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REVIEW ARTICLE **OPEN ACCESS**

A Review on Floating Drug Delivery Systems

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ABSTRACT
Recent scientific and patent literature demonstrates rising interest in academic and industry research organisations for novel dosage forms that can be kept in the stomach for a lengthy and predictable period of time. By overcoming physiological challenges such as short gastric residence periods (GRT) and unpredictably long stomach emptying times, rate-controlled oral drug delivery devices have recently made scientific and technological advances (GET). Controlling the duration of gastric residence with gastro-retentive dosage forms will give us new and significant treatment possibilities, and is one of the most practical methods for obtaining a longer and predictable drug delivery patterns in the gastrointestinal system. The floating drug delivery system is a fairly simple and sensible idea from a formulation and technological standpoint. A gastro-retentive medication delivery system that continuously regulates the administration of sparingly soluble medicines at the site of absorption includes a floating drug delivery system. This review article makes an effort to acquaint readers to the most recent technological advancements in floating medication delivery systems.
Keywords: *Floating drug delivery system, Gastric residence time, Gastrointestinal system, sparingly soluble, Floating medication.*

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INTRODUCTION

Floating drug delivery systems (FDDS) also known as low-density systems have enough resistance to float on the stomach and remain there for an extended period of time without having any impact on the rate at which the stomach empties. These are low-density systems having sufficient buoyancy to float over the contents of the stomach and remain there for a long time. The medicine will release gradually at the desired concentration in the system while the body floats on the contents of the stomach. As a result, the stomach will be emptied of the residue. These outcomes will then lead to an increase in GRT and better control of drug concentration flux.(1-2)In 1968, Davis discovered the first floating systems. In order to float over the gastric juices in the stomach and retain longer action, floating systems explain that the systems have low density and have a greater buoyancy property. Drugs with a short biological half-life can be maintained via floating drug delivery systems, increasing their efficacy and aiding in a reduction in dosage frequency. This feature of feds helps to improve pharmaceutical therapy and patient compliance. Many buoyant systems have been created using granules, powders, capsules, tablets, laminated films, and hollow micro-spheres. The purpose of floating drug delivery systems is to increase absorption by extending the time the dosage form spends in the gastrointestinal tract. Drugs that are highly soluble in acidic conditions and have a specific absorption location in the upper section of the small intestine are more suited to these mechanisms. Floating multi-particulate are gastro-retentive drug free-flowing synthetic polymer powders, preferably smaller than 200 micrometers in size. Floating multi-particulate are effervescent and non-effervescent drug delivery methods that are gastro-retentive. The drug's gastric residence time will be greatly prolonged by gastro retentive systems, which will stay over several hours in the environment of the stomach. In a high pH situation, continuous stomach retention promotes bioavailability, lowers drug wastes and improves solubility for pharmaceuticals that are less soluble delivery systems based on non-effervescent and effervescent approach.The ability of the system to exert some therapeutic control is referred to as "controlled release". It aids in maximizing efficiency and adherence. The typical stomach residence time is between 2-5 hours. A promising new dosage form that is fast gaining acceptance is floating dosage forms. By incorporating gas-generating agents and the proper excipients, floating dosage forms can be created as tablets or capsules that float in gastrointestinal fluids. As the medication is floating on the contents of the stomach, it is slowly and effectively removed from the body. After the drug has been discharged, the stomach's residual system is emptied. (3)

