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A Review on: Floating Drug Delivery System

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ABSTRACT

Floating drug delivery systems (FDDS) don't alter the rate at which the stomach empties since their bulk density is lower than that of gastric fluids. This allows them to stay in the stomach for several decades.While the medication is floating on the contents of the stomach, it is gradually and regulated expelled from the system. After the medication is released, any leftovers in the stomach are emptied. This improves the Gastric Residence Time (GRT) and allows for more precise regulation of variations in plasma drug concentration. In order to produce a cohesive gel barrier and dissolve gradually enough to serve as a drug reservoir, the system needs to be structurally sound enough to keep its overall specific gravity below 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. Our review paper aims to provide thorough information on the pharmaceutical foundations of FDDS design, classification, preparation factors influencing FDDS, benefits, uses, limitations, and potential future applications.

KEYWORDS: Gastro retentive system, Floating drug delivery system, Classification, Methods, Evaluation.

1. Introduction

All the dosage forms created to date for human administration, oral formulations have gained a prominent position. A quick stomach emptying time is one of the numerous factors that contribute to the poor bioavailability of conventional oral delivery systems in the majority of situations [1-2]. To address this issue, however, recent technology advancements have produced a plethora of innovative pharmaceutical devices, chief among them being controlled release medication delivery systems. One such device is the gastro-retentive drug delivery system (GRDDS). An instance where the combination of a long-term drug release and a stomach retention period has greatly increased patient compliance. The interest in this new delivery technique has been sparked by some inherent constraints of the traditional oral drug delivery systems. Many drug molecules (such as pranlukasthydrate, metformin HCl, baclofen, etc.), of which the primary site of absorption is the stomach or the proximal part of the small intestine, or have the absorption issue in the distal part of the intestine, have problems with bioavailability when fast gastric emptying associated with conventional oral medications occurs [3-5]. Drugs that are less soluble in an environment of higher pH in the intestine can also have their solubility increased by keeping them longer in the stomach [2]. Numerous medications, such as captopril, metronidazole, ranitidine hydrochloride, and others, are susceptible to deterioration in the colon [2-6]. Recurrent dosing is necessary for medications with short half-lives since they tend to be rapidly removed from the systemic circulation in order to achieve the necessary therapeutic effect. However, by releasing the medication gradually in the stomach and maintaining an effective drug concentration in the systemic circulation for a considerable amount of time, an oral sustained-controlled release formulation with additional gastric retention characteristic can bypass these restrictions [7]. In addition to its systemic effects, GRDDS has shown promise in treating gastric and duodenal ulcers, including esophagitis, locally by removing the Helicobacter pylori bacteria that is deeply buried in the stomach's sub mucosal tissue [2, 5, 8-10]. GRDDS formulations have been around for approximately three decades [11]. The fundamental fabrication methods are also well-established, as are their in vitro characterizations. Very few reviews on GRDDS have been published, even recently [5, 12-18]. The formulation elements, in vitro characterization studies conducted by different researchers, or the overall GRDDS are the main topics of these reviews. Pawar et al. have evaluated the industrial elements of GRDDS that include physicochemical, biopharmaceutical, and regulatory factors [19]. Nevertheless, there aren't many marked gastro-retentive formulations. The pharmacokinetic performances of the created systems must thus be ascertained by looking through the in vivo experiments conducted with GRDDS, given their crucial functions in the successful commercialization of any dose form. Our examination of the literature revealed that, as of right now, no review has been published that focuses on in vivo performances of GRDDS, particularly on current studies. In this regard, the review's objective is to provide an overview of the pharmacokinetic parameters, gastro-retention periods, and intrinsic difficulties or limitations associated with the in vivo assessments that different researchers have documented.

2. Basic Gastrointestinal Tract Physiology

The stomach is composed of three anatomical regions: the fundus, the body, and the antrum (pylorus). The antrum is the primary location for mixing motions and functions as a pump for stomach emptying via thrusting actions, while the proximal portion, composed of the fundus and body, serves as a reservoir for undigested material [20]. Both when feeding and when fasting, gastric emptying takes place. Nonetheless, the motility patterns in the two states differ. Every two to three hours, an interdigestive sequence of electrical events occurs in the stomach and intestines during the fasting state [21]. This is known as the interdigestive myoelectric cycle, or migrating myoelectric cycle (MMC), and Wilson and Washington have further classified it into the following 4 phases [22].

