FLOATING DRUG DELIVERY SYSTEM AS A TOOL TO IMPROVE DISSOLUTION RATE IN GASTRIC

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ABSTRACT:

In recent years, new drug research and development have increased due to physical problems such as not spending long in the stomach and not being able to digest in the stomach. Gastric Persistent Dosage Form (GRDF) will remain in the stomach. Techniques to extend the stomach residence time include floating delivery systems, inflation and expansion systems, polymer bioadhesive systems, and intestinal delay,as highperformance systems. Drugbased therapy is entering a new era in which more and more drug based strategies are used and utilized to treat drugs. Floating drug delivery system (FDDS) is a medical device used for prolonged gastric emptying. The primary purpose of writing this review on floating drug delivery systems (FDDS) is to gather the current literature, particularly the literature that has most extensively examined floating systems for the purpose of inducing bowel movements.Sustained oral delivery from the colon has many benefits for drugs absorbed from the upper gastrointestinal tract and for drugs that act locally along the gut. This review includes an indepth discussion of physical handling, factors determining retention time in the stomach**,** variables affecting digestion, unit formation methods, hydrodynamically balanced systems**,** and multiunit floating structures and their distribution, design, and evaluation. These systems have a variety of applications**.**

Keywords: Floating drug delivery systems, Gastric retention, Mechanism.

INTRODUCTION:

Floating drug delivery systems (FDDS) have been developed to store drugs in the stomach and are suitable for drugs that are insoluble and stable in gastric fluid**.** The principle behind FDDS is to make the paper less dense than fruit juice so that it floats on the paper. FDDS are hydrodynamically controlled devices that are strong enough to float on the stomach and remain in the stomach for long periods without affecting the intestine. As the drug is released, the rest of the stomach is also released. This leads to longer stomach residence times and better control of plasma exchange. The principle of buoyant formulations provides a simple and effective way to hold the stomach in time to increase the amount of information and release of the drug [1]**.** In some cases, it is necessary to extend the duration of the drug's stay in the digestive tract for a better effect. For example, drugs that are recommended to be absorbed in the proximal part of the intestine and drugs that are insoluble and break down at alkaline pH can be used in the stomach for a long time. In addition, in the treatment of some ulcerative diseases, the stomach can provide many advantages such as the ability to deliver drugs to the stomach and small intestine during the long term treatment process, thus increasing bioavailability and therapeutic effect [2].

Classification of floating drug delivery system

A) Effervescent FDDS

1. Gas generating system.
2. Volatile liquid containing system

B) Non-Effervescent FDDS

1. Colloidal gel barrier system.
2. Microporous compartment system
3. Floating microspheres / micro balloons
4. Alginate floating beads.

C) Raft forming system

A) Effervescent system

Effervescent systems include use of gas generating agents, carbonates (e.g Na bicarbonate) and alternative organic acid (e.g acid and salt acid) gift within the formulation to supply CO2 gas so reducing the density of system and creating it float on the gastric fluid. an alternate the incorporation of matrix containing portion of liquid that manufacture gas that evaporate at body temperature [3].

1. Gas generating systems

These are formulated by intimately mixing the CO2 generating agents and the drug within the matrix tablet. these have a bulk density lower than gastric fluids and therefore remain floating in the stomach unflattering the gastric emptying rate for a prolonged period.

2.Volatile liquid vacuum containing systems

This system is created to float within the abdomen owing to floatation chamber which can be a vacuum or full of air or a harmless gas, whereas drug reservoir is encapsulated within a microporous compartment.[4]

(B) Non- Effervescent system

This type of system prevents the restricted flow of mucus during swallowing, preventing its expulsion from the stomach. These systems are also called plug systems because they must be bent to remain close to the pyloric valve. One idea developed for this unrestricted form involves mixing the drug with a gel that swells with the mucus while controlling the mouth and maintaining the relative integrity and density
of form**,** but in the external jelly barrier. The compound imparts buoyancy to the indefinite amount of paper present. The most commonly used excipients are non-effervescent floating delivery products, gel-forming or swellable polysaccharide hydrocolloids, polysaccharides**,** and matrix-
forming polymers such as polyacrylates, polymethacrylates**,** and polymethacrylates.[5]

