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FLOATING DRUG DELIVERY SYSTEM: AN OVERVIEW

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ABSTRACT

Floating drug delivery systems (FDDS) have a lower bulk density than gastric fluids, consequently they float in the stomach for longer decades of time without altering the gastric emptying rate. The medicine is released gradually and at a controlled pace from the system while it is floating on the stomach contents. The residual approach in the stomach is emptied once the medicine is released. As a consequence, the Gastric Residence Time (GRT) is enhanced, and differences in plasma drug concentration are better controlled. The system must have enough structure to formulate a cohesive gel barrier and disintegrate gradually enough to act as a drug reservoir while maintaining an overall specific gravity lower than that of stomach contents. The techniques used to create both non-effervescent and effervescent floating tablets based on buoyancy mechanisms in order to expand FDDS. Using the previously effective. Thus, it is possible to provide medications with a limited window of therapeutic action. The goal of our review paper is to provide thorough information on the pharmaceutical foundations of FDDS's design, classification, preparation factors that affect FDDS, benefits, uses, disadvantages, and potential future applications.

KEYWORDS: Gastroretentive System, Gastric emptying rate, HBS and Floating Drug Delivery System.

INTRODUCTION

Floating systems, also known as dynamically regulated systems, are low density systems with enough buoyancy to pass over the contents of the stomach and stay afloat in the stomach for an extended amount of time without slowing down the rate at which the stomach empties.

This outcome isa longer period of stomach retention and improved management of plasma medication concentration variations.[1] Certain drug concentrations are delivered in systemic blood circulation by solid oral dose forms like capsules and tablets without causing any control over the medication delivery mechanism can significantly alter the drug concentrations in plasma. Oral administration is the most practical and recommended method of delivering any medication to the systemic circulation. Factors as medication formulation versatility, patient compliance with the product, and convenience of dose administration. Drugs with short half-lives and easy absorption from the gastrointestinal tract (GIT) are rapidly removed from the systemic circulation. To prevent this, sustained-controlled release oral formulations are being developed. The reduced effectiveness of the dose given as a result of partial drug release from the DDS brought on by humans' comparatively short stomach residence time across the main absorption zone, such as the proximal portion of the GIT. Therefore, factors have resulted in the creation of oral controlled release. The capacity to precisely place a drug delivery system in a particular area of the GI tract, particularly for medications with stability issues or an absorption window, is one of the many benefits of using CR dosage forms with gastric retention characteristics. In order to create an effective medication delivery system that is gastroretentive or stomach specific, numerous currently, methods such as hydro dynamically balanced systems (HBS) / floating drug delivery systems, low density systems, raft systems with alginate gels, bioadhesive or mucoadhesive systems, high density systems, super porous hydro gels, and magnetic systems are used to extend gastric residence times (GRT).[2]

Floating system

Floating drug delivery systems (FDDS) have a lower bulk density than gastric fluids; they float in the stomach for extended periods of time without slowing down the rate at which the stomach empties. As the medication is floating on the stomach contents, the system is removed from the system gradually and at the appropriate pace. Following drug release, the stomach's residual system is emptied.[3]

STOMACH ANATOMY

The basic operate of the abdomen is to method and transport food in little intestine the duration of food is tiny and largely protein square measure digestible.

1. Phase I (basal phase)
2. Phase II (pre burst phase)

3. Phase III (burst phase)
4. Phase IV.

Phase I

Due to the delayed initiation of MMC, the stomach emptying rate is sluggish during this period. This stage often lasts between 30 and 60 minutes. In this period, contraction does not take place. Another name for it is basal phase. Due to the lasts between thirty and sixty minutes.

Phase II

Delayed initiation of MMC, the stomach emptying rate is sluggish during this period.
During this phase, mucus discharge and bile secretion occur. There is a contraction. It is 20 to 40 minutes long. Another name for it is the pre-burst period.

Phase III

During this period, there are brief, frequent, and strong contractions. Usually, it lasts 10 to 20 minutes. this stage is also known as housekeeper wave as it tends to release the stomach's contents after fasting. During this phase, the large goal passes down to the intestine but stays in the stomach in the fed condition.