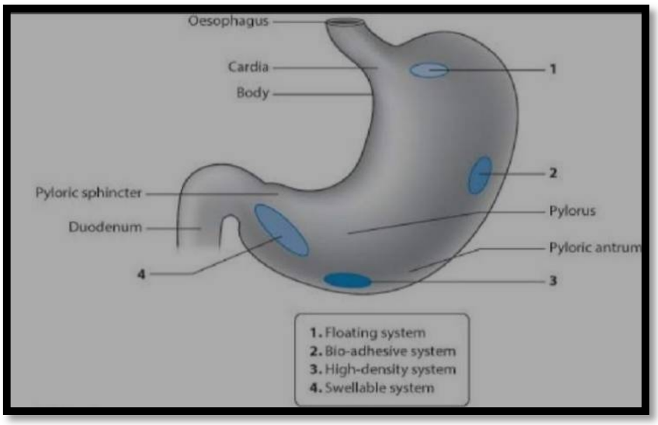

Fig. No.1: Floating drug delivery system

HISTORY OF FLOATING DRUG DELIVERY SYSTEMS IN DRUG DELIVERY

FDDS has just lately been used in the administration of medication since the mid-1900s. One of the early applications of FDDS in the delivery of medication was the creation of floating drug injectors for intravenous (IV) drug administration. These devices delivered medications into the bloodstream directly with great precision and accuracy, reducing the possibility of problems and negative consequences. Over the next decades, the application of FDDS increased in a variety of fields, including the design of pumps for dispensing medications and other fluids in medical applications. These devices relied on hydrodynamic principles to maintain a fluid flow that was seamless and continuous, enhancing the precision and efficacy of medication administration. Due to recent technical developments, even more advanced FDDS systems for the administration of medication have been created. These systems include implanted pumps, wearable pumps, and portable pumps. These technologies let doctors to more accurately administer drugs and other therapies just where a patient needs them, reducing the risk of problems and negative side effects.

Even now, floating drugs are often utilized in the delivery of medical care, and as new technology and applications are developed, its use is anticipated to grow. This is an exciting field of research and development where the concepts of floating systems are applied to the design of next generation medical devices and systems. (4)

Principles of FDDS and its importance in various applications: (5)

In the development and operation of several medical equipment and systems, notably in the area of drug administration, the concepts of floating systems are crucial. The following are some of the fundamental ideas of floating property in medicine and medication delivery:

Consistent Flow: By ensuring a steady and controlled flow of fluids, such as medications or other medical treatments, floating of drugs helps to lower the chance of alterations and errors. This is crucial in situations like the administration of chemotherapy medications when exact control over the flow rate is essential.

Reduced Wear and Tear: Hydrodynamically floating property extends the life of medical equipment by minimizing friction and wear, which also lowers the frequency of maintenance and repairs. This is crucial for implanted equipment, such as pumps and catheters, which have long-term dependability requirements.

Increased Accuracy: Floating drugs contributes to increased fluid delivery accuracy in medical devices, lowering the possibility of over- or under-delivery of medications or other treatments. This is crucial in situations when using the incorrect dosage of a medication might have negative effects.

Leakage, obstructions, and clots are just a few of the difficulties and adverse effects related to medication delivery that can be minimized through hydrodynamically balanced floating mechanism. This is crucial in situations where maintaining fluid flow is necessary to avoid potentially dangerous medical issues.

Floating property is a crucial part of a wide range of medical equipment and systems, from wearable and implantable pumps to portable implantable devices. The potential to deliver medications and other therapies with more precision and control, lowering the possibility of problems and side effects, and enhancing patient outcomes, is what makes it so important.

NEED OF FLOATING DRUG DELIVERY SYSTEMS (FDDS): (6)

Floating drug delivery systems (FDDS) are designed to prolong the stay of the dosage form in the gastrointestinal tract and aid in enhancing the absorption. Such systems are best suited for drugs having a better solubility in an acidic environment and also for the drugs having specific sites of absorption in the upper part of the small intestine. To remain in the stomach for a prolonged period of time. The dosage form must have a bulk density of less than 1.

There are several reasons why floating drug delivery systems are becoming increasingly important in the medical field:

- **Regulated Release:** Drugs may be released over a prolonged period of time using floating drug delivery

