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A REVIEW ON FLOATING DRUG DELIVERY SYSTEMS

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ABSTRACT

Oral drug delivery is a convenient and easy method for administering drugs, but it has disadvantages such as inability to determine the site of action, low bioavailability, and potential interactions with the gastric gastrointestinal tract. Gastro-retentive drug delivery systems offer a novel approach, allowing controlled drug release to prolong absorption and transport the medication to its intended location. This method requires increased gastric residence time, increased bioavailability, reduced drug waste, and increased solubility. It is particularly useful for local action in the stomach, such as treating peptic ulcers or drugs less soluble in basic pH sites. Floating Drug Delivery System (FDDS) is a novel approach targeting the upper GIT of the stomach, enhancing absorption and bioavailability. This system, formulated with a hydrodynamically balanced system (HBS), gradually releases the medication at a regulated pace, allowing it to stay in the stomach and improve the availability of drugs with low stability. This extended duration of gastric residence time (GRT) and improved plasma drug concentration fluctuations are key benefits. HBS systems can release medication gradually in the stomach due to their low bulk density, addressing short gastric residence time issues.

INTRODUCTION

Oral drug delivery is the simplest form of drug delivery and has been used since older times. Oral drug delivery allows us to deliver the drug with very ease and convenience. GIT allows us to incorporate various polymers that can be used to enhance drug delivery. Many drugs are not absorbed from the GIT (gastrointestinal tract) due to their incompatibilities in the GIT area. (1)

Oral dosage form allows multiple advantages like ease of administration, patient adherence, and easy to incorporate different types of sustained and controlled formulations. However conventional drug delivery has some disadvantages like its unable to determine the site of drug action, has low bioavailability, degradation by the gastric HCL, low absorption of some drugs, interaction with the bile juice etc (2). Many drugs that are absorbed easily from the GIT are eliminated quickly from the systemic circulation due to short half-lives. To keep these medications in the systemic circulation and provide the best possible therapeutic benefit, they must be taken several times. A revolutionary method of medication administration that enables the use of specialised procedures is the gastro-retentive drug delivery system. And some drugs are formed in a way that they release the drug in a controlled way i.e. controlled drug delivery. Controlled drug delivery allows the drug to be released in a slower rate extends the absorption time to obtain a prolonged drug delivery, and delivers the drug to the site of action. (1).

1. When the site-specific drug delivery is formulated, it is necessary to gastric residence time is increased and the bioavailability is gradually increased, drug waste is reduced, drug solubility is increased.
2. It can be helpful if there is a requirement to have a localised effect on the stomach, such as when treating a peptic ulcer, therefore it is an approach in treating ulcers and if the drug is less soluble in a high pH environment.

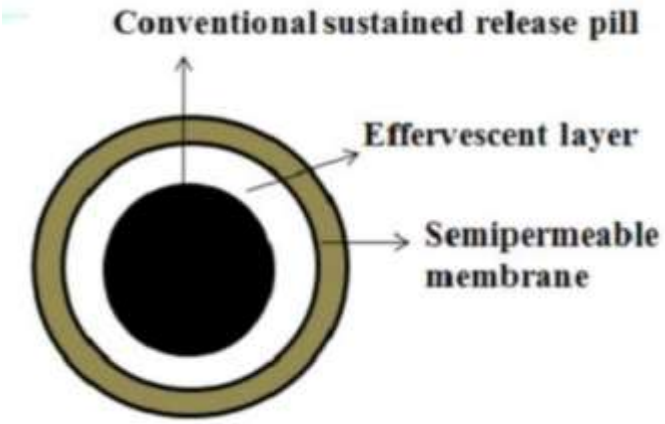

Fig.1- Different layers of FDDS (tablets) (1)

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GRDDS is a novel approach targeting the drug to upper GIT, improving drug solubility, enhancing absorption, and improving bioavailability. In recent years, numerous strategies have been formulated and explored for gastroretentive drug delivery. These include sinking systems with high density that remain at the stomach's base, floating systems with lesser density that float in the gastric fluid, mucoadhesive systems that adhere to the stomach mucosa, and un-foldable, extendible, or swellable systems that impede the release of dosage forms through the pyloric sphincter. Additionally, superporous hydrogel systems and magnetic systems have also been developed. (1)

To allow the drug to stay in the stomach (upper GIT) and to improve the availability of drugs with low stability, Floating Drug Delivery System (FDDS) are formulated. The hydrodynamically balanced system (HBS), also referred to as a floating drug delivery system, floats on the gastric contents and gradually releases the drug at a controlled rate. Following the medication's release, the stomach's residual contents are emptied, resulting in a longer gastric residence time (GRT) and better control over changes in plasma drug concentration. (1).

