MgSt) is primarily utilized to improve the flow characteristics of powders.
- The optimal quantity of MgSt, which maximizes powder flow, can be identified when a complete coating is formed around each particle.
- Recently, research has focused on modifying the surfaces of lactose carriers by incorporating MgSt to enhance the in vitro aerodynamic performance of these formulations by minimizing adhesion.
- Furthermore, recent studies have explored the viability of a novel solid coating technique called Mechanofusion to demonstrate how MgSt can be used to enhance the effectiveness of carrier-based DPIs. [40,43]

9. Talc

- Talc is a naturally occurring hydrous magnesium silicate used in pharmaceutical formulations as a glidant, lubricant, and diluent
- .It improves powder flow properties in tablet and capsule manufacturing and helps prevent ingredients from sticking to processing equipment.

Talc is chemically inert, making it ideal for use in both oral and topical formulations.

III. METHODOLOGY

Direct Compression

This is the simplest and most economical method for tablet production.

This technique can be utilized to create orally disintegrating tablets (ODT) by carefully choosing combinations of excipients that ensure quick disintegration and adequate physical stability.

Sugar-based excipients are commonly employed as bulking agents due to their solubility in water, sweetness, enjoyable mouth feel, and effective taste masking.

Tablets made using traditional compression techniques tend to be less friable but take longer to disintegrate.

The compression technique, either with or without the use of wet granulation, is an efficient and cost-effective approach to create tablets that maintain satisfactory structural durability

IV. RESULTS

Odour	Odourless
Melting Point	Approx. 140°C–142°C

1. . Preformulation Studies

Property	Observation
State	Solid
Colour	Off-white to yellow

Parameter	Standard Range	F1	F2	F3
Angle of Repose (°)	25–30° (Excellent); 30–40° (Good)	32.5° (Good)	28.9° (Excellent)	30.7° (Good)
Bulk Density (g/cm³)	0.2–0.8 g/cm³	0.48 g/cm³	0.52 g/cm³	0.50 g/cm³
Tapped Density (g/cm³)	Higher than bulk density	0.59 g/cm³	0.61 g/cm³	0.58 g/cm³
Carr's Index (%)	5–15% (Excellent); 16–20% (Good)	18.64% (Good)	14.75% (Excellent)	13.79% (Excellent)
Hausner's Ratio	1.00–1.25 (Good flow)	1.22 (Good)	1.17 (Good)	1.16 (Good)

2. Post-Compression Evaluation Table (F1 – F3)

Solvent	Solubility
Distilled Water	Sparingly Soluble
Hydrochloric Acid	Freely Soluble
Methanol	Soluble
Ethanol	Slightly Soluble
Buffer pH 6.8	Slightly Soluble

Parameter	Standard Value	F1 Batch	F2 Batch	F3 Batch	Acceptance Criteria
Thickness (mm)	4.0 ± 5%	3.95	4.05	3.90	±5% variation from standard
Diameter (mm)	8.0 ± 5%	7.9	8.1	7.95	±5% variation from standard
Hardness (kg/cm²)	3.5 ± 0.5	3.4	3.6	3.2	3–5 kg/ cm²
Friability (%)	<1.0	0.5	0.4	0.6	<1%
Weight Variation (%)	±5%	3.2	2.9	4.5	±5% from average
Wetting Time (seconds)	25 ± 5	27	24	29	<30 s

