Formulation And Evaluation of Enteric Coated Tablets of Pantoprazole

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Abstract*—Pantoprazole is a proton pump inhibitor widely used in the treatment of acid-related gastrointestinal disorders such as gastroesophageal reflux disease, peptic ulcer disease, and Zollinger–Ellison syndrome. Despite its therapeutic effectiveness, pantoprazole is highly unstable in acidic environments and undergoes rapid degradation in gastric fluid, leading to reduced bioavailability and therapeutic failure when administered as conventional oral dosage forms. To overcome this limitation, enteric coating technology has been extensively employed to protect the drug from acidic degradation and ensure its release in the intestinal environment Enteric-coated tablets are designed to resist disintegration in the acidic pH of the stomach while allowing rapid drug release in the higher pH of the intestine. This targeted release not only enhances drug stability but also improves bioavailability and patient compliance. The present review focuses on the formulation and evaluation aspects of enteric coated tablets of pantoprazole, highlighting the rationale behind enteric coating, selection of polymers, formulation techniques, and evaluation parameters. Various formulation strategies, including core tablet development, selection of suitable enteric polymers such as methacrylic acid copolymers and cellulose derivatives, and coating processes, are discussed in detail. Critical evaluation parameters, including pre-compression studies, post-compression characteristics, in-vitro disintegration, dissolution studies in simulated gastric and intestinal fluids, and stability studies are reviewed. The role of enteric coating in enhancing therapeutic efficacy, reducing gastric irritation, and improving drug stability is also emphasised. Overall, enteric-coated tablets of pantoprazole represent an effective and well-established approach for targeted intestinal drug delivery and improved clinical performance.

***Index Terms*—Pantoprazole; Enteric coating; Proton pump inhibitors; Delayed-release tablets; Acid-labile drugs; Oral drug delivery; Pharmaceutical formulation; Dissolution studies**

I. INTRODUCTION

Acid-related gastrointestinal disorders such as gastroesophageal reflux disease (GERD), peptic ulcer disease, and Zollinger–Ellison syndrome are among the most commonly encountered conditions in clinical practice. Excessive gastric acid secretion plays a key role in the pathophysiology of these disorders, leading to mucosal damage, inflammation, and discomfort. Proton pump inhibitors (PPIs) are considered the most effective class of drugs for the management of acid-related diseases due to their ability to irreversibly inhibit the gastric H^+/K^+-ATPase enzyme, thereby suppressing gastric acid secretion. Pantoprazole is a widely prescribed proton pump inhibitor owing to its potent acid suppression, favourable safety profile, and high therapeutic efficacy. It is commonly used in the treatment of GERD, gastric and duodenal ulcers, and other hypersecretory conditions. However, pantoprazole is highly acid-labile and undergoes rapid degradation in the acidic environment of the stomach. This instability significantly reduces its oral bioavailability when administered in unprotected conventional dosage forms, leading to reduced therapeutic effectiveness. Oral drug delivery remains the most preferred route of administration because of its convenience, patient compliance, and cost-effectiveness. However, for acid-sensitive drugs such as pantoprazole, oral administration presents a major formulation challenge. Exposure of the drug to gastric acid can result in chemical degradation before it reaches the site of absorption in the intestine. Therefore, an appropriate formulation strategy is essential to protect the drug from acidic conditions and ensure its release at the desired site. Enteric coating technology has been extensively used to overcome these limitations. Enteric-coated tablets are designed

to resist disintegration and drug release in the acidic pH of the stomach while allowing rapid dissolution in the higher pH environment of the intestine. This delayed-release approach not only protects acid-labile drugs from gastric degradation but also minimises gastric irritation and improves bioavailability. Enteric coating thus plays a crucial role in enhancing the stability and therapeutic performance of proton pump inhibitors like pantoprazole. The formulation of enteric-coated tablets involves multiple critical steps, including the development of a stable core tablet, selection of suitable enteric polymers, and optimisation of coating parameters. Polymers such as methacrylic acid copolymers and cellulose derivatives are commonly employed to achieve pH-dependent drug release. Proper evaluation of enteric-coated tablets through physicochemical tests, in vitro dissolution studies, and stability studies is essential to ensure product quality and performance. This review focuses on the formulation and evaluation of enteric-coated tablets of pantoprazole, emphasising the need for enteric protection, formulation strategies, coating techniques, and evaluation parameters. Understanding these aspects is essential for the development of effective delayed-release formulations that improve drug stability, bioavailability, and patient compliance.

