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FLOATING DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

The motive of scripting this overview on floating drug delivery systems (FDDS) was to collect the current literature with unique recognition at the essential mechanism of floatation to obtain gastric retention. The current trends of FDDS such as the physiological and formulation variables affecting gastric retention, strategies to layout single-unit and multiple-unit floating systems, and their type and components factors are blanketed in detail. Gastric emptying is a complicated method and makes in vivo overall performance of the drug shipping structures uncertain. In order to keep away from this variability, efforts had been made to increase the retention time of the drug-delivery systems for extra than 12 hours.

Keywords*: Gastric Retention, Single unit dosage, multiple unit Floating systems.*

1. INTRODUCTION

Gastric emptying of dosage forms is an exceptionally variable procedure and capacity to extend and manipulate emptying time is a precious asset for dosage forms, which live withinside the stomach for an extended time period than traditional dosage forms. Several problems are confronted in designing controlled release systems for higher absorption and more advantageous bioavailability. One of such problems is the incapability to restrict the dosage form withinside the favored place of the gastrointestinal tract. Drug absorption from the gastrointestinal tract is a complicated system and is problem to many variables. It is extensively recounted that the volume of gastrointestinal tract drug absorption is associated with contact time with the small intestinal mucosa. Thus small intestinal transit time is an critical parameter for pills which can be incompletely absorbed.

Floating systems are described as systems with a low density, a better buoyancy attribute, and the capacity to go with the flow over gastric fluids withinside the stomach, making an allowance for longer movement times.

2. HISTORY

Davis first brought FDDS in 1968. These systems are recognised to have decrease densities than the gastric fluid, remaining buoyant for a long term withinside the stomach. They are identified as an critical way of attaining good enough gastric retention and drug bioavailability(Badoni, Ojha, Gnanarajan, & Kothiyal, 2012). In addition, they may be suitable systems for the delivery of drugs, that have a narrow absorption window withinside the higher small gut or stomach (Singh & Kim, 2000). In view of the buoyancy mechanisms, non-effervescent systems and effervescent systems, were implemented to expand FDDS.

Attempts are being made to expand a controlled drug delivery system that may offer therapeutically effective plasma drug concentration stages for longer durations, thereby lowering the dosing frequency and minimizing fluctuations in plasma drug concentration at constant state with the aid of using delivering drug in a controlled and reproducible manner (Hirtz J. et al. 1985).which can be much less soluble in excessive pH environment. Gastric retention to offer new therapeutic possibilities and considerable advantages from patients. The controlled gastric retention of solid dosage forms can be finished with the aid of using the mechanism of muco adhesion (Ponchel G et Al.1998)(Lenaerts VM et al.1990), floatation (Deshpande AA et Al.1997), sedimentation (Rednick AB et al. 1970) (Davis SS et Al.1986), expansion (Urguhart J et al.1994) (Mamajek RC et Al.1980), changed form systems (Fix JA et al. 1993) (Kedzierewicz F et al.1999) or with the aid of using the administration of pharmacological agents (Groning R et al.1984,1989) that delaying gastric emptying. Based on those approaches, floating drug delivery systems appears to be the promising delivery systems for control release of drugs.

3. FLOATING DRUG DELIVERY SYSTEM

Floating system or Hydrodynamically managed structures are low-density structures which have enough buoyancy to drift over the gastric contents and stay floating withinside the stomach with out affecting the gastric emptyingf rate for a extended length of time. While the system is floating at the gastric contents, the drug is released slowly on the favored rate from the system. After release of drug, the residual system is emptied

from the stomach. This end results in an expanded GIT and a higher manipulate of the fluctuations in plasma drug concentration. However, except a minimum gastric content material had to permit the right success of the floating retention principle, a minimum stage of floating force (F) is likewise required to hold the dosage shape reliably buoyant at the floor of the meal. Many floating structures had been evolved primarily based totally on granules, powders, capsules, tablets, laminated movies and hole microspheres.

Basic Gastrointestinal Tract Physiology:

Anatomically the stomach is split into three regions: fundus , body, and antrum (pylorus). The proximal component fabricated from fundus and body acts as a reservoir for undigested material, while the antrum is the primary site page for blending motions and a to behave as a pump for gastric emptying with the aid of using propelling actions.

