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Floating Tablet for Drug Delivery System

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Abstract: *The purpose of developing novel delivery systems was to address some issues with the physicochemical properties of pharmaceutical compounds as well as formulation creation, as well as some flaws in conventional dosage forms. The controlled release floating system is a way of medication administration that shows promise. Device for dispensing a potential drug with a narrowing window of absorption. Medicines are insoluble or just very slightly soluble, as well as those that release locally in the stomach and have a low rate of absorption in the colon. Under the floating drug delivery system is a continuous supply gastroretentive medicine administration system. minimally soluble medications are delivered to the absorption site in a controlled manner. These points discuss the floating drug delivery system's advantages and disadvantages in comparison to more conventional drug administration technique. The floating medication delivery system is covered in great length in the review, along with its benefits and drawbacks compared to more traditional drug administration methods.These considerations must be examined when developing dosage forms. There are numerous ways that this dosage type was developed. The review's primary objectives were the formulation and evaluation of the effervescent floating medication delivery system. The goal of this comprehensive study is to bring together the ongoing research on this delivery method, which highlights the different effects that can affect and lessen stomach retention and offers crucial information on its formulation.*

Keywords: Floating tablet

I. INTRODUCTION

Oral administration is the most Famous and convenient technique of many medications.
Because it contains several important qualities, the oral route is frequently considered to be the most effective medication delivery mechanism. Its some key characteristics:

a) To prolong the action, it should only be given once.
b) Only the necessary amount of the active drug should be administered.

These elements together to form a sustained or regulated delivery system.
One example of a medication delivery system that distributes the medicine gradually and/or continuously is sustained deliver. 1, 2, and the main objective These systems were developed to improve a product's safety and extend its shelf life. These techniques have a number of disadvantages, including dosage dumping, a longer time to reach therapeutic blood levels, a greater first pass impact, and a higher bioavailability. These systems often cost more than conventional systems do.[3]
Due to the fact that these goods are made for the general public as opposed to an individual, different people may have higher or lower steady state drug levels as a result. If a medication's therapeutic window is broad enough, it might not b e a problem.4Despite the flaw in the system, there is still a lot of potential for research in this area.Despite the shortcom ings of the systems, research in this area is still underway because there is still much space for advancement. medicatio n delivery system for oral use over prolonged release formulationControlled release drug delivery systems (OCRDDS) with protracted stomach retention have considerable advantages over sustained release formulations.
A prescription drug delivery system operating under the direction of a releases the taking medicine over an extended pe riod of time in order to continually distribute the medication to the upper side of the gastrointestinal tract, where it will be absorbed.
For some formulations of oral continuous medication delivery, the stomach emptying time represents a limitation.

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The ability to limit the dose form in the desired region of the gastrointestinal system is one of these criticalities.
As a remedy for this physiological problem, several pharmaceutical administration techniques with prolonged stomach retention durations have been investigated.
In an effort to decrease the frequency of dosing and limit changes in plasma drug concentration at steady state, The dev elopment of a controlled medicine delivery system that can sustain therapeutically effective plasma medication concentr ation levels over long periods of time is ongoing.[5]
For dosing method that stay longer in the stomach than standard dosing method, the capacity for extend and control vacating time Dosing forms' gastric emptying is a highly varied procedure.
Gastric emptying of dosing forms is a highly variable process. One of these challenges is having the dosing method contained in the desired region of the digestive system Several medication administration methods with extended stomach retention times have been researched a solution to this physiological issue.
As a remedy for this physiological problem, several pharmaceutical administration techniques with prolonged stomach retention durations have been investigated. Delivered drug under control system that supplying level of plasma medication concentrations that are therapeutically effective for protracted periods of time are being developed in an effort to decrease the frequency of dosing and minimise variation in plasma drug concentration at steady state. Due to their propensity to leave in the stomach part for some hours, drugs stomach residence durations can be significantly prolonged by , gastro retentive mechanisms. Long-term stomach retention boosts medication bioavailability and decrease dosage concentration, and makes in high pH, the medicines that are less soluble settings more soluble.
Along with several benefits, gastric retention gives patients additional treatment opportunities.
Modulating the stomach ability to retain solid dose form accomplished via variety of techniques, including expansion, flotation, sedimentation and shape is altered type System and the use of pharmaceuticals that postpone gastric emptying. Depend on this techniques, floating drug delivery system seem to be the most promising way to regulate medication release.