Phase IV

Occur between phases III and I of two consecutive cycles and last for 0 to 5 minutes. Following the consumption of a mixed meal, the sequence of contractions shift from fed to fasting states.

This is also referred to as the "digestive motility pattern," and it consists of constant contraction similar to that of phase II fasting.

Stomach Physiology

The digestive tube that runs between the oesophagus and the small intestine is enlarged to form the stomach. With the exception of the stomach's additional, oblique layer of smooth muscle inside the circular layer, which aids in the execution of complex grinding actions, the stomach's wall is physically similar to the other portions of the digestive tube. The stomach contracts when it is empty, causing the mucosa and submucosa to rise into separate folds known as rugae. Secretary epithelial cells, which cover the stomach's surface and extend into gastric pits and glands, can be classified into four primary categories. They exude an alkaline

mucus that shields the epithelium from acid and shear stress. Hydrochloric acid is secreted by parietal cells. Chief cells: release the proteolytic enzyme pepsin. Gastrin is secreted by G cells. There are two main reasons why the smooth muscle of the stomach contracts. Chyme is created when food is consumed and is pulverized, combined, and liquefied. Gastric emptying is the process by which chyme is pushed into the small intestine through the pyloric canal.[4,5]

Gastric Emptying Rate

Both when feeding and when fasting, gastric emptying takes place. Nonetheless, the motility patterns in the two states differ. An electrical sequence of inter-digestion occurs during fasting, revolving through the colon and stomach every two to three hours. The frequency of drug absorption may be influenced by the close contact between the absorbing membrane and the drug delivery algorithm, as well as by the algorithm's ability to maximize drug absorption. Due to these factors, oral controlled release (CR) dose formulations with the ability to retain in the stomach have become more popular. Because the dosage form may be swiftly transferred from the more absorbent upper portions of the colon to the lower areas where the drug is absorbed, the medicine may not be absorbed evenly along the length of the gastrointestinal tract.[4,5]

Drug selection criteria for the floating drug delivery system

1. Quick absorption occurs via the upper gastrointestinal tract.
2. Medication having unionized characteristics and a low pKa
3. At higher pH values, the solubility of drugs is decreased.
4. Medicines that degrade in alkaline pH conditions; by making them gastro retentive, their bioavailability can be increased.
5. Lessening gastrointestinal discomfort, which could cause the stomach's concentration of medication to rise.[6,7]

Advantages of FDDS

1. This method can be used to administer drugs with a short half-life that nonetheless have a major therapeutic impact.
2. Higher bioavailability for drugs that the upper gastrointestinal tract can metabolize.
3. They are also superior to the traditional method since they can be utilized to address the problems of stomach retention and emptying time.
4. The amount of time it takes for an active module to be released over a century from a single dosage.

5. Adverse effects are minimized or eliminated when the active ingredient is delivered directly to the site of action.
6. Lowers the dosage frequency.
7. It improves the medications' bioavailability.
8. Higher bioavailability for certain substances that the upper gastrointestinal tract may metabolize.[8,9,10]

Disadvantages of FDDS

1. There are numerous factors that affect stomach retention, such as pH, gastric motility, and the presence of food. Float cannot be predicted because these factors are never constant.
2. Drug delivery devices that float shouldn't be made of substances that irritate or harm the stomach mucosa.
3. The stomach emptying time varies greatly because of its all-or-none emptying process.
4. Floating types shouldn't be administered to patients soon before bed.[11]

Mechanism of floating system

Various attempts have been made up to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introduction floating dosage forms mucoadhesive systems, high – density system, modified shape system, gastric emptying delaying drugs. Among these the floating dosage forms are the most commonly used. Floating drug delivery systems FDDS.Have bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolong period of time. While the system is floating on the gastric contents the drug is released slowly at the desired rate from the system. After release of drug the residual system is eliminated from the stomach. This results in an increased GRT and a better control of the fluctuation in plasma drug concentration.oral dosage forms (capsule or tablet) that are designed to prolong the retention time of the drug within the GI tract. The recent literature survey shows that interest increased in academics and industrial research regarding the development of novel dosage forms that can be sustained in the stomach for a longer and predictable period of time. The numerous marketed FDDS are given in table.[12,13]

Factors Affecting Gastric Retention

The following variables influence the dose form's gastric retention time (GRT) and, consequently, its effectiveness as a gastroretentive system:

Density: Density is a variable that influences the role and duration of gastric retention.