Stomach Physiology:

The stomach is an elevated segment of the digestive tube among the oesophagus and small intestine. The wall of the stomach is structurally just like the opposite components of the digestive tube, with the exception that stomach has an extra, indirect layer of easy muscle withinside the round layer, which aids withinside the overall performance of complicated grinding motions. In the empty state, the stomach is shrunk and its mucosa and sub mucosa are thrown up into wonderful folds known as rugae (Fig.1)(Banker GS et al. 1996).

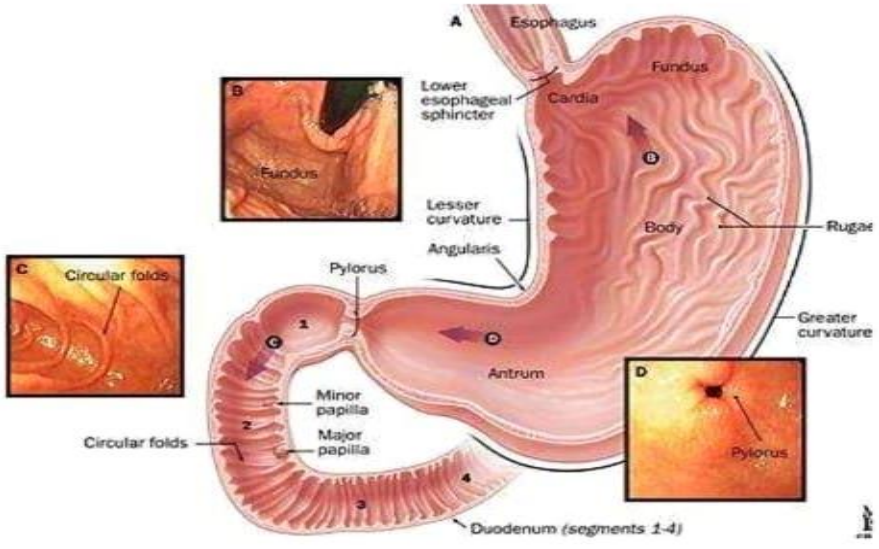
There are pix to 4 most important sorts of secretary –

Epithelial cells that cowl the floor of the belly and amplify down into gastric pits and glands:

- Mucous cells: secrete alkaline mucus that protects the epithelium against shear stress and acid.
- Parietal cells: secrete hydrochloric acid.
- Chief cells: secrete pepsin, a proteolytic enzyme.
- G cells: secrete the hormone gastrin.

The contraction of gastric smooth muscle serves two basic functions -

- Ingested food is crushed, ground, mixed and liquefying to form Chyme.
- Chyme is forced through the pyloric canal into the small intestine, a process called gastric emptying.



Gastric motility:

Gastric motility is managed through a complicated set of neural and hormonal signals. Nervous manage originates from the enteric apprehensive system in addition to parasympathetic (predominantly vagus nerve) and sympathetic systems. A huge battery of hormones has been proven to persuade gastric motility- for e.g. each gastrin and cholecystokinin act to loosen up the proximal stomach and contractions withinside the distal stomach.

Theng quantity of the stomach is 25-50 ml. There is a huge distinction in gastric secretion of everyday and achlorhydric individuals. Gastric pH additionally has stated impact of absorption of drug from release system. The pH of fasting stomach is 1.2-.2.0 and in fed situation 2.0-6.0 (Hoffmann a et al.1998)

Gastric empty rate:

Gastric emptying happens at some stage in fasting in addition to fed states. The sample of motility is but awesome withinside the 2 states. During the fasting kingdom an interdigestive collection of electrical occasions take place, which cycle each thru belly and gut each 2 to three hours. (Stanley S D et al.1998).

This is referred to as the interdigestive mylo electric powered cycle or Migrating myloelectric cycle (MMC), that is similarly divided into following four stages as defined through Wilson and Washington.(Vyas SP et al.2002)

1. Phase I (Basal phase) lasts from 40 to 60 minutes with rare contractions.
2. Phase II (Preburst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (burst phase) lasts for 4 to 6 minutes. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the Housekeeper wave.
4. Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

