Floating Drug Delivery System : A Review

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Abstract : Floating drug delivery systems (FDDS) are engineered to possess a bulk density lower than that of gastric fluids, thereby enabling prolonged buoyancy within the stomach without significantly altering the gastric emptying rate. While remaining afloat on gastric contents, these systems facilitate the controlled and sustained release of the incorporated drug. Following complete drug release, the system either disintegrates or is subsequently eliminated from the stomach.

This approach effectively enhances gastric residence time (GRT), contributing to improved regulation of plasma drug concentration and minimizing pharmacokinetic fluctuations. To achieve optimal performance, FDDS must exhibit adequate structural integrity to form a stable and cohesive gel barrier, ensuring gradual drug release while maintaining a density lower than that of the surrounding gastric medium.

FDDS are generally formulated using either effervescent or non-effervescent mechanisms, both of which rely on buoyancy principles to achieve gastric retention. These systems are particularly advantageous for the delivery of drugs characterized by a narrow therapeutic window.

The present review aims to provide a comprehensive overview of the pharmaceutical principles underlying the design, classification, and formulation of FDDS. Furthermore, it examines the critical factors influencing system performance, along with their advantages, applications, limitations, and prospective advancements in this evolving drug delivery technology.

Keywords: Floating drug delivery system, Polymer, Gastroretentive system, Prolonged Gastric Retention, Controlled Drug Release.

INTRODUCTION : [1-5]

A floating tablet is a type of gastroretentive drug delivery system (GRDDS) that is designed to remain buoyant in the stomach for a prolonged period. This allows the drug to be released slowly and in a controlled manner, thereby increasing the time the drug stays in the stomach. The buoyancy of the tablet is achieved by using low-density polymers or gas-generating agents, which help the tablet float on gastric fluids without being quickly emptied.

Floating drug delivery systems (FDDS) are formulated to remain on the surface of gastric contents for an extended time without significantly affecting the normal gastric emptying process. These systems are especially useful for drugs that are unstable in intestinal fluids or have limited absorption in the lower parts of the gastrointestinal tract. While floating, the drug is released gradually, and once the drug is completely released, the system is eliminated from the stomach.

This approach increases gastric residence time (GRT), which helps maintain more consistent drug levels in the blood and reduces fluctuations. As a result, it improves the overall therapeutic effect of the drug.

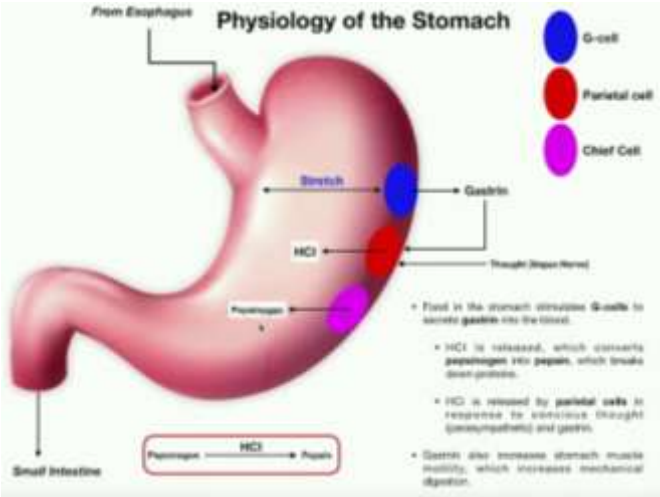
FDDS are particularly beneficial for drugs that are mainly absorbed in the upper part of the gastrointestinal tract or those that degrade in alkaline conditions. They are also useful for delivering drugs locally to the stomach or the upper small intestine. This can improve bioavailability, enhance treatment effectiveness, and may reduce the required dose.

The main goal of any drug delivery system is to provide effective treatment, reduce side effects, and improve patient compliance in a cost-effective way. Oral drug delivery systems are the most commonly used, accounting for more than half of all dosage forms.

Controlled Release Drug Delivery Systems (CRDDS) are designed to release drugs at a predictable and controlled rate over a long period. This helps maintain stable drug levels in the body, reduces the frequency of dosing, and minimizes side effects. Gastric retention systems, such as floating, mucoadhesive, swelling, and delayed gastric emptying systems, increase the time a drug remains in the stomach. This leads to better drug absorption, reduced drug loss, and improved effectiveness of the therapy.