1.1 Definition

Floating systems, often referred to as dynamically regulated system, are buoyant enough to float above and stay above the contents of the stomach while also remaining buoyant when the stomach empties. The period of stomach retention is therefore increased, and fluctuations drug concentration in plasma are better prevented. There have been many granules, powder-, capsule, tablet, laminated-film-, and follow-microsphere-based buoyant systems developed.6

1.2 Need for Controlled Release Gastroretentive Drug Delivery (CRGRDF'S)

Gastroretentive Dosage Forms

(GRDF), which have prolonged GRT, may provide significant new treatment options, such as 6 With insoluble and spar ingly soluble medications, this application is very effective.It is generally known that the amount of time available for d rug dissolution decreases as a medication's solubility drops, and as a result, the transit time has a substantial impact on d rug assimilation. To solve this issue, erodible, Gastroretentive dose form which give regulated release of slightly soluble medications at the place of absorption.
Through local medication release, CRDF'S significantly enhance stomach pharmacotherapy resulting increased drug concentration at the stomach mucosa as a result. For example, penicillin from the stomach's submucosal tissue Helicobacter pylori enables the delievery of nonsystemic controlled release antacid formulations in order to gastritis, oesophagitis, and duodenal and stomach ulcer (Calcium carbonate). GRDF's can be used to transport medications with so-called absorption windows.
Penicillin , aminoglycosides cephalosporin Sulphonamides and other antibacterial , antiviral, and antifungal chemicals are only absorbed from a relatively small number of GI mucosal sites.For controlled release gastroretentive dose forms, molecules with Good absorption but low colonic absorption but excellent capabilities the higher of the GIT are typically acceptable choices (CRGR DF). Amoxicillin trihydrat is one example of a medicine that changes the normal intestinal flora.

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II. BIOLOGICAL ASPECTS OF CRGRDF'S

2.1 Stomach Physiology

A substantial portion of the digestive system is the stomach located between the small intestine and the oesophagus architecturally speaking, the wall of stomach's is same as the wall of other parts of the digestive tract, but it has a circular layer of smooth muscle with an additional obliquely, layer inside., that aids the stomach in performing intricate grinding movements.

Rugae are the unique fold that are formed by the elongation of mucosa and submucosa when the stomach is empty because it contracts.

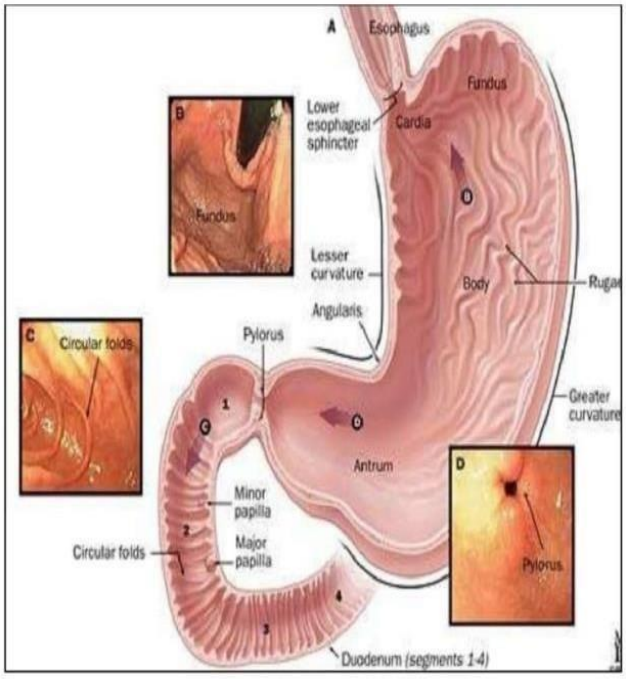

Figure: Physiology of the stomach

The following are the main categories of gastric epithelial cells, which line the surface of the stomach and migrate into t he pits and glands of the stomach.

