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# A REVIEW ON FLOATING DRUG DELIVERY SYSTEM

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## ABSTRACT

Pharmaceutical industries have received much interest in pharmaceutical research in the area of oral drug delivery more over on Gastro retentive drug delivery system that is Floating Drug Delivery System (FDDS). Oral delivery of medicine is far and away the foremost desirable route of drug delivery. This route has high patient acceptableness, primarily because of easy administration. The purpose of writing this review on floating drug delivery systems (FDDS) was to compile the recent literature with special focus on the principal mechanism of floatation to achieve gastric retention. The recent developments of FDDS together with the physiological and formulation variables moving viscous retention, approaches to style single-unit and multiple-unit floating systems, and their classification and formulation aspects square measure covered in detail. This review additionally summarizes the in vitro techniques and in vivo studies to judge the performance and application of floating systems, and applications of those systems.

**KEYWORDS:** Floating drug delivery system, mechanism of floatation, formulation aspect.

## INTRODUCTION

Oral administration of drugs is by far the most preferable route of drug delivery due to the ease of administration, minimum cost of therapy, patient compliance and flexibility in formulation etc. Oral sustained drug delivery system the formulations show some limitations connected with the gastric emptying time. Variables and too rapid gastrointestinal transit time could result in incomplete drug release from the device into the narrow absorption window leading to diminished efficacy of the administered dose. Floating drug delivery systems or dynamically controlled systems are low density systems that have sufficiently buoyancy time to flow over the gastric contents and stay buoyant in the stomach without affecting the gastric emptying rate for a prolonged time.[1] Gastro retentive drug delivery system is the systems which are retained in the stomach for a longer period and thereby improve the bioavailability of drugs that are preferentially absorbed from upper part of the GIT.[2] Gastro retentive dosage forms can stay in the gastric region for long periods and hence much prolong the gastric retention time of drugs. Over the last few decades, the several gastro retentive drug delivery approaches being design and development, including: sinking systems that is retained in the bottom part of the stomach[3, 4], The floating systems that causes buoyancy in gastric fluid[5, 6, 7], However, the recent technological development has resulted to many novel pharmaceutical products, mainly the controlled release drug delivery systems to overcome this problem. Gastro-retentive drug delivery system (GRDDS) is one such example where the attribute like gastric retention time coupled with the drug release for extended time has much improved patient compliance. Therefore to overcome such problems gastro retentive drug delivery systems are designed to prolong the gastric retention time of the drugs which are:

1. Locally active in the stomach.
2. Unstable in the intestinal environment.
3. Have narrow absorption window in the git.
4. Have low solubility at the high pH regions.[8,9]

Various approaches has been proposed to increase the gastric residence of the drug delivery that includes floating drug delivery system (FDDS), mucoadhesion or bioadhesion system, high density system, expansion system, magnetic system, super porous hydrogel, raft forming system and floating ion exchange resins.[10]

## ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM

1. It increases patient compliance by reducing dosing frequency
2. Buoyancy increases gastric residence time
3. Better therapeutic effect of short half life drugs
4. Site specific drug delivery to stomach can be achieved
5. In this drug is released in a controlled manner
6. Gastric irritation can be avoided by designing sustained release.

7. No risk of dose dumping by making single unit floating unit such as microspheres releases drug uniformly.[11]

**DISADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM**

1. Floating drug delivery system is not feasible for those drugs that have solubility or stability problem in GI tract.
2. These floating systems require a high level of fluid in the stomach for drug delivery to float and work efficiently.
3. Drugs such as nifedipine, which under goes first pass metabolism may not be desirable for the preparation of these types of systems.
4. Drugs which are irritant to Gastric mucosa are also not desirable.
5. The drug substances that are unstable in the acidic environment of the stomach are not suitable drug candidates to be incorporated in the systems.[1]

**SUITABLE DRUG CANDIDATES FOR GASTRO RETENTION**

In general, appropriate candidates for GRDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT:

1. Narrow absorption window in GI tract e.g., riboflavin and levodopa.
2. Primarily these drugs absorbed from stomach and upper part of GI tract, e.g., calcium supplements, chlordiazepoxide and cinnarazine
3. Drugs that act locally in the stomach, e.g.,antacids and misoprostol
4. Drugs that degrade in the colon, e.g., ranitidine HCl and metronidazole
5. Drugs that are disturb normal colonic bacteria e.g., amoxicillin trihydrate.[12,13,14]

**DRUGS UNSUITABLE FOR GASTRO RETENTIVE DRUG DELIVERY**

1. Drugs that has been very limited acid solubility e.g. phenytoin etc.
2. Drugs are specially suffer instability in the gastric environment e.g. erythromycin etc.
3. Drugs that are intended for selective release in the colon e.g. 5- amino salicylic acid and corticosteroids etc.[13,14]

**ANATOMY OF THE STOMACH**

The basic function of the stomach is to process and transport food in small intestine. The residence time of food is small and mostly proteins are digested. The gastro intestinal tract may be divided into three main regions

- Stomach
- Small intestine- duodenum, jejunum, and ileum
- Large intestine.[15]

