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Floating drug delivery system: A review

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Abstract
Controlled-release oral delivery systems are programmed to deliver drugs in a predictable time frame. This improves efficacy, minimizes side effects, and increases drug bioavailability. This is the most prevalent route of administration among all routes investigated. Systemic delivery of drugs via pharmaceuticals in different dosage forms. Latest technology and scientific research have been devoted to developing rate-controlled drug delivery systems to Overcome physiological disadvantages such as short gastric residence time and unpredictable stomach time to empty. Inter-subject variability with significant impact on gastric residence time and drug delivery action. This has led to increased interest in formulating new delivery systems. It is retained in the stomach for long, predictable periods. some approaches like floating drug delivery systems (FDDS), swelling and expansion systems, bio adhesive systems, modified Systems, high-density systems, or other devices have been discovered to delay gastric emptying. FDDS is particularly important for locally active drugs with narrow absorption windows. Unstable and low in the gastric or upper small bowel, intestinal, or colonic environment solubility at high pH values. This review article aims to provide detailed information about their design, classification, benefits, pharmacological rationale for *in vitro* and *in vivo* evaluation parameters, and the future of FDDS.

Keywords: floating drug delivery systems, GRDDS, GIT

Introduction

The term "drug delivery system" refers to a pure, unprocessed form of the drug that can be in solid, liquid, or semi-solid form. It should be therapeutically effective, safe, and stable enough to deliver the necessary quantity of the drug to the target site in the body quickly, to reach the target site with the required concentration, and to maintain the target concentration. Oral medication delivery techniques are widely used in drug delivery systems that are commercialized [1]. Oral drug delivery is typically favored because it has lower treatment costs, higher patient compliance, and is simpler to administer. Even though taking medication has many advantages, it should be taken more frequently because the stomach can easily empty it [2]. The distribution of medications must offer a longer duration of stomach residence to get beyond these obstacles. The duration of drug release is improved, drug waste is reduced, and drug solubility is improved for drugs that are less soluble in high environmental pH levels thanks to gastro retention [3]. As their release is continuously delayed and regulated, many medications that are released in the stomach offer the strongest therapeutic effects. The need for repeated dosages would be unnecessary and this form of drug delivery technology would have significantly fewer negative effects [4]. The packaging of medications in multilayered or bilayered tablets is a novel method for delivering the loading dose and maintenance dose in a tablet in pharmaceutical dosage. With the use of an instant-release amount of medicine in one layer and an extended-release proportion in the second, this design enables the manufacture of extended-release while maintaining a sustained blood level. The immediate release section, which delivers the initial dose of medication for immediate action and, for the most part, travels through the intestine with an intact matrix layer, gradually dissolves from its exposed phases along this path, helping to maintain the blood level that was initially reached [5].

Conventional controlled-release dosage forms often delay the beginning of effect following oral administration and prolong drug release. Because the drug is rapidly released from the rapid-release layer, the plasma concentration of the drug increases quickly, and the drug is then continuously released from the sustained-release layer, the layered tablets have a pharmacokinetic advantage over conventional controlled-release dosage forms [6].

Gastro-retentive drug delivery system-approved drugs [7]

- Medicines that work locally in the stomach, such as antacids and misoprostol, etc.
- Medicines with a limited window of absorption in the gastrointestinal system, such as riboflavin and furosemide.
- Medicines that exhibit instability in the intestinal environment, such as captopril and ranitidine HCl.
- Medicines that work well against common intestinal microorganisms, such as antibiotics for Helicobacter pylori.
- Medicines that are poorly soluble at high pH levels, such as chlordiazepoxide, diazepam, etc.

Gastro retentive drug delivery system unsuitable medicines

- Medicines whose solubility in an acidic medium is very low, such as phenytoin, etc.
- Medicines that are unstable in the stomach environment, such as Erythromycin, etc.
- Medicines that are primarily used for their controlled release in the colon, such as corticosteroids and 5-amino salicylic acid.

Classification of GRDDS

Dosage forms that can be held within the stomach are called Gastroprotective Dosage Forms (GRDF) [12].