- Mucous cell: By creating astringent , this shields the epithelium from acid &shear stress.
- Parietal cell :Transmit the acid hydrochloric acid.
- Chief cells : A proteolytic enzyme called pepsin is released.
- G cells : gastrin hormone release

There are two main purpose for the stomach smooth muscle to contract:

- Chyme is produced when food is crushed, ground, combined, and liquefied during digestion.
- Chyme is pushed into the small intestine through the pyloric canal during stomach emptying.

2.2 Gastric Motility

A complex network of neural and hormonal impulses regulates gastric motility. The sympathetic, vagus nerve-dominated parasympathetic, and enteric nervous systems are the origins of neurological control.

It has been demonstrated that many hormones have an impact on gastric motility. For instance, gastrin and chole cystokinin both calm enhance the concentration of the distal stomach and the proximal stomach .In conclusion, it has been proposed that the patterns of stomach motility are produced by the integration of a variety of inhibitory and stimulatory impulses by smooth muscle cells.

Solid must first be sized down to less than 1 to 2mm in diameter. Order to pass the pyloric gatekeeper, order to pass the pyloric gatekeeper, although fluids can easily flow through the pylorus in spurts. For the dose form to dissolve in vivo, the stomach volume is required. The stomach may hold 25–50 ml when at rest.

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In achlorhydric and normal individuals, the amount of stomach output varies greatly. The impact of stomach pH on medication delivery method-mediated drug absorption is also noteworthy.
While fasting, the stomach's pH is between 2.0 and 6.0 under fed settings. 8
Gastric empty rate
The stomach empties both after eating and after fasting.
The patterns of mobility in the 2 states are different, though.When a person is fasting,
Every two to three hours, a sequence of electrical events known as the interdigestive cycle pass through the stomach an d intestine. 9
Wilson and Washington claim that this is sometimes known as the The migrating myloelectric cycle (MMC) is further b roken down into the steps listed below.10

1. Phase l During this stage, sporadic contractions can continue for 40 to 60 minutes.
2. Sporadic contractions and action potentials characterise the 40 to 60 minute Phase II (Preburst Phase). The fre quency and intensity gradually rise as the phase goes on.
3. .Between 4 and 6 minutes are spent in the burst phase. It has strong, frequent, repeated contractions that are bri f. The entire undigested material is pushed into the by this wave the stomach and the small intestine are released Additionally called the "housekeeping wave."

2.3 Factors Affecting Gastric Retention

How successful dosage forms are as gastroretentive systems depends on a variety of factors that control the dosage types' gastric retention times (GRT).

- **Density**- GRT is a dose-form buoyancy function that depends on density.12
- **Size** – GRT has been found to be higher in dosage form units having a diameter of more than 9.5 mm.
- **Shape of dosage form -** Tetrahedron with a ring Shaped devices with flexural moduli of 48 and 22.5 kilogrammes per square inch are said to offer better GRT (KSI). Retention varied from 90% to 100% after 24 hours when compared to all of her forms.13
- **Single or multiple unit formulation –** Multiple unit formulations feature a more predictable release profile when compared to single unit dosage forms, allow coadministration of units with different release profiles or containing incompatible medications, and provide a higher margin of safety against dosage form failure.
- **Fed or Unfed State:** Every 1.5 to 2 hours, the migrating myoelectric complex (MMC), which is a phenomenon, a type of intense motor activity that is unique to the gastrointestinal tract (GI) motility of people who are fasting.If the formulation is delivered at the same time as the MMC, which clears out undigested food from the stomach, the unit's GRT should be relatively brief. However, in the fed situation, MMC is slowand GRT takes a lot longer.
- **Nature of Meal** - The sort of food eaten can change the stomach's motility pattern to a fed state, reducing gastric emptying and lengthening the duration that medications stay in the body. 14
- **Caloric Content** - In terms of calories, a meal with a high protein and fat content can prolong GRT by four to ten hours.
- **Feeding Frequency –** Due to the low frequency of MMC, if multiple meals are supplied consecutively rather than one, the GRT can rise by more than 400 minutes.
- **Gender –** Regardless of weight, height, or body shape, men's mean ambulatory GRT (0.6 hours) is smaller than that of their (3.4 age and race-matched) female counterparts (1.2 hours).
- **Age -** Seniors, especially those over 70, live substantially longer lives.
- **Posture -** Both supine and upright ambulatory patient situations can be evaluated with GRT.
- **Biological Variables -** include diabetes and Crohn's diseases.