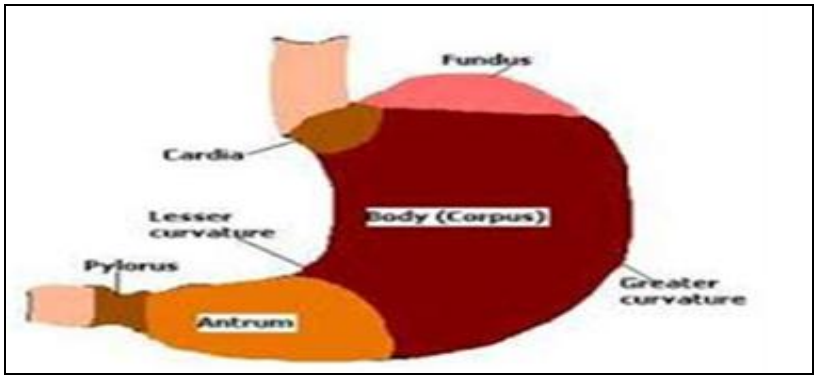


**Figure 1: Shows parts of Stomach.**

**PHYSIOLOGY OF THE STOMACH** The stomach is an expanded section of the digestive tube between the oesophagus and small intestine. In the empty state the stomach is contracted and its mucosa and sub mucosa are thrown up into folds called as rugae. There are 4 major types of secretary an epithelial cell that covers the stomach and extends into gastric pits and glands.

1. Mucous cells- secrete alkaline mucus
2. Parietal cells – secrete HCL
3. Chief cells- secrete pepsin
4. G cells- secrete hormone gastrin[16]
   It is divided into 4 phases[17]

- phase I (basal phase) it lasts from 40-60 min with the rare contractions
- Phase II (preburst phase) last with intermittent potential and contractions.
- Phase III (burst phase) it last for 4-6 min. in these intense and regular contraction occur in the short periods. Due to these contractions the indigestive food is swept from stomach to intestine. These are known as house keeper waves.
- Phase IV it lasts for 0-5 min a phases III and I for two consecutive cycles.

After the hyperacidity of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state. These contractions changes result in reducing the size of food particles (to less than 1 mm) which are propelled toward the pylorus in a suspension form. During the fed

state onset of MMC is delayed resulting in slowdown of gastric emptying rate.[18]

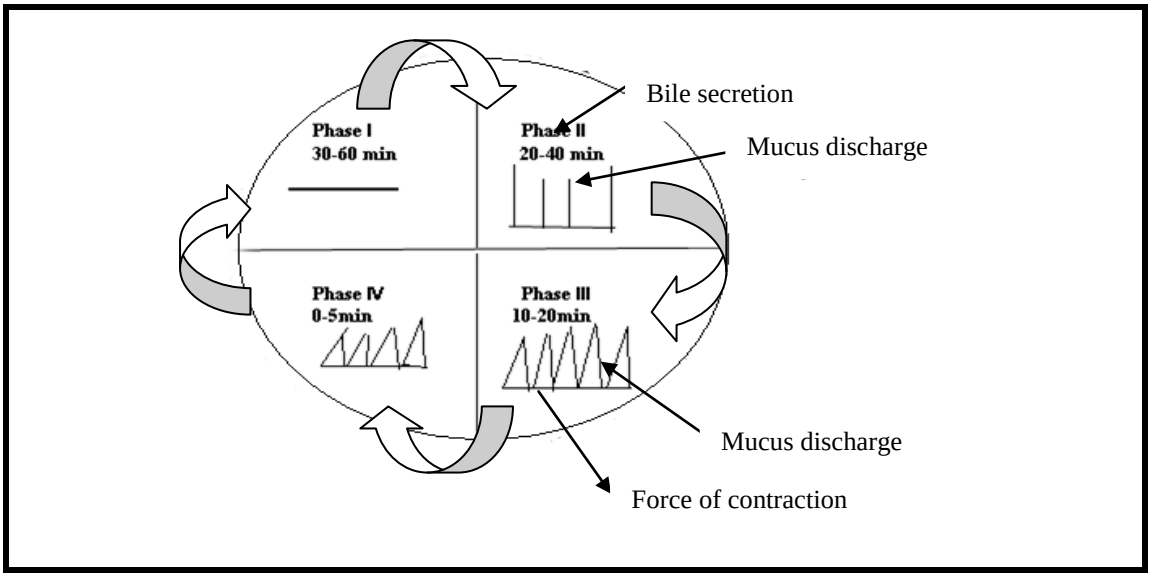


**Fig. 2: Motility Pattern in GIT.**

## FLOATING SYSTEM

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While this system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach.[19]