1.Colloidal gel barrier systems (hydrodynamic balanced system)

This system maximizes the amount of drug reaching the absorption site by extending the residence time in
the stomach**.** It contains only gelforming hydrocolloids to maintain the buoyancy of the stomach content. Examples include polycarbophil, polystyrene**,** and polyacrylates. When in contact with the fluid in the stomach, hydrocolloids in the body hydrate and form a colloidal gel barrier around themselves.[6]

2. Microporous compartment systems

This technology incorporates the encapsulation technique of a drug reservoir inside a microporous compartment along with pores at top and bottom walls. In the stomach the floatation chamber composed of entrapped air causes the delivery system to float over the gastric content.[6]

3.Floating Microspheres/Micro balloons

Hallow microspheres also are known as micro balloons are considered as a most efficient buoyant system. It is composed of central hallow space inside the microsphere. Hallow microsphere is loaded with a drug in their outer polymer shelf are fabricated by a novel solvent Diffusion method for emulsion.[7]

4. Alginate beads/Floating beads

Multi-unit floating dosage forms have been developed from calcium alginate spherical beads of about 2.5 mm in diameter and can be fabricated by adding sodium alginate solution into aqueous solution of calcium chloride, resulting in the precipitation of calcium alginate, the beads are further separated, snap-frozen in liquid nitrogen and freeze-dried at 400 °C for 24 h, leads to generation of a porous system. This fabricated system would maintain a floating force for over 12 h and these floating beads provide a longer residence time of more than 5.5 h.[8]

(C) Raft- forming systems

Raft – forming system are in much attention for the delivery of antacid and drug delivery for gastro infection and disorders. On contact with gastric fluid, a gel – forming solution swells and forms a viscous of gastric fluid thus facilities release drug slowly in the stomach.[6]

ADVANTAGES OF FDDS:

1.Floating dosage forms such as tablets or capsules remain in solution for long periods of time even at alkaline intestinal pH.

2. FDDS is beneficial for drugs intended to act locally in the stomach, such as antacids.

3.FDDS formulations are advantageous in cases of strong bowel movements and severe diarrhea, as they keep the drug floating in the stomach, resulting in a relatively better response.

4.Acidic substances such as aspirin cause irritation to the stomach wall upon contact, so FDDS formulations can be useful for taking aspirin and other similar drugs.

5.FDDS is advantageous for drugs that are absorbed through the stomach, such as iron salts.

6.Since the drug is released slowly into the body, adverse effects are minimized and the drug efficacy is increased.

7.FDDS reduces fluctuations in drug concentration above the critical concentration, enhancing pharmacological effects and improving clinical outcomes.

8. Floating formulations are a common approach**,** especially for drugs with limited absorption sites in the upper small intestine.[9]

DISADVANTAGES OF FDDS:

1. This system requires a high level of fluid in the stomach to deliver the drug so that it floats and works effectively. It is not suitable for drugs that have problems with solubility or stability in the gastrointestinal tract.

2. Drugs such as nifedipine (a calcium channel blocker) that are well absorbed throughout the gastrointestinal tract and undergo first-pass metabolism may not be desirable.

3. Drugs that irritate the gastric mucosa are also undesirable or inappropriate**.**

4.Drugs that are unstable in the acidic environment of the stomach are not suitable.

5.The formulation should be taken with a glass of water.

6.The formulation should be taken with a glass of water (200-250 ml).