BIOLOGICAL ASPECTS OF CONTROL RELEASE GASTRO RETENTIVE FLOATING DRUG DELIVERY SYSTEM:[6-7-8]

Stomach Physiology :



Dig: Stomach Physiology

The stomach is an expanded part of the digestive system located between the esophagus and the small intestine. Its wall structure is similar to other parts of the gastrointestinal tract, but it contains an additional inner oblique layer of smooth muscle. This extra muscle layer allows the stomach to perform strong mixing and grinding movements.

When the stomach is empty, it remains contracted, and its inner lining (mucosa and submucosa) forms folds known as *rugae*. These folds allow the stomach to expand when food is consumed.

The inner surface of the stomach is lined with specialized epithelial cells that extend into gastric pits and glands. The major types of cells include:

1. **Mucous cells** – These cells secrete alkaline mucus, which protects the stomach lining from mechanical stress and acidic conditions.
2. **Parietal cells** – These cells produce hydrochloric acid (HCl), which helps in digestion and maintains an acidic environment.
3. **Chief cells** – These cells release pepsinogen, which is converted into pepsin, an enzyme responsible for protein digestion.
4. **G cells** – These cells secrete the hormone gastrin, which regulates gastric activity and acid secretion.

The contraction of gastric smooth muscles performs two main functions:

- Mechanical digestion: Food is crushed, mixed, and converted into a semi-liquid form called *chyme*.
- Gastric emptying: Chyme is gradually pushed through the pyloric sphincter into the small intestine.

Gastric Motility

Gastric motility refers to the movements of the stomach that aid in digestion and emptying. It is regulated by both neural and hormonal mechanisms.

- **Neural control** involves the enteric nervous system, along with the parasympathetic (mainly via the vagus nerve) and sympathetic nervous systems.
- **Hormonal control** includes substances such as gastrin and cholecystokinin, which influence stomach relaxation and contraction.

The volume of gastric fluid plays an important role in dissolving orally administered drugs. The resting gastric volume is typically around 25–50 mL. Variations in gastric acid secretion (such as in achlorhydric individuals) can significantly affect drug dissolution and absorption.

Gastric pH also plays a critical role:

- In the fasting state: pH is approximately 1.2–2.0
- In the fed state: pH ranges from 2.0–6.0

These pH variations can influence drug stability and absorption.

Gastric Emptying Rate

Gastric emptying occurs under both fasting and fed conditions, but the patterns differ.

In the fasting state, the stomach exhibits a cyclic pattern of electrical and motor activity known as the **migrating myoelectric complex (MMC)**. This cycle occurs every 2–3 hours and helps clear residual contents from the stomach and intestine.

In the fed state, gastric motility changes to allow slower and more controlled emptying, which supports digestion and enhances drug absorption in certain delivery systems.

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEMS (FDDS) [9]

Floating drug delivery systems can be broadly classified based on their mechanism of buoyancy and design:

1. Non-Effervescent Floating Drug Delivery Systems

Non-effervescent FDDS depend on the swelling ability of polymers or their bioadhesive interaction with the gastrointestinal mucosa to remain in the stomach. These systems use gel-forming agents or highly swellable hydrocolloids, such as cellulose derivatives, which form a viscous gel barrier when in contact with gastric fluid.

Matrix-forming polymers like polyacrylates, polymethacrylates, and polystyrene are commonly used. In addition, bioadhesive polymers such as chitosan and carbopol help the system adhere to the stomach lining, thereby increasing gastric residence time and enabling sustained drug release.

2. Effervescent Floating Drug Delivery Systems

Effervescent FDDS utilize gas-generating agents to achieve buoyancy. These formulations typically contain sodium bicarbonate along with organic acids such as citric acid or tartaric acid.

When these components come into contact with gastric fluid, they react to produce carbon dioxide gas. The generated gas becomes trapped within the system, reducing its density and allowing it to float on gastric contents. Some formulations may also include volatile components that generate gas at body temperature, further supporting flotation and controlled drug release.

3. Volatile Liquid-Containing Systems

These systems contain an inflatable chamber filled with volatile liquids such as cyclopentane or ether. At body temperature, these liquids vaporize, causing the chamber to expand and maintain buoyancy.

They are designed as hollow, deformable units with two compartments:

- One compartment contains the drug
- The other contains the volatile liquid

This design allows prolonged gastric retention and controlled drug delivery.