## CLASSIFICATION OF FLOATING SYSTEM

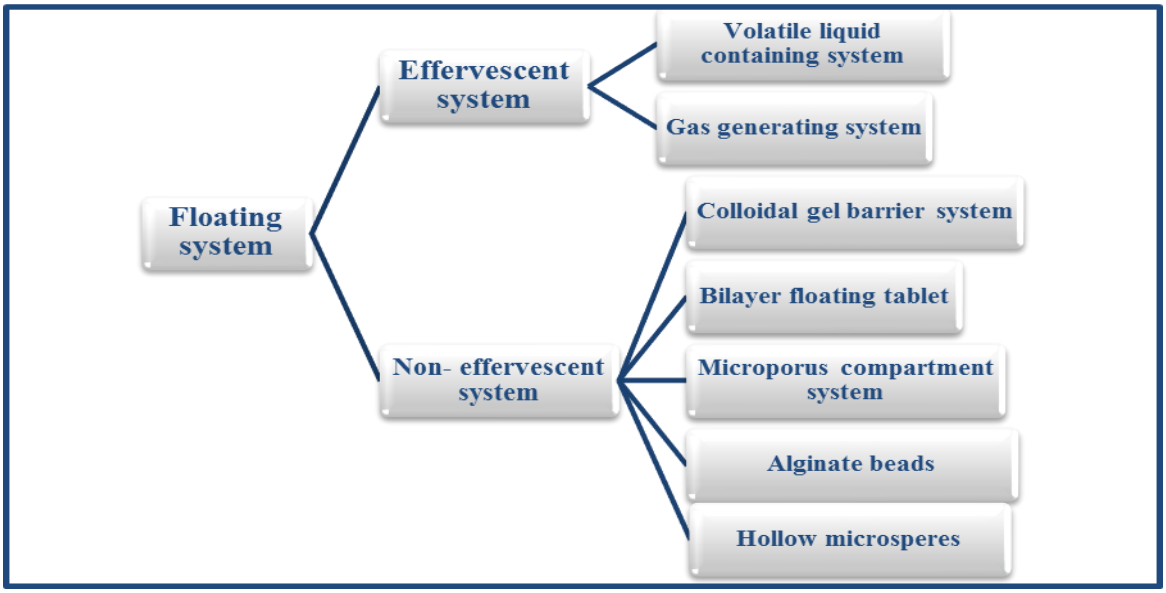


**Fig. 3: Classification of floating system.**

## EFFERVESCENT FLOATING SYSTEM

Effervescent floating systems include use of gas generating agents, carbonates (e.g. Sodium bicarbonate) and other organic acid (e.g. citric acid and tartaric acid) present in the formulation to produce carbhus reducing the density of system and making it float on the gastric fluid. An alternative used is the incorporation of matrix containing portion of liquid, which produce gas that evaporate at body temperature.[20]

These effervescent systems further classified into two types.

## VOLATILE LIQUID CONTAINING SYSTEMS

Inflatable chamber with a liquid can be incorporated which provide sustained gastric retention of drug delivery system. Liquids in this system include cyclopentane, ether that gasifies at body temperature which causes inflatation of the chamber in the stomach.

They contains hollow deformable unit which are osmotically controlled floating systems. System is divided into two compartments first compartment contains drug and there is volatile liquid in the second compartment.[21]

**GAS GENERATING SYSTEMS**

It basically contains polymers that gasify at body temperature effervescent compounds such as sodium bicarbonate, citric acid, tartaric acid, swellable polymers like methocel, and polysaccharides like chitosan. Resin beads loaded with bicarbonate and coated with ethylcellulose is the most common approach for preparation of these systems. The ethycellulose coating is insoluble but permeable to water which release carbon dioxide due to which it float.[22]

**NON-EFFERVESCENT SYSTEM**

The non effervescent FDDS supported mechanism of swelling of compound or bioadhesion to tissue layer in alimentary tract. The most normally used excipients in non effervescent FDDS are a unit gel forming or extremely swellable polysaccharide kind hydrocolloid s, polysaccharides and matrix forming material like polycarbonate, polyacrylate, polymethacrylate, phenylethylene as Well as bio-adhesive polymer such as chitosan and carbopol.The various type of this systems are as follows:[23]

**COLLOIDAL GEL BARRIER SYSTEM**

Hydrodynamically balanced system is first designed by Sheth and Tossounian. They remain buoyant in the stomach due to gel-forming hydrocolloids and this enhances GRT and increases the amount of drug at the absorption site. Various gel forming agents used in this system are highly soluble cellulose type hydrocolloids which are hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, polysaccharides and matrix forming polymers such as polycarbophil, polystyrene.[24]

**BILAYER FLOATING TABLET**

A two layer floating tablet contain two layer immediate release layer which release initial dose from system while the another sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintain a bulk density isless than unity and thereby it remains buoyant in the stomach.[25]

**MICRO POROUS COMPARTMENT SYSTEM**

In this inside the micro porous compartment which has pores in the top and bottom walls contains encapsulated drug reservoir. In drug reservoir peripheral walls are completely sealed due to this sealing direct contact of undissolved drug with gastric surface is prevented. Entrapped air in the floating chamber stimulates the system to float over gastric content. Through an aperture the gastric fluid enters which dissolves the drug for absorption across intestine.[26]

**ALGINATE BEADS**

Multiple unit dosage forms are developed from freeze dried calcium alginate. Spherical alginate beads of roughly 2.5 mm diameter can be prepared by dropping a sodium alginate solution into aqueous solution of calcium chloride, causing precipitation of calcium alginate leading to development of the porous system, which can maintain a floating force for over 12 hours. When compared with solid beads, which gave a short residence, time of 1 hour, and these floating beads gave a prolonged residence time of more than 5.5 hours.[28]

**HOLLOW MICROSPHERES**

Hollow microspheres (microballons), loaded with drug in their outer polymer shells were prepared by a novel emulsion solvent diffusion method. The ethanol: dichloromethane solution of drug and enteric acrylic polymer was emerged into an agitated aqueous solution of PVA that was thermally controlled at 400 C. The gas part originated in spread polymer droplet by evaporation of dichloromethane formed an internal cavity in microsphere of polymer with drug. The microballons floated continuously over the surface of acidic dissolution media containing surfactant for more than 12 hours *in vitro*.[27]

**MECHANISM OF FLOATING SYSTEMS**

Various aims have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introducing floating dosage forms (gas-generating systems and swelling or expanding systems), mucoadhesive systems, high-density systems, modified shape systems, gastric-emptying delaying devices and co-administration of gastric-emptying delaying drugs. Among these, the floating dosage form has been most commonly used. Floating drug delivery systems has a bulk density less than gastric fluids and so remains buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the dosage form is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of the floating drug, the remaining system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration However, besides a token viscous content needed to allow the proper accomplishment buoyancy retention principle, a smallest level of floating force (F) is additionally needed to stay the dose steady buoyant on the surface of the meal. To evaluate the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats higher if F is on the upper positive aspect. This equipment helps in modifying FDDS with regards to stability and sturdiness of floating forces created so as to stop drawbacks of unpredictable intra gastric buoyancy capability variations