4. FACTORS AFFECTING GASTRIC RETENTION

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

- Density – GRT is a function of dosage form buoyancy that is dependent on the density.
- Size – Dosage form units with a diameter of more than 9.5mm are reported to have an increased GRT.
- Shape of dosage form – Tetrahedron and ring-shaped devices with a flexural modulus of 48 and 22.5 kilopounds per square inch (KSI) are reported to have better GRT. 90% to 100% retention at 24 hours compared with other shapes.
- Single or multiple unit formulation – Multiple unit formulations show a more predictable release profile and insignificant impairing of performance due to failure of units, allow coadministration of units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.
- Fed or unfed state – Under fasforms conditions, the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.
- Nature of meal – Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release.
- Caloric content – GRT can be increased by four to 10 hours with a meal that is high in proteins and fats.
- Frequency of feed – The GRT can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC.
- Gender – Mean ambulatory GRT in males (3.4 □0.6 hours) is less compared with their age and race-matched female counterparts (4.6 □1.2 hours), regardless of the weight, height and body surface.
- Age – Elderly people, especiallysurface over 70, have a significantly longer GST.
- Posture – GRT can vary between supine and upright ambulatory states of the patient.15
- Concomitant drug administration– Anticholinergics like Atropine and Propantheline, Opiates like Codeine and Prokinetic agents like Metoclopramide and Cisapride.
- Biological factors – Diabetes and Crohn’s disease.

5. APPROACHES TO GASTRIC RETENTION

Various approaches have been pursued to increase the retention of an oral dosage form in the stomach.

Practical approaches in designing FDDS –

The idea of FDDS become first defined withinside the literature as early as 1968, whilst Davis (1968) disclosed a way to conquer the problem skilled with the aid of using a few folks of gagging or choking after swallowing medicinal pills. The writer recommended that such problem might be conquer with the aid of using presenting tablet having a density of much less than 1.0g/cm3, in order that tablet will drift on water surface. Since then numerous procedures were used to broaden a super floating drug transport system (Moya Nakagawa et al. 2006).

Approaches to Design Single and Multiple Unit Dosage Form –

The following approaches have been used for the design of floating dosage forms of single and multiple unit systems. (Yie W. et al, 1992)

For Single Unit Dosage Forms(Eg: tablets)

I. Floating lag time: It is the time taken by the tablet to emerge onto the surface of dissolution medium and is expressed in seconds or minutes.

II. In vitro drug release and duration of floating: This is determined by using USP II apparatus (paddle) stirring at a speed of 50 or 100 rpm at 37 ± 0.2 °c in simulated gastric fluid (pH 1.2 without pepsin). Aliquots of the samples are collected and analysed for the drug content. The time (hrs) for which the tablets remain buoyant on the surface of the dissolution medium is the duration of floating and is visually observed.

III. In vivo evaluation for gastro-retention: This is carried out by means of X-ray or Gamma scintigraphic monitoring of the dosage form transition in the GIT. The tablets are also evaluated for hardness, weight variation, etc.

In low density approaches, (Deshpande AA et al.1997)The globular shells reputedly having decrease density than that of gastric fluid may be used as a service like popcorn, poprice, polystrol for the drug for its managed launch. The polymer of preference may be both Ethyl cellulose or HPMC. Depending on kind of launch desired. Finally the product floats at the gastric fluid whilst liberating the drug steadily over a extended duration. Fluid stuffed floating chamber kind of dosage paperwork consists of incorporation of a fueloline stuffed floatation chamber in to a micro porous thing that homes as a reservoir having apertures gift at pinnacle and backside partitions thru which the gastrointestinal tract fluid enters to dissolve the drug.

- **Hydro Dynamically Balanced System :**

These systems are designed to lengthen the live of the dosage forms withinside the gastric intestinal tract and resource in improving the absorption. Drugs having a higher solubility in acidic surroundings and additionally having unique web website online of absorption withinside the higher a part of small intestine is executed through those HBS structures. To maintain in stomach for a extended time frame the dosage shape have to have bulk density of much less than '1' and has to hold its structural integrity and launch drug continuously from the dosage shape. Among all of the benefits single-unit formulations are related to a few limitations/issues inclusive of sticking collectively or being obstructed withinside the GIT which can also additionally cause capability risk of producing irritation (Przemyslaw Dorozynski et al.2007).

- **For Multiple Unit Dosage Forms (Eg: microspheres) –**

Apart from the In vitro release, duration of floating and in vivo gastro-retention tests, the multiple unit dosage forms are also evaluated for:

(i) Morphological and dimensional analysis with the aid of scanning electron microscopy (SEM). The size can also be measured using an optical microscope.