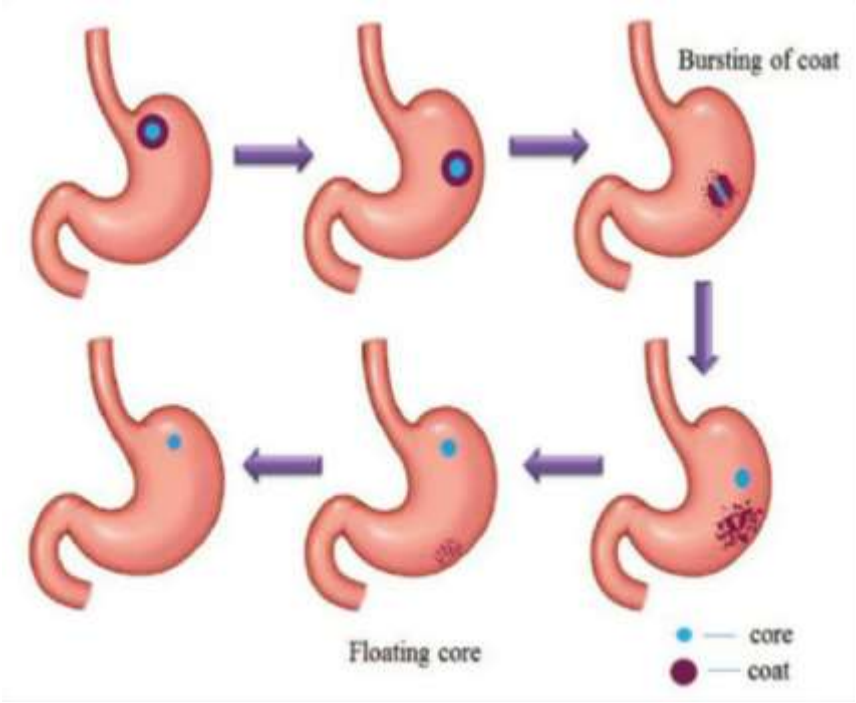

Fig2. Schematic representation of Floating DDS (10)

The principle of the FDDS is that Drug dose forms are designed to have a lower weight than the stomach fluid so that they can float, and increase the gastric residence time, which will allow the drug to be released in a controlled way throughout floating (2).

The importance of contact time with the small intestinal mucosa for drug absorption is widely recognized. Therefore, the duration of small intestinal transit is a crucial factor for drugs that are not fully absorbed. The ability to prolong retention time offers multiple benefits, such as extending the effectiveness of drugs with short half-lives, improving drug bioavailability, minimizing side effects, reducing the frequency of dosing, saving medication, enhancing solubility for medications that are not well soluble at high pH levels, enhancing treatment, and eventually boosting patient adherence. (1)

DRUGS SUITABLE FOR FORMING FLOATING TABLETS

1. Those drugs with narrow absorption range in Gastro intestinal tract. (Riboflavin, Furosemide, PABA derivatives)
2. Drugs whose site of action is stomach. (Antacids)
3. Drugs that degrade and are unsuitable for intestinal and colonic-environment. (ranitidine, metronidazole, captopril)
4. Medications which solubilize less in basic pH. (diazepam, verapamil)
5. Medications that react with the good bacteria in the colon. (Amoxicillin) (2).

ADVANTAGES OF THE FDDS

1. Floating DDS can be useful for drugs giving local action in Upper GIT like antacids
2. In conditions like diarrhoea, floating tablets can be useful for its treatment.
3. Drugs that have limited absorption receptors can be given by this.

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4. Drugs with acidic pH can cause irritation in the stomach and they can be given by FDDS.
5. FDDS cause fast action in comparison to the conventional drugs e.g. Effervescent tabs and powder. (2)
6. Improves bioavailability of drugs.
7. Enhanced 1st pass metabolism.
8. Fewer doses are required as drug release is extended.
9. Plasma drug level is maintained at a constant level.
10. Selectivity of receptors is enhanced. (11)

