International Journal of Engineering Research Excellence and Applied Science (IJEREAS)

Volume-II (Issue 3) – September 2024 ISSN: 3048-5355

Advances in Formulation and Evaluation of Gastroretentive Floating Tablets: Challenges and Opportunities

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Abstract

Gastroretentive drug delivery systems (GRDDS) are innovative pharmaceutical approaches specifically designed to extend the duration of a drug's retention in the stomach. By prolonging the gastric residence time, these systems optimize the absorption of drugs that are primarily absorbed in the upper gastrointestinal tract, thereby enhancing their bioavailability and overall therapeutic efficacy. Among the various types of GRDDS, floating tablets have emerged as a particularly promising technology. Their ability to remain buoyant in gastric fluids ensures they can float on the surface of the stomach contents, maintaining their position within the stomach for an extended period. This floating mechanism not only facilitates prolonged gastric retention but also enables a controlled and sustained release of the active pharmaceutical ingredient, thereby improving treatment outcomes and reducing dosing frequency.

This review provides a comprehensive exploration of gastroretentive floating tablets, focusing on their formulation strategies, key evaluation parameters, and diverse therapeutic applications. Furthermore, it delves into the challenges encountered during their development, such as physiological and manufacturing hurdles, while offering insights into emerging innovations and future directions to address these limitations and enhance their clinical utility.

Keywords: Gastroretentive drug delivery systems (GRDDS), Gastric residence time, Enhanced bioavailability, Therapeutic efficacy, Floating tablets, Buoyancy.

1. INTRODUCTION

The oral route remains the most preferred and widely utilized method for drug administration due to its simplicity, patient compliance, cost-effectiveness, and non-invasive nature. However, certain drugs face significant limitations when administered orally, particularly those with poor bioavailability. These limitations often arise from their short gastric residence time, which reduces the window available for effective absorption, or their narrow absorption window, where drug uptake is confined to specific regions of the upper gastrointestinal (GI) tract, such as the stomach and proximal small intestine. Additionally, drugs that are poorly soluble or unstable in the intestinal environment are particularly susceptible to reduced therapeutic efficacy when they pass rapidly through the gastrointestinal system.[1-4]

To address these challenges, **Gastroretentive drug delivery systems (GRDDS)** have been developed as innovative pharmaceutical approaches. These systems are designed to prolong the retention of drugs in the stomach, ensuring that the drug remains in the region where it can be optimally absorbed. Among various GRDDS, floating tablets have emerged as a particularly promising technology. These systems rely on the principle of buoyancy, where the tablets are formulated to remain afloat on gastric fluids, thereby preventing their rapid transit to the intestines. This prolonged gastric retention enhances the drug's exposure to the

gastric mucosa and maintains a steady drug release rate, leading to improved absorption and bioavailability. [5-8]

Floating tablets are especially beneficial for drugs that are poorly soluble in alkaline environments or degrade in the intestinal pH, as they provide an extended period of stability and dissolution in the acidic gastric environment. By enabling a controlled and sustained release of the drug over time, floating tablets not only improve therapeutic outcomes but also reduce the frequency of dosing, enhancing patient compliance. This makes them a valuable solution for addressing the challenges associated with oral drug delivery, particularly for drugs requiring targeted gastric absorption or sustained therapeutic action. [9-12]

2. MECHANISM OF FLOATING TABLETS

Floating tablets are a type of gastroretentive drug delivery system (GRDDS) designed to prolong the residence time of drugs in the stomach, enhancing their absorption and bioavailability. The fundamental mechanism behind these tablets is **buoyancy**, which allows the tablets to float on the surface of gastric fluids, preventing them from moving too quickly through the stomach and allowing for controlled, sustained drug release. [13]

Buoyancy and Floating Mechanism: The key factor for the functioning of floating tablets is their **density**. For the tablet to float, its density must be lower than that of the stomach's gastric fluids, which typically have a density of around 1 g/cm³. By using excipients that reduce the overall density of the tablet, it remains buoyant and floats on the surface of the stomach's contents, thus maintaining its position and ensuring extended residence time. [14-15]

There are two primary mechanisms of floating tablets:

1. Effervescent systems
2. Non-effervescent systems

1. Effervescent Floating Systems

In effervescent floating tablets, the mechanism relies on a **gas-generating reaction**. These tablets contain **acidic** and **alkaline** components, such as citric acid and sodium bicarbonate, which react upon contact with gastric fluids. This acid-base reaction generates **carbon dioxide (CO_2)**, forming gas bubbles within the tablet matrix.

- **Reaction:** When the tablet encounters gastric fluid (acidic environment), the acid and base react to produce carbon dioxide, which gets trapped within the tablet.
- **Effect on Buoyancy:** The gas trapped inside the tablet causes it to swell and reduces its density, allowing the tablet to float on the stomach contents. The sustained generation of gas ensures that the tablet maintains its buoyant state for an extended period, facilitating prolonged gastric retention.

