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“Floating Drug Delivery System And its Applications: An Overview”.

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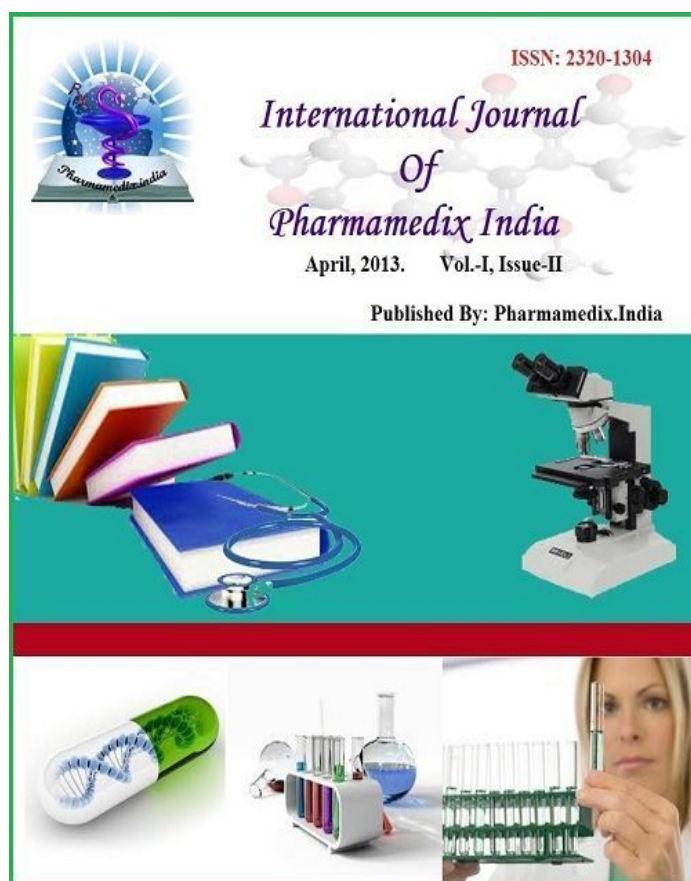
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Abstract:

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 including the physiological and formulation variables affecting gastric retention, approaches to design single-unit and multiple-unit floating systems, and their classification and formulation aspects are covered in detail. This review also summarizes the *in vitro* techniques, *in vivo* studies to evaluate the performance and application of floating systems, and applications of these systems. These systems are useful to several problems encountered during the development of a pharmaceutical dosage form.

Keywords: Evaluation *in vitro* and *in vivo*, floating drug delivery systems, multiple units, single unit.

Introduction:

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract. Drug absorption from the gastrointestinal tract is a complex procedure and is subject to many variables. It is widely acknowledged that the extent of

gastrointestinal tract drug absorption is related to contact time with the small intestinal mucosa^[1] Thus, small intestinal transit time is an important parameter for drugs that are incompletely absorbed. Basic human physiology with the details of gastric emptying, motility patterns, and physiological and formulation variables affecting the gastric emptying are summarized. Gastroretentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the

stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients. The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion^[2,3] flotation^[4] sedimentation^[5,6] expansion,^[7,8] modified shape systems,^[9,10] or by the simultaneous administration of pharmacological agents^[11,12] that delay gastric emptying. Based on these approaches, classification of floating drug delivery systems (FDDS) has been described in detail. In vivo/in vitro evaluation of FDDS has been discussed by scientists to assess the efficiency and application of such systems^[13,14]. Several recent examples have been reported showing the efficiency of such systems for drugs with bioavailability problems.

Basic git physiology^[15,16]

Anatomically the stomach is divided into three regions:

Fundus, Body and Antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested materials, whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions^[17]. Gastric emptying occurs in both the fasting and fed states. During the fasting state an interdigestive series of electrical events take place which cycle both through stomach and intestine every 2-3 hrs^[18] which

is called as interdigestive myoelectric cycle or migrating myoelectric cycle (MMC) which is further divided into four phases. After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state which is also termed as digestive motility pattern.

