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"Advances in Gastroretentive Drug Delivery Systems: Enhancing Bioavailability and Therapeutic Efficiency"

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ABSTRACT:

The aim of composing a review, on gastric retentive drug delivery systems (GRDDS) is to outline the literature focusing on the emergence of various gastric pathways. This serves as an approach in the realm of supplementation and drug control. Research efforts have been dedicated to developing oral delivery mechanisms to address challenges like gastrointestinal residence time (GRT) and gastric emptying time (GET). GRDDS aims to prolong GRT enabling targeted drug release at sites in the gastrointestinal tract (GIT) resulting in localized or systemic effects. Oral medications often face bioavailability due to stomach changes particularly when the drug is insoluble, in the alkaline pH of the intestines. Furthermore, drugs designed for stomach effects tend to act and do not linger long enough in the stomach. Numerous endeavours have been undertaken to extend drug delivery system retention time reducing frequency. Gastroretentive drug formulations do not extend medication duration. Also enhance patient adherence by facilitating better medication regimen comprehension. This piece presents an overview of drug delivery pros, cons and characteristics while also discussing products containing patented nutrients.

Keywords: Gastroretentive drug delivery systems (GRDDS), gastrointestinal residence time (GRT), gastric emptying time (GET), gastrointestinal tract (GIT), bioavailability, drug control, oral medications, alkaline pH, drug retention, patient adherence, targeted drug release, drug delivery mechanisms, localized effects, systemic effects, supplementation, patented nutrients.

INTRODUCTION :

Because of its known value, the language of management always plays an important role in therapy. Some reasons make this method convenient for patient role, and these formulations are cheaper, easier to transport and store, more flexible in composition, and easier to administer (Pinto, 2010).

However oral management faces some physical barriers due to differences within the digestive device. moreover, many variables inside the digestive machine can exchange and influence the absorption of the drug. among these elements, pH, digestion time, enzymatic pastime and the region in which useful plants are positioned are the maximum essential (Rouge et al., 1996).

Approach isn't sufficient to conquer all troubles bobbing up from the intestines. for instance, drug formulations aren't suitable for capsules that are preferentially absorbed within the upper part of the digestive tract, as they can't deal with stomach ulcers; permit go of time consequently, incomplete launch of the drug and decreased effectiveness of the drug are a result of the mixed device now not closing within the belly (Kagan and Hoffman, 2008). and over time several them are already on the market.

The failure of conventional gastric retention structures has led to the improvement of oral gastric retention systems. those shipping structures are designed to remain inside the gastrointestinal tract for a long time and release the drug in a managed manner for the duration of this time. prolonged contact of intestinal micro organism with tissue may additionally increase the bioavailability of the drug (Boldhane and Kuchekar, 2010). other advantages of those structures include (Garg and Gupta, 2008): (i) accelerated treatment efficacy, (ii) decreased drug loss, (iii) extended drug solubility within the presence of low solubility in high pH environment, and (iv) increased drug solubility in the presence of low solubility in the high pH surroundings and (iv) discount of drugs appearing regionally within the stomach and duodenum.

DEFINE GRDDS?

Gastric retention drug administration is a method of prolonging the residence time in the belly by means of targeting the discharge of the drug to unique web sites within the higher gastrointestinal tract (GIT) to provide nearby or systemic results.

Monitoring of HIV-2 Infection

HIV-2 infection diagnosis typically involves testing for both HIV-1 and HIV-2.Reagent screening tests are followed by confirmation testing with antibody differentiation assays, which differentiate between HIV-1 and HIV-2 antigens. Once a patient is confirmed to be HIV-2 positive, the initiation of Antiretroviral Therapy (ART) is warranted. For patients with HIV-2 infection under ART treatment, monitoring is essential. This involves regular assessment of CD4+ T-cell counts and plasma viral loads (VLs). The monitoring frequency is typically every 3 months or at least twice a year, depending on the patient's clinical status, baseline CD4+ cell count, and the rate of CD4+ cell count decline. In cases of detectable VL, confirmation should be sought by taking a following sample, which is typically done one month apart.

ANATOMY OF STOMACH:-

The stomach has four area:
(1) Cardia (2) Fundus (3) Body (4) Pylorus 6

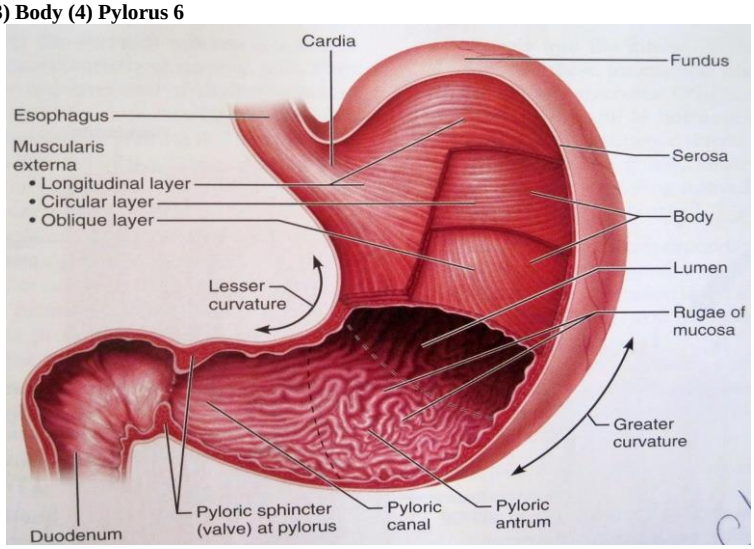


Figure 1:- Anterior view of regions of stomach

Gastric emptying:

The procedure of gastric emptying occurs in both frugality and eating situations. Within case of fasting, it is divided according to the cycle of the stomach and intestines, which occurs every 2-3 hours. This activity is called the interdigitate myoelectric loop or migrating myoelectric complex (MMC). It has four stages (Figure 2).

