

Formulation and Evaluation of Fast Dissolving Tablet of Piperazine Citrate

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Abstract: Piperazine is a well-established broad-spectrum anthelmintic commonly used to treat parasitic infections such as those caused by roundworms and pinworms. Its mechanism of action involves inducing flaccid paralysis in the parasites, facilitating their elimination from the host's body. Although piperazine demonstrates good oral bioavailability (60%-80%), its poor aqueous solubility leads to slow dissolution, potentially delaying absorption and therapeutic onset. This limitation is particularly critical in cases requiring immediate relief. To address this issue, fast-dissolving tablets (FDTs) offer a promising solution. These dosage forms rapidly disintegrate in the oral cavity, enhancing dissolution and promoting faster absorption. The formulation of piperazine as FDTs not only improves therapeutic efficacy but also enhances patient compliance, especially in pediatric and geriatric populations with swallowing difficulties. This review highlights the need for and advantages of developing fast-dissolving formulations of piperazine citrate for improved clinical outcomes.

Keywords: Piperazine Citrate, Fast Dissolving Tablet, Superdisintegrants, Anthelmintic, Dissolution Enhancement, Direct Compression

I. INTRODUCTION

The oral route is the most favored and convenient method of drug administration because of its simplicity, high patient compliance, and economical nature. However, conventional solid oral dosage forms, such as tablets and capsules, often present challenges for patients who have difficulty swallowing, including pediatric, geriatric, and bedridden patients. This limitation has led to the development of fast-dissolving tablets (FDTs), which disintegrate rapidly in the oral cavity without the need for water, providing a convenient alternative to conventional dosage forms.

Fast-dissolving tablets (FDTs) have gained significant attention in recent years due to their ability to enhance drug absorption and bioavailability. These tablets dissolve or disintegrate within seconds to minutes when placed on the tongue, allowing the drug to be rapidly absorbed through the mucosal membrane or swallowed with saliva. The benefits of FDTs include improved patient adherence, rapid onset of action, and ease of administration. They are particularly useful for drugs with poor solubility or drugs that require rapid therapeutic action.

Piperazine Citrate is a widely used anthelmintic drug that has been effective in the treatment of parasitic worm infections such as ascariasis and enterobiasis. It acts by paralyzing the neuromuscular system of parasites, making them susceptible to expulsion from the gastrointestinal tract. Despite its efficacy, conventional piperazine formulations face challenges related to poor dissolution and delayed drug absorption, which may lead to inconsistent therapeutic outcomes. The bioavailability of piperazine is often limited by its slow disintegration in the gastrointestinal tract, necessitating the need for an improved formulation that ensures faster dissolution and absorption.

To address these limitations, fast-dissolving formulations of piperazine can be developed to enhance drug release, improve patient compliance, and provide faster therapeutic action. The formulation of a fast-dissolving tablet of piperazine can be particularly beneficial in treating pediatric and geriatric patients, who may have difficulty swallowing conventional tablets.

The key to achieving rapid disintegration in fast-dissolving tablets lies in the selection of an appropriate superdisintegrant. Superdisintegrants are excipients that facilitate the rapid breakup of tablets into smaller particles, enhancing drug dissolution and absorption. Various superdisintegrants, such as sodium starch glycolate, croscopovidone, and croscarmellose sodium, have been explored for their effectiveness in FDT formulations.



Overview of Piperazine Citrate:

Piperazine citrate is a widely used anthelmintic agent effective against intestinal worm infections, particularly ascariasis (roundworm) and enterobiasis (pinworm). It belongs to the chemical class of heterocyclic compounds and is commonly available in the form of citrate salt due to its enhanced solubility in water.

Chemical Properties

- Chemical Name: Piperazine citrate
- Molecular Formula: $C_{10}H_{16}N_2 \cdot C_6H_8O_7$
- Molecular Weight: Approximately 324.35 g/mol
- Solubility: Freely soluble in water & slightly soluble in alcohol
- Appearance: White crystalline powder with a slightly salty taste

Mechanism of Action

Piperazine works by blocking neuromuscular transmission in parasites. It acts as a GABA (gamma-aminobutyric acid) agonist, causing flaccid paralysis of the worms. The paralyzed worms detach from the intestinal wall and are eliminated from the body by the action of peristalsis.

Therapeutic Uses

- Ascariasis (Roundworm infection)
- Enterobiasis (Pinworm infection)

Occasionally used in combination therapies for mixed worm infestations.

Pharmacokinetics

- Absorption: Well absorbed from the gastrointestinal tract with oral bioavailability of around 60-80%.
- Onset of Action: Typically a few hours Post-administration, but may be delayed due to poor solubility.

Limitations

- Bitter taste
- Poor aqueous solubility slow dissolution
- Delayed onset of action
- Compliance issues in pediatric and geriatric patients.

These drawbacks make Piperazine Citrate a suitable candidate for fast-dissolving tablet (FDT) formulation to enhance its dissolution rate, improve therapeutic effect, and increase patient acceptability.

Overview of Fast Dissolving Tablet:

Fast-Dissolving Tablets (FDTs) are solid oral dosage forms designed to disintegrate or dissolve quickly in the mouth without requiring water. They are designed to improve patient convenience, particularly for populations who have difficulty swallowing conventional tablets, such as children, elderly, and bedridden patients.

Advantages of FDTs

- Rapid onset of action due to faster disintegration and absorption.
- Improved patient compliance and ease of administration.
- Ideal for emergency or on-the-go medication use.
- Improved bioavailability for drugs that have poor solubility or undergo significant first-pass metabolism.
- Sufficient mechanical strength for handling and packaging
- Minimal or no water required for intake



Techniques Used in FDT Formulation

- Direct Compression simple and cost-effective; requires superdisintegrants.
- Freeze Drying (Lyophilization) produces highly porous and rapidly dissolving tablets.
- Sublimation removal of volatile ingredients to create pores for faster disintegration.
- Spray Drying and Molding – advanced methods to improve solubility and taste.