4. Bilayer Floating Tablets

Bilayer floating tablets consist of two distinct layers:

- An **immediate-release layer** that provides an initial dose of the drug
- A **sustained-release layer** that forms a gel barrier upon contact with gastric fluid

The gel layer helps maintain buoyancy and ensures prolonged drug release in the stomach.

5. Micro-Porous Compartment Systems

These systems contain a drug reservoir enclosed within a compartment that prevents direct contact with the gastric mucosa.

The system includes small pores or openings through which gastric fluid enters, dissolves the drug, and allows it to diffuse out. Entrapped air within the system provides buoyancy, helping it float on gastric contents.

6. Raft-Forming Systems

Raft-forming systems are commonly used for antacid formulations and the treatment of gastrointestinal disorders such as acid reflux.

Upon contact with gastric fluid, these systems form a viscous gel or “raft” that floats on the stomach contents. The formation of carbon dioxide helps the raft remain buoyant. This floating layer acts as a barrier, preventing the backflow of gastric acid into the esophagus.

7. Colloidal Gel Barrier Systems

Also known as hydrodynamically balanced systems, these were developed to enhance gastric retention time and drug absorption.

They use gel-forming hydrocolloids and matrix-forming polymers such as polystyrene and polycarbophil, along with cellulose-based polymers like hydroxypropyl methylcellulose. These materials form a stable gel barrier that maintains buoyancy and allows controlled drug release over an extended period.

Overall, these different types of FDDS are designed to improve gastric retention, enhance drug bioavailability, and provide controlled and sustained drug release for better therapeutic outcomes.

FACTORS AFFECTING GASTRIC RETENTION:[10-11]

The gastric retention time (GRT) of capsule form is controlled by several factors that affect their effectiveness as a gastroretentive system.

Density - GRT is a function of capsule form buoyancy that is dependent on the density.

Size - capsule form units with a fringe of further than 9.5 mm are reported to have an increased GRT.

Shape of dosage form - Tetrahedron and ring- shaped bias with a flexural modulus of 48 and 22.5 kilopounds per square inch (KSI) are reported to have better GRT. 90 to 100 retentions at 24 hours compared with other shapes.

Single or multiple unit formulation - Multiple-unit formulations offer more predictable release profiles, reduce the risk of dose dumping, enable coadministration of incompatible substances, and provide greater safety compared to single-unit forms.

Gender - Mean ambulatory GRT in males (3.4 + 0.6 hours) is less compared with their age and racematched womanish counterparts (4.6 + 1.2 hours), anyhow of the weight, height and body face.

Age - Elderly people, especially those over 70, have a significantly longer GRT.

Posture - GRT can vary between supine and upright ambulatory countries of the case.

Biological factors - Diabetes and Crohn's complaint.

POLYMERS USED IN FLOATING DRUG DELIVERY SYSTEM : [12,13,14]

1] Natural Polymers

Chitosan: Biodegradable, biocompatible, and forms a gel in acidic pH, promoting sustained medicine release and buoyancy.

Guar gum: Provides gel- forming capability and helps sustain medicine release.

Xanthan gum: Used as a thickening agent and stabilizer, promoting floating and controlled release.

Alginates: Form hydrogels that swell in the stomach, enabling floatation and controlled medicine delivery. Hydroxypropyl Methylcellulose (HPMC): A extensively used polymer for controlled release phrasings due to its gel- forming capability. Different grades (e.g. HPMC K4M, K15M) can conform medicine release rates.

Methylcellulose: Provides buoyancy and a prolonged floating effect due to its high water immersion capacity.

Ethylcellulose: frequently used in combination with other polymers to modify medicine release and enhance floatation.

2] Synthetic Polymers

Eudragit (Methacrylic acid copolymers):

a) Eudragit RL and RS give controlled medicine release and help maintain buoyancy.

b) Eudragit NE 30D used in coatings for floatable phrasings.

Polyvinyl Alcohol (PVA): Biocompatible, forms stable hydrogels, and aids in floatation.

Polyethylene Oxide (PEO): Offers high lump capacity, perfecting the floatation and release profile.

Polylactic-co-Glycolic Acid (PLGA): Used in advanced FDDS to achieve sustained release.