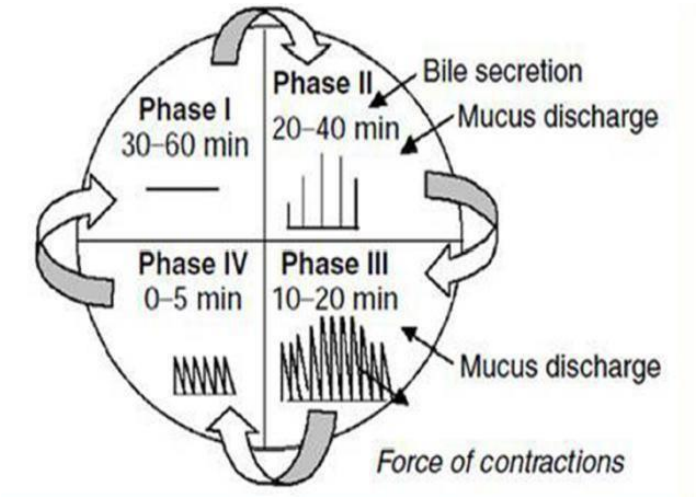


Figure 2. Gastrointestinal motility patterns

Phase	Duration
Phase-I (Basal phase)	30-60 min within frequent contractions
PhaseII (Pre burst phase)	20-40 min with the irregular action potential and contractions as the phase developments,the intensity and the frequency also rise gradually
Phase-III (Burst phase)	10-20 min, it containsintense And regular contractions for short periods. It's due to this wave that all the undigested materialis swept from stomach to the small intestine
Phase-IV	0-5 min and happens between phases three & one of two successive cycles

Table 1:-phases of gastric emptying

After the mixed food is digested, the contraction sample changes from the fasting state to the sated state. This is also considered a standard digestive movement and involves the same endless contractions as the second phase of the fasting state. Contraction causes a reduction in the size of the food (<1 mm), which pushes the suspended food towards the pylorus. The beginning of MMC is delayed throughout the nutritional state, resulting in a slower rate of intestinal absorption. Scintigraphy studies involving empty stomach measurements in healthy individuals show that orally administered and released materials face two important physiological problems:

1. Low GRT
2. Uncertain gastric emptying price but additional principal problem come across through the oral route is first bypass impact that leads to lessen systemic bioavailability of numerous tablets.

GASTRORETENTIVE DRUG DELIVERY SYSTEMS:

Medicines that are easily sock up from the intestine and have a low lifespan are quickly excrete from the body and therefore need to be taken more frequently. To overcome this difficulty, gastric drug delivery systems have been designed that provide a good plasma dose over a long period of duration, thus minimize the frequency of drug administrationand the advantage of reducing the changes in plasma concentrations by delivering the drug in a managed and duplicable manner. If the drug is not well in the intestine is caused by alkaline pH, the stomach may produce more liquid before elimination, which narrows the treatment window for digestive drug and makes the drugs follow a certain absorption-release limit. Drugs that may be beneficial for gastric retention include medicine that are less soluble in the intestinal pH than the stomach (such as cinnarizine, chlordiazepoxide, etc.), drugs that are easily broken down in the intestinal pH (such as captopril), and drugs that are less soluble in the intestinal pH than the stomach . Medicines that act locally on the stomach (such as misoprostol). Depressant , antibiotics, catecholamines, anticonvulsants, analgesics, antihypertensives, vitamins and muscle lightening can also be deliver in hydrodynamic balancing system (HBS) dosage (Figure 3). Antibiotics can prolong the duration of drug therapy, thus increasing patient adherence. The appearance of the drug in the prescription is an essential prerequisite for the absorption of the drug. However, if the solubility of the drug is low, it will take a long duration of time for the drug to dissolve in the stomach and transit time will become the most important, which will affect the absorption of drugs. Therefore, the amount of this medicine needs to be repeated in half a day. However, liposomes, nanoparticles, microspheres, etc. Other formulations/formulations such as can also be utilise for controlled release, but GRDDS is often examine a good replacement to improve bowel movements.