Applications of FDTs

- Pediatric and geriatric medicine
- Anti-allergic, anti-emetic, and pain relief medications
- Drugs with poor solubility or bitter taste (e.g., piperazine citrate)

Challenges in Traditional Dosage Forms

Traditional solid oral dosage forms like tablets and capsules are widely used for drug delivery because of their stability, ease of production, and patient-friendly nature. However, they present several limitations, especially for certain patient groups and specific drugs like piperazine citrate.

Difficulty in Swallowing

Pediatric, geriatric, and bedridden patients often struggle with swallowing large tablets or capsules.

This can lead to non-compliance, improper dosing, or skipped medications.

Delayed Onset of Action

Solid dosage forms require disintegration and dissolution in the gastrointestinal tract before absorption.

Drugs with poor solubility, such as piperazine, dissolve slowly, resulting in delayed therapeutic effect.

Poor Patient Compliance

Bitter-tasting drugs (like piperazine citrate) often cause discomfort and aversion, especially in children.

The need for water during administration adds inconvenience in emergency or travel situations.

Inconsistent Bioavailability

Variability in gastric pH, gastric emptying time, and food intake can affect the dissolution and absorption of drugs.

Drugs with low solubility may have erratic absorption profiles.

Risk of Dose Dumping

Improper disintegration can cause a sudden release of the drug, leading to side effects or reduced efficacy.

These challenges justify the need for improved formulations such as Fast-Dissolving Tablets (FDTs), which can overcome the drawbacks of conventional oral dosage forms by offering faster onset of action and improved patient compliance.

Role of Superdisintegrants in Fast Dissolving Tablet

Superdisintegrants play a crucial role in the formulation of fast-dissolving tablets by enabling rapid disintegration and dissolution of the tablet upon contact with saliva. They act mainly through mechanisms such as swelling and water wicking, which help the tablet break apart quickly in the oral cavity.

The selection of an effective Superdisintegrant is essential to ensure the tablet dissolves within seconds without leaving residue or causing discomfort. Commonly used superdisintegrants include croscopovidone, croscarmellose sodium, and sodium starch glycolate. Among these, croscopovidone is particularly effective due to its high capillary activity, porous structure, and non-gelling nature, which make it ideal for enhancing the disintegration and dissolution of poorly soluble drugs like piperazine citrate. Incorporating an appropriate concentration of superdisintegrant significantly improves drug release, bioavailability, and ultimately, the therapeutic performance of the formulation.

Fast Dissolving Tablet Formulation Approach

The formulation of fast-dissolving tablets requires a strategic selection of excipients and manufacturing techniques to ensure rapid disintegration, acceptable taste, mechanical strength, and drug stability. The most commonly used method



is direct compression, which is simple, cost-effective, and suitable for heat- and moisture-sensitive drugs like piperazine citrate. In this approach, the active pharmaceutical ingredient (API) is blended with superdisintegrants, fillers, sweeteners, and other excipients, then compressed into tablets using minimal processing steps.

Key excipients include superdisintegrants to accelerate tablet breakup, diluents to provide bulk, lubricants to aid in tablet formation, and flavoring agents to mask any unpleasant taste. Crospovidone is often preferred as the superdisintegrant in piperazine formulations due to its rapid wicking properties and non-gelling behavior. The formulation must also ensure uniform drug distribution, good flow properties, and adequate hardness to withstand handling without compromising disintegration speed.

Successful FDT formulation involves optimizing the concentration of each excipient, maintaining tablet uniformity, and achieving a balance between fast disintegration and mechanical integrity. This approach not only enhances the drug's onset of action but also improves patient compliance, particularly in populations with swallowing difficulties.

Assessment Techniques for Fast-Dissolving Tablets (FDTs)

To ensure the effectiveness and quality of fast-dissolving tablets, several analytical tests are conducted during formulation development. These assessments help verify that the tablets meet expected pharmaceutical standards and provide quick therapeutic action.

Initial evaluations include checking the tablet's physical features such as size, shape, texture, weight consistency, and resistance to breaking or crumbling. The most critical characteristic of FDTs is their ability to disintegrate quickly—ideally within 30 seconds—when placed in the mouth. This is measured through disintegration testing, along with related assessments like wetting time and moisture absorption, which indicate how fast the tablet begins to dissolve after contact with saliva.

The uniform distribution of the active drug is also tested to confirm that each unit delivers an accurate dose. Additionally, dissolution studies are performed using standard equipment to observe how efficiently and rapidly the drug is released into solution, mimicking the conditions in the body. Together, these evaluation methods ensure that the final product is both reliable and patient-friendly, offering quick relief with consistent drug delivery.

II. CONCLUSION

The development of fast-dissolving tablets (FDTs) of piperazine citrate presents a promising approach to enhance patient compliance, particularly in populations with swallowing difficulties such as children and the elderly. By overcoming the limitations of conventional dosage forms—like delayed onset of action and poor dissolution—FDTs offer rapid drug release and improved bioavailability. The use of superdisintegrants, especially crospovidone, plays a vital role in achieving quick tablet disintegration and effective drug delivery. This formulation strategy not only improves therapeutic efficiency but also provides a more convenient and acceptable dosage form. With further research and optimization, FDTs of piperazine could significantly enhance the management of parasitic infections by offering a safer, faster, and more patient-friendly treatment option.

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