(ii) In vitro floating ability (Buoyancy %): A known quantity of microspheres are spread over the surface of a USP (Type II) dissolution apparatus filled with 900 ml of 0.1 N HCl containing 0.002% v/v Tween 80 and agitated at 100 rpm for 12 hours. After 12 hours, the floating and settled layers are seperated, dried in a dessicator and weighed. The buoyancy is calculated from the following formula.

$$\text{Buoyancy (\%)} = Wf / (Wf + Ws) \times 100$$

Where Wf and Ws are the weights of floating and settled microspheres respectively

(iii) Drug-excipient (DE) interactions: This is done using FTIR. Appearance of a new peak, and/or disappearance of original drug or excipient peak indicates the DE interaction. Apart from the above mentioned evaluation parameters, granules are also evaluated for the effect of ageing with the help of Differential Scanning Calorimeter or Hot stage polarizing microscopy.

- **Approaches to gastric retention:**

1. Floating drug delivery systems (FDDS): These devices float over the gastric contents due to their low density.

2. Bioadhesive systems: These systems bond to the stomach mucosa, allowing for the system's localized retention.

3. Swelling and expanding systems: Swelling and expanding systems absorb water and grow in size as a result.

4. High-density systems: They settle into the folds of the stomach, allowing them to stay in the stomach for longer periods of time.

Classification of floating drug delivery System:

1. Single Unit Floating Dosage Systems
    a) Effervescent Systems (Gas-generating Systems)
    b) Non-effervescent Systems
2. Multiple Unit Floating Dosage Systems
    a) Non-effervescent Systems
    b) Effervescent Systems (Gas-generating System.
    c) Hollow Microspheres
    d) Raft Forming Systems.

1. Single unit floating dosage system-

Single-unit dosage forms are less difficult to manufacture, however due to the fact they empty absolutely or partly from the stomach, they run the chance of dropping their outcomes too soon, ensuing in excessive variability in bioavailability and nearby discomfort because of a big extent of drug administered at a selected region withinside the gastrointestinal tract.

(a) Effervescent Systems (Gas-generating Systems)-

These are matrix kinds of structures made with effervescent substances like sodium bicarbonate, citric acid, and tartaric acid, in addition to swelling polymers like chitosan and methylcellulose. When CO2 comes into contact with acidic gastric contents, it is generated and fixed in swollen hydrocolloids, giving dosage kinds buoyancy.

(b) Non-effervescent Systems

Polysaccharides, hydrocolloids, and matrix-forming polymers consisting of polyacrylate, polycarbonate, polystyrene, and polymethacrylate are used to generate a gel-forming or swelling cellulose kind in non-effervescent floating dosage bureaucracy. A straightforward strategy to absolutely integrate the drugs and the hydrocolloid-forming gel is protected withinside the formulation method. Following oral administration, this dosage form swells in contact with stomach juices and achieves a bulk density of 1. The air contained withinside the swelling matrix offers buoyancy to the dose form.

2. Multiple unit dosage form:-

(a) Non-effervescent Systems-

Unlike effervescent systems, there may be little studies on effervescent a couple of-unit systems withinside the literature. However, few researchers have investigated the feasibility of growing an indomethacin-containing approach using chitosan because the polymeric excipient. A version drug synthetic the usage of the extrusion manner is a couple of HBS unit containing indomethacin.

(b) Effervescent Systems

A calcium alginate center and a calcium alginate/PVA membrane have been separated via way of means of an air compartment in a multi-unit system. In the presence of water, the PVA leaches out and will increase the permeability of the membrane, keeping the integrity of the air compartment. The floating residences of the system have advanced because the molecular weight and PVA content material have increased. The freeze-drying process for making floating calcium alginate beads is likewise addressed.

(c) Hollow Micro spheres

Hollow microspheres filled with prescription drugs have been created of their outer polymer shelf the usage of a completely unique method of emulsion solvent diffusion. At four hundred stages Celsius, the drug's ethanol/dichloromethane answer and enteric acrylic polymer have been poured right into a thermally regulated, agitated Poly Vinyl Alcohol (PVA) solution.