1. Phase 1-(Basic phase)-last from 30-60 minutes with rare contractions.
2. Phase 2-(Preburst phase)-last for 20-40 minutes with intermittent action potential and contractions.
3. Phase 3-(Burst phase)- last for 10-20 minutes which includes intense and regular contractions for short period.
4. Phase 4-last for 0-5 minutes and occurs between phase 2 and 1 of 2 consecutive cycles (Fig1).

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state which is also termed as digestive motility pattern.

factors influencing gastric retention:

Gastric residence time of an oral dosage form is influenced by many factors. To pass through the pyloric size should be in the range of 1-2 mm^[19]. The pH of the stomach in fasting state and fed state are 1.5-2.0 and 2.0-6.0 respectively. A large volume of waste administered in oral dosage form raises the pH of the stomach contents to 6-9. The rate of gastric emptying depends mainly on viscosity, volume and

caloric contents of meals. It does not make any difference whether the meal has high protein, fat or carbohydrate contents as long as the caloric content is the same while there is decrease in gastric emptying time by increasing acidity and caloric value. Other factors influences such as biological factors which includes age, body mass, index, gender, posture and diseased states (Hepatic failure, Diabetes, Chrons' disease). In case of elderly persons gastric emptying is slowed down. Females have slower gastric emptying rates than that of males. Stress increases the gastric emptying rates where as depression slows it down. Volume of liquids administered also effects the gastric emptying time. Larger the liquid content, faster the emptying. Several formulations parameters can effect the gastric residence time such as size, shape, density, diameter etc of the dosage unit which affects gastric emptying^[20]. Out of all ring shaped devices have better gastric rates when compared to all other shapes. Formulations having a diameter more than 7.5mm shows better gastric residence time compared with formulations having 9.9mm. Density of a dosage form influences the gastric emptying rate. buoyant dosage form having a density of less than that of the gastric fluids. So the unit is retained in the stomach for a prolonged period.

floating drug delivery system:

Floating systems or Hydrodynamically

controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal (Fig 1). Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres. Table 1 enlists examples of various drugs formulated as different forms of FDDS

approaches to gastric retention

Various approaches have been pursued to increase the retention of an oral dosage form in the stomach, for example, bioadhesive approach in which the adhesive capacity of some polymer with glycoprotein is closely applied to the epithelial surface of stomach.

Other approaches include: high density and low density approach.

1) high density

approach

For preparing such type of formulations, the density of the pellets should be higher than the stomach fluid. It would be at least 1.50 g/ml. In this type, the drug can be coated or mixed with heavy, non-toxic materials such as barium sulfate, titanium dioxide, etc.

2) low density

approach

Floating systems come under low density approach. In this approach, the density of pellets should be less than 1 g/ml, so as to float the pellets or tablets in the gastric fluid and, release the drug slowly for a longer period of time. This type is also called as Hydrodynamically Balanced System (HBS).

approaches To Design Floating Dosage Forms^[21]:

The following approaches have been used for the design of floating dosage forms of single and multiple units

single-unit dosage forms:

In low density approaches, the globular shells apparently having lower density than that of gastric fluid can be used as a carrier for drug for its controlled release. A buoyant dosage form can also be obtained by using a fluid-filled system that floats in the stomach. In coated shells^[22] popcorn, poprice, and polystyrol have been exploited as drug carriers. Sugar polymeric materials such as methacrylic polymer and cellulose acetate

phthalate have been used to undercoat these shells. These are further coated with a drug-polymer mixture. The polymer of choice can be either ethylcellulose or hydroxypropyl cellulose depending on the type of released desired. Finally the product floats on the gastric fluid while releasing the drug gradually over a prolonged duration. Fluid-filled floating chamber type of dosage forms includes incorporation of a gas-filled floatation chamber into a microporous component that houses a drug reservoir^[23]. Aperture or opening are present along the top and bottom walls through which the gastrointestinal fluid enters to dissolve the drug. The other two walls in contact with the fluid are sealed so that the undissolved drug remains therein. The fluid present could be air, under partial vacuum or any other suitable gas, liquid, or solid having an appropriate specific gravity and an inert behavior. The device is of swallowable size, remains afloat within the stomach for a prolong time, and after the complete release the shell disintegrates, passes off to the intestine, and is eliminated.