1. The 40–60 minute Phase I (base phase) is punctuated by sporadic contractions.

2. The Preburst phase, or Phase II, is characterized by sporadic contractions and action potentials that last 40 to 60 minutes. Both the intensity and frequency steadily rise as the phase goes on.

3. Three to six minutes make up Phase III, or the blast phase. It consists of brief intervals of time with strong, regular contractions. All of the undigested material is carried out of the stomach and into the small intestine by means of this wave. The housekeeping wave is another name for it.

4. Phase IV, which happens in the interval between phases III and I of two successive cycles, lasts for 0 to 5 minutes.

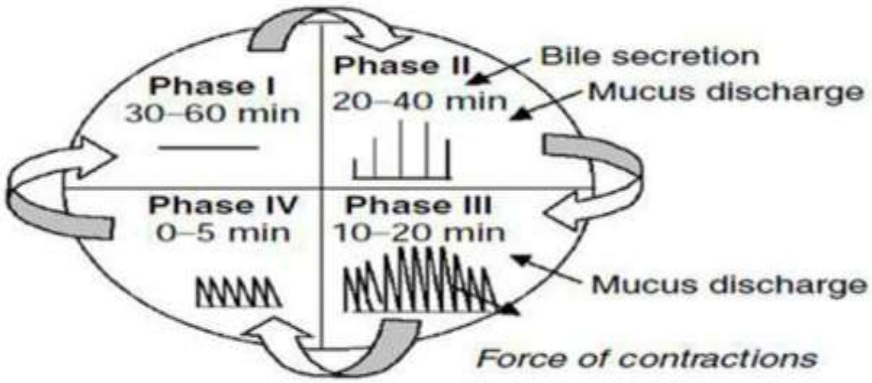

Fig no. 1 Motility pattern of GIT

The pattern of contractions shifts from the fasted condition to the fed state following the consumption of a mixed meal. This pattern, also called the digestive motility pattern, consists of continuous contractions similar to those seen in phase II of the fasting condition. Food particles are reduced in size by these contractions to less than 1 mm, and then they are sent in a suspension state in the direction of the pylorus. The delayed start of MMC during the fed state causes the pace of stomach emptying to slow down [23].

3. FDDS design

A] Gastric Motility

Many neuronal and hormonal signals interact to regulate stomach motility. The enteric nervous system, along with the parasympathetic (mostly vagus nerve) and sympathetic nervous systems, are the sources of nervous control. Numerous hormones have been shown to affect stomach motility; for example, cholecystokinin and gastrin both work to increase distal stomach contractions and calm the proximal stomach. In summary, the patterns of stomach motility most likely result from the integration of a significant amount of stimulatory and inhibitory impulses by smooth muscle cells. Spurts of liquid easily flow through the pylorus, but solids must shrink to a diameter of less than 1-2 mm in order to pass through the pyloric gatekeeper. For the dose form to dissolve in vivo, the stomach capacity is crucial. The stomach holds 25 to 50 milliliters at rest. Standard and a chlorohydrin person differ significantly in their stomach secretions. The impact of gastric pH on drug absorption via the delivery method is also significant. The stomach's pH ranges from 1.2 to 2.0 when fasting and from 2.0 to 6.0 when eaten.

B] 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 drug delivery algorithm and the absorbing membrane, 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. Drug absorption from the colon is typically irregular and ineffective, and dosage forms may be swiftly transferred from more absorbent top sections of the intestine to lower regions where the drug is less absorbed. As a result, drug absorption may not occur consistently along the length of the gastrointestinal tract. Furthermore, certain medications can only be absorbed by the top part of the small intestine or the stomach.

C] Potential drug candidates for gastro retentive drug delivery systems [24-26]

Medications that operate locally in the stomach, such as antacids and misoprostol. Medications that have a limited window of absorption in the gastrointestinal tract (GIT), such as riboflavin, levodopa, furosemide, and Para amino benzoic acid. Medications that can be unpredictably found in the intestine or colon, such as captopril and ranitidine HCl. Medications that disrupt common colonic bacteria, such as helicobacter pylori antibiotics. Medications that show poor solubility at high pH levels, such as verapamil hydrochloride, diazepam, and chlordiazepoxide.

D] The following criteria were implement to choose a drug candidate for the floating drug delivery system [27-28]

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. The effect of medications on the local level, such as the treatment of Helicobacter pylori in ulcerative conditions.

5. Medicines that degrade in alkaline pH conditions; by making them gastro retentive, their bioavailability can be increased.