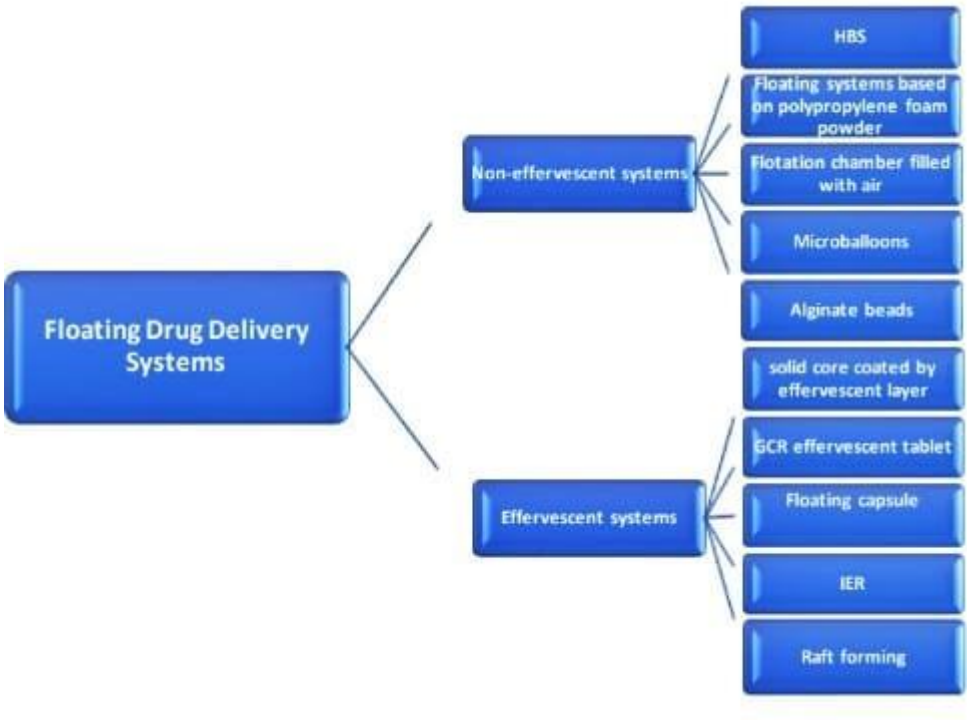


Fig. Classification of FDDS

Mechanism of action is as follows:

Because FDDS has a decrease bulk density than gastric fluid, it may go with the flow withinside the stomach for longer durations of time without affecting the rate at which it empties. The medication is lightly released from the system on the preferred pace at the same time as the systems are floating at the belly material. Once the drug is launched, the stomach's residual system is empty. As a result, GRT is increased, and plasma drug concentration fluctuations are higher managed. A new equipment for estimating the ensuing weight has been recorded withinside the literature for the computation of floating pressure kinetics. The system works with the aid of using constantly measuring the pressure required to maintain the submerged object afloat, that's same to F (as a feature of time).

Methods of Developing Floating Drug Delivery Systems:

1. Direct compression technique-

It entails compressing tablets directly from powder without changing the physical structure of the material. The most common carriers are dicalcium trihydrate phosphate, tricalcium phosphate, and others.

2. Wet granulation technique

Wet powder massaging, grinding, or drying are all involved. Instead of compacting the powders, wet granulation forms them by binding them together with an adhesive.

3. Effervescent Technique

The floating chamber of the medication delivery system will be filled with inert gas as a result of an effervescent reaction between organic acid (citric acid) and bicarbonate salts (CO2).

4. Ionotropic Gelation Technique

The basic polymer of natural origin, anionic polysaccharide sodium alginate, was gelled with oppositely charged calcium ions (counter-ions) with the goal of creating immediate microparticles.

5. Solvent evaporation technique

The capacity of a continuous phase to remove the entire amount of liquid dispersal solvent is insufficient. To obtain hardened microspheres, solvent evaporates from the dispersal surface.

6. Spray drying technique

Dispersing the core layer into the liquid coating content and spraying the core coating mixture into the environment to solidify the coating by rapidly evaporating the coating material

7. Melt solidification technique

This method entails emulsifying the molten mass in an aqueous phase before cooling it and solidifying it. The carriers for this technique include lipids, waxes, polyethylene glycol, and others.

8. Melt Granulation Technique

This is a granulation technique that uses a meltable binder to agglomerate pharmaceutical powders without the need for water or organic solvents.

Evaluation of floating drug delivery systems:

Various parameters that need to be evaluated in gastroretensive formulations include floating duration, dissolution ,profiles, specific gravity, content uniformity, hardness, and friability in case of solid dosage forms. In the case of multiparticulate drug delivery systems, differential scanning calorimetry (DSC), particle size analysis, flow properties, surface morphology, mechanical properties and X-ray diffraction studies are also performed.

1. Bulk density: It's the proportion of a powder's total mass (m) to its bulk volume (Vo).

$$Db=m/Vo$$

2. Tapped density: It's the ratio of powder total mass (m) to powder tapped volume (Vi).

$$Dt = m/Vi$$

3. Compressibility index: The bulk density (o) and tapped density (t) of powder, as well as the rate at which it packs down, can be used to determine the flowability of powder.