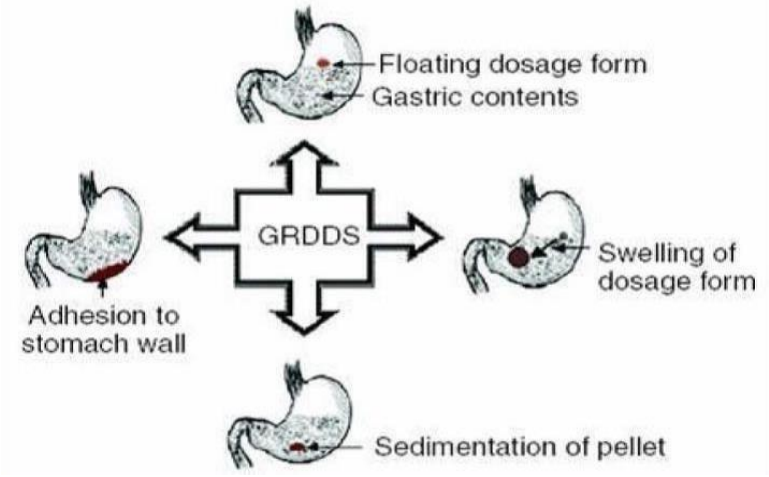
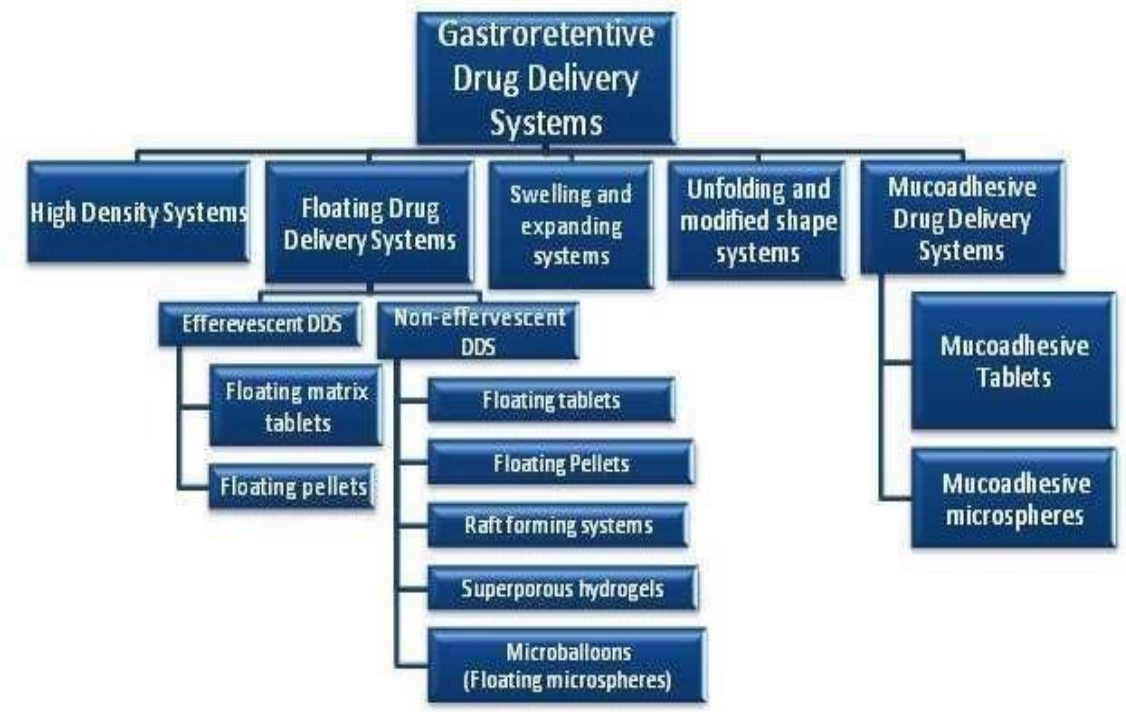


Figure3.Techniques of GRDDS

CLASSIFICATION OF GRDDS :-



1. HIGH DENSITY SYSTEM

How much data has a density between 1.0 and a higher value can cause the average GI to change over time? The system, whose density is approximately 3.0 g/cm3, remains in the stomach and can resist peristaltic movements.

However, it is difficult to produce such materials in large quantities and reach a density of 2.4-2.8 g/cm3. Solvent such as barium sulfate, zinc oxide, and titanium dioxide can be used for preparation of quantitative data. and titanium dioxide [17]. In 1930, Hoelzel first observed the outcome of a high dose form of GRT in various animal species. The density of the test paper is from 0.9 to 10.5 g/cm3

2. FLOATINGSYSTEMS

Since floating drug delivery systems hold a lower thickness than gastric fluid, they continue to exist in the stomach without affecting the empty stomach in the long term. Since the system floats in the stomach contents, the drug is free from the system in a controlled manner. After the drug is released, the remaining parts are evacuated from the stomach.

Variable performance is split into:

1. Effervescent systems are less effective due to oil production and trapping.
2. non-effervescent systems with inherently low density orless density cause for expansion

A) EFFERVESCENT FLOATING SYSTEMS

Effervescent flotation systems involve gas-producing substances and vaporous liquids. This procedure has been used for both single-unit and multi-unit systems. Effervescent substances E.g.- calcium carbonate, tartaric acid and citric acid are used together with water soluble polymers in electric generators. When the system meets fruit juice, carbon dioxide is released due to the reaction of the effervescent substance with the fruit juice. The released CO_2 is trapped in the hydrocolloid mold, giving the tablets lagging time , and affecting their unbind properties. In volatile liquids, vaporous liquids such as ether and cyclopentane enter the gas chamber and the liquid evaporates at body temperature, causing the chamber in the stomach to expand. Hydrophilic polymers are constantly used to control the drug release concentration in this system.

Effervescent floating machine can be divided into single-layer, double-layer effervescent floating tablet and multi-unit effervescent floating machine. A sheet of effervescent tablets is completely mixed with effervescent substances, polymers, drugs and excipients. However, in two-layer effervescent floating tablets, one layer contains the drug, polymer, and CO2 gas-generating agent, while the other layer produces the immediate-release drug and CO2 and polymer-free excipients. In a recent study, sodium bicarbonate in HPMC matrix formulation was used to improve GRT by increasing the water content of the layer and increasing the diffusion area.

Additionally, increasing sodium bicarbonate reduces the release of the drug from the matrix, possibly due to carbon dioxide bubbles interfering with the diffusion process. In another study, this method was used to evaluate the in vitro and in vivo behavior of ciprofloxacin hydrochloride effervescent floating tablets.