**F = F buoyancy - F gravity**

**= (Df - Ds) gv**

Where, F= total vertical force, Df = fluid density, Ds = object density, v = volume and g = acceleration due to gravity.[29]

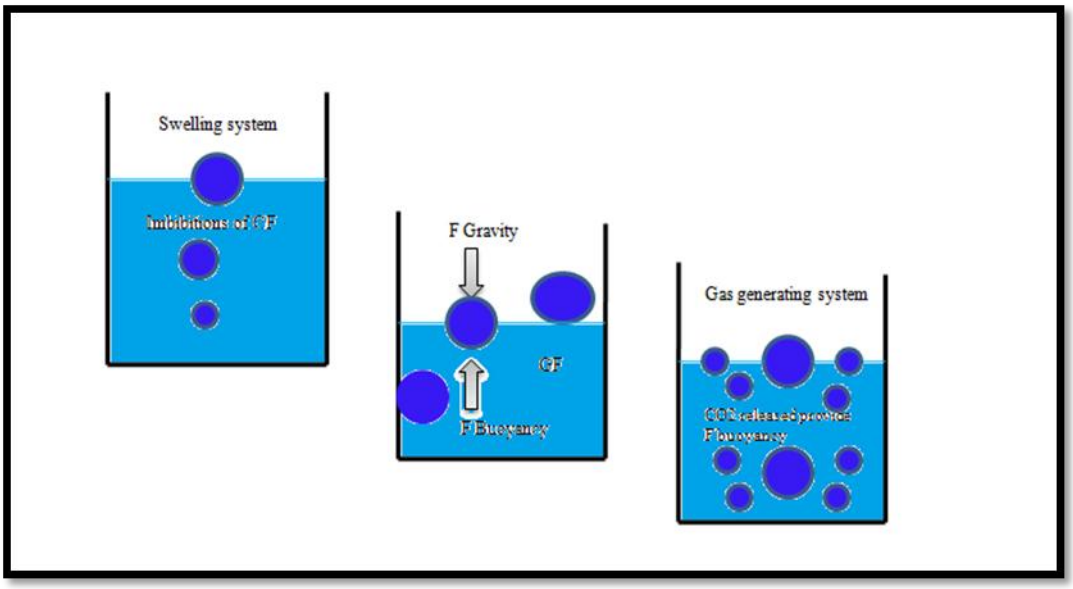


**Figure 4: Mechanism of floating systems, GF= Gastric fluid.**

**FACTORS AFFECTING GASTRIC RETENTION[30]**

**a) Idiosyncratic factors**

- **Density**: GRT is a function of dosage form buoyancy that is dependent on the density.
- **Size:** Dose units with a diameter of more than 7.5mm are reported to have an increased GRT compared with those with a diameter of 9.9mm.
- **Shape of dosage form**: Tetrahedron and ring shaped tools with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better GRT 90% to 100% retention at 24 hours compared with different shapes
- **Biological factors:** Diabetes and Crohn's disease.
- **Fed or unfed state:** under fasting conditions: GI motility is identified by periods of strong motor activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the abdomen and, if the temporal order of administration of the formulation coincides there with of the MMC, the GRT of the unit will be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.
- **Nature of meal:** feeding of undigestible polymers or fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release.
- **Caloric content**: GRT can be expanded by 4 to 10 hours with a meal that is high in proteins and fats.
- **Frequency of feed:** the GRT can expanded by over 400 minutes, when successive meals are given compared with a single meal due to the low frequency of MMC.
- **Gender:** Mean ambulatory GRT in males (3.4±0.6 hours) is low compared with their age and race matched female counterparts (4.6±1.2 hours), regardless of the weight, height and body surface.
- **Age:** Elderly people, especially those over 70, have a significantly longer GRT.
- **Posture:** GRT can vary connecting supine and upright ambulatory states of the patient.
- **Concomitant drug administration:** Anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramide and cisapride.
- **Single or multiple unit formulation:** Multiple unit formulations show a high Predictable release profile and insignificant impairing of performance due to failure of units, allow to administration of units with completely different profiles or containing incompatible substances and allow a bigger margin of safety indefinite quantity kind failure compared with single unit indefinite kind.

**b) FORMULATION FACTORS[31]**

- **SIZE OF TABLETS** Retention of floating dosage forms in stomach depends on the size of tablets. Small tablets square measure empty from the abdomen throught the biological process section, but large ones are expelled during the house keeping waves9. Floating and non floating capsules of 3 different sizes having a diameter of 4.8 mm (small units), 7.5 mm (medium units), and 9.9 mm (large units), were formulated and analyzed for their different properties. It was found that indefinite quantity units remained buoyant despite their sizes on the gastric contents throughout their residence

within the digestive tube, while the non floating dosage units sank and remained in the lower part of the stomach. Floating unit's far away from the gastro-duodenal junction were protected against the peristaltic waves throughout the biological process section whereas non floating forms stayed getting ready to the opening and were subjected to dynamic and retropelling waves of the biological process part.

- **DENSITY OF TABLETS** Density is the main important factor affecting the gastric residence time of dosage form. A buoyant indefinite quantity type having a density but that of the internal organ fluids floats, since its far away from the pyloric valve, the dosage unit is retained in the stomach for a prolonged period. A density of less than 1.0g/ml i.e. less than that of gastric contents has been reported. However, the floating force kinetics of such dosage form has shown that the bulk density of a dosage form is not the most appropriate parameter for describing its buoyancy capabilities.
- **SHAPE OF TABLETS** The shape of dosage form is one of the factors that affect its gastric residence time. Six shapes (ring polyhedron, cloverleaf, string, pellet, and disk) were screened *in vivo* for their gastric retention potential. The tetrahedron (each leg 2cm long) rings (3.6 cm in diameter) exhibited nearly 100% retention at 24 hr.
- **VISCOSITY GRADE OF POLYMER** Drug release and floating properties of FDDS are greatly affected by viscosity of polymers and their interaction. Low viscosness polymers (e.g., HPMC K100 LV) were found to be more beneficial than high viscosity polymers (e.g., HPMC K4M) in improving floating properties. In addition, a decrease in the release rate was observed with an increase in polymer viscosity.