4. Hausner's Ratio: It is calculated by taking the Tapped density and dividing it by the Bulk density using the formula below.

$$\text{Hausner's Ratio} = \text{Tapped density} / \text{Bulk density}$$

5. Angle of repose: In this experiment, a funnel is filled with an accurately weighed mixture of powder, granules, and microparticles.

$$\tan \theta = (h/r)$$

$$\Theta = \tan^{-1} (h/r)$$

Θ = angle of repose

H = height of the heap

R = radius of the heap

6. Tablet dimensions: A calibrated Vernier Caliper was used to measure thickness and diameter. Three tablets of each formulation were chosen at random and measured separately for thickness.

7. Hardness: Hardness indicates a tablet's capacity to withstand mechanical shocks while in use. A Monsanto hardness tester was used to assess the tablets' hardness. It was measured in kilogrammes per square meter. Three tablets were chosen at random and their hardness was determined.

8. Friability test: The Roche Friabilator was used to assess the friability of tablets. It was given as a percentage (percent). To begin with, ten tablets were weighed (W) and placed in the friabilator. The friabilator was spun at 25 rpm for 4 minutes, or turned up to 100 times. The tablets were weighed once again (Wo). A formula was used to compute the percent friability.

$$\%F = 100 (1-Wo/W).$$

9. Table density: For floating tablets, tablet density was an excellent criterion. When the tablet's density is substantially lower than that of gastric juice, it can float most effectively (1.04). The density was calculated using the following

Formula:

$$V = \pi r^2 h$$

$$D = m/v$$

Where,

V = volume of tablet (cc)

r = radius of tablet (cm)

h= crown thickness of tablet (g/cc)

m = mass of tablet

10. Weight variation experiment: To test for weight variation, ten pills were chosen at random from each batch and weighed individually. The United States Pharmacopoeia allows for some variation in tablet weight.

11. Determination of buoyancy lag time: The buoyancy lag is the time it takes for the tablet to rise to the surface and float. The buoyancy of pills was investigated in 900ml of artificial stomach fluid at 370.5oC. The buoyancy lag time was measured with a stop watch, and the entire floating time was visually observed.

12. Floating time: throughout the investigation, float time was monitored using a USP dissolving apparatus-II at 50 rpm with 900ml of 0.1N HCl and a temperature of 370.5 oC.

The Benefits of a Floating Drug Delivery System:

1. Due to the alkaline pH of the intestine, floating drugs of all kinds, such as capsules or tablets, will linger in the fluid for a long time.

2. The dissolving of the medicine in the stomach fluid occurs when prolonged release floating dosage forms, such as tablets or capsules, are administered. They dissolve in gastric fluid and are available for absorption in the small intestine after the stomach contents have been emptied. As a result, even at the alkaline pH of the intestine, it is envisaged that a medication will be fully absorbed from floating dosage forms if it remains in the solution sstate

3. The gastro-retentive system is beneficial for medications that are absorbed through the stomach. e.g. Ferrous salts and antacids.

4. Advantageous for medications that have a local effect in the stomach, such as antacids.

5. The FDDS formulation is effective in intestinal movement and diarrhoea to keep the medicine in a floating state in the stomach, allowing for a greater reaction.

6. FDDS promotes patient compliance by reducing dosage frequency.

7. Treatment for gastrointestinal problems such as gastroesophageal reflux.

8. Despite the first-pass effect, bioavailability is not affected since the plasma drug concentration is not affected.

9. Because aspirin and other similar drugs are acidic and cause stomach irritation, HBS/FDDS formulations may be useful for their administration.

10. Benefits from medications that are absorbed by the stomach, such as ferrous salts and antacids.

11. The medicine is delivered to a specific location.

Disadvantages of the floating drug delivery System:

1. Drugs that are unstable in the stomach's acidic environment are not ideal candidates for incorporation into the system. The presence of food is frequently required in these systems to prolong stomach emptying.

2. It is not recommended for medications that have an issue with GIT stability or solubility.

3. Medications that have a substantial absorption rate and those that have first-pass effect only desirable candidates are found throughout the gastrointestinal tract.

4. The dosage form's tendency to float is determined by its hydration condition. Water that comes and goes from administration is beneficial in keeping these tablets afloat.18

5. Many factors influence stomach retention, including gastric motility, pH, and the presence of food. Because these variables are never consistent, buoyancy cannot be anticipated.