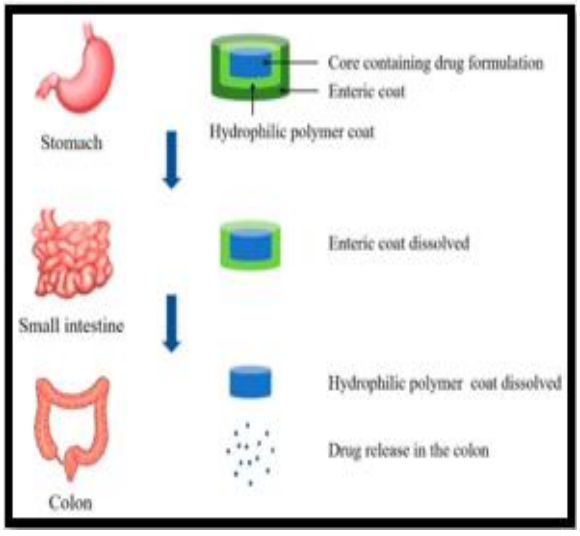

Figure 1: Mechanism of enteric coating for the protection of acid-labile drugs like pantoprazole and targeted intestinal drug release

The figure illustrates the mechanism of action of enteric-coated tablets designed for acid-labile drugs such as pantoprazole. Pantoprazole is unstable in the acidic environment of the stomach and undergoes rapid degradation when exposed to gastric fluid. As shown in the figure, the enteric-coated tablet remains intact in the stomach due to the presence of a pH-dependent polymer coating that resists dissolution at low pH. This protective coating prevents premature drug release and degradation in gastric conditions. Once the tablet reaches the higher pH environment of the intestine, the enteric coating dissolves, allowing the rapid release of pantoprazole at the site of absorption. This targeted drug delivery enhances drug stability, improves oral bioavailability, and ensures effective acid suppression. Thus, enteric coating plays a crucial role in improving the therapeutic performance of pantoprazole.

II. NEED FOR ENTERIC COATING OF PANTOPRAZOLE

Pantoprazole is a proton pump inhibitor that is highly effective in the treatment of acid-related gastrointestinal disorders; however, its clinical performance is limited by its instability in acidic environments. Pantoprazole is an acid-labile drug and undergoes rapid degradation in the gastric pH of the stomach. When administered as an uncoated conventional tablet, a significant portion of the drug degrades before reaching the site of absorption, resulting in reduced bioavailability and suboptimal therapeutic efficacy. The absorption of pantoprazole primarily occurs in the small intestine, where the pH is more favourable for drug stability and absorption. Exposure of the drug to gastric acid not only causes chemical degradation but may also lead to variability in drug release and absorption. Therefore, protecting pantoprazole from the acidic gastric environment is essential to ensure consistent drug delivery and therapeutic effectiveness. Enteric coating provides a pH-dependent protective barrier that prevents drug release in the stomach while allowing rapid disintegration and dissolution in the intestinal environment. Enteric polymers remain intact at low pH and dissolve only at higher pH values, typically above pH 5.5. This selective dissolution ensures that pantoprazole is released at the desired site, minimizing degradation and improving oral bioavailability. Additionally, enteric coating helps reduce gastric irritation and improves patient compliance by preventing direct contact of the drug with the gastric mucosa. The use of enteric coated tablets also allows

for better control over drug release, improved stability during storage, and enhanced overall therapeutic performance. Hence, enteric coating is a critical formulation strategy for pantoprazole to achieve targeted intestinal delivery and optimal clinical outcomes.