**APPROACHES TO GASTRORETENTION** Several techniques are reported in the literature to increase the gastric retention of drugs.[32- 35]

1) **HIGH DENSITY SYSTEMS** These systems, which have a density of ~3g/cm3, are retained in the rugae of stomach and capable of withstanding its peristaltic movements18, 20. The only major disadvantage with these systems is that it's technically difficult to manufacture them with an oversize quantity of drug (>50%) and attain needed density of 2.4-2.8g/cm3. Diluents such as barium sulphate (density= 4.9), zinc oxide, titanium oxide, and iron powder must be used to manufacture such high-density formulation.[32]
2) **SWELLING AND EXPANDING SYSTEM** These systems are also called as "Plug type system", since they exhibit tendency to remain logged in the pyloric sphincters. These polymeric matrices remain in the gastric cavity for several hours by selection of polymer with the proper molecular weight and swelling properties controlled and sustained drug release can be achieved. Upon returning in touch with gastric fluid, the polymer imbibes water and swells. The in depth swelling of those compounds may be a result of the presence of physical-chemical cross links within the deliquescent polymer network. These cross link prevents the dissolution of polymer and thus maintain the physical integrity of the dosage form. A high degree of cross linking retards the swelling ability of the system and maintains its physical integrity for prolonged period of time. On the opposite hand, a low degree of cross linking results in extensive swelling followed by the rapid dissolution of polymer.[38]
3) **INCORPORATING DELAYING EXCIPIENTS** Another detained gastric emptying approach of interest include feeding of digestible polymers or fatty acid salts that charges the motility pattern, of the stomach to a fed stage thereby decreasing the gastric emptying rate and permitting considerable prolongation of the drug release. Prolongation of GRT of drug delivery system consists of incorporating delaying excipients like trietanolamine myristate in a delivery system.[39]
4) **MODIFIED SYSTEMS** with non disintegrating geometric appearance molded from silastic elastomers or extruded from polyethylene blends, which extend the GRT depending on size, shape and flexural modules of drug delivery device.[40]
5) **MUCOADHESIVE & BIOADHESIVE SYSTEM** Bioadhesive drug delivery systems are used to localize a delivery device within the lumen to enhance the drug absorption in a site specific manner. This approach involves the utilization of bioadhesive polymers, which can adhere to the epithelial surface in the stomach. Some of the for most promising excipients that are used usually in these systems embrace polycarbophil, carbopol, lectins, chitosan, CMC and gliadin, etc.[41,42]
6) **FLOATING SYSTEMS** Floating drug delivery systems have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the internal organ, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach [43]. Floatation of a drug delivery system within the abdomen is achieved by incorporating floating chamber full of vacuum, air, or inert gas.

**FORMULATION EXCIPIENTS USED IN FDDS[44, 45, 46]**

1) **Polymers** The following polymers used in preparations of FDDS -HPMC K4 M, Calcium alginate, Eudragit S100, Eudragit RL, Propylene foam, Eudragit RS, ethyl cellulose, poly methyl methacrylate, Methocel K4M, Polyethylene oxide, β Cyclodextrin,HPMC 4000, HPMC 100, CMC, Polyethylene glycol, polycarbonate, PVA, Polycarbonate, Sodium alginate, HPC-L, CP 934P, HPC, Eudragit S, HPMC, Metolose S.M. 100, PVP, HPC-H, HPC-M, HPMC K15, Polyox, HPMC K4, Acrylic polymer, E4 M and Carbopol.

2) **Inert fatty materials (5%-75%)** Edible, inert fatty material having a specific gravity of less than one can be used to decrease the hydrophilic property of formulation and hence increase buoyancy. E.g. Beeswax, fatty acids, long chain fatty alcohols, Gelucires 39/01 and 43/01.
3) **Effervescent agents** Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di-Sodium Glycine Carbonate, CG (Citroglycine).
4) **Release rate accelerants (5%-60%)** eg. lactose, mannitol.
5) **Release rate retardants (5%-60%)** eg. Dicalciumphosphate,talc, magnesium stearate.
6) **Buoyancy increasing agents (upto80%)** eg. Ethyl cellulose.
7) **Low density material** Polypropylene foam powder (AccurelMP 1000).

**METHODS OF PREPARATION**

**1. METHODOLOGY FOR SINGLE LAYER FLOATING TABLETS:** Basically single layer floating tablets are prepared by compression methods. For this normally three basic compression methods are used. They are as follows:-