6. Lessening gastrointestinal discomfort, which could cause the stomach's concentration of medication to rise.

4. Classification

Floating drug delivery system is of 3 types

1. Effervescent systems

2. Non-effervescent systems

3. Raft-forming systems

1. Effervescent systems

These matrix-type systems were created by mixing effervescent substances including citric acid, sodium bicarbonate, tartaric acid, and calcium carbonate with swelling polymers like polysaccharides or hydroxy-propyl methylcellulose. These are formulated such that when they come into contact with an acidic stomach, CO2 is produced and becomes trapped in swelling hydro colloids, giving the dosage forms buoyancy [29].

These systems subdivided into two categories:

A. Gas generating systems

The foundation of low-density FDDS is the release of CO2 that occurs after oral administration and interacts with stomach acids. The materials are made in a way that when they come into contact with the acidic gastric juice in the stomach, they release carbon dioxide and get trapped in the gel-based hydrocolloid. It keeps the dose form buoyant while causing it to rise. Ultimately, it causes the dose form's specific gravity to decrease, which causes a float to appear on the chime. The CO2 producing components are mixed in a single layer or multi-layered form to construct a gas-production mechanism in the tablet matrix's hydrocolloid layer. The medicine was then released from the other layer over an extended period of time [31-32].

- Floating capsule
- Floating pills

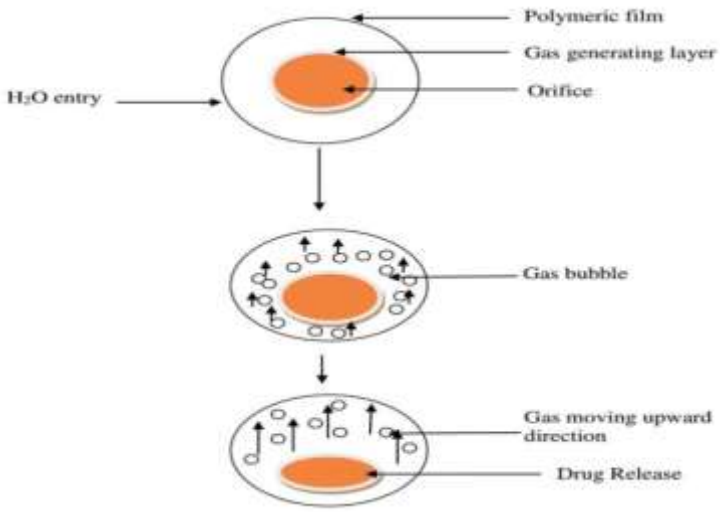

Fig.2: Floating mechanism releasing CO2

B. Volatile liquid

This osmotically regulated floating system is comprised of a device consisting of a hollow deformable unit in a compressed convertible condition. The housing would be fastened to its deformable unit, which would be internally divided into a first and second chamber and divided by an impermeable, pressure-sensitive movable unit. The drug reservoir floats because a volatile liquid, like cyclopentane or ether, evaporates in the second chamber at a temperature equivalent to body temperature, becoming a gas. An active ingredient is usually found in the first chamber. The unit is expelled from the stomach with the help of a bioerodible stopper that permitted the vapour to escape [31-32].

- Intra gastric osmotically controlled
- Gastrointestinal inflatable

2. Non-effervescent systems

This technique is predicated on the bioadhesion or swelling of polymers in the GI traction mucosal layer. An extrusion method is used to manufacture a model medicine. A needle is used to extract a mixture of acetic acid and chitosan, and the extracted material is then dried and chopped. By changing the drug polymer ratio, the essential drug release can be produced while the chitosan hydrates float in acidic environments.

A. Alginate beads

B. Hollow microspheres

C. Ring capsule

D. Films

E. Magnetic system

F. Matrix layered tablets [29-30]

3. Raft-forming systems

Antacids and prescription drugs for ailments and stomach infections are being administered via raft-forming devices, which are attracting a lot of attention. A gel-forming solution expands and produces a thick, cohesive gel that is trapped in CO2 bubbles when it comes into touch with stomach contents. This raft layer helps the medication release gradually in the stomach by forming on top of the gastric fluid. [31-32].

5. Factors affecting gastric retention [33-35]

A few variables influence the dose form's gastric retention time (GRT), which in turn influences how effective it is as a gastro retentive system:

A) Formulation factors

Dimension of tablets

The floating retention of dosage forms in the stomach is mostly caused by the size of the pills. During the digestion process, smaller tablets get through the stomach more rapidly than larger ones.