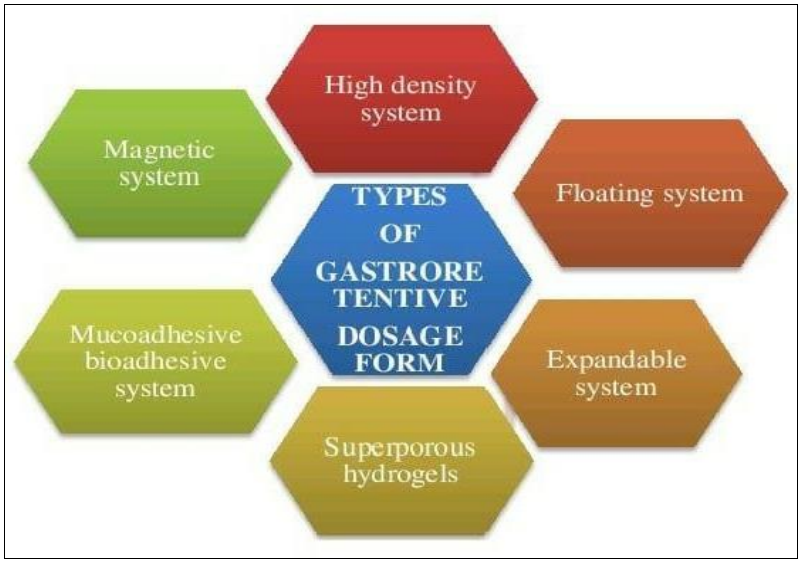

Fig 1: Types of Gastroprotective Dosage Form.

High-density system

These GRDF types are stored in the stomach rugae and have a density of -3g/cm^3. Once these systems reach a maximum threshold density of 2.4–2.8g/cm^3, they can be kept operating in the lower region of the stomach. Its main drawback is that they require a lot of medication products and are technically challenging to create.

Swelling and expandable system

The expandable GRDF normally comes in three configurations: a tiny configuration that is easy to swallow; an expanded form that is achieved in the stomach, blocking the pyloric sphincter; and finally, another small form that is accomplished in the stomach when retention is no longer required. Osmosis typically causes swelling, while mechanical shape memory causes unfolding**.**

Mucoadhesive and bio adhesive system

These systems enable the inclusion of bio adhesive substances that enable the system to stick to the stomach's walls and prevent gastric emptying. By enhancing the closeness and duration of contact between the dose type and the biological membrane, bio/mucoadhesive systems extend the GRT by adhering to the surface of the stomach epithelial cell, or mucin.

Super porous hydrogels

They are swellable systems with an average pore size of greater than 100 micrometers; they reach equilibrium in less than a minute as a result of quick water absorption by capillary wetting through numerous connected open holes. They swell to a size that will allow them to exert enough mechanical strength to withstand the pressure caused by the contraction of the stomach**.**

Magnetic system

The magnetic dosage forms have an extra-corporal magnet and a tiny internal magnet that regulates the dosage form's gastrointestinal transit.

The Floating Drug Delivery System (FDDS) is a very simple and logical approach to the creation of GRDF from a formulation and technology standpoint [8, 9, 11].