Hydrodynamically balanced systems (HBS) are designed to prolong the stay of the dosage form in the gastro intestinal tract and aid in enhancing the absorption. Such systems are best suited for drugs having a better solubility in acidic environment and also for the drugs having specific site of absorption in the upper part of the small intestine. To

remain in the stomach for a prolong period of time the dosage form must have a bulk density of less than 1. It should stay in the stomach, maintain its structural integrity, and release drug constantly from the dosage form. Single unit formulations are associated with problems such as sticking together or being obstructed in the gastrointestinal tract, which may have a potential danger of producing irritation.

multiple-unit dosage forms

The purpose of designing multiple-unit dosage form is to develop a reliable formulation that has all the advantages of a single-unit form and also is devoid of any of the above mentioned disadvantages of single-unit formulations. In pursuit of this endeavor many multiple- unit floatable dosage forms have been designed. Microspheres have high loading capacity and many polymers have been used such as albumin, gelatin, starch, polymethacrylate, polyacrylamine, and poly alkyl cyanoacrylate. Spherical polymeric microsponges also referred to as “microballoons” have been prepared. Microspheres have a characteristic internal hollow structure and show an excellent in vitro floatability^[24]. In Carbon dioxide-generating multiple-unit oral formulations several devices with features that extend, unfold, or are inflated by carbon dioxide generated in the devices after administration have been described. These dosage forms are excluded from the passage of the pyloric

sphincter if a diameter of ~12 to 18 mm in their expanded state is exceeded.

advantages of floating drug delivery^[24-27]

- Enhanced bioavailability
- Enhanced first-pass biotransformation
- Sustained drug delivery/reduced frequency of dosing
- Targeted therapy for local ailments in the upper GIT
- Reduced fluctuations of drug concentration
- Reduced counter-activity of the body
- Extended time over critical (effective) concentration
- Minimized adverse activity at the colon
- Site specific drug delivery
- stomach for drug delivery to float and work efficiently

limitations^[28,29].

- Not suitable for drugs that have solubility or stability problem in GIT.
- Drugs such as nifedipine which is well absorbed along the entire GIT and which undergoes first pass metabolism, may not be desirable.
- Drugs which are irritant to gastric mucosa are also not suitable.
- The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the systems.
- The dosage form should be administered with a full glass of water (200-250 ml).

- These systems are not advantageous over the conventional dosage forms for those drugs, which are absorbed throughout the gastrointestinal tract

mechanism of floating of floating effervescent tablet:^[30]

When the dosage form administered it contact with gastric fluid and produce effervescent and evolved CO₂ gas. This support to penetrate the fluid in tablet and float, the low density polymer HPMC various grade provide low density system so it buy out efficiently in gastric fluid. The system is as design to float and shows sustains release for better patient compliance and reduces dose frequency and adverse effect of drug.

classification of floating drug delivery:

Floating drug delivery systems are classified depending on the use of two formulation variables: effervescent and non-effervescent systems.

A. non-effervescent systems

a) colloidal gel barrier systems:

Hydrodynamically balanced system (HBS) of this type contains drug with gel forming or swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers. They help prolonging the GI residence time and maximize drug reaching its absorption site in the solution form ready for absorption. These systems incorporate high levels (20 to 75 % w/w) of one or more gel forming highly

swellable cellulose type hydrocolloids e.g. hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC), hydroxypropyl methylcellulose (HPMC), sodium carboxy methyl cellulose (NaCMC) incorporated either in tablets or capsules. When such a system comes in contact with the gastric fluid, the hydrochloride in the system hydrates and forms a colloidal gel barrier around its surface. This gel barrier controls the rate of the fluid penetration into the device and consequent release of drug from it. As the exterior surface of the dosage form goes in to the solution, the adjacent hydrochloride layer becomes hydrated and thus maintains the gel layer. The air trapped inside the swollen polymer maintains the density less than unity and confers buoyancy to these dosage forms^[31].