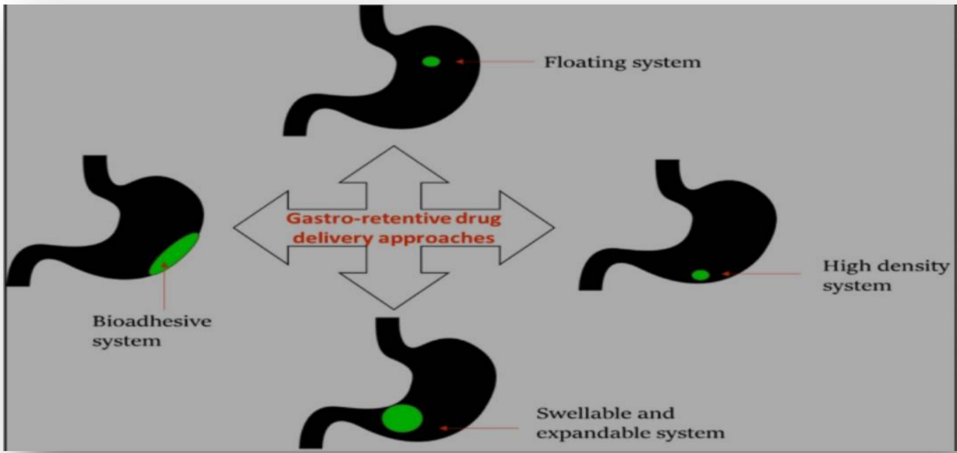

Fig. No. 2: Approaches of GRDDS

  systems, making the active ingredient's release more predictable and controlled. This may lead to a more successful course of therapy, better patient outcomes, and fewer adverse effects.
- **Targeted Delivery:** Floating medication delivery systems may be made to target particular GI tract regions, resulting in increased active ingredient absorption. This is crucial in situations where the medicine has to reach a specific area of the GI system, such as the colon or small intestine.
- **Reduced Risk of Stomach Irritation:** Because floating drug delivery systems release drugs farther from the gastric wall, they can lower the risk of stomach irritation. This is crucial while using medications like non-steroidal anti-inflammatory medicines, which may induce gastrointestinal discomfort or other adverse effects (NSAIDs).
- **Improved compliance:** Floating drug delivery systems may be made more pleasant and simple for patients to use, which can increase adherence to the recommended course of therapy and patient compliance. This is crucial in situations when a medicine must be administered for a long time, including in the treatment of chronic illnesses.

BACKGROUND OF FLOATING DRUG DELIVERY SYSTEMS (FDDS): (5)

The idea of FDDS was first introduced to the literature in 1962. Floating drug delivery systems (FDDS) float in the abdomen without slowing down the gastric emptying since their bulk density is lower than that of gastric fluids. The medicine is slowly withdrawn from the system at the desirable rate while the body continues floating on the contents of the stomach. The stomach's residual system is emptied after the medication has been released. As a result, the GRT is elevated, and fluctuations in plasma drug concentration are better managed.

Polymers, hydrophilic polymers, and natural polymers, among other materials, were used to create the first floating medication delivery devices. These early systems had a fairly straightforward construction and were supported in the stomach by the buoyant of the device.

With the invention of novel materials, better manufacturing processes, and more complex release mechanisms, floating medication delivery devices have evolved over time. Today, a variety of uses for floating drug delivery systems exist, including the treatment of chronic illnesses including diabetes and cardiovascular disease as well as the distribution of medications for pain relief, inflammation, and cancer.

VARIOUS APPROACHES OF FDDS

Floating drug delivery systems (FDDS) can be used in a variety of ways, including: (7)

(A) Effervescent system:

1. Gas generating system: These floating delivery systems use effervescent interactions between citric/tartaric acid and carbonate/bicarbonate salts to liberate CO2, which is then trapped in the systems' jellified hydrocolloid layer, reducing its specific gravity and causing it to float over chyme. These are matrix-type systems that have been created using effervescent substances including sodium bicarbonate, tartaric acid, and citric acid, as well as swellable polymers like chitosan and methylcellulose. They are designed in such a manner that when they come into contact with the acidic contents of the stomach, CO2 is released and captured in swelling hydrocolloids, giving the dosage forms buoyancy.(8-11)