Floating drug delivery system

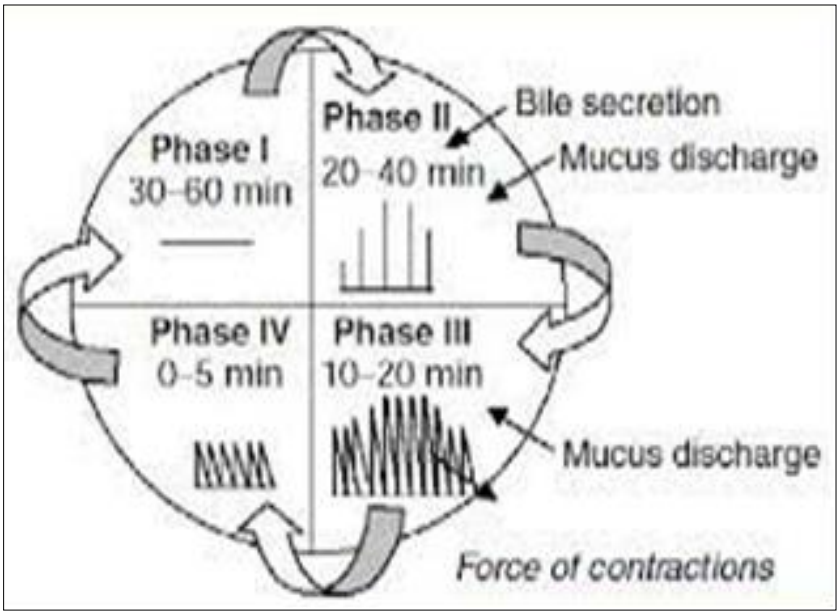

Fig 2: Motility Pattern in GIT

After the ingestion of a blended dinner, the example of compressions changes from abstained to that of taken care of state which is likewise named as stomach-related motility design [9].

Stage1
(Fundamental stage)- last from 30-60 minutes with uncommon constrictions.

Stage2
(Preburst stage)- keep going for 20-40 minutes with discontinuous activity potential furthermore, compressions.

Stage3
(Burst stage) - keep going for 10-20 minutes which incorporates extreme and normal withdrawals for brief periods.

Stage4
keep going for 0-5 minutes and happens between stage 2 and 1 of 2 back-to-back cycles.[11]

Considering the component of lightness, two particularly various advances have been used being developed FDDS which are:[1]

Effervescent System
1. Gas generating system.
2. Volatile liquid-containing system.

Non-Effervescent System
1. Colloidal gel barrier system.
2. Bi-layer floating system.
3. Microporous compartment system.
4. Floating beads/ Alginate Beads.
5. Microballoons/ Hallow Microsphere.

Effervescent system
Effervescent systems include the use of gas-generating agents, carbonates (e.g. Sodium bicarbonate), and other organic acids (e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide (CO2) gas, thus reducing the density of system and making it float on the gastric fluid. An alternative is the incorporation of a matrix containing a portion of liquid, which produce gas that evaporates at body temperature. These effervescent systems are further classified into two types [10].