Density of tablets

Another factor that influences how long a dose form remains in the stomach is density. A buoyant dosage with a density lower than the gastric fluids would float because it is far enough from the pyloric sphincter to promote greater retention in the stomach for an extended period of time. It has been discovered that tablets with a density of 1.0 g/ml or less, which are generally believed to be less dense than stomach contents, are more effective. However, it has been shown by the floating force kinetics that the bulk density of a dose form does not directly affect its buoyancy qualities.

Shape of tablets

The dosage form's shape is also thought to be an influential factor because it has an impact on the stomach residence time. The capacity of six different kinds of forms—ring, tetrahedron, cloverleaf, thread, pellet, and disk—to stay in the stomach is examined in vivo. In this investigation, after 24 hours, the tetrahedron-shaped rings—each leg measuring 2 cm in length—passed with nearly 100% retention.

Viscosity of polymers

The drug release and floating properties of FDDS are greatly influenced by the viscosity of different polymer grades and their interactions. It has been demonstrated that low viscosity polymers (like HPMC K100 LV) enhance the floating properties of the dosage form better than high viscosity polymers (like HPMC K4M). Furthermore, a drop in the release rate was found to correlate with an increase in polymer viscosity.

B) Idiosyncratic factors

Gender

Women's stomach emptying times are longer than men's, according a study. The mean ambulatory stomach retention time in men (3.4+0.4 h) is lower than that in age- and race-matched females (4.6+1.2 h), regardless of weight, height, or body surface.

Age

Additionally, older adults have faster gastric emptying times than younger adults. There may be differences in the transit periods of the intestines and stomach between individuals. The typical duration of stomach retention is significantly longer in the elderly, particularly in those over 70.

Posture: Upright position

Postprandial emptying is delayed by the floating shape because, in an upright position, it remains above the gastric contents regardless of size. Floating dose forms show longer and more reproducible gastric retention durations than conventional dosage forms, which tend to sink towards the bottom of the distal stomach from whence they are released through the pylorus by peristaltic motions [36].

Posture: Supine position

There is no reliable defense in this attitude against erratic and premature emptying. In patients who are supine, large dosage forms—both floating and conventional—may be retained for longer. The gastric retention of floating forms does not seem to be significantly impacted by the lesser and larger curvatures of the stomach. When these units travel distally, the peristaltic motions that drive the stomach contents toward the pylorus may sweep them away, which would significantly shorten the gastric retention period in comparison to those who were standing up straight.

Concomitant intake of drugs

A wide range of simultaneously taken medications, including opiates (like codeine), prokinetic medicines (like metoclopramide and cisapride), and anticholinergics (like atropine or propantheline), may have an effect on the floating drug delivery system's performance. When using medications that reduce GI motility, the time it takes for the stomach to empty can be extended, and vice versa.

Feeding regimen

Food lengthens the gastric residence time, which speeds up the pace at which the drug dissolves in the dose form at the absorption site of choice. Between four and ten hours have been reported to be spent with stomach retention after a diet high in fats and proteins [37-39].

6. Mechanism of floating system [40]

Several approaches are available to extend the dosage form's retention time in the stomach. These include the introduction of floating dosage forms (gas-generating and swelling or expanding systems), mucoadhesive systems, high-density systems, modified-shape systems, gastric-emptying delaying devices, and co-administration of drugs that delay the stomach's emptying. The most used dose form is the floating form. Due to its lower density compared to gastric fluid, this method allows for the retention of buoyant in the stomach without affecting the rate of gastric emptying for an extended duration. The floating drug delivery system is an excellent method; when the formulation enters the stomach, the dosage form interacts with the gastric fluid and floats on the surface of it. Following dosage form floating, the drug is progressively removed from the system at the chosen frequency. After the medication is released, the stomach's residual system is emptied. Increased stomach retention time is a better way to manage changes in plasma medication concentration resulting from these findings. According to the floating system's retention principle, the right buoyancy must be achieved by the stomach content. Maintain the dosage form on the meal's surface in the stomach; a little range of floating force (F) is also necessary. In order to compute the floating force kinetics, a novel piece of equipment for determining the resultant weight has been reported in the literature. If F is higher on the positive side, then the object floats more easily. With the goal of avoiding the restrictions caused by unpredictable fluctuations in intragastric buoyancy ability, this equipment aids in the optimization of FDDS with respect to stability and endurance of floating forces created.