Size: The dosage form's size may have an impact on the duration of gastric retention. It is recommended that the dosage form size not exceed 9.5 mm in diameter, since this may result in an extended stomach retention period.

Dosage form shape: Tetrahedron and ring-shaped devices with flexural moduli of 48 and 22.5 kilo pounds per square inch (KSI) are claimed to have good and better stomach retention times. 90% to 100% retention at 24 hours in contrast to other forms.

Formulation with one or more units: When compared to single module dosage forms, multiple unit formulations show a more predictable release profile, allow for the co-administration of units with different release profiles or containing incompatible substances, and permit a larger margin of safety against dosage form failure. Additionally, the tiny performance impairment resulting from unit incapacity is negligible.

Feeding frequency: Because the migrating myoelectric complex (MMC) occurs infrequently, the stomach retention period might rise by more than 400 minutes when multiple meals are provided instead of only one.

Gender: Regardless of weight, height, or body surface, the mean ambulatory gastric retention time in males is 3.4 - 0.6 hours or less when compared to their age, and 4.6 1.2 hours in females of the same race.

Age: Individuals over 70 years of age were shown to have a longer stomach retention period.

Posture: The patient's gastric retention time (GRT) can change from a supine to an upright ambulatory position.[14,15]

Methods of Preparation of Floating Tablets

Procedure for single-layer floating tablets: Compression techniques are primarily used to create single-layer floating tablets. Usually, three fundamental compression techniques are applied for this. They are listed below.

1. Direct compression method
2. Dry granulation method
3. Wet granulation method

Direct compression method: This technique involves compressing tablets straight from powdered ingredients without changing the ingredients' physical makeup. This technique is applied to crystalline substances with good flow and compressibility characteristics. Characteristics like ammonium chloride, sodium chloride, methenamine, and potassium salt (chloride, chlorate, and bromide), among others. Tablet computers are used to prepare compressed tablets through a single compression process. Following the passage of a certain amount of granulated or powdered tabletting material into a die, the material is compressed at a high pressure (~tons/in2) by the tablet machine's upper and lower punches.[16,17]

Dry granulation method: It is described as the slugging process that forms granules when tablet components are moisture-sensitive or cannot tolerate high temperatures during the drying process.[18]

Wet granulation method: In wet granulation, a rapid mixer granulator (RMG) is used to thoroughly mix or blend the active ingredient, diluents, and disintegrates. The RMG is a versatile chopper that combines a chopper and an impeller for rapid dispersion of dry particles.as well as solvent or aqueous granulations. After the wet milling process, the moist materials are spread out on sizable trays and put in drying chambers equipped with thermostable heat controllers and circulating air currents. Tray dryers and fluidized bed dryers are common types of dryers. The process of passing the granules through a smaller mesh screen reduces their particle size after drying. The lubricant, also known as the glideant, is then applied as a fine powder to encourage granule flow. After that, these granules are compacted. To purchase a tablet. When compared to wet granulation, the production method for dry granulation is quicker and less expensive. Dry granulation is particularly useful for active substances that are labile to moisture and high temperatures, or that are sensitive to solvents, as it doesn't require heat or moisture.[19]

METHOD OF EVALUATION

There are two types

1. Pre-compression
2. Post-compression

1. Pre-compression

Bulk density: Bulk density is the mass of powder divided by the bulk volume. Particle shape, cohesion, and size distribution all affect bulk density. A huge funnel was used to gently pour

a precisely weighed quantity of powder into a graduated measuring cylinder. Original bulk volume—which was measured—was found. It is provided by the following formula and is represented in gm/ml:[20]

M/Vo is the bulk density.

where M is the powder's mass

Vo is the powder's bulk volume.