- Direct compression,
- Dry granulation,
- Wet granulation.
- **DIRECT COMPRESSION METHOD:** Direct compression is the process of compressing tablets directly from powdered materials without modifying physical nature of materials into the tablets. This method is used for crystalline chemicals having good compressible characteristic and flow properties such as: Potassium salt (chloride, chlorate, bromide), Ammonium chloride, Sodium chloride, Methenamine etc. Compressed pills are prepared by single compression using tablet machines. After a quantity of powdered or granulated tabletting material flow into a die, the upper and lower punches of the tablet machine compress the material under a high pressure (~tons/in2).
- **DRY GRANULATION METHOD:** It is defined as the formation of granules by slugging, if the tablet ingredients are sensitive to moisture and/or unable to withstand elevated temperature during drying
- **WET GRANULATION METHOD:** In wet granulation the active ingredient, diluents and disintegrants are mixed or blended well in a rapid mixer granulator (RMG). The RMG could be a multi-purpose chopper that consists of an impeller and a chopper and is is employed to prime speed dispersion of dry powders and binary compound or solvent granulations. Moist materials from wet edge steps are placed on massive trays and placed in drying chambers with a current wind and thermo stable heat controller. Commonly used dryers are tray dryer, fluidized bed dryer. After drying, the granules are reduced in particle size by passing through smaller mesh screen. After this, the lubricating substance or glidant is added as fine powder to promote flow of granules. These granules are then compressed to urge a tablet. Dry granulation when compared with wet granulation has a shorter, more cost-effective manufacturing process. Because it does not entail heat or moisture, dry granulation is especially suitable for active ingredients that are sensitive to solvents, or labile to moisture and elevated temperatures

**2. METHODOLOGY FOR BILAYER FLOATING TABLETS**

- Oros ® Push Pull Technology
- L-Oros Tm Technology
- DUROS Technology
- Elan Drug Technologies' Dual Release Drug Delivery System
- EN SO TROL Technology
- Rotab Bilayer
- Geminex Technology

- **OROS ® PUSH PULL TECHNOLOGY**
- It is two or three layer system, a drug layer and push layer. Drug layer contain drug with alternative agents and because of this drug is a smaller amount soluble. Sometimes suspending agent and diffusion agent also are other. The pill core is enclosed by semi semi permeable membrane.

- **L-OROS TM TECHNOLOGY**
- Alza developed L-OROS system due to solubility problem. The system contain a drug in dissolved state in a lipid soft gel product which is produced first and then barrier membrane, after which osmotic membrane and semi permeable membrane coat is applied and is then trained out through opening.

- **DUROS TECHNOLOGY**
- This technology is also known as miniature drug dispensing system which works like a miniature syringe and release small quantity of drug consistently over a period of time .There is Associate in Nursing outer cylindrical metallic element alloy reservoir that has high impact strength because of that drug molecules within it are shielded from enzymes.

- **ELAN DRUG TECHNOLOGIES' DUAL RELEASE DRUG DELIVERY SYSTEM**
  The DUREDASTM Technology provides combination release of drugs together and different release pattern of single drug i.e. it provides sustained unharness furthermore as immediate unharness. This technology provides various advantages i.e. two drug components provide tailored release and it's another benefit is that it consist of bilayered tablet technology in which it contain modified as well as immediate release

pattern in one tablet. In these different controlled release formulations are combined together.

**EN SO TROL TECHNOLOGY**

- An integrated approach is used by Shire laboratory for drug delivery system which focuses on identification and incorporation of enhancer which is identified to form optimized dosage form in controlled release system. By this enhancement in solubility is achieved.

**• ROTAB BILAYER**

- RoTab bilayer when using is switched to production mode. Dose and compression force is mechanically regulated by adjusting filling speed and die table. Hardness is also regulated when required.

**• GEMINEX TECHNOLOGY**

- In this drug delivery system at different times more than one drug can be delivered. This technology essentially will increase the therapeutic effectiveness of the drug by decreasing its facet effects. It is useful both to industry as well as patient as in single tablet it provides delivery of drug at different rates.[47]

- **IN VITRO AND IN VIVO EVALUATION PARAMETERS OF STOMACH SPECIFIC FDDS** Different studies reported within the literature indicate that pharmaceutical dose exhibiting gastric residence in vitro floating behavior show prolonged internal organ residence in vivo. Although, in vitro floating behavior alone is not adequate proof for economical gastric retention therefore *in vivo* studies will offer definite proof that prolonged gastric residence is obtained.

- **HARDNESS, FRIABILITY, ASSAY, CONTENT UNIFORMITY (TABLETS)** these tests are performed as per represented in fixed monographs.

- **FLOATING LAG TIME AND TOTAL FLOATING TIME DETERMINATION** The time between the introduction of the pill into the medium and its rise to higher one third of the dissolution vessel is termed as floating lag time and also the time that the indefinite quantity kind floats is termed because the floating or flotation time. These tests are typically performed in simulated internal organ fluid or 0.1 mole.lit-1 HCl maintained at 37o C, by mistreatment USP dissolution equipment containing 900 mil of 0.1 molar HCl because the dissolution medium.[48]

- **DRUG RELEASE**

The take a look at for in vitro drug release studies are typically allotted in simulated internal organ and enteric fluids maintained at 370 C. Dissolution tests are performed mistreatment the USP dissolution equipment. Samples are withdrawn sporadically from the dissolution medium, replaced with a similar volume of recent medium every time, so analyzed for his or her drug contents once associate degree applicable dilution. Recent methodology as delineated in USP XXIII states that the indefinite quantity unit is allowed to sink to all-time low of the vessel before rotation of blade is started. A small, loose piece of non reactive material like no more than many turns of wire helix is also connected to the indefinite quantity units that may otherwise float. However, normal dissolution ways supported the USP or British accumulation (BP) is shown to be poor predictors of in vitro performance for floating indefinite quantity forms.