CLASSIFICATION OF TYES OF FLOATING DDS

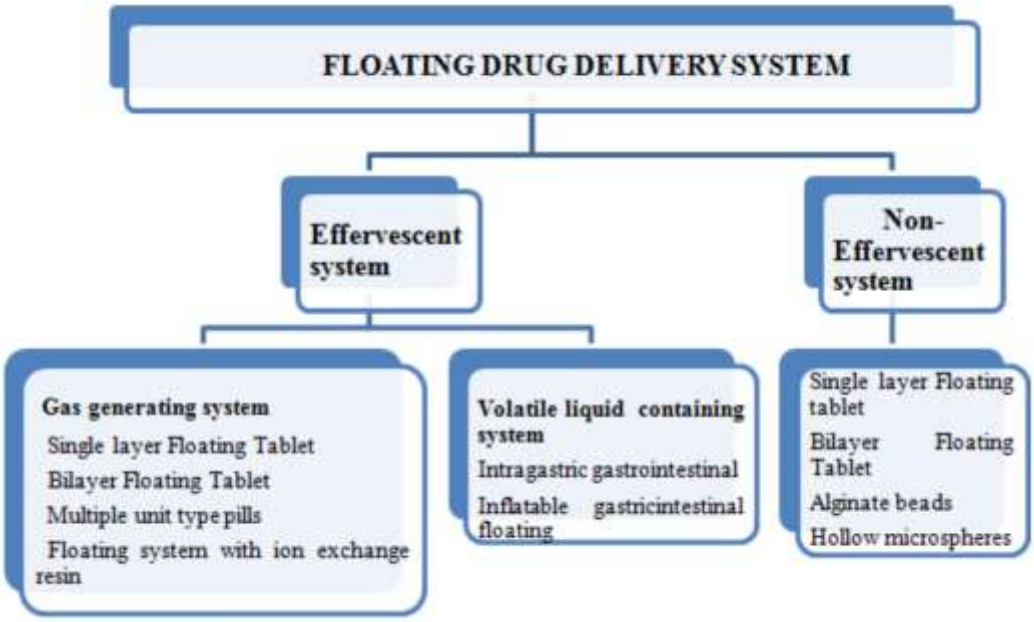

Fig.2- Types of FDDS. (3)

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEM

Because of the narrow absorption window of some drugs in the upper gastrointestinal tract, drugs with low bioavailability can be given by floating drug delivery in several ways. By keeping the dosage form where it is absorbed, it increases the bioavailability. Here is a summary of them:-

1. Sustained Drug Delivery
   HBS have the ability to hold in the stomach for long periods and release the drug gradually. Thus, these methods can address the problem of the short stomach residence time that occurs when using an oral CR formulation. These systems' bulk densities of less than 1 allow them to float atop the contents of the stomach. These systems are really big, and it's not allowed to pass via the pyloric aperture. Nicardipine HCL sustained-release floating capsules were recently created and tested in vivo. (1)
2. Site-Specific Drug Delivery
   For drugs like furosemide and riboflavin, which are mostly absorbed from the stomach or the proximal section of the small intestine, these systems are quite helpful. Furosemide is primarily absorbed in the stomach and then in the duodenum. There have been reports of the creation of a monolithic floating dosage form that has a longer length of stomach residence and improved absorption. The floating tablet'sAUC was around 1.8 times higher than that of traditional furosemide tablets.
3. Absorption Enhancement
   Pharmaceuticals with Low bioavailability sites in the upper gastrointestinal tract might be used to build floating medication delivery devices that maximise absorption. (1)

MANUFACTURING OF FLOATING TABLETS

Methods of manufacture for the floating medication delivery system:
The following procedures are used to make the floating tablets based on the qualities of the medicine and excipient, the required d uration (immediate or sustained), the drug's stability (against temperature, oxidation, etc.), and their practicality. (11)

A. Dry granulation
B. Wet granulation
C. Direct compression

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EVALUATION OF FDDS

Interaction between Drug & Excipients:
Utilizing FTIR, drug-excipient (DE) interactions are conducted. The DE interaction is indicated by the emergence of a new high and/or the loss of the original medication or excipient peak. In addition to the evaluation parameters already indicated, the impact of ageing can be examined using a DSC or hot-stage polarising microscopy. (11)

Precompression and post-compression parameters:
Pharmacopeial standards should be followed when monitoring precompression factors like bulk density, compressibility index, and angle of repose, and post-compression characteristics such as hardness, friability, and weight uniformity.

Morphology and surface topography:
Contact angle metre, scanning electron microscopy (SEM), atomic force microscopy (AFM) which must be running at a 10 k.v. acceleration voltage, and contact profilometer 40 were used to determine the surface topography and structures. (11)

Time of Total Floating of tablet: The amount of time that passes after the tablet is inserted into the medium until it rises to the upper third of the dissolving vessel is known as the floating lag time. The amount of time that the dosage form floats is known as the floating/flotation time/Total floating time. The USP dissolving apparatus is typically used as the dissolving medium for these experiments, which are typically conducted in Simulated Gastric Fluid (SGF) or 0.1 N HCl (900ml) kept at 37°C.