F = F buoyancy

F gravity = (Df Ds) g v

Where, F= total vertical force,

DF = fluid density,

Ds = object density,

g = acceleration due to gravity,

and also v = volume

7. Methods of Developing Floating Drug Delivery System [41]

1) **Direct compression technique**

It entails compressing tablets straight from their powdered form without changing the material's physical composition. The most widely used carriers include tricalcium phosphate, dicalcium trihydrate phosphate, etc.

2) Effervescent Technique

Citric acid, an organic acid, and bicarbonate salts will react effervescently to produce inert gas (CO2), which will fill the floating chamber of the medication delivery mechanism.

3) Wet granulation technique

Involves rubbing, grinding, or drying powder moist. Rather than compacting the powders, wet granulation forms the granules by gluing them together with an adhesive.

4) Ionotropic Gelation Technique

In order to create instantaneous microparticles, the anionic polysaccharide sodium alginate, the main polymer derived from nature, was eluted using oppositely charged calcium ions, or counter-ions. This process is referred to as a physicochemical way of hardening microdroplets through the chelation of polyvalent ions with polyelectrolyte. This kind of chelation results in the formation of a shell around the polyelectrolyte molecules in a polymeric system that is widely used. It works by gelating aqueous sodium alginate, gellan, or carrageenan and then adding divalent cations like calcium, barium, or potassium chloride, which causes the polymers to cross-link and instantly forms discrete, solid microparticles. This technique produces robust, spherically-shaped, narrow, high-yield microparticles that are then used to carry numerous NSAID medications, reducing dose-related adverse effects and extending the drug's release potential.

5) Solvent evaporation technique

The amount of liquid dispersal solvent cannot be completely eliminated by continuous phase capability. To receive the hardened microspheres, the solvent evaporation from the dispersal surface occurs. This method allows the dispersion or dissolution of the core material by dissolving the polymer in a volatile organic water-impermeable solvent, such as chloroform or dichloromethane. In order to create tiny polymer droplets surrounding encapsulated material, the resultant solution is then added drop-wise to a stirring aqueous solution with an inappropriate stabilizer, like polyvinyl alcohol. Solvent extraction or evaporation can be used to harden the resulting microsphere.

6) Spray Drying Technique

Involves distributing the core layer into the liquid coating content and spraying the core coating mixture into the surrounding air to solidify the coating by a rapid evaporation process that solubilizes the coating material. The drying of the drug and polymer mist in air is the first step in the spray dying or spray congealing process. Spray congealing involves cooling the solution, while spray drying involves removing the solvent. First, the polymer is dissolved in a suitable organic volatile solvent, like acetone or dichloromethane. Next, under high-speed homogenization, the solid medication is distributed throughout the polymer solution. The process is then followed by atomization in a hot air stream, which creates tiny droplets in a fine mist from which the solvent solvent instantly evaporates to form floating microspheres.

7) Melt Solidification Technique

This process involves cooling the molten mass to solidify after emulsifying it in the aqueous phase. For this method, lipids, waxes, polyethylene glycol, etc. are used as carriers.

8) Melt Granulation Technique

This process uses a meltable binder to agglomerate the pharmaceutical powder; it doesn't use water or organic solvents for granulation.

9) Emulsion solvent diffusion method [42-43]

System of Conflation Detergent Prolixity Concave microspheres known as micro-balloons that contain medication within their polymer shell were created with the use of a novel conflation detergent prolixity technique. Pouring methylene chloride and a polymer and medication into an agitated waterless polymer result (vinyl alcohol) yields ethanol. The methylene chloride that is entangled evaporates, causing the microparticles to create interior depressions.

Excipients Incorporated in Different Floating Dosage Form [41]

- Effervescent Agents: E.g. citric acid, tartaric acid, sodium bicarbonate, Di-SGC (Disodium glycine carbonate), CG (Citroglycine).
- Rate of release Retardants: A few materials are employed to slow down the rate of release, including magnesium stearate, talc, and dicalcium phosphate.
- Inert Fatty Materials: E.g. Long chain fatty alcohols, Beeswax, Fatty acids, Gelucires 39/01 and 43/01
- Release rate Accelerants: E.g. Mannitol, lactose, etc.
- Hydrocolloids: E.g.β-cyclodextrin, carbopol, alginates, gelatin, pectin, HPMC, and Acacia, among others.
- Buoyancy increasing Agents: E.g. Ethyl Cellulose and Polypropylene Foam Powder (Accurel MP 1000)

8. Evaluation parameters of floating drug delivery system for single module dosage form [44-49]

1) Hardness:

It shows how well a tablet can handle mechanical shocks without breaking. The Monsanto hardness tester is used to measure the tablets' hardness. The unit of measurement is kg/cm^2. The tablets' hardness was assessed after three were chosen at random. When the tablet is used properly, the minimum hardness range is less than 5 or 5.5 kg/cm^2.