Tapped density: A 100 ml dry measuring cylinder was filled with 10 gram of powder. The tapped volume of the cylinder was then measured after it had been tapped 100 times from a fixed height.[21]

Angle of repose (θ): The maximum angle that can exist between the horizontal plane and the powder pile's surface is known as the angle of repose (θ). The fixed funnel approach was applied. A graph paper was placed on a flat horizontal surface, above which a funnel with its tip fixed at a specific height 'h' was positioned. A funnel was carefully filled with powder until the conical pile's peak barely touched the funnel's tip.[22]

$$\text{Repose angle } Ø = \tan 1 \ (h/r)$$

Hausner's ratio: To forecast the powders' flowability, utilize Hausner's ratio. This approach bears resemblance to the compressibility index. Equation can be used to express Hausner's ratio: Tapped density / bulk density equals Hausner's ratio.

2. Post-compression

Weight Variation test (U.S.P.): Weigh each of the 20 tablets separately. After calculating the average weight, weigh each tablet separately and compare the results. If just two tablets deviate from the % limit and if no tablet has more than two differences, the tablet passes the U.S.P. test. multiplied by the percentage threshold.[23]

Thickness and Diameter: By verniar caliper. Vernier Caliper will be used to measure diameter of each tablet. It will be measured by simply placing the tablet in between the jaws of verniar caliper and slide the scale arm to press the tablet against the stationary arm then the reading displayed will be noted.

Hardness: To ensure that the tablet can withstand shock and stress during manufacture, packing, and shipping, as well as when handled by the patient, it is crucial to consider the

tablet's hardness and strength. To gauge the tablet's hardness Testers from Monsanto, Strong-Cobb, Pfizer, and Erweka, Schleuniger testers are employed.[24]

Friability: 20 tablets of each batch will be weigh and then tested by friabilator at speed 25 rpm for 4 min. Then weigh will be checked and calculated.

Floating lag time and total floating time: The dissolution equipment type II, which contained 100 mL of 0.1 N HCl and a paddle rotating at 50 rpm (pH 1.2) at 37 ± 0.5 °C, was used to visually assess the floating lag time (FLT) and total floating time (TFT) of floating tablets.[25]

Dissolution Study: The USP dissolution apparatus type II paddle type was used to perform the in vitro drug release of the formulation at a temperature of 37 ± 0.5 °C and a rotating speed of 50 rpm in a sink condition. 900 milliliters of 0.1NHCl dissolving media were utilized. Using a UV/visible spectrophotometer, the samples were taken out at prearranged intervals for a duration of six hours, and they were replaced with fresh medium that had been appropriately diluted.[26]

Disintegration Test (U.S.P.): The U.S.P. apparatus for testing disintegration consists of six three-inch glass tubes with 10 mesh screens at the bottom and an open top. One tablet is put in each tube, and the basket rack is set up in a 1-liter beaker of water, simulated gastric fluid, or simulated intestinal fluid at 37 ± 2 0 C to test the disintegration time. The tablet must stay 2.5 cm below the liquid's surface during its upward movement and not come any closer to the beaker's bottom during its downward movement. Move the tablet-containing basket up and down at a frequency of 28 to 32 cycles per minute over a distance of 5 to 6 cm. Placing perforated plastic disks on each pill will stop it from floating. The tablet needs to break down and all of the particles need to get through the 10 mesh screen within the allotted time, according to the test. mentioned. If any residue is left, it ought to be soft in texture. Breakdown duration: Tablet without coating: 5–30 minutes pill coated: 1-2 hours.[27]

Drugs that suitable for Floating drugdelivery systems

1. Medication that acts locally in the stomach, such as misoprostol, antacids, and H2 receptor antagonists.
2. Medication that breaks down in the colon, such as metronidazole and ranitidine HCL.
3. Medication that disrupts healthy colonic bacteria, such as trihydrate and amoxicillin.

4. GI tract's narrow absorption window

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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