**DRUG LOADING, DRUG ENTRAPMENT EFFICIENCY, PARTICLE SIZE ANALYSIS, SURFACE CHARACTERIZATION, MICROMERITICS STUDIES AND PERCENTAGE YIELD (FOR FLOATING MICROSPHERES AND BEADS)** Drug loading is assessed by crushing accurately weighed sample of beads or microspheres during a mortar and another to the acceptable dissolution medium that isthencentrifuged, filteredand analysed by varied analytical ways like spectrophotometry. The share drug loading is calculated by dividing the number of drug within the sample by the burden of total beads or microspheres. The particle size and also the size distribution of beads or microspheres are determined within the dry state mistreatment the optical research methodology. The external and cross-sectional morphology (surface characterization) is completed by scanning microscope (SEM). The measured weight of ready microspheres was divided by total quantity of all non-volatile parts used for the preparation of microspheres, which is able to offer the full proportion yield of floating microspheres.[49, 50]

- **RESULTANT WEIGHT DETERMINATION**

Bulk density and floating length are the most parameters to explain the adequacy of a indefinite quantity type's buoyancy though single density determination doesn't predict the floating force evolution of the indefinite quantity type as a result of the dry material of it's created increasingly reacts or interacts with within the stomachal fluid to unleash its drug contents ``So to calculate real floating capabilities of indefinite quantity form as a perform of your time a unique methodology has been planned. It operates by force cherish the force F needed to stay the article wholly submerged within the fluid. This force determines the resultant weight of the article once immersed and will be accustomed quantify its floating or non floating capabilities. The magnitude and direction of the force and also the resultant weight corresponds to the Victoria add of buoyancy (Fbuoy) and gravity (Fgrav) forces functioning on the objects as shown within the equal

F = Fbuoy – Fgrav

F = dfgV – dsgV = (df-ds) gV
F = (df – M/V) gV

- In which the F is total vertical force (resultant weight of the object), g is that the acceleration thanks to gravity, df if the fluid density, ds is that the object density is that the object mass and V is that the volume of the article.

- **WEIGHT GAIN AND WATER UPTAKE (WU)**

Weight gain or water uptake is studied by considering the swelling behavior of Floating indefinite quantity type. The study is completed by immersing the indefinite quantity type in simulated stomachal fluid at 37oC and determinative the dimensional changes like pill diameter and/ or thickness at regular 1-h time intervals till twenty four h, the tablets were far away from beaker, and also the excess surface liquid was removed fastidiously victimisation the paper. The swollen tablets were then reweighed and Shanghai dialect is measured within the terms of % weight gain, as given by equation

$$WU = (Wt – Wo) X 100 / Wo$$

Within which Wt and Wo area unit the weights of the indefinite quantity type at time t and ab initio, respectively11.

- **XRAY/ GAMMA SCINTIGRAPHY**

For in vivo studies, X-Ray/Gamma Scintigraphy is that the main analysis parameter for floating indefinite quantity type. In every experiment, the animals area unit allowed to quick long with free access to water, and a exposure is created simply before the administration of the floating pill to confirm the absence of radio-opaque material. visual image of indefinite quantity type by X-ray is thanks to the inclusion of a radio-opaque material. The formulation is run by natural swallowing followed by fifty cc of water. The picture taking imaging is taken from every animal during a standing position, and also the distance between the supply of X-rays and also the animal ought to unbroken constant for all imaging, so the pill movement can be simply noticed. Stomachal radiography was done at 30-min time intervals for a amount of five h victimisation AN X-ray machine. Gamma scintigraphy could be a technique whereby the transit of a indefinite quantity type through its meant web site of delivery is non-invasively imaged in vivo via the considered introduction of AN applicable short lived gamma emitting isotope. The inclusion of a γ-emitting radionucleide during a formulation permits indirect external observation employing a γ-camera or scintiscanner. however the most downside of γ-scintigraphy area unit the associated radiation for the patient, the restricted geography info, low resolution inherent to the technique and also the sophisticated and high-priced preparation of pharmaceutical.[51,52]

- **PHARMACOKINETIC STUDIES** Pharmacokinetic studies include AUC (Area under Curve), Cmax, and time to reach maximum plasma concentration (Tmax) were estimated using a computer. Statistical analyses were performed using a Student t test with p, 0.05 as the minimal level of significance.[53]

- **SPECIFIC GRAVITY** Displacement method is used to determine the specific gravity of floating system using benzene as a displacing medium.[54]

- **FLOATING PROPERTIES** Effect of formulation variables on the floating properties of gastric floating drug delivery system was determined by using continuous floating monitoring system and statistical experimental design.[55]

- **SURFACE TOPOGRAPHY** The surface topography and structures were determined using scanning electron microscope (SEM, JEOL JSM – 6701 F, Japan) operated with an acceleration voltage of 10k.v, Contact angle meter, Atomic force microscopy (AFM), and Contact profiliometer.[56]

- **DETERMINATION OF MOISTURE CONTENT** The water content per se is seldom of interest. Rather, it shows whether or not a product supposed for trade and production has standard properties like
- Storability
- Agglomeration in the case of powders
- Microbiological stability
- Flow properties, viscosity
- Dry substance content
- Concentration or purity
- Commercial grade (compliance with quality agreements)

Thus moisture content of the prepared formulations was determined by Karl fisher titration, vacuum drying, Thermo gravimetric methods, Air oven method, Moisture Meters, Freeze drying as well as by physical methods.[57]

- **SWELLING STUDIES** Swelling studies were performed to calculate molecular parameters of swollen polymers**.** Swelling studies was determined by using Dissolution apparatus, optical microscopy and other sophisticated techniques which include H1NMRimaging, Confocal laser scanning microscopy (CLSM), Cryogenic scanning electron microscopy (Cryo SEM), Light scattering imaging (LSI) etc. The swelling studies by using Dissolution apparatus (USP disso-lution apparatus (usp-24) lab india disso 2000) was calculated as per the following formula.[58]