While the outer layer consists of a swellable substance, the internal structure contains effervescent substances such as sodium bicarbonate, calcium carbonate and tartaric acid. . polymer composition. Rare diseases may be associated with problems such as joint or intestinal infections, which can cause

abdominal pain. For this process to float and work well in the stomach, there needs to be a lot of fluid. Therefore, drugs that affect the gastric mucosa are not suitable for weak bacteria.

b) NON-EFFERVESCENT FLOATING SYSTEMS

In non-effervescent systems, use cellulose derivatives or gel-forming polymers. The standard technique for non-effervescent systems involves mixing the drug with a gelforming polymer. Various non-effervescent systems include hydrodynamically balanced systems (HBS), one- and two-layer floating tablets, and microspheres/hollow microspheres.

The HBS system was developed by Sheth and Tossounian in 1984. HPMC, hydroxypropylcellulose (HPC).

Hydroxyethyl cellulose, sodium carboxymethylcellulose, carrageenan, agar and alginic acid are some of the polymers used to create HBS systems. In this case, the drug is mixed with a polymer and filled into a gelatin capsule. Floating tablets can be made from the combination of a drug and a gel-forming hydrophilic polymer that hydrates and swells upon contact with gastric fluid, maintaining the density of the tablet at <1 g/cm3. As a result, the low volume floats on gastric fluid and prolongs GRT. Hydrophilic polymers commonly used in floating tablets include HPMC, polyethylene oxide, HPC, cellulose acetate phthalate, etc. takes place.

A two-layer floating tablet with an immediate-release layer and a sustained-release layer of the drug was studied. While current delivery systems contain disintegrants to help release the drug quickly, delivery systems contain hydrophilic polymers that control the release rate of the drug and provide buoyancy of the tablet. Drug-loaded microspheres/hollow microspheres are produced by simple solvent evaporation or solvent diffusion technology, and many floating systems are available. Polycarbonate, cellulose acetate, calcium alginate, Eudragit S, agar, and low methoxylated pectin are polymers commonly used to form microspheres. Many variables, such as the amount of polymer, the ratio of plasticizer to polymer, and weight, can affect the buoyancy behavior and drug release of these dosage forms. One 13of the disadvantages of HBS is that the system is a matrix system consisting of a mixture of chemicals and low polymer materials. It is not possible to change the release kinetics of the drug without changing the buoyancy properties of the dosage form and vice versa.

3. SWELLING AND EXPANDING SYSTEM:

The prevalence of this type of DDS is mainly due to the presence of hydrogel-forming substances when ingested; This increase in size prevents them from leaving the stomach through the pylorus. For this reason, the amount of paper remains in the stomach for a long time. These systems will be referred to as "plug systems" because they favor the pyloric sphincter. The main mechanism of swelling and release of drug from the system is diffusion. These systems use hydrophilic polymers (such as HPMC, polyethylene oxide, and carbomers) that absorb water from gastric fluid and increase the volume of the body. Expandable drug delivery systems are designed to increase their volume (Figure 4a).). Originally used to treat animals, their use was later expanded to include humans. For proper functioning of the body, three general configurations should be considered: small to facilitate oral intake, expanded form in the stomach to avoid contamination of the pyloric sphincter, and reduced size of the body for urination after the drug is finished. This system is also called the "plug system" because it can block the pyloric sphincter.

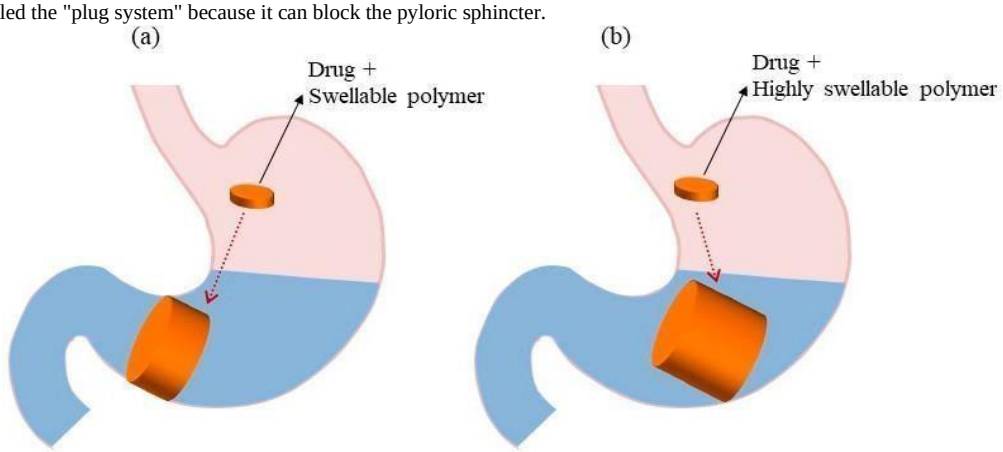


Figure: -4.GRDDSbasedon(a)expandable systems and(b)super porous hydrogel system

4. UNFOLDING AND MODIFIED SHAPE SYSTEMS

These are non-fragmentable geometries, molded from silicone elastomers or polyethylene blends, that extend into the stomach over time according to the size, shape and bending modulus of drug delivery. Materials with different geometries such as continuous solids, tetrahedrons, rings, trefoils, flat discs, strings, and particles/spheres are examined. These systems contain at least one wearable polymer (e.g. Eudragit® E, hydroxypropyl cellulose (HPC)) and one non-wearable polymer (e.g. polyamide, polyolefin, polyurethane) dispersed in the chemical polymer composition in the matrix. Trilobal, disc, linear and granular shapes are molded from silicone elastomer, while tetrahedral and rigid toroidal shapes are made from a mixture of low-density polyethylene and ethylene: vinyl acetate copolymer.