2) Friability test:

Using the Roche Friabilator, assess the tablets' friability in this parameter. Take ten tablets at first and record their average weight in this parameter. Take these ten tablets now and insert them into the Friabilator. The Friabilator can be run up to 100 revolutions or turned at 25 rpm for four minutes. Take those tablets out of the Friabilator and weigh them again when the 100 revolutions are complete. After that, compare the tablets from the before and after the revolution. Friability was expressed in percentage ratio (%). The % friability is then computed by % Friability = 100 * (W0 W) / W0

Where, W0 = Initial weight

W = Final weight % Friability of tablets less than 1% was considered acceptable.

3) Weight variation test:

To check for weight variance, ten tablets are randomly chosen from each batch and weighed separately. The U.S. Pharmacopoeia permits a slight variation in a tablet's weight. As shown in the table, the following % variation in weight dissimilarity is permitted.

4) Density of the tablet:

For floating tablets, one important factor is the tablet's density. Only when the tablet's density is lower than that of stomach fluid will it float (1.004). The density is determined utilizing following relationship.

V = r2 h d

Where, v = volume of tablet (cc)

r = radius of tablet (cm)

h = crown thickness of tablet (g/cc)

d = mass/volume

5) Floating test:

Estimates were made of the intervals between the dosage structure's presentation and buoyancy on the replicated stomach fluid and the duration of the dose structure's presence. Total Floating Time (TFT) is the total amount of time that the dosage structure remains on the medium's surface once it raises, also known as Floating Lag Time (FLT) or Buoyancy Lag Time (BLT).

6) Swelling study:

A dosage structure's swelling behavior is assessed by taking into account its weight growth or water absorption. Dimensional changes, such as the expansion of the tablet's diameter across and thickness over time, can also be measured. Water take-up is estimated regarding percent weight gain, as given by the equation:

WU = (Wt W0) x 100

Where, Wt = Weight of dosage form at time t

W0 = Initial weight of dosage form

7) In-vitro drug release studies:

In vitro drug release studies and buoyancy checks are usually conducted in simulated stomach and intestinal fluids maintained at 37^{0}C. Practically, the USP dissolution apparatus with 900 ml of 0.1 HCl as a testing medium maintained at 37^{0}C is used to assess the in vitro drug release time. Floating (or flotation) time is the amount of time required to allow the hydrodynamic balanced system (HBS) dosage structure to float.

8) Determination of the drug content:

The process of determining the drug content is used to verify the amount of drug substance present in the dose form. It shouldn't go over the amount of points obtained through standard monographs. Drug assay and the UV technique are used to assess the drug's substance.

For multiple module dosage form

9) Percentage entrapment efficiency:

The phase distribution of the drug in the produced formulations can be accurately measured using the percentage entrapment efficacy. Three methods, including pressure ultra-filtration, ultra centrifugation, and the microdialysis method, are used to calculate entrapment efficiency.

10) Scanning Electron Microscopy (SEM):

Under a SEM, the surface morphology for examining the units' homogeneous coating was seen.

11) In-vitro dissolution:

USP equipment 2 is used to measure the drug release incidence from various dosage forms (paddle method). 900 ml of 0.1 N HCl are used in the dissolution test, which is run at 37^0C and 50 rpm. Every hour for ten hours, a sample of the solution (5 milliliters) is taken out of the dissolving apparatus, and the samples are replaced with brand-new dissolution medium. The samples are diluted with 0.1 N HCl to an appropriate concentration after being filtered using a 0.45-mm membrane filter. These solutions' absorbance is measured at 274 nm with a UV/Vis double-beam spectrophotometer.

12) Floating properties:

As part of dissolution studies, the duration of the formulation's continuous floating on the medium's surface (the floating duration) and the time elapsed between the addition of the FDDS to the medium and its buoyancy to the upper third of the dissolution vessel (the floating lag time) were simultaneously measured.