2.4 Approaches to Design Floating Drug Delivery System

The idea of FDDS was initially introduced to the literature by Davis (1968), who described a method to avoid the problem that some people have with gagging or choking after taking prescription medications.

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By dispersing pills with a density of less than 1.0g/cm3, the author claims that this problem might be handled and that they would float on the water's surface.
Other techniques have since been employed to create the ultimate floating pharmaceutical delivery system.

2.5 Approaches to Design Single unit Dosage Form
The design of floating dosage form for Single and Multiple System has been done using the following Strategies :

Single Unit Dosage Form

1. The floating lag time: This measurement, which is given in seconds or minutes, determine how long take tablet to surface on a dissolution medium's surface.
2. Using a USP II equipment (paddle), agitate simulated gastric fluid at a speed of 50 or 100 rpm at 37 0.2 °C to measure in vitro drug release and floating time (pH 1.2 without pepsin).
   The samples are divided into aliquots, and the presence of medicines is subsequently examined. The duration of floating is clearly indicated by the number of hours the tablets float on the dissolution medium's surface.
3. Xray or gamma scintigraphic monitoring of the dose form transition in the GIT is used to asses Gastro retention in vivo.

Additionally, the tablets are assessed for characteristics including weight variation and hardness. Low density methods, which enclose drugs in globular shells that seem to have a lower density than stomach contents, enable for the controlled release of drugs. Either HPMC or ethyl cellulose are suitable options for the polymer. Depending on the type of release sought.

2.6 Hydro Dynamically Balanced System
By increasing the amount of time dose forms stay in the stomach and intestinal tract, these methods are designed to imp rove absorption.With the help of these HBS systems, drugs can be administered with better acid solubility and to a spec ific area of the upper small intestine for absorption.

2.7 Approaches to Gastric Retention
To increase the retention of an oral dose form in the stomach, various strategies have been tested.
These systems consist of:

1. Floating System
2. Bioadhesive System
3. Swelling and Expanding System
4. High Density System
5. Modified System

A. Floating Drug Delivery System
A hydrodynamically balanced system is another name for the floating medicine delivery system.
Because they Floating drug delivery systems (FDDS) float in the stomach for a long time without slowing down how q uickly the stomach empties since they have a lower bulk density than gastric fluids.
While floating on the stomach's contents, the drug is gradually and at the desired rate removed from the body.
When the drug is expelled from the stomach, the stomach's residual system is emptied.
GRT is boosted as a result, and the fluctuations in plasma medication concentration are better managedThere are two ty pes of this distribution mechanism :

- Non-effervescent System
- Effervescent System

Non-effervescent System
Either a polymer's bioadhesion to the mucosa of the GI tract or the mechanism of a polymer's swelling serves as the fou ndation for the Noneffervescent FDDS.The majority of excipients used in noneffervescent FDDS are of the gelforming

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or highly swellable cellulose type, hydrophilic gums, polysaccharides, matrix-forming substances like polycarbonate, polyacrylate, polymethacrylate, & polystyrene, as well as Bioadhesive polymers like chitosan and carbopol.
It has Various type as fallow :

Colloidal Gel Barrier System / Single Layer Floating Tablets

The first system with a balanced hydrodynamics, developed by Sheath and Tossounian in 1975, contained drugs containing hydrocolloids, which form gels.
one or more cellulose type E hydrocolloids that are extremely swellable and form gels.

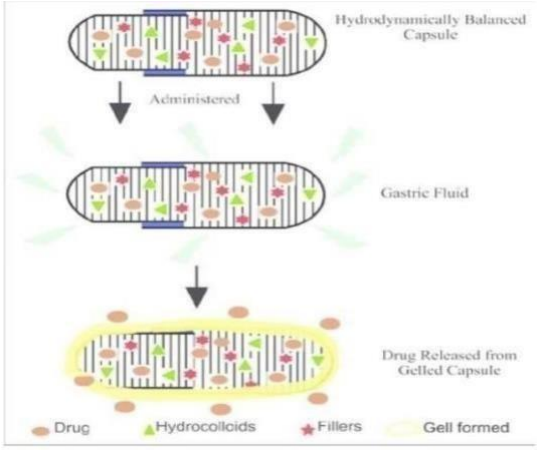

Figure 2: Hydrodynamically Balanced System within gel structure

Bi-layer floating tablets:

The bilayer tablet can maintain buoyancy in the stomach because the sustained release layer absorbs gastric fluid and pr oduces an impenetrable colloidal gel barrier on its surface while maintaining a bulk density of less than unity.
The initial dose is flushed from the body by the quick release layer.