5. BIOADHESIVE OR MUCOADHESIVE SYSTEMS

Bioadhesive or mucoadhesive drug delivery systems are used to introduce delivery materials into the lumen to enhance drug absorption in specific areas. This approach involves the use of bioadhesive polymers that adhere to the epithelial surface of the stomach. Some of the best excipients commonly used in these systems include polycarbophil, Carbopol®, lectins, chitosan, CMC, etc. takes place.) Long stay in the upper gastrointestinal tract

1. Increasing absorption, thus increasing the bioavailability of the drug. > 1Strong hydrogen bonding group [-OH,-COOH]
2. Strong anionic charge
3. Flexible enough to penetrate the mucus network
4. Suitable for moisturizing mucus / mucosal tissue surface energy
5. The polymer must have a molecular weight that will support the connection between the polymer and mucus. Matrices created with polymers swell when placed in an aqueous environment, followed by dissolution of the matrix. Polyelectrolytes have more mucoadhesive properties than neutral polymers.

For example,

a) PVP, methylcellulose, sodium carboxymethylcellulose, hydroxypropylcellulose
b) Hydrogel: This type of polymer swells and adheres to the mucosa when in contact with water. These are subdivided: Synthetic Polymers - Cellulose Derivatives, Carbopol Natural Polymers - Tragacanth, Pectin, Gelatin, Sodium Alginate, Gum Arabic

FACTOR AFFECTING ON GRDDS:-

a) **Density**: Stomach retention time (GRT) is a function of the buoyancy of the bulk paper, which depends on the density. The density of the dosage form should be lower than the stomach contents (1.004 gm/ml).
b) **b.Size:** Doses larger than 7.50 mm in diameter are said to improve GRT compared to doses larger than 9.90 mm in diameter.
c) **Paper quantity:** Tetrahedral and toroidal with a flexural modulus of 48 and 22.50 kg per square inch are reported to have better GRT at 24 hours compared to other shapes.
d) **d.Single or multi-unit formulations:** Multi-unit formulations show a more precise release profile and suffer less from efficacy due to unit failure; It allows units with different release profiles to be co-applied depending on how much paper is per unit.
e) **Full/Unfed State:** In emergency situations, bowel movement is classified as a cycle of motor activity that occurs every 1.5 to 2 hours if the control period of the overlapping process of the MMC, the unit of the digestive system, is very short. However, in the case of satiety, MMC is delayed and the time it stays in the stomach is longer.
f) **Good nutrition:** Eating fatty acids or indigestible foods can transform the intestinal structure into nutritional state, thereby reducing intestinal inflammation.
g) **Calorie content**: Foods high in protein and fat can increase GRT by 4 to 10 hours.
h) **h.Age:** Generally, older people over the age of 70 have longer bowel movements.
i) **Frequent feeding:** Due to the low frequency of MMC, the time it stays in the stomach will exceed 400 minutes if you eat consecutive meals with a single meal.
j) **Gender:** Although weight, body position, and height, mean abdominal breathing time in men (3.4 ± 0.6 hours) is less correlated with age and race in women (4.6 ± 1.2 hours).
k) **k.Posture:** The duration of holding the stomach will be different between patients lying supine and patients walking upright.

➢ **EVALUATIONPARAMETERSOFGRDDS :-**

❖ **INVITRO EVALUATION PARAMETERS:-**

In vitro assays of GRDDS can be used to estimate in vivo efficacy. Standard tests for gastroretentive tablets include determining tablet tensile strength, weight change, friability, drug content, consistency, and in vitro drug release. Buoyancy behaviors such as buoyancy delay time and total buoyancy length have been used to evaluate the buoyancy behavior of low-density systems. In addition, buoyancy force is also used to measure the buoyancy of floating tablets. Additionally, the swelling rate, water absorption capacity, and gel strength of the polymer layer can be evaluated using an antibiotic and tested for at least 8 hours to ensure the flotation mechanism, drug release, and energy gel. Table 6 describes various in vitro parameters of GRDDS.

1. **Buoyancy lag time:-**The time required for the digestate to rise to the surface of the dissolution medium. It was determined to use a USP dissolution apparatus containing 900 mL of 0.1 N HCl solution as the measurement medium and maintained in a flotation time delay at 37 °C.
2. **Floating time:-**This determines the buoyant force of the paper. This test uses a special dispersion device according to the dosage form with 900 mL of separation medium stored at 37°C. Determining the floating time or amount of floating time of parts by visual inspection.
3. **Specific gravity/density**: - Specific gravity estimates are important for both low- and high-density GRDDS. Specific gravity is determined using theory.
4. **Swelling index**: - The swelling index was determined by soaking the tablets in 0.1 N HCl at 37°C and removing them periodically.
5. **Water uptake**: - In this study, quantitative data were removed from the separation medium after a period of delay and the weight change was determined. Water absorption (WU) = (Wt - Wo) * 100 / Wo where W_t= weight of the dosage form at time t, W_o= initial weight of the dosage for
6. **Weight variation**: - Various official methods are recommended by pharmacopeia's to calculate the weight variation. Usually, the individual and average weight of 20 tablets is recorded. From these data, average weight and weight variation is calculated.
7. **Hardness and friability: -** Monsanto tester, Joncobb tester, Pfizer tester etc. Determine hardness or crushing strength using
8. **In vitro dissolution tests**: - The purpose of this experiment is to determine the time release of GRDDS in gastric and intestinal fluids at 37°C using a USP Type II dissolution apparatus (flap type).

❖ **INVIVO EVALUATION PARAMETERS: -**

Well-designed in vivo studies in animal models or humans are needed to provide evidence of the in vivo efficacy of GRDDS. In vivo studies provide information on GRT and bioavailability of drugs. Selecting an appropriate animal model is the first prerequisite for successful in vivo research. For

example, problems may occur with small animals such as rats, mice, guinea pigs and rabbits, especially when handling large animals. Therefore, GRT and bioavailability remain difficult to measure.