6. Drugs that irritate or damage the stomach mucosa should not be incorporated into floating drug delivery devices.

7. Due to its all-or-none-emptying method, there is a lot of variation in gastric emptying time.

8. In supine subjects, gastric emptying of floating forms can happen at any time and is strongly dependent on the diameter and size. As a result, floating forms should not be given to patients right before bedtime.

9. Because of solubility and stability concerns in the GIT, drugs that induce irritation to the gastric mucosa are not ideal for this system.

6. MECHANISM OF ACTION OF FDDS

The system floats on gastric contents (see in figure 3), the gradual drug release with fundamental contents. The discharge is accompanied with the aid of using elimination of the residual system for the stomach. But, along side an appropriate floating force (f), minimal levels of gastric contents are had to permit attainment of buoyancy retention precept and additionally to maintain dosage form buoyant over meal surface. To measure the kinetics of floating force, a singular equipment is used for the calculation of resultant weight (rw) has been reported. Its operation composes measuring a force equal to f (with respect to time) which continues theobject submerged. Object floats better if the rw is on the higher positive side.

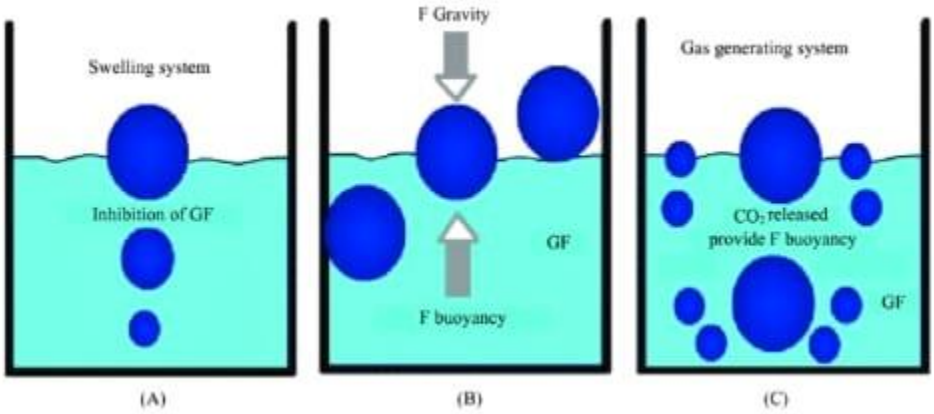


Fig. Mechanism of action of FDDS

Factors affecting the floating drug delivery system:

1. Density: The density of a dose form determines its buoyancy and, as a result, its floating efficiency. The dose form's density should be lower than the stomachic contents (1.004 gm/ml).

2. Shape of dosage form: Tetrahedron and ring-shaped devices have a higher floating potential than other shapes. They have a 90-98 percent higher rate of 24-hour retention.

3. Fed or unfed state: GI motility is characterized by periods of robust motor activity, or migrating myoelectric complexes (MMC), which occur every 1.5 to 2 hours under abstinence settings.

4. Formulation of a single or multiple units: Multiple unit formulations permit a larger margin of safety against dosage form failure compared with single unit dosage forms.

5. Nature of meal: Feeding indigestible polymers or fatty acid salts to the stomach can cause it to shift its motility pattern to a fed state, slowing gastric emptying and prolonging medication release.

6. Calorie content: A high-protein, high-fat meal can extend floating time by 4–10 hours.

7. Frequency of feed: Because of the low frequency of migratory myoelectric complex, the GRT will increase by over 40 minutes when successive meals are provided instead of a single meal (MMC).

8. Posture: The GRT will differ between the patient's supine and upright ambulant stages. In the case of the floating systems, it was rumored that when individuals were kept in an upright ambulant position, the dosage type stayed consistent on stomachic content, as opposed to when they were in a supine position. As a result, the floating drugdelivery system inside the upright position of the patients is safeguarded against post-prandial evacuation.

9. Age: Elderly people, those over the age of 60, have a much longer floating time.

10. Biological factor: Floating might vary depending on a person's health or physiological status. Diabetes and Crohn's illness, for example, affect floating time.

11. Concomitant drug administration: Floating time is affected by anticholinergics like atropine, opiates like codeine, and prokinetic drugs like metoclopramide and cisapride.

Application of FDDS:

1. Maximize bioavailability gastro retentive fdds is applied for increasing the activity of the dosage type of drug to extended action bioavailability is maximized.