2. Non-effervescent Floating Systems

Non-effervescent floating tablets rely on **physical properties** of the excipients used, rather than gas generation, to maintain buoyancy. There are two main types of non-effervescent floating systems: **swelling systems** and **low-density systems**.

A. **Swelling Systems:** These tablets are made using **hydrophilic (water-attracting)** polymers such as **HPMC (Hydroxypropyl methylcellulose)**, **guar gum**, or **xanthan gum**. When the tablet comes into contact with gastric fluids, these polymers absorb water, causing the tablet to swell.
   - **Effect on Buoyancy:** The swelling increases the tablet's size while its density remains low, allowing it to float. The swelling process also helps control the release of the drug by forming a gel-like matrix that slowly releases the active pharmaceutical ingredient (API) over time.

B. **Low-Density Systems:** Tablets formulated with **low-density materials** such as **hollow microspheres**, **microcrystalline cellulose**, or **floating beads** are designed to have an

inherently low density, allowing them to float even without the need for swelling or gas generation.

- **Effect on Buoyancy:** These materials inherently have a lower density than the stomach's contents, so they can float without relying on any chemical reactions or physical swelling, offering another mechanism for maintaining gastric retention. [16]

3. FACTORS AFFECTING FLOATING TABLET PERFORMANCE

Several factors influence the effectiveness of floating tablets, including:

- **Tablet Size and Shape:** Larger tablets or tablets with irregular shapes may float more effectively than smaller, smooth tablets. The larger surface area allows for better retention and a slower release of the drug.
- **Tablet Composition:** The use of hydrophilic polymers and low-density materials plays a critical role in determining the floating properties. The formulation must balance factors such as swelling, density, and drug release rate to achieve optimal performance.
- **Gastric pH and Volume:** The acidic pH of the stomach (pH 1.5–3.5) is crucial for the effervescent reaction in gas-generating floating tablets. The gastric fluid volume also impacts the floating behavior, as larger volumes of liquid may lead to faster tablet dissolution.
- **Food Intake:** The presence of food can alter the gastric pH, volume, and motility, which may affect the floating behavior. Floating tablets generally perform better in the fasting state but can still provide extended retention during the fed state. [17-20]

4. FORMULATION STRATEGIES

Formulating floating tablets involves careful selection of excipients and the use of specific techniques to ensure that the tablet remains buoyant in the gastric fluid and delivers the drug in a controlled and sustained manner. The key factors in the formulation of floating tablets

include the choice of excipients that influence buoyancy, drug release rate, and the overall stability of the dosage form. The following sections describe the formulation strategies used to design effective floating tablets. [21-22]

1. Selection of Excipients

The choice of excipients plays a crucial role in achieving the desired floating properties, controlled drug release, and overall tablet stability. The main excipient categories include:

1.1. Buoyancy-generating Agents: To ensure the tablet remains afloat in the stomach, buoyancy-generating agents are incorporated. These agents either generate gas (effervescent systems) or reduce the tablet's density (non-effervescent systems).

- **Effervescent Systems:** The most commonly used buoyancy-generating agents in effervescent floating tablets are **acid-base reactants**, such as:**Citric acid**, **Tartaric acid**, **Sodium bicarbonate**. These ingredients react with water or gastric fluid to generate **carbon dioxide (CO_2)**, which is trapped within the tablet structure, making the tablet less dense and buoyant.
- **Non-effervescent Systems:** In non-effervescent floating tablets, low-density materials and polymers are used to reduce the tablet's density.
  - ✓ **Low-density materials:** Materials such as **microcrystalline cellulose (MCC)**, **hollow microspheres**, and **floating beads** are used to create a tablet that is light enough to float.
  - ✓ **Swelling agents:** Hydrophilic polymers such as **hydroxypropyl methylcellulose (HPMC)**, **xanthan gum**, **guar gum**, and **carbopol** are used to swell and form a gel-like matrix when exposed to gastric fluid. The swelling increases the tablet's volume, which decreases its density and enhances buoyancy. [23-24]

1.2. Polymer Matrix and Drug Release Control: The polymer matrix is crucial not only for buoyancy but also for the **sustained release** of the drug. The choice of polymer will determine the release profile, as well as the mechanical strength of the tablet. [25]