The HBS must comply with following three major criteria:

1. It must have sufficient structure to form cohesive gel barrier.
2. It must maintain an overall specific density lower than that of gastric contents.
3. It should dissolve slowly enough to serve as reservoir for the delivery system.

A bilayer tablet can also be prepared to contain one immediate release and other sustained release layer. Immediate release layer delivers the initial dose whereas sustained release layer absorbs gastric

fluid and forms a colloidal gel barrier on its surface. This results in system with bulk density lesser than that of gastric fluid and allows it to remain buoyant in the stomach for an extended period of time^[32].

A multi-layer, flexible, sheath-like device buoyant in gastric juice showing sustained release characteristics have also been developed. The device consists of at least one dry self-supporting carrier film made up of water insoluble polymer matrix having a drug dispersed/dissolved therein, and a barrier film overlaying the carrier film. Both carrier and barrier films are sealed together along their periphery and in such a way as to entrap a plurality of small air pockets, which bring about the buoyancy to the laminated films.

b) micro porous compartment system:

This technology is comprised of encapsulation of a drug reservoir inside a micro porous compartment with pores along its top and bottom surfaces. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of gastric mucosal surface with undissolved drug. In stomach, the floatation chamber containing entrapped air causes the delivery system to float over the gastric contents. Gastric fluid enters through the pores, dissolves the drug and carries the dissolved drug for continuous transport across the intestine for absorption. Intra-gastric floating and

sustained release granules of Diclofenac sodium were developed using hydroxypropyl cellulose, ethyl cellulose and calcium silicate as floating carriers which had a characteristically porous structure with numerous pores and a large individual pore volume. The coated granules acquired floating ability from the air trapped in the pores of calcium silicate when they were coated with a polymer.

c) alginate beads:

Multiple unit floating dosage forms have been developed from freeze-dried calcium alginate. Spherical beads of approximately 2.5 mm in diameter were prepared by dropping a sodium alginate solution into aqueous solution of calcium chloride, causing a precipitation of calcium alginate. These beads were then separated; snap frozen in liquid nitrogen and freeze-dried at -40°C for 24 hrs, leading to formation of porous system that maintained floating force for over 12 hrs. They were compared with non-floating solid beads of same material. The latter gave a short residence time of 1 hr, while floating beads gave a prolonged residence time of more than 5.5 hrs¹⁰. Floating systems comprising of calcium alginate core separated by an air compartment from a membrane of calcium alginate or a calcium alginate/polyvinyl alcohol (PVA) have also been developed. The porous structure generated by leaching of PVA (water

soluble additive in coating composition) was found to increase membrane permeability and thus preventing the collapse of air compartment.

d) hollow microspheres :Hollow microspheres (micro balloons), loaded with ibuprofen in their outer polymer shells were prepared by novel emulsion solvent diffusion method. The ethanol: dichloromethane solution of the drug and an enteric acrylic polymer were poured into agitated aqueous solution of PVA that was thermally controlled at 40⁰c. The gas phase was generated in dispersed polymer droplet by evaporation of dichloromethane and formed an internal cavity in micro sphere of polymer with drug (Fig 6). These micro balloons floated continuously over surface of acidic solution media that contained surfactant, for greater than 12 hrs *in vitro*.The drug release was high in pH 7.2 than in pH 6.8 ^[33-34].

B. effervescent systems:

A drug delivery system can be made to float in the stomach by incorporating a floating chamber, which may be filled with vacuum, air or inert gas. The gas in floating chamber can be introduced either by volatilization of an organic solvent or by effervescent reaction between organic acids and bicarbonate salts ^[35].

I. volatile liquid containing systems: These devices are osmotically controlled floating systems containing a hollow deformable unit

that can be converted from a collapsed to an expanded position and returned to collapse position after an extended period. A deformable system consists of two chambers separated by an impermeable, pressure responsive, movable bladder. The first chamber contains the drug and the second chamber contains volatile liquid. The device inflates and the drug is continuously released from the reservoir into the gastric fluid. The device may also consist of bioerodible plug made up of PVA, polyethylene,etc. that gradually dissolves causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable system from the stomach.