Angle of repose:

The grains were allowed to flow through the channel fixed to a stage at definite height (h). The angle of repose was also calculated by measuring the height a d compass of the mound ograins formed. tan=h/r

Ø=tan-1(hr)

Ø=angle of repose

h=height of the mound

r = compass of the mound

13) Stability study:

The stability study of the multiple dosage form is submitted, in accordance with ICH requirements, to a temperature of 400C/20C and a relative humidity of 75%5% for three months in an appropriate packing mode in a programmable environmental test chamber. The formulations are analyzed for drug content, floating behavior, and in vitro drug release every month at the end of the month.

14) In vivo method

1) X-Ray method

These days, X-ray is a highly used evaluation criterion for floating dosage forms. Finding the dosage form in the GIT is helpful because it allows one to forecast and correlate the time it takes for the stomach to empty and the dosage form to transit through the GIT. In this case, radioopaque substance is added to a solid dosage form so that X-rays can see it.

2) Gamma-Scintigraphy

Gamma-emitting radioisotopes combined with cr-DFs are now the gold standard for assessing the gastroretentive formulation in volunteers in good health. When DF is being prepared, a tiny quantity of a stable isotope, such as Sm, is compounded into it. The primary disadvantages of gamma-scintigraphy include the radiation exposure that comes with it for the patient, the restricted topographic data it provides, the method's intrinsic low resolution, and the difficult and costly process of preparing radiopharmaceuticals.

3) Gastroscopy

Peroral endoscopy, when combined with fibereoptic and video devices, is part of it. It is suggested that the effect of a longer stay in the stomach mileu on the FDDS may be visually inspected using a gastroscopy. As an alternative, FDDS may be extracted from the stomach for a more thorough analysis.

4) Ultrasonography

Certain abdominal organs can be seen thanks to ultrasonic waves that reflect significantly varying acoustic impedances across interfaces. The majority of DFs lack noticeable auditory discrepancies throughout their contact with the physiological environment. For this reason, ultrasonography is not frequently employed in the assessment of FDDS. The hydrogels' intragastric position, solvent penetration into the gel, and the interactions between the gastric wall and FDDS during peristalsis were all evaluated as part of the characterisation process.

Advantages of FDDS [50-53]

1. This method can be used to administer drugs with a short half-life that nonetheless have a major therapeutic effect.

2. Higher bioavailability for drugs that the upper gastrointestinal tract can metabolize.

3. They can also be utilized to address the problems of stomach retention and emptying time, which is an advantage over the traditional method.

4. The duration of a long century required for the release of an active module from a single dosage.

5. Adverse effects are minimized or eliminated when the active ingredient is delivered directly to the site of action.

6. FDDS is advantageous for medications that cause stomach vexation in the first place. such as Antacids.

7. FDDS is beneficial in treating gastrointestinal disorders such gastroesophageal reflux illness.

8. Simplicity in case compliance and administration.

9. Lowers the dosage frequency.

10. It improves the medications' bioavailability.

11. Higher bioavailability for certain substances that the upper gastrointestinal tract may metabolize16.

12) There is no gastrointestinal discomfort due to the multi-particulate system's sustained release effect, floatability, and invariant release of the medication1.

13) It helps relieve GERD (gastric influx problem).

14) Advantageous when experiencing diarrhea.

Disadvantages of FDDS [54]

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. Medications that irritate or harm the mucosa of the stomach shouldn't be made into floating drug delivery systems.

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.

5. A floating method is not an option for medications that have a problem (difficulty, challenge) with solubility (or)consistency in stomach fluids.

6. Use a full glass of water (200–250 ml) to provide the dosage form.

7. Drugs that are absorbed throughout the GI tract and undergo first-pass metabolism, such as nifedipine and propranolol, are not suitable options.

HOW FDDS WORKS?

One of the main methods for attaining sufficient medication bioavailability and stomach retention is FDDS. This system only accepts medications with a window for absorption in the upper small intestine or stomach. Since it is less dense than gastric fluids, the medication is administered gradually and at the proper pace while floating in the stomach and not slowing down the rate at which the stomach empties. After the medicine is discharged, the stomach's residual system is cleared out. Consequently, there is a longer period of stomach retention and better management of the volatility in plasma drug concentration [55-58].