I. **Radiology: -** This technique is mainly used to determine the time-dependent position of diet containing barium sulphate (radio-opaque marker) in the body using X-rays. Xrays are taken at different times to record the exact dose

II. **Scintigraphy: -**Similar to radiography, it is used to determine the in vivo Variable character of gastric permanent dosage data. In scintigraphy, 99mTc pertechnetate is used as an emitting material instead of X-rays to absorb the preparation that will record the image. This procedure uses a lighted, optical, tubular, thin instrument called an "endoscope" to look deep inside the body, such as the stomach, esophagus, and intestines.

III. **Ultrasound:** - For diagnostic purposes. Technique that uses ultrasound to take pictures of the inside of the body. The disadvantage of this test is that it cannot detect internal organs.

IV. **13C Octanoic Acid Breath Test:** - Radioactive 13C Octanoic Acid is used to measure the breath of the drug in GRDDS. This drug is absorbed from the duodenum and when radiolabeled, the amount of carbon dioxide exhaled after its metabolism is related to the amount of caprylic acid absorbed. Radiolabeled CO2 isotope ratio is measured by mass spectrometry. It deals with the immediate analysis of the amount of information in the intestine. These systems are only used to determine the intestinal motility and dissolution behavior of drugs. In this process, a lot of information is recorded as magnetic dipoles by connecting lines of ferromagnetic particles and recording the magnetic dipole field by a device that responds to biomagnetic measurements.

➢ **POLYMERS AND OTHER INGREDIENTS USED IN FORMULATIONS OF GASTRORETENTIVE DOSAGE FORMS:-**

- **Hydrocolloids (20%-75%):**Modified cellulose derivatives can be anionic, synthetic or nonionic, such as hydrophilic gums. For example, Gum Arabic, Agar, Chitosan, Casein, Bentonite, Veegum, Gellan Gum, Sodium CMC, Pectin, MC, HPC, HPMC K4 M, HPMC K15 M, Eudragit S100, Calcium Alginate, HPMC K100 M, Eudragit, Acrylic Foam, Ethyl Cellulose, Polyethylene Oxide, Beta Cyclodextrin, Polyethylene Glycol, Sodium Alginate, PVA, Polycarbonate, Carbopol, PVP, E4 M, Acrylic Polymer and CP 934P.
- **Inert fatty materials (5%-75%):** Lean foods with a specific gravity <1 can be used to reduce the hydrophilicity of the process and therefore increase buoyancy. For example, fatty acids, beeswax, Gelucires 39/01 and 43/01, long-chain fatty alcohols, etc.
- **Effervescent agents:** Citric acid, sodium bicarbonate, tartaric acid, citric acid, glycin disodium carbonate, tiablwm yam.
- **Release rate accelerants (5%-60%):** Lactose, Mannitol, etc
- **Release rate retardants (5%-60%):** Dicalcium phosphate, Talc, Magnesium stearate, etc.
- **Low density material:** Polypropylene foam powder.
- **Buoyancy increasing agents (up to 80%):** Ethyl cellulose.

ADVANTAGES OF GRDDS:-

1. **Enhanced bioavailability:-** The bioavailability of riboflavin CR-GRDF was significantly improved compared to the application of non-GRDF CR polymer formulations. There are many different processes involved in the absorption and transport of drugs in the gastrointestinal tract, and these processes simultaneously affect drug absorption.
2. **Enhanced first-pass biotransformation:-** Similar to the activity of transporters capable of being inactive, the presystemic metabolism of the drug may be increased if the drug is exposed to supplemental metabolizing enzymes (cytochrome P450s, especially CYP3A4). Instead of entering the 23rd of the bolus.
3. **Sustained drug delivery/reduced frequency of dosing:-** For drugs with short biological half-lives, continuous and slow infusion of CR-GRDF may result in pharmacokinetic drift and frequent dose reductions. This feature is associated with increased patient compliance and therefore improved treatment.
4. **Targeted therapy for local ailments in the upper GIT**:-Long-term application of GRDF to the stomach will be effective in the local treatment of the stomach and intestines. Thanks to this type of application, the therapeutic effect can be achieved locally, while the body's potency after absorption and distribution is minimal.
5. **Reduced fluctuations of drug concentration Continuous:-**Injection of the drug after administration of CRGRDF results in a narrower plasma concentration compared to the immediate-release version. Therefore, side effects of the drug can be prevented by reducing drug changes. These properties are particularly important for drugs with a narrow therapeutic index24.

DISADVANTAGES OF GRDDS:-

1. **Influence of Food:** The presence of food in the stomach affects the activity of GRDDS. Eating food can alter the digestive system, making the medicine less digestible and absorbable.
2. **Formulation Complexity:** Creating effective GRDDS often requires a complex design process, increasing the complexity and cost of drug development. Achieving the perfect balance of buoyancy, bioadhesion or turgor while maintaining stability and safety is a difficult task.
3. **Potential for Incomplete Gastric Emptying:** In some cases, GRDDS does not fill the entire stomach, causing complications and complications. Incomplete bowel movements will affect subsequent doses and may increase the risk of overdose.
4. **Risk of Gastrointestinal Irritation:** Some GRDDS models, especially those using bio adhesive methods, may irritate the intestinal mucosa. Prolonged contact with the abdominal wall may cause local irritation or swelling.
5. **Limited Applicability to All Drugs:**Not all medications are suitable for GRDDS. Some drugs will not be beneficial if left in the stomach for a long time and their formulation will not be suitable for the physical and chemical properties of the drug.