Formulation Of Enteric Coated Tablets Of Pantoprazole

The formulation of enteric coated tablets of pantoprazole involves the development of a suitable core tablet followed by the application of a protective enteric coating to achieve delayed release of the drug. Since pantoprazole is acid-labile, the formulation strategy is designed to protect the drug from degradation in the acidic environment of the stomach and to ensure its release in the intestinal pH.

1. Formulation of Core Tablets

The core tablets were formulated to provide adequate mechanical strength, uniform drug distribution, and rapid disintegration once the enteric coating dissolves. Pantoprazole sodium was mixed with suitable excipients including diluents, binders, disintegrants, lubricants, and glidants. Microcrystalline cellulose was used as a diluent to provide compressibility, while Polyvinylpyrrolidone (PVP K30) acted as a binder to impart sufficient tablet strength. Superdisintegrants such as croscarmellose sodium or sodium starch glycolate were incorporated to ensure rapid disintegration of the core tablet in intestinal conditions. Lubricants and glidants were added to improve flow properties and prevent sticking during compression. The core tablets were prepared using either direct compression or wet granulation method.

2. Seal Coating of Core Tablets

Before applying the enteric coating, the core tablets were seal coated with a thin layer of Hydroxypropyl Methylcellulose (HPMC). Seal coating serves multiple purposes, including protection of the core tablet from moisture, prevention of drug–polymer interaction, and improvement of adhesion between the core tablet and the enteric coating layer. This step is particularly important for moisture-sensitive drugs like pantoprazole.

3. Enteric Coating of Tablets

Enteric coating was applied over the seal-coated tablets using pH-sensitive polymers such as Hydroxypropyl Methylcellulose Phthalate (HPMCP), Cellulose Acetate Phthalate (CAP), or methacrylic acid copolymers (Eudragit L100/S100). These polymers remain intact in acidic pH and dissolve only at higher intestinal pH. The enteric coating solution was prepared using a suitable solvent system along with plasticizers such as polyethylene glycol or triethyl citrate to improve film flexibility. Coating was performed using a conventional coating pan or spray coating technique until a uniform and acid-resistant coating was achieved.

4. Rationale of Formulation Strategy

The selected formulation approach ensures that pantoprazole remains protected from gastric acid while enabling targeted drug release in the intestine. The combination of core tablet optimization, seal coating, and enteric coating provides enhanced drug stability, improved bioavailability, and reduced gastric irritation. Thus, the formulation strategy plays a critical role in the successful development of enteric coated tablets of pantoprazole.

III. MATERIALS AND METHODS

Methods

1. Pre-formulation Studies

Pre-formulation studies were carried out to evaluate the suitability of pantoprazole and excipients for tablet formulation. Flow properties of the drug–excipient blend were assessed by determining bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio. These parameters were evaluated to ensure adequate flowability and compressibility of the blend. Compatibility studies of pantoprazole with selected excipients were performed using Fourier Transform Infrared Spectroscopy (FTIR) and/or Differential Scanning Calorimetry (DSC), wherever available, to detect any possible drug–excipient interactions.

2. Preparation of Core Tablets

Core tablets containing pantoprazole were prepared using either the direct compression or wet granulation method. Pantoprazole, diluents, binder, and disintegrants were accurately weighed and blended uniformly. Subsequently, lubricant and glidant were added to the blend and mixed gently to ensure uniform distribution. The final blend was compressed into tablets using a tablet compression machine with suitable punches to obtain core tablets of desired hardness and weight.

3. Application of Coating

a) Seal Coating

The compressed core tablets were initially subjected to seal coating using a thin film of Hydroxypropyl Methylcellulose (HPMC). Seal coating was applied to prevent moisture penetration, protect the drug core, and improve adhesion of the enteric coating layer.

b) Enteric Coating

Enteric coating was applied over the seal-coated tablets using pH-sensitive polymers such as Eudragit L100/S100, Cellulose Acetate Phthalate (CAP), or Hydroxypropyl Methylcellulose Phthalate (HPMCP). The coating solution was prepared using a suitable solvent system and plasticizer. Coating was carried out using a conventional coating pan or spray coating method until acid-resistant tablets with uniform coating thickness were obtained.