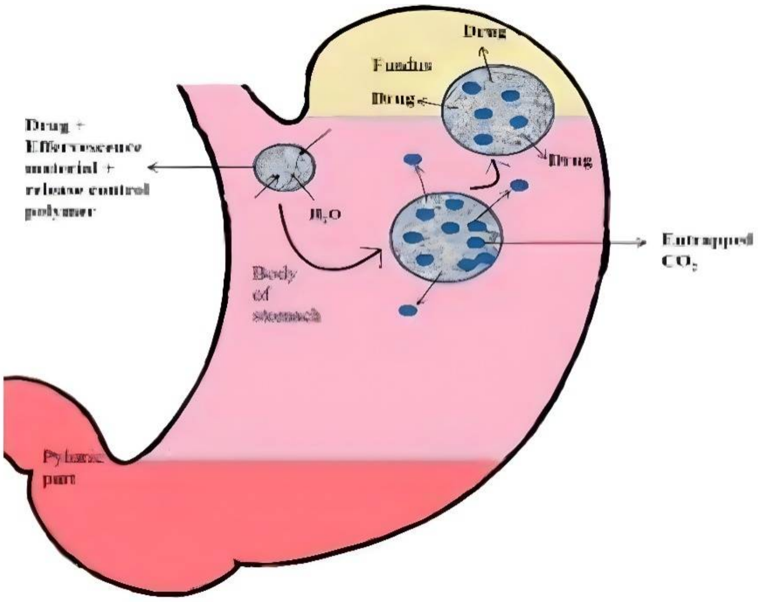

Fig. No. 3: Gas generating systems

2. Volatile liquid containing system: By including an inflatable chamber that holds a liquid, such as ether or cyclopentane, that gasifies at body temperature to induce the chamber to inflate in the stomach, a drug

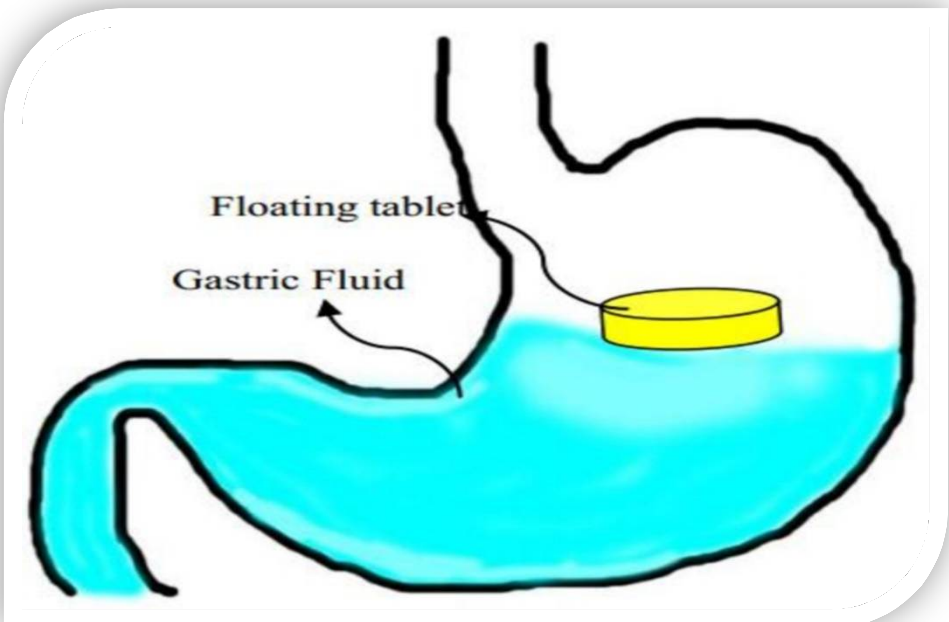

Fig. No. 4: Volatile liquid containing system

delivery system's GRT may be maintained. The apparatus could also include a bio erodible plug made of PVA, polyethylene, or another material that gradually dissolves and causes the inflatable chamber to release gas and collapse after a predetermined period of time, allowing the inflatable systems to spontaneously eject themselves from the stomach. (12-14)

(B) Non- effervescent system:

1. Colloidal gel barrier system: Drugs containing gel-forming hydrocolloids are included in the Hydrodynamically Balanced System (HBS), which is designed to keep stomach contents buoyant. These systems contain a significant amount of one or more hydrocolloids of the cellulose type that generate highly swellable gels. A few examples are HEC, HPMC, Sodium CMC, polysaccharides, and matrix-forming polymers including polycarbophil, polyacrylates, and polystyrene that are included in either tablets or capsules. The hydrocolloid in the system hydrates and creates a colloidal gel barrier around the gel surface when it comes into touch with stomach fluid. The air held by the expanded polymer keeps the density below one and adds buoyancy. (12-17)

2. Microporous compartment system: This method works by enclosing the compound inside a microporous compartment with openings on the top and bottom walls. To avoid any unintentional direct contact of the undissolved medication with the stomach mucosal surface, the outer walls of the drug reserve compartment are totally sealed.