Intra-gastric, osmotically controlled drug delivery system consists of an osmotic pressure controlled drug delivery device and an inflatable floating support in bioerodible capsule. When the device reaches the stomach, bioerodible capsule quickly disintegrates to release the drug delivery system. The floating support is made of a deformable hollow polymeric bag containing a liquid that gasifies at body temperature to inflate the bag^[36].

ii. gas generating systems:

These buoyant delivery systems utilize effervescent reaction between carbonate/ bicarbonate salts and citric/tartaric acid to liberate CO₂ which gets entrapped in the

jellified hydrochloride layer of the system, thus decreasing its specific gravity and making it float over chyme. These tablets may be either single layered wherein the CO₂ generating components are intimately mixed within the tablet matrix or they may be bilayer in which the gas generating components are compressed in one hydrocolloid containing layer, and the drug in outer layer for sustained release effect. Multiple unit type of floating pills that generate CO₂, have also been developed. These kinds of systems float completely within 10 minutes and remain floating over an extended period of 5-6 hrs [37,38]

evaluation of floating drug delivery systems:

Various parameters that need to be evaluated in gastro retentive formulations floating effervescent tablet include pre compression evaluation like flow properties, bulk density, tapped density, hausner ratio, and carrs index. Post compression evaluation floating lag time, floating duration, swelling index and dissolution profiles, generally performed in simulated gastric fluids at 37°C.

measurement of buoyancy capabilities of the fdds:

The floating behaviour was evaluated with resultant weight measurements. The experiment was carried out in two different media, deionised water and simulated meal, in order to monitor possible difference. The

apparatus and its mechanism are explained earlier in this article. The results showed that higher molecular weight polymers with slower rate of hydration had enhanced floating behaviour and it was observed more in simulated meal medium compared to deionised water.

floating lag time :-

The test for floating time measurement is usually performed in stimulated gastric fluid or 0.1 mole/lit HCl maintained at 37°C. It is determined by using USP dissolution apparatus containing 900 ml of 0.1mole/lit HCl as the dissolution medium at 37°C. The time taken by the dosage form to float is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time [39]

in-vitro dissolution:-

The proposed relevant *in vitro* dissolution method to evaluate a floating drug delivery system (for tablet dosage form). A 100-mL glass beaker was modified by adding a side arm at the bottom of the beaker so that the beaker can hold 70 ml of 0.1 mole/litre HCl dissolution medium and allow collection of samples. A burette was mounted above the beaker to deliver the dissolution medium at a flow rate of 2 ml/min to mimic gastric acid secretion rate. The performance of the modified dissolution apparatus was compared with USP dissolution Apparatus 2

(Paddle). The problem of adherence of the tablet to the shaft of the paddle was observed with the USP dissolution apparatus. The tablet did not stick to the agitating device in the proposed dissolution [40]

method:

The drug release followed zero-order kinetics in the proposed method. Similarity of dissolution curves was observed between the USP method and the proposed method at 10% difference level. The proposed test may show good invitro-in vivo correlation since an attempt is made to mimic the in vivo conditions such as gastric volume, gastric emptying, and gastric acid secretion rate. [41]

drug release:

Dissolution tests are performed using the dissolution apparatus. Samples are withdrawn periodically from the dissolution medium with replacement and then analyzed for their drug content after an appropriate dilution. [42]

determination of swelling index:

The swelling behavior of the dosage unit was measured by studying its weight gain. The swelling index of tablets was determined by placing the tablets in the basket of dissolution apparatus using dissolution apparatus using dissolution medium distilled water at $37 \pm 0.5^\circ\text{C}$. After 0.5, 1, 2, 3, 4, 5 and 6 hours each dissolution basket containing tablets was withdrawn and blotted with tissue paper to

remove the excess of water and weighed on the analytical balance. The swelling index was calculated by using the following formula. [43]

$$\text{Swelling Index} = \frac{\text{Wet weight} - \text{Dry weight}}{\text{Dry weight}} \times 100$$

content uniformity, hardness, friability (tablets): drugs used in the FDDS] [44-45]