6. **Potential for Incomplete Drug Release:** Not all medications are suitable for GRDDS. Some drugs will not be beneficial if left in the stomach for a long time and their formulation will not be suitable for the physical and chemical properties of the drug.
7. **Patient Acceptance and Compliance:** Patients must understand and follow special instructions for taking medications for GRDDS, which may cause problems with acceptance and compliance. Patients may have difficulty meeting their specific needs, which may affect the quality of treatment.
8. **Risk of Device Malfunction:**Some GRDDS have systems such as flotation devices that can malfunction or malfunction in certain situations. This may lead to premature release or inadequate retention of the drug..
9. **Limited Application to Lower Gastrointestinal Conditions:**GRDDS is usually produced in the intestine and may not be suitable for intestinal diseases. Targeting drugs to specific sites in the digestive tract will require multiple delivery strategies.

APPLICATION OF GASTRORETENTIVE DRUG DELIVERY SYSTEMS:-

1. **Enhanced Bioavailability:-**The bioavailability of riboflavin controlled-release gastroprotective materials is better compared to theapplication of noncontrolledrelease gastroprotective polymeric formulations. In the absorption and transport of drugs in the gastrointestinal tract, there are many different mechanisms that work simultaneously to affect drug absorption.
2. **Sustained Drug Delivery:**Problems such as intestinal GRT have been encountered in oral administration-release preparations. Since HBS systems float on food in the stomach, it can be used to solve the problem of the possibility of remaining in the stomach for a long time with density <1. This system is very small and does not pass through the pyloric opening.
3. **Site Specific Drug Delivery Systems:** These systems are often particularly useful for drugs that are absorbed through the stomach or near the small intestine. Controlling/delaying the drug reaching the stomach provides adequate local treatment and limits the effects of the drug. This reduces the side effects of the drug in the bloodstream. Additionally, long-term feeding at a dedicated dispensing point may reduce the frequency of drug use. For example, furosemide and riboflavin.
4. **Absorption Enhancement:** Drugs with poor bioavailability due to their specific location in the upper gastrointestinal tract are candidates for FDDS formulation to maximize their absorption..
5. **Minimized adverse activity at the colon:** Keeping the drug in the stomach, the HBS system reduces the passage of the drug into the intestine. Therefore, the negative activities of the drug in the intestine will be prevented. This pharmacodynamic property gives the reason for the gastroretentive dosage forms of beta-lactam antibiotics to be absorbed only by the small intestine, and their presence in the intestine leads to the development of microbial rejection.
6. **Reduced fluctuations of drug concentration:**Controlled-release GRDF is administered by a continuous injection, resulting in a narrow plasma concentration range associated with immediate release data. Thus, changes in the drug are reduced and side effects resulting from the interaction can be maximized.

CONCLUSION: -

Developing effective gastroenteric drug materials for the delivery of diarrheal medication is a challenging task. For this reason, various methods have been used to create the needs of the gastrointestinal tract, and among them, the floating drug delivery method has emerged as the best method. These systems have the advantage of good absorption of the drug absorbed from the upper stomach. Remaining the body in the stomach for a long time increases the local effect of the drug. This leads to less medication and better treatment. Good stability and better drug release make the system more reliable compared to other drug models. The absorption of drugs in the gastrointestinal tract is a very different process, and taking a long time to digest the prescription will lead to a longer time for the absorption of the drug. Floating drug delivery systems show promise as a potential gastric storage method. Although there are many complex issues that need to be solved to ensure long-term GI retention, many companies are trying to commercialize this approach.

REFERENCES: -

1. Pinto, J.F., 2010. Site-specific drug delivery systems within the gastro-intestinal tract: from the mouth to the colon. Int. J. Pharm. 395, 44–52
2. Rouge, N., Buri, P., Doelker, E., 1996. Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery. Int. J. Pharm. 136, 117–139
3. Kagan, L., Hoffman, A., 2008. Selection of drug candidates for gastroretentive dosage forms: pharmacokinetics following continuous intragastric mode of administration in a rat model. Eur. J. Pharm. Biopharm. 69, 238–246.
4. Boldhane, S.P., Kuchekar, B.S., 2010. Development and optimization of metoprolol succinate gastroretentive drug delivery system. Acta Pharm. 60, 415–425.
5. Garg, R., Gupta, D.G., 2008. Progress in controlled gastroretentive delivery systems. Trop. J. Pharm. Res. 7, 1055–1066.
6. (Friedman et al., 2004, 2005; Garg and Gupta, 2008; Gerard et al., 2014; Grenieret al., 2015; Hassan, 2014; Pathak et al., 2015; Tsabari et al., 2013).
7. Tortora GJ, Grabowski SR. Principles of Anatomy and Physiology; New York; John Wiley and Sons; 2002
8. Marinaganti RK, Bonthu S, Nagakanyaka DP, Sheik M; A comprehensive review on gastro retentive drugdeliverysystem; 2013; 3(2); 149-164.