APPLICATION OF FDDS [59-61]

Because of the upper gastrointestinal tract's short absorption window, floating drug delivery offers many possibilities for medications with low bioavailability. It increases the bioavailability by retaining the dose form at the site of absorption. Here is a summary of them.

a) Sustained Drug Delivery:

Because HBS systems can stay in the stomach for several decades, they can release the medication over an extended period of time—up to a century. These approaches thereby solve the problem of the short stomach residence time associated with an oral CR formulation. These systems can float because of their bulk density of less than 1. on the contents of the stomach. These systems are relatively bigger and cannot pass via the pyloric aperture. Nicardipine hydrochloride sustained release floating capsules were recently created and tested in vivo. The formulation was tested on rabbits and compared with MICARD capsules that are sold commercially. The sustained release floating capsules' plasma concentration time curves revealed a longer administration period (16 hours) than those of the traditional MICARD capsules (8 hours) [62].

Comparative research was also conducted between the Madopar HBS and Madopar standard formulations, demonstrating that while the medication was released in vitro for up to 8 hours in the former instance, it was essentially completed in less than 30 minutes in the latter [63].

b) Site-Specific Drug Delivery:

These systems are especially useful for medications like furosemide and riboflavin, which are specifically absorbed from the stomach or the proximal portion of the small intestine. The stomach absorbs furosemide the most, followed by the duodenum. According to reports, a monolithic floating dosage form with an extended period of stomach residence was developed, leading to an increase in bioavailability. The floating tablets' AUC was around 1.8

times higher than that of traditional furosemide tablets [64].For the local delivery of misoprostol, a synthetic prostaglandin E1 analog used to prevent gastrointestinal ulcers brought on by NSAID use, a bilayer-floating capsule was created. Drug waste might be minimized and targeted therapeutic levels could be reached by slowing the transport of misoprostol to the stomach [65].

c) Absorption Enhancement:

Pharmaceuticals that exhibit low bioavailability due to site-specific absorption from the upper gastrointestinal tract may be developed as floating drug delivery systems to optimize absorption. For instance. When floating dosage forms are compared to commercially available LASIX tablets (33.4%) and enteric coated LASIX-long product, a significant improvement in bioavailability (42.9%) can be achieved [64].

d) Enhanced Bioavailability:

When riboflavin CR-GRDF is administered instead of non-GRDF CR polymeric formulations, the bioavailability is considerably higher. The amount of drug absorption is influenced by a number of concurrent processes related to drug absorption and transit in the gastrointestinal system [66].

e) Minimized adverse activity at the colon:

The amount of medication that enters the colon is reduced when the drug is retained in the HBS systems of the stomach. As a result, the drug's unwanted effects on the colon may be avoided. The GRDF formulation for beta lactam antibiotics, which are absorbed exclusively from the small intestine and whose presence in the colon leads to the development of microorganism resistance, is justified by this pharmacodynamic factor. Decreased variations in medication concentration: In contrast to instant release dosage forms, continuous drug input after CRGRDF treatment results in blood drug concentrations within a tighter range. As a result, variations in the effects of the drug are reduced, and the concentration-dependent negative effects linked to peak concentrations can be avoided. This particular feature is especially beneficial for medications with a limited therapeutic index [66-68].

Future Potential

Numerous recent papers have made it evident that the gastro-retentive floating medication delivery method has a lot of potential. The process of drug absorption in the gastrointestinal tract varies greatly, and the duration of stomach retention of the dose form prolongs the absorption period. FDDS shows promise as a possible gastric retention method. Many of the newly approved clinical medications have limited absorption windows and could benefit from compounding into an FDDS. Oral medication would be a far better form of treatment than parenteral drug administration. It's possible that FDDS will make it more likely. Effective delivery of drugs can maximize absorption and optimize their absolute bioavailability, even if they have poor bioavailability due to limited absorption to the upper gastrointestinal tract. The use of buoyant delivery systems as a helpful treatment strategy for duodenal and stomach tumors is also being investigated. There are several approaches to use the floating notion in the development of anti-reflux medications. Creating a controlled release technique for medications with the potential to treat Parkinson's disease is another crucial area of research.

9. CONCLUSION

Because their absorption is limited to the upper gastrointestinal tract and they may be administered effectively, GRDDS (FDDS) offers a number of potential advantages for drugs with low bioavailability. This maximizes their absorption and optimizes their bioavailability. Nowadays, there are several methods for extending the stomach retention period. These include of extrusion and swelling systems, bio adhesive systems, ion exchange systems, high density systems, floating drug delivery systems, and various delayed stomach emptying excipients. Floating pills offer a steady dose form with a sustained release of medication. Many efforts are being made these days to create diverse gastroretentive medication delivery systems. The FDDS is becoming increasingly promising for a promising future.

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