The delivery system floats above the gastric contents of the stomach due to the air-filled flotation chamber. Through the holes, gastric fluid enters, dissolves the medication, and transports it continuously all across the intestine for absorption. (18)

3. Floating microspheres: Low-density systems known as gastro-retentive floating microspheres have enough buoyancy to float over gastric contents and remain in the stomach for an extended period of time. The medicine is gently delivered at the correct pace while the system floats over the contents of the stomach, increasing gastric retention while minimizing changes in plasma drug concentration.

Gel formers, polysaccharides, and polymers hydrate to create a colloidal gel barrier when microspheres come into contact with stomach fluid, regulating the pace of fluid uptake into the device and subsequent medication release. The adjacent hydrocolloid layer's hydration preserves the gel layer as the external surface of the dosage form dissolves. The air captured by the expanded polymer reduces density and gives the microspheres buoyancy. (19)

4. Alginate floating beads: Calcium alginate that has been freeze-dried has been used to create floating dosage forms with multiple units. By adding a sodium alginate solution to aqueous calcium chloride solutions, calcium alginate precipitates, yielding spherical beads with a diameter of around 2.5 mm.

The beads are split into individual pieces, quickly frozen in liquid nitrogen, then frozen at -40°C for 24 hours. This creates a porous structure that can sustain a floating force for up to 12 hours. (20-21)

Table No. 1: Various floating dosage forms (21)

Dosage forms	Drugs
Microspheres	Aspirin, Ibuprofen, Tranilast.
Granules	Diclofenac sodium, Indomethacin, Prednisolone.
Capsules	Diazepam, Furosemide, L-Dopa and Benserazide.
Tablets / pills	Amoxycillin Trihydrate, Ampicillin, Diltiazem, p-Amino benzoic acid, Riboflavin-5'-phosphate, Theophylline, Verapamil HCl.

5. **Raft forming system:** Raft forming systems have drawn a lot of interest as a means of delivering medications for gastrointestinal illness and infections. The production of a viscous adherent gel in combination with stomach fluids, where each piece of the liquid expands to create a continuous layer known as a raft, is one of the mechanisms involved in the formation of rafts. Due to the low bulk density produced by the production of CO_2, this raft floats on stomach juices. Alkaline carbonates or bicarbonates that are thick and float on gastric fluids are typically included in the system's components along with a gel-forming agent. (22-23)

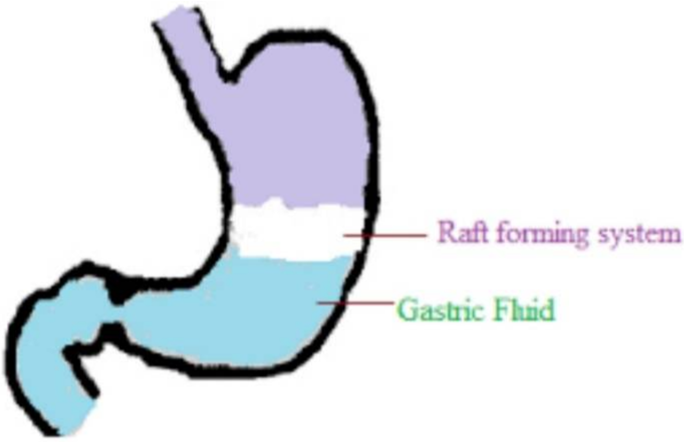

Fig. No. 5: Raft forming system

IMPORTANCE OF FLOATING DRUG DELIVERY SYSTEMS (FDDS): (24)
1. Traditional oral administration is frequently employed in the pharmaceutical industry to treat illnesses.
2. Conventional delivery, however, has a number of disadvantages, with non-site specificity being the most significant one. They call for a release at a particular place or a release where the maximum amount of the medicine is delivered to the particular site.
3. HBS is one type of site-specific delivery for the distribution of medications to either the stomach or the intestine.
4. The pharmaceutical industry is now focusing on such drugs that require site specificity.
5. It is achieved by keeping the dose form in the stomach, after which the medication is released in a controlled manner to a specified location in the stomach, duodenum, or intestine.