METHODS OF PREPARATION OF FLOATING TABLET :

The preparation of floating tablets typically involves one of the following methods:

1. **Direct Compression:** Ingredients, including the drug, floating agents (e.g. sodium bicarbonate, citric acid), polymers (e.g. HPMC) and excipients are mixed and directly compressed into tablets.[15]]

2. **Wet Granulation:** The drug and excipients are mixed with a granulating agent (e.g. water, ethanol). The wet mass is granulated, dried and compressed into tablets.[16]

3. **Effervescent Technique:** Effervescent agents like sodium bicarbonate and citric acid are incorporated to produce C02, allowing the tablet to float. These are combined with the drug and compressed into tablets.[17]

4. **Hot-Melt Extrusion:** Polymers are melted and mixed with the drug, shaped into tablets, and cooled. This method is used for controlled-release floating tablets.[18]

ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM : [19-20]]

1] Increases the oral bio availability of medicine.

2] Enhanced first pass bio-transformation.

3] Sustained medicine delivery/ reduced frequency of dosing.

4] Reduced oscillations of tube medicine attention.

5] Bettered receptor activation selectivity.

6] Give advanced effectiveness due to reduced counteractivity of body.

7] Extended time over critical (Effective) attention.

8] Minimized adverse exertion at the colon.

9] Targeted remedy for original affections within the upper GIT.

10] Point specific medicine delivery.

CHALLENGES OF FLOATING DRUG DELIVERY SYSTEM : [21-22]

Medicines having solubility or stability problem in GIT are not suitable for FDDS.

1. Medicines like Nifedipine, Propranolol etc. which are well absorbed throughout GIT and which undergoes first pass metabolism are not be desirable seeker.
2. Medicines which are irritant to Gastric mucous also are can't desirable.
3. Medicines that are unstable in the acidic terrain of the stomach are not suitable in this type of systems.
4. High position of fluid in the stomach is needed for maintaining buoyancy; float and work efficiently.

APPLICATION OF FLOATING DRUG DELIVERY SYSTEM :[23-24]

1. Sustained Drug Delivery: Floating systems prolong gastric residence, enabling controlled drug release over time. E.g., sustained-release floating capsules of nicardipine showed effective in vivo performance.
2. Site-Specific Delivery: Ideal for drugs absorbed in the stomach or upper intestine, like diuretics and vitamin B2, enhancing bioavailability significantly.
3. Absorption Enhancement: Improves bioavailability for drugs with site-specific absorption in the upper GI tract. E.g., floating formulations showed superior absorption compared to conventional forms.
4. Constant Blood Levels: Ensures steady drug release, maintaining consistent blood levels, with easy administration and better patient compliance.

FORMULATION OF FLOATING TABLETS :[25,26,27]

1. **Active Pharmaceutical Ingredient (API):** The drug intended for controlled or sustained release.

Example: Metformin, Ciprofloxacin.

2. **Polymers:**

a) Hydrophilic Polymers: Control drug release and form the matrix.

Examples: Hydroxypropyl methylcellulose (HPMC), Carbopol.

b) Effervescent Agents: Generate gas for buoyancy. Examples: Sodium bicarbonate, citric acid.

3. **Buoyancy Enhancers:** Provide low density.

Examples: Low-density materials like polyethylene oxide or ethyl cellulose.

4. **Binders:** Ensure tablet integrity.

Examples: Polyvinylpyrrolidone (PVP), starch.

5. **Lubricants and Glidants:** Facilitate manufacturing.

Examples: Magnesium stearate, talc.

6. **Gas-Generating System:** Sodium bicarbonate and organic acids (e.g., citric acid) react in the gastric medium to release C02.

IN-VITRO EVALUATION OF FLOATING DRUG DELIVERY SYSTEMS (FDDS) : [28,29,30]

1. **Pre-compression Parameters** (before tablet punching)
   - Angle of repose
   - Bulk density & tapped density
   - Carr's index & Hausner's ratio
2. **Post-compression Parameters** (after tablet punching)
   - Appearance – shape, color, surface texture.
   - Thickness & diameter – using vernier caliper.
   - Weight variation test – to ensure uniformity of dosage.
   - Hardness test – mechanical strength, usually 4–6 kg/cm².
   - Friability test – resistance to abrasion (should be <1%).
3. **Specific Floating Tablet Tests**
   - Buoyancy / Floating test

   -Place the tablet in 0.1 N HCl (pH 1.2) at 37 ± 0.5 °C.

   Floating lag time (FLT): Time taken to rise and float on the surface.

   Total floating time (TFT): Duration tablet remains buoyant.
4. **Swelling Studies**
   - Wt = weight after swelling, W0 = initial weight.
5. **Drug Content Uniformity**
6. **In-Vitro Dissolution Studies**

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