9. GargS,SharmaS;GastroretentiveDrugDeliverySystem;BusinessBriefing:Pharmatech;2 003;160-166. 10)Wen H, Park K. Introduction andoverview of oral controlledreleaseformulationdesign.In:WenH,Park
10. K.editors.OralControlledReleaseFormulationDesignandDrugDelivery:Theory toPractice,JohnWileyandSons Inc;2010. p. 21.
11. Thapa, P.; Jeong, S. Effects of Formulation and Process Variables on Gastroretentive Floating Tablets with AHigh-Dose Soluble Drug and Experimental Design Approach. Pharmaceutics 2018, 10, 161. [CrossRef]
12. Rahim, S.A.; Carter, P.; Elkordy, A.A. Influence of calcium carbonate and sodium carbonate gassing agentson pentoxifylline floating tablets properties. Powder Technol.
    2017, 322, 65–74. [CrossRef]
13. Talukder, R.; Fassihi, R. Gastroretentive delivery systems: A mini review. Drug Dev. Ind. Pharm. 2004, 30,1019–1028. [CrossRef] [PubMed]
14. Kim, S.; Hwang, K.-M.; Park, Y.S.; Nguyen, T.-T.; Park, E.-S. Preparation and evaluation of non-effervescentgastroretentive tablets containing pregabalin for oncedaily administration and dose proportionalpharmacokinetics. Int. J. Pharm. 2018, 550, 160–169. [CrossRef] [PubMed]
15. Sheth, P.; Tossounian, J. The hydrodynamically balanced system (HBS™): A novel drug delivery system fororal use. Drug Dev. Ind. Pharm. 1984, 10, 313–339.
16. [CrossRef]
17. Hilton, A.; Deasy, P. In vitro and in vivo evaluation of an oral sustained-release floating dosage form of
18. Hilton, A.; Deasy, P. In vitro and in vivo evaluation of an oral sustained-release floating dosage form ofamoxycillin trihydrate. Int. J. Pharm. 1992, 86, 79–88. [CrossRef]
19. 19)Wen H, Park K. Introduction and overview of oral controlled release formulation design. In: Wen H, Park K. editors. Oral Controlled Release Formulation Design and
    Drug Delivery:Theory to Practice, John Wiley and Sons Inc; 2010. p. 21
20. Garg, R.; Gupta, G. Progress in controlled gastroretentive delivery systems. Trop. J. Pharm. Res. 2008, 7,1055–1066.
21. Klausner, E.A.; Lavy, E.; Friedman, M.; Hoffman, A. Expandable gastroretentive dosage forms. J. Control.Release 2003, 90, 143–162.
22. Bardonnet, P.; Faivre, V.; Pugh, W.; Piffaretti, J.; Falson, F. Gastroretentive dosage forms: Overview andspecial case of Helicobacter pylori. J. Control. Release 2006, 111, 1–18.
23. Wen H, Park K. Introduction and overview of oral controlled release formulation design. In: Wen H, Park K. editors. Oral Controlled Release Formulation Design and Drug Delivery: Theory to Practice, John Wiley and Sons Inc; 2010. p. 21
24. Mule MS, Kshirsagar RV. Gastroretentive mucoadhesive microsphere: a review. Indo Am J Pharm Res 2011;1:483–505
25. Brahmankar DM, Jaiswal SB; Biopharmaceutics and pharmacokinetics a treatise; New Delhi; Vallabh Prakashan; 2003.
26. Patel GM, Patel HR, Patel M; Floating drug delivery system: An innovative approach to prolong gastric retention; Pharmainfo.net 2007; 5(6)
27. Hilton AK, Deasy PB. In vitro and in vivo evaluation of an oral sustained release floating dosage form of amoxycillin trihydrate. *Int J Pharm.* 1992;86:79–88.
28. Pham AT, Lee PI. Probing the mechanisms of drug release from hydroxypropyl methyl cellulose matrices. *Pharm Res.* 1994;11:1379–1384.
29. Burns SJ, Corness D, Hay G, Higginbottom S, Whwlan I, Attwood D, Barnwell SG. Development and validation of an in vitro dissolution method for a floating dosage form with biphasic release characteristics. *Int J Pharm.* 1995;121:37–34
30. Klausner, E.A.; Lavy, E.; Friedman, M.; Hoffman, A. Expandable gastroretentive dosage forms. J. Control.Release 2003, 90, 143–162.
31. Mandal, U.K.; Chatterjee, B.; Senjoti, F.G. Gastro-retentive drug delivery systems and their in vivo success:A recent update. Asian J. Pharm. Sci. 2016, 11, 575–584.
32. Wang YP, Gan Y, Zhang XX. Novel gastroretentive sustained-release tablet of tacrolimus based on self-microemulsifying mixture: in vitro evaluation and in vivo bioavailability test. Acta Pharmacol Sin. 2011;32:1294–1302.
33. Jiménez-Martínez I, Quirino-Barreda T, Villafuerte-Robles L. Sustained delivery of captopril from floating matrix tablets. Int J Pharm. 2008;362:37–43.
34. Klausner, E. A., Lavy E., Friedman, M., Hoffman, A., (2003) Expandable gastroretentive dosage forms. J. Control. Release 90, 143–162.
35. Garg R., Gupta G.D. (2008) Progress in Controlled Gastroretentive Delivery Systems. Trop. J. Pharm. Res., 7 (3): 1055-1066
36. Hoffman A. (1998) Pharmacodynamic aspects of sustained release preparation. Adv.
    Drug Deliv. Rev. 33: 185-199.
37. Vyas SP. Controlled drug delivery: Concept and Advances. Vallabh Prakashan. 2006, 196-217.
38. Joseph R. Controlled drug delivery fundamentals and application. Revised and Expanded Marcell. Dekker Inc. 2nd edition. New York, 2009.
39. Joseph R. Controlled drug delivery fundamentals and application. Revised and Expanded Marcell. Dekker Inc. 2nd edition. New York, 2009.
40. Fabrcgas JL, Cucala CG, Pous J; Sites R.A. In vitro testing of an antacid formulation with prolonged gastric residence time; Drug Development and Industrial Pharmacy; 1994; 20; 1199-1212.