MERITS OF FLOATING DRUG DELIVERY SYSTEMS: (25)
1. Longer stomach residence time may be favorable for local action within the upper section of the small intestine, such as the treatment of peptic ulcers.
2. Delivery of medications with a restricted window of absorption in the intestine region.
3. For medications that are quickly absorbed after release in the GI tract, such as cyclosporine, ciprofloxacin, ranitidine, amoxicillin, captopril, etc., improved bioavailability is anticipated.
4. Increased therapeutic effectiveness
5. Decreases dosage frequency.
6. Targeted treatment for conditions affecting the upper Intestinal tract locally.
7. Prolongs the dosage form's retention at the absorption site.
8. Drugs that release slowly and at a controlled rate cause less mucosal irritation.
9. A rise in drug bioavailability brought on by first pass metabolism.
10. Drug delivery at a specified site.
11. Drug dosage forms that provide local therapeutic effect in the small and large intestine can create a prolonged and sustained release of medication when administered through gastro-retentive drug delivery. As a result, they are helpful for treating conditions that affect the stomach and small intesutine.

CHALLENGES AND LIMITATIONS: (26)
1. The drawback of floating systems is that they need a lot of fluids in the stomach to function properly and float. Thus, a higher water intake is advised when using this dose form.
2. If the floating dose form is not larger in size and is in a supine position (such when sleeping), contractile waves may sweep it away. Therefore, the patient shouldn't take a floating dose form right before night.
3. Drugs that have a difficult time remaining stable in highly acidic environments, have a very poor solubility in acidic environments, or irritate the intestinal mucosa cannot be included into GRDDS.
4. Numerous elements, including stomach motility, pH, and the presence of food, might affect gastric retention. Since these variables are never consistent, it is impossible to forecast buoyancy.
5. Drugs that have issues with stability and solubility in the gastrointestinal tract are not good choices for these kinds of systems.

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS (FDDS):
Numerous possible uses for hydrodynamic systems in medication delivery include:
1. **Targeted delivery**: To transport medications more precisely and effectively to particular target regions of the body, such as tumors or sites of inflammation, hydrodynamic systems can be utilized.

2. **Controlled release**: Drugs may be released using hydrodynamic systems over an extended period of time at a controlled pace, which eliminates the need for frequent dosage and improves patient compliance.
3. **Improved bioavailability**: Hydrodynamic devices can increase a drug's bioavailability by ensuring that it is delivered consistently and effectively to the site of action, enhancing the efficacy of therapies.
4. **Reduced side effects**: Hydrodynamic devices can decrease the accessibility of healthy tissues to the medication, minimizing the risk of adverse effects and increasing patient outcomes. This is accomplished by delivering pharmaceuticals to the site of action.
5. **Enhanced solubility**: Hydrodynamic systems can make poorly soluble medicines more soluble, improving medication delivery effectiveness and efficiency.
6. **Improved delivery of large molecules**: Big molecules may now be delivered more effectively thanks to hydrodynamic systems, which make it possible to distribute biologics and other large molecules that would otherwise be challenging to deliver using conventional methods.

These are a few possible uses for hydrodynamic systems in medication administration, and further study is required to fully comprehend their advantages and restrictions in these contexts. (27)

CONCLUSION

Due to its capacity to increase delivery system effectiveness and decrease potential adverse effects, hydrodynamically balanced systems are becoming more and more common in the medical and medication delivery fields. This is accomplished by stabilizing the fluid flow inside the system, lowering turbulence, and assuring reliable medication administration.

Floating delivery systems have been demonstrated to enhance the efficacy of drug delivery systems overall, improve the bioavailability of pharmaceuticals, and improve the precision of dosage. For instance, floating delivery systems may be utilized to carry medications to the body's specified locations, making distribution more accurate and regulated.

Floating devices can be employed in a variety of medical settings, including hemodialysis, where they can enhance the elimination of waste from the blood and lower the risk of problems.

In general, the application of hydrodynamically balanced floating systems to drug delivery and therapeutic diagnosis has the potential to significantly enhance the quality of patient outcomes and the efficiency of these therapies. To completely comprehend the advantages and restrictions of these systems in various disciplines, more study is necessary.

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