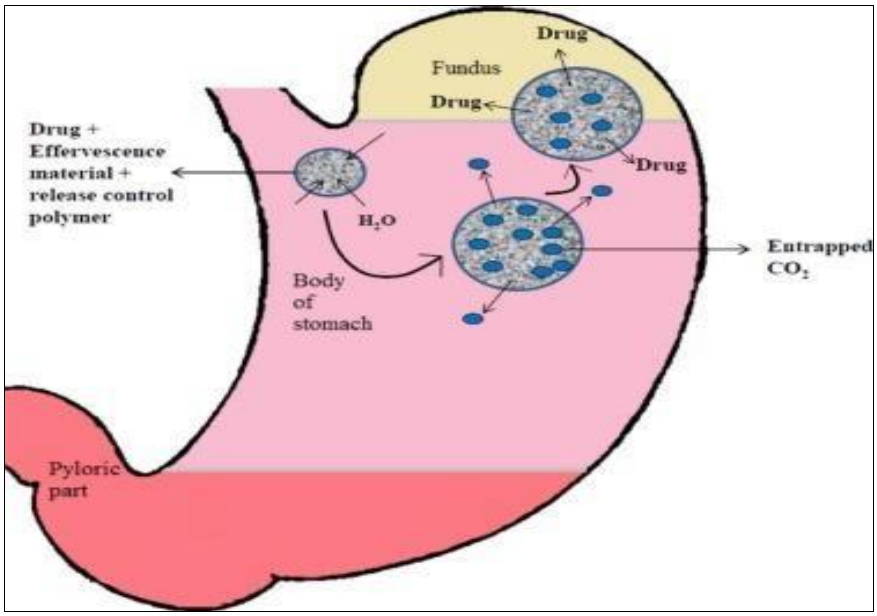

Fig 3: GRDDS based on effervescence

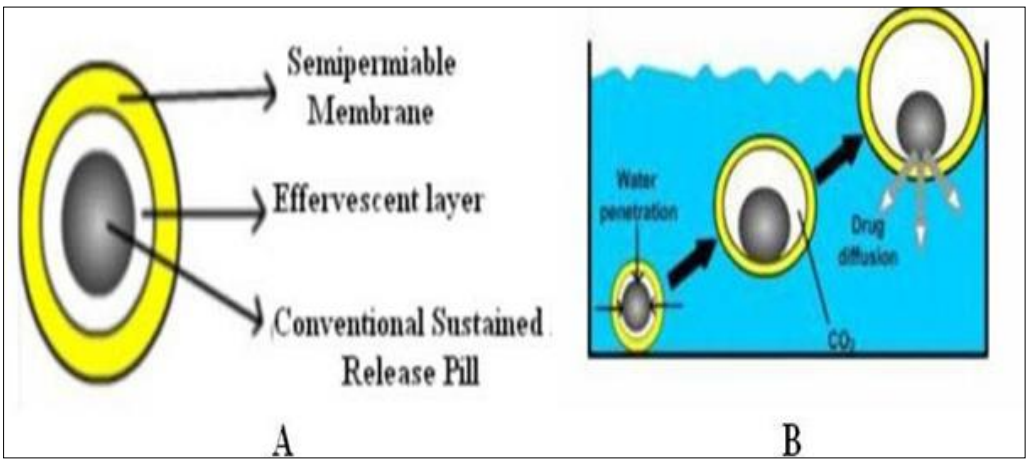

Fig 4: Multiple-unit oral drug delivery system.

Gas generating systems [14].
This buoyant distribution device exploits an effervescence reaction between carbonate and bicarbonate salts and citric or tartaric acid to release CO2, further lowering its specific gravity and causing it to float over the chime.

Volatile liquid/vacuum systems
They have an inflatable chamber made of a liquid, such as ether or cyclopentane, that gasifies at body temperature to cause expansion of the chamber in the stomach. The system consists of two chambers: the volatile liquid is in the second chamber, while the first chamber contains the medicine.

Non-Effervescent system
The non-effervescent FDDS in the GI tract works by adhering to the mucosal layer of the polymer by polymer swelling. The following excipients are used most commonly in non-effervescent FDDS:
Hydrophilic gums and hydrocolloids of the cellulose type create gels or are extremely swellable
Polysaccharides, matrix-forming substances like polycarbonate, polystyrene, polymethacrylate, and polyacrylate, as well as bioadhesive polymers like Carbopol and Chitosan.

Colloidal gel barrier systems / Single layer floating tablets
In such systems, one or more gel-forming hydrocolloids of the cellulose type, polysaccharides, and matrix-forming polymers are present in large concentrations and have a high swelling potential.

Bi-layer floating tablets
The immediate release layer of a bi-layer tablet releases the initial dose from the system. The sustained release layer absorbs stomach fluid, forming an impermeable colloidal gel barrier on its surface, and maintaining a bulk density of less than 1 [15].

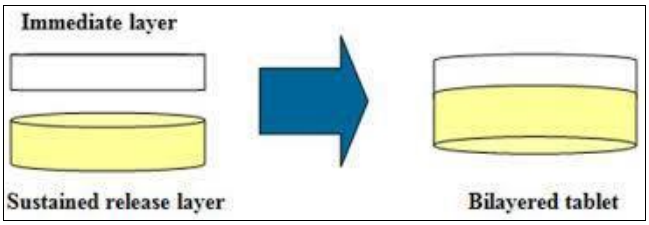

Fig 5: Bi-layer tablet

Based on this technology, a drug reservoir is enclosed inside a small, porous space that has perforations running the length of its top and bottom walls.

Multi-particulate system: floating beads / alginate beads
Oral dosage forms with a variety of small discrete units make up multi-particulate drug delivery systems.

Micro balloons/hollow microspheres
Hollow microspheres, commonly referred to as micro balloons, were discovered to float *in vitro* for 12 hours when submerged in an aqueous solution.