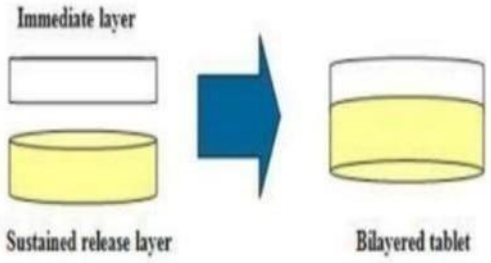

Fig 3:Bilayer Tablet[17]

Micro Porous Compartment System

This device's mechanism entails squeezing a drug reservoir into a tiny, porous chamber having perforations along the upper and lower walls. lower The drug reservoir compartment's outer walls are totally sealed, thus there is no possibility of the undissolved medication making touch with the gastric mucosal surface.

Multi Particulate System

The method of medicine delivery that uses alginate and floating beads with numerous particles.Most multiparticulate dr ug delivery methods are oral dosage forms made up of a number of tiny discrete units, each of which has a variety of de sired properties.
These techniques allow for the division of the drug dosage into a number of subunits, each of which is composed of tho usands of spherical particles with a diameter ranging from 0.05 to 2.00 mm.

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Many floating unit forms have been produced using freeze dried calcium alginate. Calcium alginate precipitates and creates a breathable material that is able to resist a floating force is a more than a 12 hours of a forces.
when a calcium chloride aqueous solution is combined with sodium alginate solution.
These floating beads had a longer residence period of more than 5.5 hours compared to solid beads, which only provide d a short residence time of an hour.The active component is split up into numerous tiny, independent subunits and is inc luded in pharmaceutical formulations referred to as multiparticulate dosage forms. These components are combined int o a sachet to produce the necessary overall dose.
tablets with numerous units and their floating behaviour.

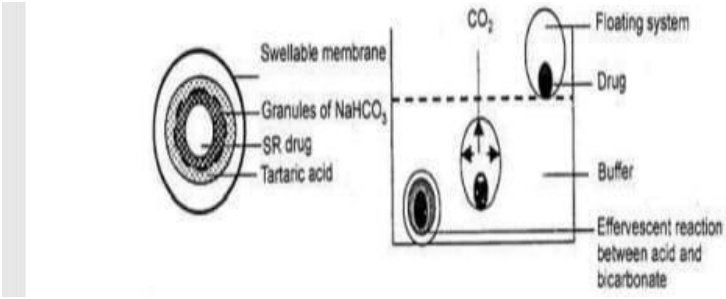

Figure: Multi particulate

Micro balloons / Hollow Microspheres

These floating beads had a longer residence period of more than 5.5 hours compared to solid beads, which only provided a shorter time of an hour. The active component is split up into numerous tiny, independent subunits and is included in pharmaceutical formulations referred to as multi particulate dosage forms. These components are combined into a sachet to produce the necessary overall dose. tablets with numerous units and their floating behaviour.

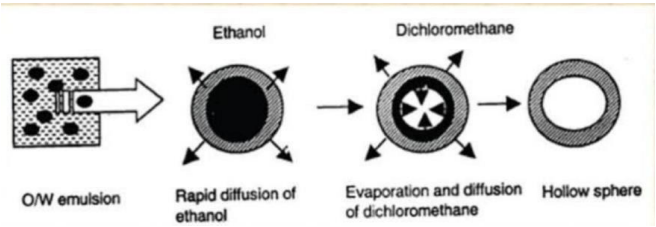

Figure: Micro balloons

Effervescent Systems

Gas Generating System

A floating chamber can be used to make a pharmaceutical delivery system float in the stomach. This chamber can be filled with air, vacuum, or inert gas. Containment systems for volatile liquids these have a liquids. filled inflatable chamber that expands when heated to body temperature, such as ether or cyclopentane. These systems are osmotically controlled floating devices and consist of a hollow deformable unit.
The device contains two chambers: one holds the medication, while the other is filled with a volatile liquid II.systems th at produce gasThese buoyant delivery techniques release CO2 through an effervescent reaction between citric/tartaric a cid and carbonate/bicarbonate salts, which is subsequently retained in the Jellification of the hydrocolloid layer in the sy stem decreased its specific gravity, causing it to float over the chime. Additionally, large-
scale CO2 emitting floating pills have been produced.
A sustained release (SR) pill with two layers around it serves as the system's foundation.
Another effervescent device with a collapsible spring and the ability to control medicine release from a polymer matrix has also been developed.