- **Hydrophilic Polymers:**
  - ✓ **HPMC (Hydroxypropyl methylcellulose)**: HPMC is a widely used polymer for floating tablets because of its ability to swell in water and form a gel matrix, controlling the release of the drug.
  - ✓ **Xanthan gum and guar gum**: These natural gums are used for their swelling properties and ability to form a controlled release matrix.
  - ✓ **Carbopol**: A strong gelling agent used in controlled release systems.
- **Hydrophobic Polymers:**
  - ✓ **Ethylcellulose**: This polymer is used for sustained-release formulations as it forms a hydrophobic barrier that slows down drug release.
  - ✓ **Acrylic polymers**: These can be used in combination with hydrophilic polymers to adjust the release rate and enhance the mechanical properties of the tablet.
- **Other Excipients:** Additional excipients like **plasticizers** (e.g., **glycerin**, **propylene glycol**) may be used to improve the flexibility and workability of the polymer matrix. [26-32]

1.3. Release Modifiers: In addition to the polymer matrix, **release modifiers** are used to adjust the rate at which the drug is released from the tablet. These can include:

- **Pore-forming agents:** Materials such as **sodium chloride**, **sorbitol**, and **mannitol** can be incorporated into the tablet to create pores during hydration, which control the release rate of the drug.
- **Crosslinking agents:** Crosslinking agents such as **glutaraldehyde** or **epichlorohydrin** are sometimes used to enhance the gel strength of the polymer matrix and slow down drug release, providing a more sustained release profile. [33]

2. Techniques for Formulation of Floating Tablets

Several techniques are used in the preparation of floating tablets to ensure proper formulation, buoyancy, and controlled release.

2.1. Direct Compression: Direct compression is a widely used technique for the preparation of floating tablets, particularly for effervescent formulations. The excipients, including the active pharmaceutical ingredient (API), buoyancy-generating agents, and polymer matrix materials, are mixed and compressed into tablets.

2.2. Wet Granulation: In this technique, the excipients and API are first blended, and then a granulating liquid (typically a binder solution) is added to form granules. These granules are then compressed into tablets. Wet granulation can be particularly useful for improving the flow properties of poorly compressible powders and ensuring uniform drug distribution. [34-38]

5. CHALLENGES AND LIMITATIONS

Despite their potential, gastroretentive floating tablets face several challenges that limit their widespread use. Variability in gastric conditions, such as changes in pH and gastric motility, can affect buoyancy and drug release, leading to inconsistent performance. The limited drug-loading capacity of floating tablets, due to the need for buoyancy agents and swelling excipients, makes them unsuitable for high-dose drugs. Additionally, achieving a consistent and controlled drug release can be difficult, and the complexity of formulation and manufacturing processes increases production costs. Patient-related issues, such as difficulty swallowing larger tablets and conditions like gastroparesis, can also hinder their effectiveness. Furthermore, stability concerns, both chemical and physical, as well as regulatory challenges in demonstrating consistent in vivo performance, add to the limitations of floating tablets. Despite these hurdles, continued research and innovation are essential to overcoming these challenges and improving the practical application of gastroretentive floating tablets.

6. FUTURE PERSPECTIVES

Advancements in technology can address the limitations of floating tablets:

- ✓ 3D Printing: Enables precise control over tablet geometry and drug release profiles.
- ✓ Nanotechnology: Incorporation of nanoparticles for enhanced drug solubility and targeted delivery.
- ✓ Hybrid GRDDS: Combining floating mechanisms with mucoadhesion or unfolding systems for improved retention.
- ✓ Patient-Centric Designs: Tailored formulations based on individual gastric conditions. **[39-40]**

7. CONCLUSION

Floating tablets offer a promising solution to the limitations associated with conventional oral drug delivery systems, particularly for drugs with poor bioavailability due to their short gastric residence time or limited absorption in the intestine. These tablets work by remaining buoyant in the stomach, effectively extending their residence time and allowing for a more controlled and sustained release of the active pharmaceutical ingredient (API). This prolonged gastric retention improves the absorption of drugs that are poorly soluble or unstable in the intestines, thus enhancing their bioavailability and therapeutic efficacy.However, the development of floating tablets is not without its challenges. Factors such as variability in gastric conditions (e.g., pH and motility), formulation complexities, excipient compatibility, and patient-related issues (e.g., difficulty in swallowing large tablets) need to be carefully addressed to ensure the effectiveness and patient compliance. Additionally, while floating tablets show great promise for enhancing the bioavailability of certain drugs, their low drug loading capacity and the need for precise formulation and manufacturing techniques present significant hurdles.

Despite these challenges, ongoing research and technological advancements are continuously improving the formulation strategies and evaluation techniques for floating tablets. Researchers are working to overcome limitations related to the size and drug loading capacity

of these systems, and to develop more efficient, patient-friendly formulations. As these advances continue, floating tablets are expected to see broader clinical applications, especially for drugs with narrow absorption windows or those that are poorly absorbed in the intestinal tract. With further innovation, gastroretentive floating tablets hold significant potential to transform the field of oral drug delivery, offering more effective and reliable treatment options for a variety of therapeutic areas.

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