Raft forming system
Raft-producing systems are frequently taken into consideration for the delivery of antacids and other drugs for gastro-infection and gastrointestinal illnesses. The gel-forming solution expands when it comes into touch with gastric fluid, generating a viscous compact gel with trapped CO2 bubbles that forms a raft layer on top of gastric fluid and releases the medication material into the stomach over time [16].

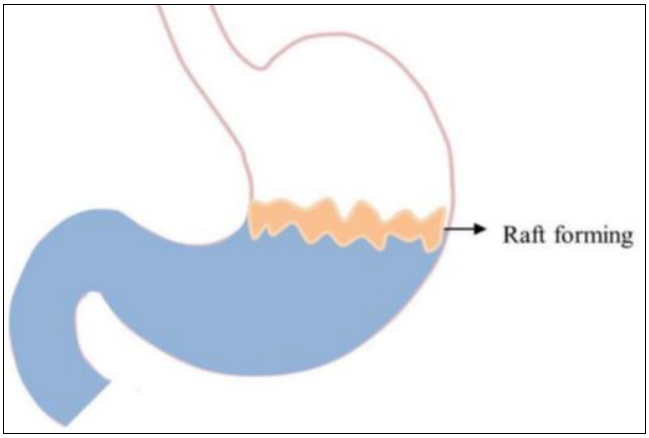

Fig 6: GRDDS based on Raft Forming System

Approaches to design floating drug delivery system
For Single Unit Dosage Forms (Ex: Tablets)

a. Floating Lag Time: This time, which is estimated in seconds or minutes, is needed for the tablet to emerge onto the surface of the dissolution media.
b. In-vitro drug release and floating duration: These are determined by using USP II devices (paddles) to stir in simulated gastric juice (pH 1.2 without pepsin) at speeds of 50 or 100 rpm at a temperature of 370.
c. Evaluation of in-vivo gastro-retention Testing of the dose form transition in the GIT using X-ray or gamma scintigraphy is used to achieve this. The pills are also examined for hardness, weight fluctuation, etc.

Hydrodynamically balanced system
The delivery method is made to prolong the time that different types of medications remain in the gastrointestinal tract and to improve absorption. Drugs created by the HBS system have a higher solubility in acidic environments and a specific absorption location in the upper small intestine. The dosage form must have a bulk density of less than "1" and continuously release the drug for the medication to remain in the stomach for an extended period [17].

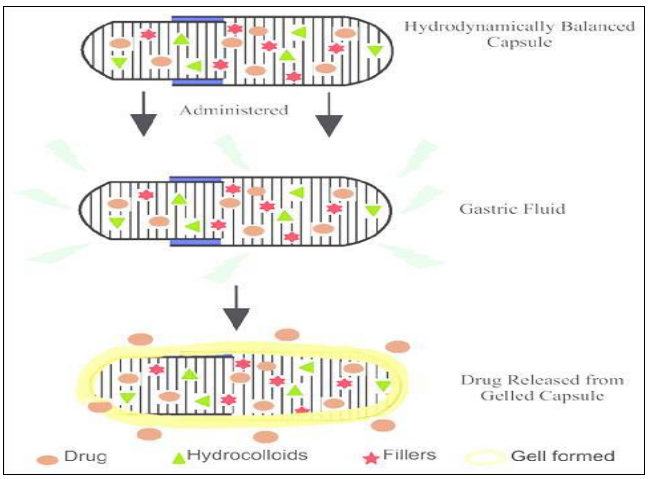

Fig 7: Working principle of Hydrodynamically Balanced System.

Methods of Developing Floating Drug Delivery System [18, 21]

- **Direct compression technique**:
  It entails compressing tablets straight from powder without changing the substance's actual physical composition. The most popular carriers include tricalcium phosphate, dicalcium trihydrate phosphate, etc.

- **Effervescent Technique**
  Citric acid and bicarbonate salts will react in an effervescent manner to produce inert gas, which will then fill the floating chamber of the medication delivery system (CO2).

- **Wet granulation technique**
  Involves grinding, drying, or massaging wet powder. Instead of compacting the powders, wet granulation forms the granules by joining them using an adhesive.