4. Evaluation of Tablets

a) Pre-compression Parameters

The powder blend was evaluated for bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose to assess flow and compression characteristics.

b) Post-compression Parameters

The enteric coated tablets were evaluated for the following quality control tests:

- Weight variation
- Hardness (using Monsanto or Pfizer hardness tester)
- Friability (using Roche friabilator)
- Thickness (using Vernier caliper)
- Disintegration time (using disintegration test apparatus)
- Drug content uniformity (analyzed using UV-Visible spectrophotometer or HPLC)

c) In-vitro Dissolution Studies

In-vitro dissolution studies were performed using a USP Type II (paddle) dissolution apparatus. The dissolution study was conducted in two stages: initially in 0.1 N HCl for 2 hours to simulate gastric conditions (acid stage), followed by dissolution in phosphate buffer pH 6.8 to simulate intestinal conditions (intestinal stage). Samples were withdrawn at predetermined time intervals, filtered, and analyzed using a UV-Visible spectrophotometer at 288 nm.

5. Optimization of Formulation

Different formulations were compared and optimized based on their acid resistance in 0.1 N HCl and drug release profile in pH 6.8 phosphate buffer. The optimized formulation was selected based on satisfactory enteric protection and desired dissolution characteristics.

6. Stability Studies

The optimized enteric coated tablet formulation was subjected to stability studies as per ICH guidelines. Tablets were stored at 40 °C ± 2 °C / 75% ± 5% RH for a period of 3 months. Samples were evaluated at predetermined intervals for parameters such as hardness, friability, drug content, and dissolution profile to assess stability.

Materials

- Drug: Pantoprazole sodium (API), obtained as a gift sample or procured from a standard pharmaceutical supplier.
- Excipients for Core Tablets:
  - Diluent: Microcrystalline cellulose (MCC)
  - Binder: Polyvinylpyrrolidone (PVP K30)
  - Disintegrant: Croscarmellose sodium or Sodium starch glycolate
  - Lubricant: Magnesium stearate
  - Glidant: Talc or Aerosil
- Coating Materials:
  - Enteric polymers: Hydroxypropyl Methylcellulose Phthalate (HPMCP), Cellulose Acetate Phthalate (CAP), or Eudragit L100/S100
  - Plasticizer: Polyethylene glycol (PEG 400/6000) or Triethyl citrate
  - Solvent: Isopropyl alcohol, dichloromethane, or purified water (depending on polymer solubility)
- Chemicals for Evaluation:
  - 0.1 N HCl (Simulated gastric fluid)
  - Phosphate buffer pH 6.8 (Simulated intestinal fluid)

All chemicals and reagents used in the study were of analytical grade.

Evaluation Of Enteric Coated Tablets Of Pantoprazole:

The prepared enteric coated tablets of pantoprazole were evaluated to ensure their quality, performance, and compliance with pharmacopeial standards. Evaluation parameters included both pre-compression

and post-compression studies, along with in-vitro performance tests.

1. Pre-compression Evaluation

Pre-compression studies were carried out on the powder blend to assess its suitability for tablet compression.

- Bulk Density: Determines the packing ability of the powder blend.
- Tapped Density: Indicates powder compressibility after tapping.
- Angle of Repose: Assesses flow properties of the blend.
- Carr's Index: Indicates compressibility and flow behavior.
- Hausner's Ratio: Used to predict flowability of powder blends.

Acceptable values of these parameters indicate good flow and compression characteristics, suitable for tablet manufacturing.