Swelling ratio = Weight of wet formulation / Weight of formulations

- **DETERMINATION OF THE DRUG CONTENT** Percentage drug content provides how much amount of the drug that was present in the formulation. It should not exceed the limits acquired by the

standard monographs. Drug content was determined by using HPLC, HPTLC methods, Near infrared spectroscopy (NIRS), Micro titrimetric methods, Inductively Coupled Plasma Atomic Emission Spectrometer (ICPAES) and also by using spectroscopy techniques (Elico Limited, Hyderabad).[59]

- **PERCENTAGE ENTRAPMENT EFFICIENCY** Percentage entrapment efficiency was reliable for quantifying the phase distribution of drug in the prepared formulations. Entrapment efficiency was determined by using three methods such as Micro dialysis method, Ultra centrifugation, and pressure Ultra filtration.[60]

- **IN-VITRO RELEASE STUDIES** In vitro release studies (USP dissolution apparatus (usp-24) lab india disso 2000) were performed to provide the amount of the drug that is released at a definite time period. Release studies were performed by using Franz diffusion cell system and synthetic membrane as well as different types of dissolution apparatus.[62]

- **POWDER X-RAY DIFFRACTION** X-ray powder diffraction (Philips analytical, model-pw1710) is the predominant tool for the study of poly-crystalline materials and is eminently suited for the routine characterization of pharmaceutical solids. Samples were irradiated with α radiation and analyzed between 2 ºC and 60 ºC .The voltage and current used were 30KV and 30mA respectively.[61]

- **FOURIER TRANSFORMS INFRARED ANALYSIS** Fourier transform infrared spectroscopy (FT-IR, Shimadzu, Model-RT-IR-8300) is a technique mostly used to identify organic, polymeric, and some inorganic materials as well as for functional group determination. Fourier Transform Infrared Analysis (FT-IR) measurements of pure drug, polymer and drug loaded polymer formulations were obtained on FT-IR. The pellets were prepared on KBr press under hydraulic pressure of 150kg/cm2; the spectra were scanned over the wave number range of 3600 to 400 cm-1 at the ambient temperature.[61]

- **DIFFERENTIAL SCANNING CALORIMETRY (DSC)** DSC (Shimadzu, Model-DSC-60/DSC-50/ Metler Toldeo) are used to characterize water of hydration of pharmaceuticals .Thermo grams of formulated preparations were obtained using DSC instrument equipped with an intercooler. Indium/Zinc standards were used to measure the DSC temperature and enthalpy scale. The sample preparations were hermitically sealed in an aluminium pan and heated at a constant rate of 10°C/min; over a temperature range of 25° C – 65°C. Inert atmosphere was maintained by purging nitrogen gas at the flow rate of 50ml/min.[61]

- **DISSOLUTION STUDIES** The dissolution test are generally performed for calculating the amount of drug release using USP dissolution apparatus.[62] The test is performed using 900ml of 0.1 N HCL, at 37ºC and 100 rpm.[63] A sample of 10 ml is withdrawn hourly and analysed under u.v and absorbance is measured. The sample is replaced by the dissolution media[64] Cumulative percentage is calculated using equation obtaine from standard curve.[65, 66]

- **X-ray / gamma scintigraphy** It helps to locate dosage form in the GIT by which one can predict and correlate the gastric emptying time and the passage of dosage form in the git. The inclusion of a radio opaque material into solid dosage form enables it to be visualized by the X-ray.[67] The inclusion of a gamma emitting radionuclide in the formulation allows indirect external observation using gamma camera, the gamma rays emitted by radionuclide is focused on the camera which helps to monitor the location of the dosage form.[68]

**APPLICATIONS OF FLOATING DRUG DELIVERY SYS-TEMS**

**1. ENHANCED BIOAVAILABILITY** The bioavailability of vitamin B2 atomic number 24-GRDF is considerably increased as compared to the administration of non-GRDF CR chemical compound formulations. There are many completely different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act con-comitantly to influence the magnitude of drug absorption.

**2. SUSTAINED DRUG DELIVERY** Oral CR formulations are encountered with issues like gastric residence time in the GIT. These prob-lems can be overcome with the HBS systems which can remain in the stomach for long periods and have a bulk density <1 as a result of which they can float on the gastric contents. These systems are relatively larger in size and passing from the pyloric opening is prohibited.

**3. SITE –SPECIFIC DRUG DELIVERY SYSTEMS** These systems are particularly advantageous for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine .The controlled, slow delivery of drug to the stomach provides suffi-cient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also reduce the dosing frequency. Eg: Furosemide and Riboflavin.

**4. ABSORPTION ENHANCEMENT** Drugs which are having poor bioavailability because of site specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, there by maximizing their ab-sorption.

**5. MINIMIZED ADVERSE ACTIVITY AT THE COLON** Retention of the drug in the HBS systems at the sto-mach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This Pharmacodynamic aspect pro-vides the rationale for GRDF formulation for betalac-tam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance.

**6. REDUCED FLUCTUATIONS OF DRUG CONCENTRA-TION**

Continuous input of the drug following CRGRDF admin-istration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse ef-fects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.[69]

## CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. Gastro-retentive floating drug delivery systems have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs. FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing towards commercializing this technique. The prolong gastric retention of the dosage form extends the time for drug absorption is now available in floating drug delivery system. Floating controlled drug delivery systems are employed to solve this problem. It also provide intimate contact between a dosage form and the absorbing tissue which may result in high drug concentration in a local area and hence, high drug flux through the absorbing tissue, producing the pharmacological effect for extended period of time with maximum bioavailability and less side effects for drugs that are absorbed primarily in the upper part of GI tract, i.e., the stomach, duodenum, and jejunum. The increasing delivery technology will ensure the development of increase number of gastroretentive drug delivery to optimize the delivery of molecules that exhibit absorption window, low bioavailability and extensive first pass metabolism.

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