- **Ionotropic gelation technique**
  To create instantaneous microparticles, the fundamental polymer of natural origin, anionic polysaccharide sodium alginate, was gelated using calcium ions that had opposite charges to one another.

- **Solvent evaporation technique**
  The amount of liquid dispersal solvent that can be removed during a continuous phase is insufficient. The dispersal surface's solvent evaporates, allowing hardened microspheres to be absorbed.

- **Spray drying technique**
  involves mixing the core layer into the liquid coating content and spraying the core coating mixture into the environment to quickly evaporate the coating material, which will solidify the coating.

- **Melt Solidification Technique**
  With this technique, the molten mass is emulsified in the aqueous phase before being cooled to solidify. The carriers employed for this approach include lipids, waxes, polyethylene glycol, etc.

- **Melt Granulation Technique**
  This technique uses a meltable binder to agglomerate the pharmaceutical powders without the need for water or organic solvents.

Advantages of Floating drug delivery system [23].

- FDDS can stay in the stomach for several hours, extending the period that different medications are retained in the stomach.
- Favorable for medications intended for localized effects in the stomach, such as antacids.
- The FDDS formulation helps keep the medicine in a floating state in the stomach so that it can be more effectively absorbed when diarrhoea and intestinal movement occur.
- FDDS increases patient compliance by reducing dosage frequency.
- The treatment of digestive problems such as gastroesophageal reflux.
- Despite the first pass impact, since the plasma drug concentration is minimized, bioavailability is maintained.
- Since that aspirin and other such medications are acidic and irritate the stomach wall, HBS/FDDS formulations may be helpful for the administration of these medications.
- advantageous for medications that are absorbed through the stomach, such as antacids and ferrous salts.
- The drug's delivery to the designated location.

Disadvantages of floating drug delivery system

- Drug compounds that are unstable in the stomach's acidic environment are not good candidates for system integration.
- Food must typically be present in these systems to delay stomach emptying.
- The only acceptable candidates are those pharmaceuticals that experience first pass effect and those that are considerably absorbed throughout the gastrointestinal tract. It is not appropriate for medications that have stability or solubility issues in the GIT.
- The dosage form's level of hydration affects its propensity to float. It is helpful to administer water intermittently to keep these tablets afloat.

- **Application of floating drug delivery system [24]**

Enhanced Bioavailability

As compared to the administration of non-GRDF CR polymeric formulations, riboflavin CR-GRDF has much higher bioavailability.

- **Drug distribution that is sustained**

Gastric residence duration was an issue for oral CR formulations. These issues may typically be solved by HBS systems that can float on the gastric contents for extended periods and have a bulk density of less than 1.

- Extended gastric availability from a site-driven medication delivery system can reduce the need for frequent doses. like riboflavin and furosemide.

- **Improvement of absorption**

By maximizing their absorption, drugs with low bioavailability caused by site-specific absorption from the upper section of the GIT are potential candidates to be created as floating drug delivery devices.

Decreased colonic adverse reaction

In HBS, the amount of medication entering the colon is reduced by the retention of the drug in the stomach. Hence, undesirable drug activity in the colon region can be prevented.

Less volatility in drug concentration

Contrary to some instant-release dosage formulations, continuous drug input after CR-GRDF treatment results in blood drug concentrations that fall within a tighter range.

Conclusion

A current study is creating an effective gastro-retentive dosage form for stomach-specific medication delivery. To achieve the desired gastro retention, a variety of techniques were employed, with the floating medication delivery system emerging as the most promising. These systems

improve the bioavailability and regulated distribution of many medications, providing new and important therapeutic alternatives. They also give the benefit of greater pharmaceutical absorption from the top of the stomach. Less frequent dosing and improved therapy effectiveness are the results of this. Such technology is more reliable since it has superior medication release and stability than other standard dose forms. The GIT is an incredibly changeable system for drug absorption, and extending GI retention of the dose form extends the period of drug absorption. A technique for stomach retention is guaranteed by the floating drug delivery system. Although many different difficulties must be worked out to achieve extended GI retention, many businesses are concentrating on commercializing this strategy. That is clear from the wide range of industrial products and patents that have been issued in this area.

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