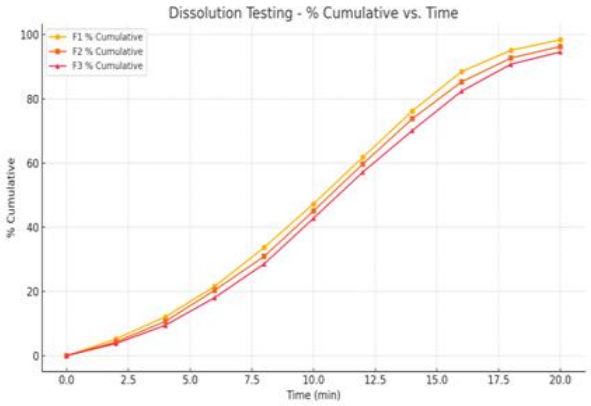
3. Evaluation Test

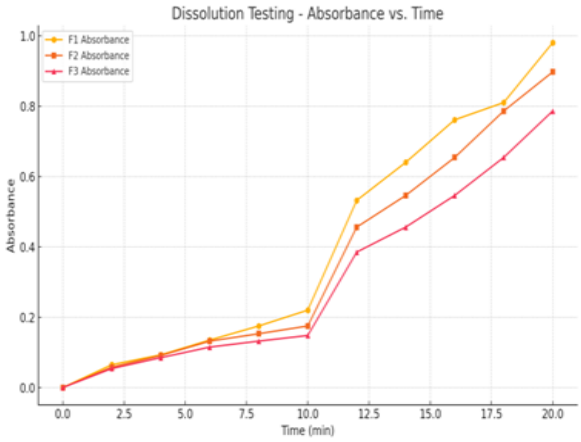
A. Disintegration Test: -

Table Disintegration Time (min)

Formulation	F1	F2	F3
Disintegration Time (min)	1.46 mim	1.23 min	4.03 min

B. Dissolution Test





Absorbance Data of Pantoprazole ODT Tablets

Time (min)	F1 (Abs)	F2 (Abs)	F3 (Abs)
0	0.000	0.000	0.000
2	0.065	0.058	0.054
4	0.093	0.091	0.085
6	0.135	0.132	0.115
8	0.175	0.153	0.132
10	0.220	0.175	0.148
12	0.532	0.456	0.385
14	0.640	0.546	0.456
16	0.761	0.654	0.546
18	0.810	0.786	0.654
20	0.980	0.897	0.786

Dissolution Testing %Cumulative vs time

Time (min)	F1 (%)	F2 (%)	F3 (%)
0	0.0	0.0	0.0
2	5.2	4.3	3.8
4	12.1	10.7	9.5
6	21.6	20.4	18.1
8	33.7	30.9	28.6
10	47.3	45.1	42.8
12	61.8	59.7	57.2
14	76.2	73.8	70.1
16	88.5	85.3	82.4
18	95.1	92.7	90.8
20	98.4	96.3	94.6

V. CONCLUSION

The present research focused on the formulation and evaluation of orodispersible tablets (ODTs) of Pantoprazole sodium, primarily aimed at improving patient compliance, especially in pediatric populations suffering from Gastroesophageal reflux disease (GERD).

Three formulations (F1, F2, and F3) were developed and systematically evaluated based on various pre- and post-compression parameters, disintegration behavior, and in vitro drug release profiles.

The organoleptic and physicochemical characterization confirmed that Pantoprazole sodium is odorless, off-white to yellow, and sparingly soluble in water and pH 6.8 phosphate buffer—properties consistent with its need for enteric protection in traditional dosage forms.

However, in this study, its incorporation into fast-dissolving tablets aimed to bypass the stomach and facilitate rapid systemic absorption via buccal or sublingual mucosa.

Among the tested formulations, F2 exhibited superior characteristics across all critical evaluation parameters. Pre-compression results showed that all formulations had acceptable flow properties, with F2 demonstrating balanced compressibility and flow indices. In the post-compression evaluation, F2 maintained ideal hardness and thickness, while showing excellent friability resistance and minimal weight variation, indicating manufacturing robustness.

The disintegration test was critical in assessing the clinical potential of the tablets. F2 disintegrated in just 1.23 minutes, well below the pharmacopeia limit of 3 minutes, making it highly suitable for rapid action in pediatric patients. Moreover, the dissolution studies highlighted F2's efficiency, achieving 98.4% drug release in 20 minutes, outperforming the other two formulations.

These results establish F2 as a stable and effective orodispersible tablet formulation for Pantoprazole sodium, fulfilling the criteria for fast disintegration, efficient drug release, and potential patient acceptability. Future directions of this study include accelerated stability testing and in vivo pharmacokinetic profiling to validate its therapeutic efficiency, bioavailability, and long-term safety. If these evaluations confirm current findings, the F2 formulation could serve as a viable alternative to conventional pantoprazole dosage forms in pediatric GERD therapy.

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