Table no.1: marketed preparations of floating drug delivery systems

applications of floating drug delivery systems:

Floating drug delivery offers several applications for drug having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability. These are summarized as follows [46]

sustained drug delivery:

HBS systems can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral controlled release formulation hence can be overcome with these systems. These systems have a bulk density of GI as a result of which they can float on the gastric contents. These systems are relatively large in size and passing from the pyloric opening is prohibited. Recently sustained release floating capsules of

nicardipine hydrochloride were developed and were evaluated in vivo. The formulation compared with commercially available MICARD capsules using rabbits. Plasma concentration time curves showed a longer duration for administration (16 hours) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hours)⁴³. Similarly a comparative study between the Madopar HBS and Madopar standard formulation was done and it was shown that the drug was released up to 8 hours in vitro in the former case and the release was essentially complete in less than 30 minutes in the latter case^[47]

site-specific drug delivery:

These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, e.g., riboflavin and furosemide. Furosemide is primarily absorbed from the stomach followed by the duodenum. It has been reported that a monolithic floating dosage form with prolonged gastric residence time was developed and the bioavailability was increased. AUC obtained with the floating tablets was approximately 1.8 times those of conventional furosemide tablets.

A bilayer-floating capsule was developed for local delivery of misoprostol, which is a synthetic analog of prostaglandin E1 used as a protectant of gastric ulcers caused by administration of NSAIDs. By targeting

slow delivery of misoprostol to the stomach, desired therapeutic levels could be achieved and drug waste could be reduced^[48]

absorption enhancement

drugs:

Those have poor bioavailability because of site specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption. A significant increase in the bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available sLASIX tablets (33.4%) and enteric coated LASIX-long product (29.5%).

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. 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 toward commercializing this technique.

future perspectives: Floating dosage form offers a great future potential as evident from several recent updated research and publications. Among the recently used clinical drugs several narrow absorption window drugs may benefit

from compounding into a FDDS. Replacing parenteral administration of drugs to oral pharmacotherapy would substantially improve treatment and patient compliances too. Drugs that have poor bioavailability because of their limited absorption to the upper gastrointestinal tract can be delivered efficiently by FDDS. Thereby maximizing their absorption and improving their absolute bioavailability. The floating concept can also be utilized in the development of various anti-reflux formulations. Developing a controlled release system for the drugs, which have potential to treat the Parkinson's disease, is also an important area of consideration. Combination therapy for FDDS needs to be developed to treat H. Pylori infection. The study of the effect of various geometric shapes must be carried out for future aspect of FDDS. A design of novel polymers can be investigated according to clinical and pharmaceutical need of a FDDS.

Figure 1:

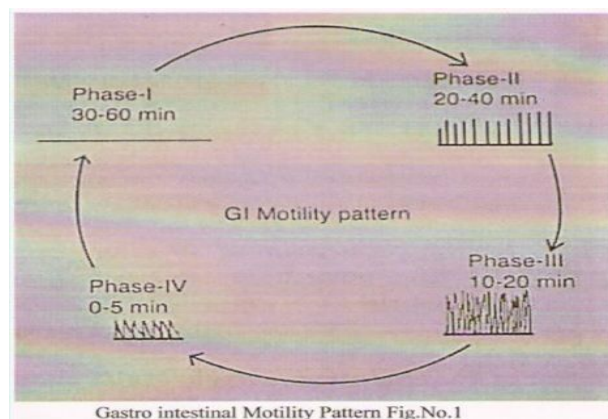
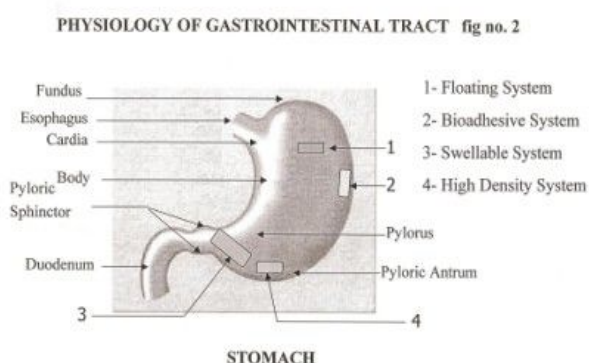