2. Sustained released drug delivery oral controlled release formulations are come across with problems such as gastric residence time in git. these problems can be controlled with the hbs system which can remain in the stomach for the long periods and having bulk density <1 as a result they can float on the gastric contents. these systems are moderately larger in size and passing from the pyloric opening is proscribed.

3. Minimize the absorption these types of dosage form have less bioavailability specific site absorption from the upper part of the git, enhancing the absorption of dosage type .

4. Site specific DDS these systems are especially important for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine. the controlled, slow delivery of the drug to stomach provides adequate local therapeutic levels and limits the systemic vulnerability to the drug. this decreases side effects that are caused by the drug in the blood circulation.

5. Decrease the adverse activity of the mi of the dosage type within the GRS (gastro retentive system), decrease the quantity Of drug that arrives in the colon.

7. LIST OF DRUGS EXPLORED FOR VARIOUS FLOATING DOSAGE FORMS

- Microspheres Tablets /Pills: Chlorpheniramine maleate, Aspirin, Griseofulvin, Acetaminophen, p-nitroaniline, Acetylsalicylic acid, Ibuprofen, Amoxycillin trihydrate, Terfenadine, Ampicillin, Tranilast,Atenolol, Theophylline, Captopril, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate.

- Films: P-Aminobenzoic acid, Cinnarizine, Piretanide, Prednisolone, Quinidine gluconate.

- Granules: Cinnarizine, Diclofenac sodium , Diltiazem, Indomethacin ,Fluorouracil, Prednisolone , Isosorbide Mononitrate ,Isosorbide dinitrate.

- Powders: Riboflavin,phosphate, Sotalol, Theophylline.

- Capsules: Verapamil HCl, Chlordiazepoxide HCl, Diazepam, Furosemide, L-,opa and benserazide Misoprostol, Propranolol HCl, Ursodeoxycholic acid, Nicardipine .

Pharmaceutical Aspects:

In designing of FDDS, following characteristics should be sought:

1) Retention in the stomach according to the clinical demand;

2) Convenient intake;

Ability to load substantial amount of drug with different physicochemical properties and release them in a controlled manners; and complete matrix integrity of the sr formulation in the stomach, an inexpensive industrial manufacture, optimization between the buoyancy time and release rate (buoyancy time increases by increasing drug: polymer ratio but release retards by increasing polymer level), lag time i.e. the time taken by the dosage form to float should be low (wong p s let al.2000) .

Most of the floating systems reported in literature are single-unit systems; these systems are unreliable and irreproducible in prolonging residence time in the stomach when orally administered, owing to their fortuitous (‘all-or-nothing’) emptying process. on the other hand, multiple-unit dosage forms appear to be better option since they reduce the inter subject variability in absorption and lower the probability of dose dumping (el-kamel a het al.2001)

8. FUTURE PERSPECTIVES IN FLOATING DRUG DELIVERY SYSTEMS

Among the medicine presently in medical use are numerous narrow absorption window drugs that can gain from compounding right into a fdds. Changing parentarl administartion of medicine to oral pharmacotherapy might extensively enhance treatment. It is predicted that fdds can also additionally enhance this possibility.moreover, it is anticipated that the fdds technique can be used for lots patentially active agents with narrow absorption window, whose improvement has been halted because of loss of suitable pharmaceutical fdds technologies. Mixture remedy to deal with h. pylori infection in a single fdds want to be developed. In addition research can also additionally concentarte on the subsequent concept:

Identification of a minimum cut-off size above that dfs retained withinside the human stomach for extended duration of time.this will allow a extra unique manage to be carried out in gestroretentivity.

Design of array of fdds, every having a narrow grt to be used in line with the medical need e.g. dosage and state of disease. This will be carried out with the aid of using compounding polymeric metrices with numerous boidegradation prpoerties.

Study of the impact of numerous geometric shape, in a extra immoderate way than preceding studies, prolonged dimensions with excessive rigidity, on gestroretentivity.

Design of novel polymers in line with medical and phamaceutical need.

9. CONCLUSION

Gastro-retentive floating drug delivery systems have emerged as an efficient means of improving the bioavailability and controlled delivery of many drugs. The growing sophistication of delivery technology will make sure the improvement of increase variety of gastro-retentive drug delivery to optimize the delivery of molecules that exhibit absorption window, low bioavailability and considerable first pass metabolism.

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