Volatile Liquid Containing System

These Systems have a hollow deformable unit and are magically floating.

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The apparatus is divided into two chambers:

- The first one keeps the medicine.
- The volatile liquid is second.

Advantages of FDDS:

1. Better drug absorption is the result of higher GRT and longer dose form stays at the location of absorption.
2. Prevented administration of medication.
3. Administration of medication for regional tommy effect.
4. Delay and controlled medication release to lessen drug-induced mucosal irritation.
5. Care for gastrointestinal conditions like gastroesophageal reflux disease.
6. Standard and conventional manufacturing tools.
7. Greater patient compliance and simpler administration's.
8. Drug delivery at specified site.

Disadvantages of FDDS:

1. Number of variables such as stomach motility ph, and the presence of food might affect gastric rretention. It is impossible to predict buoyancy since these variables are never consistent.
2. Floating drug delivery systems should not be created for medications that irritate or injure the stomach mucos.
3. There is a lot of variation in how long it takes the stomach to totally empty or not at all.
4. The supine position's random and highly dependent emptying of floating forms.
5. Some folks experience discomfort.

Formulation Aspect of FDDS

The ways that drugs are delivered and where they are administered are intrinsically maintained
When developing novel controlled release dosage forms, all of these concerns should be taken into consideration.
A technique for researching the physicochemical characteristics of pharmaceuticals is called reformulation research.The se characteristics include, among others, the pka, ph, solubility, and incompatibility.
Orally administered medications are susceptible to enzymatic and acid-base hydrolysis deterioration.
Chemicals like propantheline are unstable in the small intestine.
Use of a controlled release delivery method is directly influenced by the physiology of the digestive system. The effects of a medical condition and any accompanying medications have an impact on that designs.

1. **Absorption Window:** The location of absorption promotes formulation formation.
2. **Shorter Biological half life:** The small half life of misoprostol is advantageous for the formulation.
3. **Solubility:** Drugs with a specific site of absorption on the side of the small intestine higher up, such as ranitidine and misoprostol, which are more soluble in an acidic environment.
4. **Dose:**
   Medicine used locally in a stomach includes famotidine and ranitidine hydrochloride (H2 receptor antagonist) it is primarily treat disease of gastroesophageal reflux, duodenal ulcers, and stomach ulcers.
5. **Miscellaneous:** Other factors to take into account are the typical dosage form's low patient compliance and the medications' shorter half-lives, which require administration.

In Vitro Evaluation of Floating Tablets

The resulting formulations' physicochemical parameters and release characteristics were evaluated.

Pre-compression Parameter

Angle of Repose

Calculating the frictional forces present in grains or loose powder can be done using the angle of repose. The top of a pile of grains or powder can only be at an angle greater than this with respect to the horizontal, as depicted in fig.

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Angle of repose

The funnel was opened to let the granules flow down it; it was fastened to a platform at a specified height (h).
The angle of repose was then calculated by measuring the height and radius of the resulting pile of grains.

$\tan \theta = h/r$

$\theta = \tan\text{-}1\ (h/r)$

Where, θ = Angle of Repose h
h = Height of the heap
r = Radius of the heap

Compressibility Index

Comparing a powder bulk density (o), tapped density (t), and packing down rate allows one to determine its flowability.
The index of Compressibility was calculated by

$$\text{Compressibility Index (\%)} = \frac{\rho t - \rho 0}{\rho t} \times 100$$

Where, ρo = Bulk density /ml002E.
ρt = Tapped densityg/ml

2.8 Post-Compression Parameter

A. Shape of Tablet

To determine their form, compressed tablets were seen under a microscope.