Figure 2:

Figure 3

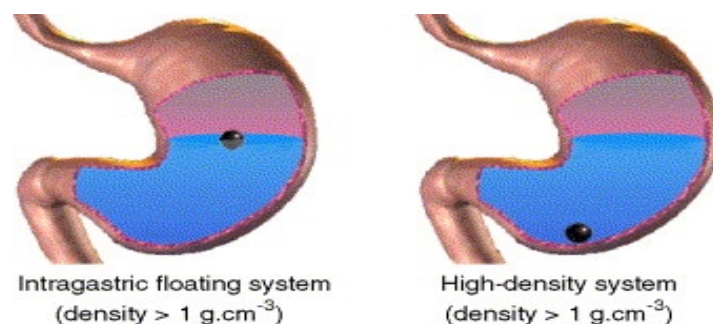


Fig. 3: Diagram of Gastroretentive drug delivery system (low density and high density systems)

Figure 4: Mechanism of Floating

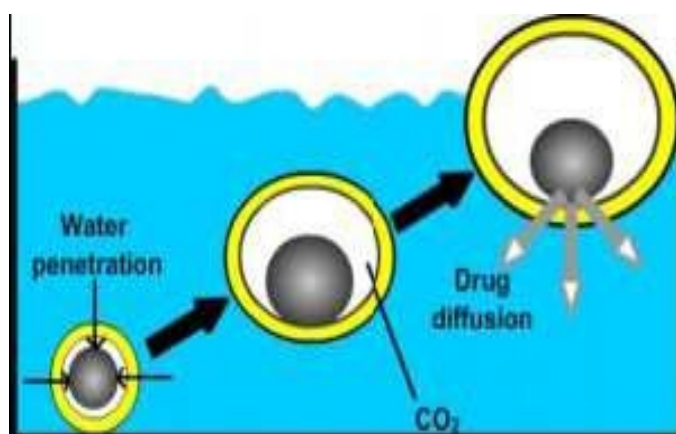


Table no. 1

Sr. No	Drug	Brand name	Manufacturer
1.	Diazepam floating capsule	Valrelease®	Roche, USA
2.	Antacid preparation	Almagate	Flot-Coat®
3.	Aluminium – Magnesium antacid	Topalkan®	Pierr Fabre Drug, France
4.	Benserazide and L-Dopa	Madopar®	Roche Products, USA
5.	Ciprofloxacin floating tablets	Cifran OD	Ranbaxy, India
6.	Effervescent floating Liquid alginate preparation	Gaviscon®	Glaxo Smithkline, India
7.	Ferrous Sulphate colloidal Gel form in GFDD	Convicon®	Ranbaxy, India
8.	Misoprostol Bilayer floating capsule	Cytotec®	Pharmacia, USA

Table no.2

Tablets	Chlorpheniramine maleate, Theophylline, Furosemide, Ciprofloxacin, Captopril, Acetylsalicylic acid, Nimodipine, Amoxycillin trihydrate, Verapamil HCl, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate, Acetaminophen, Ampicillin, Cinnarazine, Diltiazem, Fluorouracil, Piretanide, Prednisolone, Riboflavin- 5`Phosphate.
Capsules	Nicardipine, L-Dopa and benserazide, chlorthalidone HCl, Furosemide, Misoprostal, Diazepam, Propranolol, Urodeoxycholic acid.
Microspheres	Verapamil, Aspirin, Griseofulvin, and p-nitroaniline, Ketoprofen, Tranilast, Ibuprofen, Terfenadine.
Granules	Indomethacin, Diclofenac sodium, Prednisolone.
Films	Drug delivery device. Cinnarizine
Powders	Several basic drugs.

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