2. Post-compression Evaluation

The compressed and enteric coated tablets were evaluated for the following parameters:

a) Weight Variation

Weight variation test was performed to ensure uniformity in tablet weight. The tablets complied with pharmacopeial limits, indicating uniform die filling during compression.

b) Hardness

Tablet hardness was measured using a Monsanto or Pfizer hardness tester. Adequate hardness ensures mechanical strength and resistance to handling while allowing proper disintegration in intestinal conditions.

c) Friability

Friability was determined using a Roche friabilator to assess tablet resistance to abrasion. Friability values below 1% indicate good mechanical strength of tablets.

d) Thickness

Tablet thickness was measured using a Vernier caliper to ensure uniformity and proper coating application.

e) Disintegration Test

Disintegration testing was carried out using a standard disintegration test apparatus. Enteric coated tablets showed no disintegration in 0.1 N HCl for 2 hours, confirming acid resistance, and disintegrated rapidly in phosphate buffer pH 6.8.

f) Drug Content Uniformity

Drug content was estimated using a UV-Visible spectrophotometer or HPLC method. The results indicated uniform distribution of pantoprazole within the tablets.

3. In-Vitro Dissolution Studies

In-vitro dissolution studies were performed using a USP Type II (paddle) apparatus. The study was conducted in two stages:

- Acid stage: 0.1 N HCl for 2 hours, during which negligible drug release was observed, confirming effective enteric coating.
- Intestinal stage: Phosphate buffer pH 6.8, where rapid and complete drug release was observed.

The dissolution profile confirmed pH-dependent drug release and effective protection of pantoprazole from gastric degradation.

IV. RESULTS AND DISCUSSION

The formulation and evaluation of enteric coated tablets of pantoprazole were carried out to overcome the problem of acid degradation and to achieve targeted intestinal drug release. The results obtained from various pre-compression, post-compression, and in-vitro evaluation studies were analyzed and discussed to assess the effectiveness of the enteric coating approach.

Pre-compression Studies

Pre-compression parameters such as bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio indicated satisfactory flow and compressibility of the powder blend. These results confirmed that the blend possessed suitable flow properties, ensuring uniform die filling and consistent tablet weight during compression.

Post-compression Evaluation

The prepared core and enteric coated tablets complied with pharmacopeial specifications for weight variation, hardness, friability, and thickness. Tablet hardness was found to be sufficient to withstand mechanical stress during handling and coating, while friability values were below 1%, indicating good mechanical strength. Uniform tablet thickness and weight variation confirmed consistency in tablet compression.

Disintegration Studies

Disintegration testing demonstrated the effectiveness of the enteric coating. The tablets showed no disintegration or drug release in 0.1 N HCl for 2 hours, confirming adequate acid resistance. Upon exposure to phosphate buffer pH 6.8, the tablets disintegrated rapidly, indicating successful pH-dependent behavior of the enteric polymer and proper intestinal release of pantoprazole.

Drug Content Uniformity

Drug content analysis revealed uniform distribution of pantoprazole within the tablets, with assay values falling within acceptable pharmacopeial limits. This indicates minimal drug loss during formulation and coating processes and confirms the reliability of the manufacturing method.

In-vitro Dissolution Studies

In-vitro dissolution studies showed negligible drug release during the acid stage, confirming protection of pantoprazole from gastric degradation. In the intestinal stage (pH 6.8 phosphate buffer), a rapid and complete drug release was observed. The enhanced dissolution profile demonstrates the effectiveness of enteric coating in achieving delayed release and targeted intestinal delivery.

Stability Studies

Stability studies conducted under accelerated conditions as per ICH guidelines showed no significant changes in tablet hardness, friability, drug content, or dissolution profile over the study period. These results indicate that the enteric coated tablets of pantoprazole were physically and chemically stable during storage.Overall, the results confirm that enteric coating significantly improves the stability of pantoprazole in acidic conditions and ensures effective drug release in the intestine. The formulation approach successfully addresses the limitations associated with conventional pantoprazole tablets and enhances their therapeutic performance.