Tablet Swelling Index
The tablets (W1) are weighed and then put in a glass container with 200 mL of 0.1 N HCl that is kept in a H_2O bath (37 ± 0.5°C). The pill is taken out at regular intervals, and any extra liquid on the surface is gently wiped away with filter paper. Next, the enlarged tablet is weighed again (W2).

$$\text{Swellingindex} = \frac{W2 - W1}{W1}$$

Weight gain and water uptake
By taking into account the swell behaviour of the floating dose form, weight growth or water uptake may be investigated. (11)

Entrapment Efficiency
The drug's phase distribution in the prepared formulations could be accurately measured using the percentage entrapment efficiency. The medication is extracted using an appropriate technique, examined, and computed from:

$$\text{Entrapment efficiency} = \frac{\text{Practicaldrugloading}}{\text{Theoreticaldrugloading}} \text{X } 100$$

Drug release testing: In vitro drug release investigations are often tested using simulated intestinal and stomach fluids that are kept at 37°C. The USP dissolution apparatus46 is used to conduct dissolution testing. Pharmacokinetic studies: A computer was used to determine the AUC (Area under Curve), C max, and time to reach the maximum plasma concentration (Tmax). A Student t test was used for statistical analysis, with a significance threshold of p, 0.05. (11)

Evaluation of compression parameters of floating DDS:

1. **Tablet shape**: After being examined under a microscope, tablets from every formulation batch should be spherical and free of fractures. (4)
2. **Thickness:** A Vernier calliper can be used to measure each tablet's crown thickness.
3. **Hardness**: The tablet's hardness is basically evaluated using the Monsanto hardness tester. The observed hardness of each tablet formulation varied, ranging from 3.8 to 5.1 kg/cm^2. This ensures that every composition has favourable handling characteristics.
4. **Weight variation test**
   An electronic balance is used to weigh each formulation separately. That data was used to compute the average weight. The per cent deviation was calculated by comparing each tablet's weight to the average weight of tablets. (4)
5. **Friability test**
   It was performed using the friability apparatus. SOPs are followed for the standard performance of the apparatus. Each formulation was given three precisely weighted pills, which were then placed within the friability chamber. There were 100 revolutions of the apparatus. After each rotation, the pills were weighed again to ascertain the weight reduction. A loss in weight of more than 1 per cent is not acceptable.

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6. **Uniform drug content**
   The five pills in each formulation are weighed, mashed up in a mortar, and mixed together. Then, 10 mg of the material were added to a 100 ml volumetric flask. The drug's standard calibration curve was used to calculate the pantoprazole concentration in ug/ml.
   The medication was allowed to dissolve in the 0.1N HCL solvent, the mixture was filtered, and 1 ml of the sample was put in a 50 ml volumetric flask. It was then adjusted with 0.1NHCL to the 50 microliters and subjected to spectrophotometry at 291 nm 15.
7. **Studies on in vitro dissolution:** (4)
   The in vitro release of the pantoprazole floating tablet was calculated using the paddle method of the USP dissolving test device. 900ml of 0.1nhcl was used for the dissolving test, which was run at 370 0.50c and 100 rpm. A fresh dissolution media was added to the five millilitres of solution that had been removed from the dissolving apparatus. After being filtered, the samples' absorbance at 291 nm was measured using a u-v visible spectrophotometer. Plotting the cumulative percentage of drug release versus time allowed for the calculation of the controlled release.
8. **Time spent in vitro:**
   The buoyancy lag time is the length of time required for the tablet to rise to the surface and float. Using the floating lag time test, the drifting behaviour was verified and it was measured how long the floating tablets floated. The in vitro residence period was calculated using the floating lag time method. The tablets were submerged in the 0.1NHCL dissolving medium, and the duration of time it took for them to float to the surface was noted.
9. **FT-IR study of drug-polymer interaction:**
   Drug-polymer interaction was investigated using FT-IR. Pantoprazole, HEC, and -cyclodextrin infrared spectra. (4)

CONCLUSION

Gastro-retentive floating drug delivery devices have become a significant tool for improving the bioavailability and regulated distribution of numerous drugs. The delivery of molecules with a window of absorption, substantial first pass metabolism, and poor bioavailability will be optimised by the developing improved delivery technology. A floating medicine delivery system appears to be a promising strategy for gastric retention. Many organisations are concentrating on marketing longer gastric retention, despite the fact that there are numerous challenges to overcome. The creation of a suitable FDDS is a significant task, and research will not stop until the best approach that is feasible for industrial use is discovered.

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