B. Tablet Dimension

A calibrated varniear calliper is used to measuring the object's diameter and thickness.
The thickness of each of a tablet was determined after a random selection of three of each formulation.

C. Hardness

The degree of a tablet's hardness indicates how well it can manage mechanical shocks.A Monsanto hardness tester was used to gauge the tablets' hardness.
It is stated as kg/cm. These tablets' degree of hardness was measured assessed after a random selection of them.

D. Friability Test

The Roche Friabilator was used to assess tablet friability..It was stated in terms of percentages (%).
Ten pills were weighed and then put into the friabilator (W initial).The friabilator was rotated up to 100 times in 4 minu tes at a speed of 25 rpm. The tablets were once more weighed (W final).
Calculating the % friability involved :

$\%F = 100(1\text{-}W0/W)$

Tablets less than 1% amount of friability are taken into account.

E. Tablet density

A crucial component for floating tablets was tablet density. Until its density was lower than that of stomach fluid, the ta blet wouldn't float (1.004). The density was calculated using the relationship shown below.

$V = r^2h\ d = m/v$

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V = volume of tablet (cc)
r = radius of tablet (cm)
h = crown thickness of tablet (g/cc)
m = mass of tablet

F. Weight Variation Test

To assess for weight variance, ten tablets were randomly chosen from each batch and weighed individually. The U.S. P harmacopoeia allowed a tiny degree of variation in pill weight.The following weight fluctuation percentage deviation.

G. Biogency/ Floating Tablet

The duration of the dosage form's buoyancy on the simulated stomach fluid and the interval between its introduction an d its onset were both timed. The total amount of time a dose form floats is known as the total floating time. The amount of time it takes for a dosage form to appear on a medium's surface is known as the floating lag time (FLT) or buoyancy lag time (BLT) (TFT).

H. Swelling Index

Swelling behaviour was identified by tracking a dosage form's increase in weight or water consumption.
To measure the dimensional changes, one method would be to measure the gradual growth in tablet or diameter. A perc entage weight gain was used to calculate water uptake.

$$WU = \frac{Wt - W0}{W0} \times 100$$

Wt = Weight of dosage form at a time t
W0 = Initial weight of a dosage form

I. In vitro drug release studies

Typically, simulated stomach and intestinal fluids kept at a constant 37°C are used in the buoyancy test and vi tro drug r elease research.
In order to calculate floating time in practice, with 900 ml of 0.1 HCl of USP dissolution device is employed at 370C as the testing medium.The floating (or flotation) time is the length of time needed to make the HBS dosage form float. The USP dissolving device is used for dissolution tests.
After an adequate dilution, samples are regularly taken from the dissolution medium, given the same volume of new me dia, and their drug concentrations are calculated.
According to current practise as outlined in USP XXIII, the dose unit must sink to the bottom of the vessel before the bl ade can begin to rotate.19

2.9 Drugs typically used in FDDS

Sr. No	Drugs	Dosage form
1	Ibuprofen, Aspirin, Griseofulvin and Terfenadine	Microspheres
2	Prednisolone, Indomethacin and Diclofenac sodium	Granules
3	Cinnarizine	Films
4	Chlordiazepoxide HCl, Propranolol, L-Dopa, misoprostol, furosemide, benzodiazepine and HCl	Capsules
5	Ampicillin , Acetylsalicylic acid, Diltiazem, Acetaminophen, Amoxiltrihydrate, Antenolol, Chlorpheniramine, Cinnarizine, Isosorbide dinitrate, Fluorouracil, Isosorbidemononitrate	Tablets / Pills

Table 1: Drugs commonly used in FDDS

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III. CONCLUSION

The process of a medicine being absorbed in the gastrointestinal tract is very variable, and the longer t he dosage form is retained in the stomach, the longer it will take for the drug to be absorbed.

Systems for regulated and gastroretentive floating drug delivery have become effective tools for increa sing the bioavailability of various medications.

As delivery technology becomes more sophisticated, more gastroretentive drug delivery methods will be developed in order to optimize the delivery of molecules with narrow absorption windows, low bio availability, and extensive first pass metabolism.

Gastric retention could potentially be addressed with FDDS.

Numerous businesses are working to commercialize this approach despite the fact that there are still a l ot of obstacles to overcome in order to achieve prolonged gastric retention.

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