V. CONCLUSION

The present review emphasizes the importance of enteric coating technology in improving the oral delivery and therapeutic performance of pantoprazole. Pantoprazole, being an acid-labile proton pump inhibitor, undergoes rapid degradation in the acidic environment of the stomach, which significantly limits its bioavailability when administered as conventional oral dosage forms. Enteric coated tablets provide an effective formulation strategy to protect the drug from gastric acid and ensure its release in the intestinal environment, where absorption is optimal. The formulation and evaluation studies discussed in this review demonstrate that the use of pH-sensitive enteric polymers such as Eudragit L100/S100, HPMCP, and CAP successfully prevents drug release in acidic conditions while enabling rapid and complete release in intestinal pH. Evaluation parameters including pre-compression characteristics, post-compression quality control tests, disintegration behavior, in-vitro dissolution studies, and stability testing confirm that enteric coated tablets of pantoprazole meet pharmacopeial requirements and exhibit satisfactory performance. Overall, enteric coating significantly enhances the stability, bioavailability, and therapeutic efficacy of pantoprazole while minimising gastric irritation and improving patient compliance. Thus, enteric-coated tablets represent a reliable and well-established dosage form for the effective management of acid-related gastrointestinal disorders.

VI. FUTURE SCOPE

Although enteric-coated tablets of pantoprazole have proven to be effective, further research can be directed toward optimising coating materials and processes to improve dissolution consistency and reduce manufacturing variability. The development of novel enteric polymers with improved pH sensitivity and mechanical strength may further enhance formulation performance. Future studies may also focus on the development of multiple-unit enteric-coated dosage forms such as pellets or granules to reduce dose dumping and inter-patient variability. In-vivo bioavailability and pharmacokinetic studies should be conducted to establish a direct correlation between in-vitro dissolution behaviour and clinical performance. Additionally, long-term stability studies and scale-up investigations are essential for successful commercial production. Overall, continued advancements in enteric coating technology hold significant potential for improving the effectiveness, safety, and patient adherence of pantoprazole and other acid-labile drugs.

REFERENCES

[1] Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Philadelphia: Lea & Febiger; 1986.
[2] Aulton ME, Taylor KMG. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 4th ed. London: Churchill Livingstone Elsevier; 2013.
[3] Banker GS, Anderson NR. Tablets. In: Lachman L, Lieberman HA, Kanig JL, editors. The Theory and Practice of Industrial Pharmacy. 3rd ed. Philadelphia: Lea & Febiger; 1986. p. 293–345.
[4] Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. 6th ed. London: Pharmaceutical Press; 2009.
[5] Ansel HC, Allen LV, Popovich NG. Pharmaceutical Calculations. 12th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.
[6] Allen LV, Popovich NG, Ansel HC. Ansel's Pharmaceutical Calculations. 13th ed. Philadelphia: Lippincott Williams & Wilkins; 2014.
[7] Gupta R, Mishra B. Formulation and evaluation of enteric coated tablets of acid-labile drugs. Indian J Pharm Sci. 2011;73(2):153–160.
[8] Qureshi J, Patel M. Development and evaluation of enteric coated tablets for acid-labile drugs. Int J Pharm Sci Res. 2014;5(9):3784–3792.
[9] Shargel L, Wu-Pong S, Yu ABC. Applied Biopharmaceutics and Pharmacokinetics. 6th ed. New York: McGraw-Hill; 2012.
[10] Dressman JB, Krämer J. Pharmaceutical Dissolution Testing. Boca Raton: CRC Press; 2005.
[11] United States Pharmacopeia–National Formulary (USP–NF). Rockville, MD: United States Pharmacopeial Convention; latest edition.
[12] Indian Pharmacopoeia Commission. Indian Pharmacopoeia. Ghaziabad: IPC; latest edition.
[13] Khan GM, Jiabi Z. Formulation and in vitro evaluation of enteric coated tablets. J Pharm Sci. 2001;90(2):253–261.
[14] ICH Harmonised Tripartite Guideline. Stability testing of new drug substances and products Q1A(R2). International Council for Harmonisation; 2003.
[15] Rang HP, Dale MM, Ritter JM, Flower RJ. Rang and Dale's Pharmacology. 8th ed. Elsevier; 2016.