7.It is absorbed primarily from the stomach and upper gastrointestinal tract, like calcium supplements**,** chlordiazepoxide**,** and cinnarizine.[10]

Limitations of floating drug delivery system:

1. FDDS need to be administered after the meal but the residence and emptying time of drugs depends upon the digestive state which affects its absorption.
2. Floating ability depends on the hydration state of the dosage form. It is necessary of administration of water intermittent (a tumbler full, every 2 h) to keep these tablets floating in vivo.
3. Floating ability of drug in the stomach depends upon the person being positioned.
4. Drugs with solubility or stability problems with the gastric fluid are not a suitable candidate for FDDS..
5. Certain drugs though readily get absorbed in the stomach with successful first pass metabolism are not suitable as slow gastric emptying may lead to the reduced systemic bio-availability e.g. Nifedipine.[11,12,13]

Application of FDDS:

1. Sustained drug delivery:

Therefore, the disadvantages of short bowel movements encountered with the structure associated with at omic number 24 can often be overcome with these machines. The HBS system will remain in the stomac h for a long time and then release the drug to you for a long time. These systems are small in size and lim ited due to the open cavity. For example, the floating capsule that allows the release of the nicardipine joi nt has been developed and tested in vivo.[14]

2. Site specific Drug Delivery :

This system is particularly good for drugs that are absorbed from the stomach or nearby small internal or gans (such as diuretics and vitamin B2). For example, diuretics are absorbed primarily from the stomach and then from the small intestine. It is said that a significant floating unlimited species with a longer sto mach residence time is created, improving bioavailability. The AUC obtained with the floating form is ap proximately 8 times that of the diuretic form.[15]

3. Absorption Enhancement :

Drugs that have poor bioavailability as a result of site specific absorption from the higher a part of the channel area unit potential candidates to be developed as floating drug delivery systems. There by rising their absorption E.g A significantly increase within the bioavailability of floating dose forms can be achieved as compared with commercially on the market dose type.[16]

4. Maintenance of constant blood level:

These systems give a straight forward manner of maintaining constant blood level with Associate in Nursing simple administration and higher patient compliance.[17]

5. FDDS are claimed for the expanded viability of drugs as later ponders appear that the organization of Diltiazem coasting tablets twice a day would be more viable compared to typical tablets in hypertensive patients.

6. In case of Parkinson quiet, FDDS is compelling in retention of the medicate over a period of 6-8 h and kept up significant plasma concentration.
7. FDDS is site-specific sedate conveyance: These frameworks are especially beneficial for drugs that are particularly retained from the stomach or the proximal portion of the little digestive system, e. g., Riboflavin .
8. FDDS served as an great medicate conveyance framework within the annihilation of Helicobacter pylori, faulted for persistent gastritis and peptic ulcers.
9. FDDS are perfect HBS dose shape to supply way better conveyance of drugs and decreased its GI side impacts.[18,19,20]

Methods of preparation:

Methodology for single layer floating tablets: Basically single layer floating tablets are prepared by compression methods. For this normally three basic compression methods are used. They are as follows:-

- Direct compression
- Dry granulation,
- Wet granulation.

Direct compression method:

Direct compression is the process of compressing tablets directly from powdered materials without changing the physical properties of the material to be tableted**.**

This method is used for crystalline chemicals with good compressibility and flow properties**,** such as potassium salts (chlorates, chlorates, bromides), ammonium chloride, sodium chl oride, and methenamine. Compressed tablets are manufactured by one-time compression using a tableting machine. After some powder or granular tablet material enters the die, the upper and lower punches of the tableting machine compress the material under high pressure (~ton/in2).[21,22]

Dry granulation method:

It is defined as the formation of granules by slugging, if the tablet ingredients are sensitive to moisture and/or unable to withstand elevated temperature during drying.[23]

Wet granulation method:

In wet granulation**,** the active ingredient, diluent and disintegrant are mixed or thoroughly mixed in a high-speed mixing granulator (RMG). The RMG is a multi-purpose grinder consisting of an impeller and a grinder, which is used to disperse and granulate dry powders in water or a solvent at high speed. The wet materials in the wet grinding stage are placed in large trays and placed in a drying room with circulating air flow and stable thermal control. Commonly used dryers are tray dryers and fluidized bed dryers**.** After drying, the granules pass through a finer mesh sieve to reduce the particle size. Afterwards, lubricants or glidants are added in the form of fine powder to improve the fluidity of the granules. These granules are then compressed to form tablets. Dry granulation is a shorter and more cost-effective production process than wet granulation. Since it does not involve heat or moisture, dry granulation is particularly suitable for active ingredients that are sensitive to solvents or unstable to moisture and high temperatures.[24]

METHOD OF EVALUATION

1.Bulk density: This is the ratio of the mass of the powder to the bulk volume. Bulk density depends on the particle size distribution, particle shape, and cohesion. A precisely weighed amount of powder is carefully poured into a graduated cylinder through a large funnel and the volume is measured, called the initial bulk volume. It is expressed in g/ml and is determined by the following formula:[25]

Bulk density=M/Vo

Where,

M = mass of the powder

Vo = bulk volume of the powder.

2.Tapped density: 10 gm of powder was introduced into a clean, dry 100 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. It is expressed in gm/ml and is given by:[26]

Tapped density=M/Vt

Where,

M = mass of the powder

Vt = final tapping volume of the powder.

3.Angle of repose (θ): Defined as the maximum possible angle between the surface of the powder pile and the horizontal plane. The fixed funnel method was used. The funnel was fixed at the end at a given height above a flat horizontal surface on which graph paper was placed. The powder was carefully poured through the funnel until the top of the cone-shaped pile reached the end of the funnel. The angle of repose was then calculated using the following equation:[27]

Angle of repose Ø = tan1(h/r)

4.Weight change test (pharmacodynamic): Take 20 tablets and weigh them individually. Calculate the average weight and compare the weight of each tablet to the average. If no more than 2 tablets are outside the percentage limit and no tablet exceeds twice the percentage limit, the tablet passes the pharmacodynamic test.[28]

5.Hardness: The hardness and strength of a tablet are key indicators of whether the tablet can withstand shock and stress during manufacturing, packaging, transportation, and handling by the patient. Monsanto testers, Strongcobb testers, Pfizer testers, Erweka testers, and Schleuniger testers are used to determine tablet hardness.[29]

6.Dimensional analysis: The thickness and diameter of the tablets were determined using calipers. The average was calculated using 20 tablets from each batch**.**

7.Size and shape: Dimensions can be used to describe and control The thickness of the tablets may vary. The thickness of the tablets may be measured using a micrometer or other equipment. The thickness of the tablets should be controlled within ± 5% of the standard value.[30]

8.Flotation delay time and total flotation time: The flotation delay time (FLT) and total flotation time (TFT) of the floating tablets were measured visually in a Type II dissolution apparatus containing 100 ml of 0.1 N HCl (pH 1.2) using a paddle rotating at 50 rpm at 37 ± 0.5 ℃.[31]

9.Dissolution studies: In vitro drug release from the formulations was performed using a USP Type II paddle type dissolution apparatus under immersion conditions at 50 rpm and 37 ± 0.5 ℃. 900 ml of 0.1 NHCl was used as the dissolution medium. Samples were collected at reg ular intervals over a period of 6 hours and replaced with fresh medium, diluted appropriately, and analyzed using a UV/visible spectrophotometer.[32]

10.Disintegration Test (U.S.P.): The U.S.P. device to test disintegration uses 6 glass tubes that are 3" long; open at the top and 10 mesh screens at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2 0 C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass. Disintegration time: Uncoated tablet: 5-30 minutes coated tablet: 1-2 hours.[33]

Conclusion:

Floating tablets have emerged as the power full means of improving the bioavailability and providing sustained release and avoiding the adverse effects of many drugs. Floating tablets have proved to be potential approach for gastric retention. These systems have special advantage for the drug that are primarily absorbed from the upper part of GIT. So with an improved knowledge of formulation development aspect, physiochemical and pharmacological prospects of drug there is lot of future scope for designing of optimum floating drug delivery system.

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