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FLOATING DRUG DELIVERY SYSTEM FOR ENHANCEMENT OF DRUG BIOAVAILABILITY

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Abstract: *Gastric emptying* is as complex process but obstacles in the better absorption and enhance bio-availability of oral drug delivery system. Some therapeutic agents have the short biological half-life so increased dosing frequency will reduce the patient compliance. So it will give rise the need to retain the drug in stomach. Floating dosage forms will retain the in stomach for longer period of time and sustained release of drug achieved. There is some research and development of novel drug delivery system by overcoming some physiological problems such as short gastric residence time and unpredictable gastric emptying time. Oral sustained release gastro retentive dosage forms (GRDFs) have many advantages such as, absorption from upper part of GIT, locally acting in stomach and improve bio-availability of medication. Floating Drug Delivery Systems (FDDS) is achieve prolonged gastric residence time and release in controlled manner. Floating delivery systems are low density systems that have sufficient buoyancy to float over the gastric content and remain buoyant in the stomach. The purpose of writing this review is principal mechanism of floatation to achieve gastric retention and approaches to design single-unit and multiple-unit floating systems, and their classification in detail. Also summarizes the in-vitro evaluation techniques.

Keywords: Gastric emptying, gastric residence time, buoyancy, bio-availability, half-life



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INTRODUCTION

Oral route of administration is the most important and convenient route for drug delivery. Due to differential absorption from various regions of GI, the benefits of long-term delivery technology have not been fully realized for dosage forms designed for oral administration. Only recently drug delivery systems have been designed to target drugs to differential regions of GIT. These include gastroretentive systems, delayed release systems and colon targeting.

The real issue in the development of oral controlled release dosage form is not just to prolong the delivery of drugs for more than 12 hours but also to prolong the presence of dosage forms in the stomach or somewhere in the upper small intestine. Dosage forms with prolonged gastric residence time (GRT), i.e. gastro remaining or gastroretentive dosage form (GRDF) will bring about new and important therapeutic options.

The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion, flotation, sedimentation, expansion, modified shape systems. 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. Several recent examples have been reported showing the efficiency of such systems for drugs with bioavailability problems.

Floating drug delivery systems is one of the important approaches to achieve gastric retention to obtain sufficient drug bioavailability. This have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period and the drug is released slowly as a desired rate from the system.

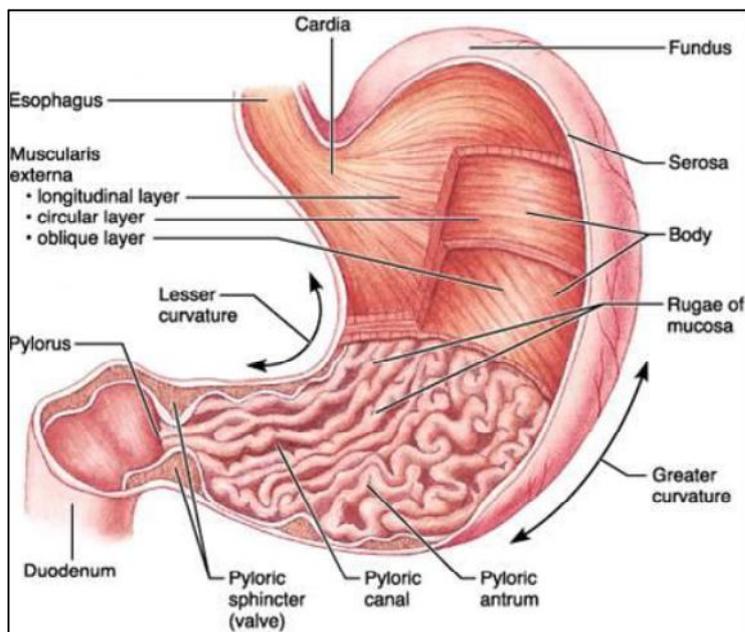
2. ANATOMY OF STOMACH⁴:

The stomach lies between the esophagus and the duodenum (the first part of the small intestine). It is on the left upper part of the abdominal cavity. The top of the stomach lies against the diaphragm. Lying behind the stomach is the pancreas. The greater omentum hangs down from the greater curvature.

Two smooth muscle valves or sphincters, keep the contents of the stomach contained. They are the esophageal sphincter (found in the cardiac region) dividing the tract above, and the Pyloric sphincter dividing the stomach from the small intestine. The stomach is surrounded by parasympathetic (stimulant) and orthosympathetic (inhibitor) plexuses (networks of blood vessels and nerves in the anterior gastric, posterior, superior and inferior, celiac and myenteric), which regulate both the secretions activity and the motor (motion) activity of its muscles.

In humans, the stomach has a relaxed, near empty volume of about 45 ml. It is a distensible organ. It normally expands to hold about 1 litre of food, but will hold as much as 2-3 litres (whereas a newborn baby will only be able to retain 30ml).

Figure 1: "Anatomy of Stomach"⁴



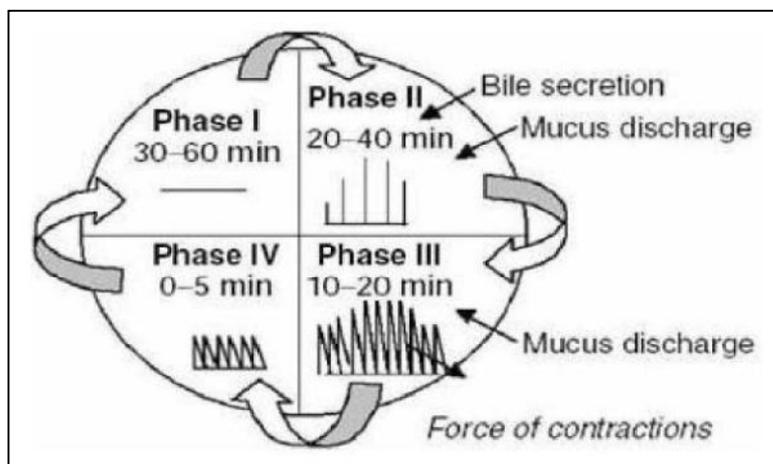
The stomach is divided into 4 sections, each of which has different cells and functions. The sections are:

Cardia	Where the contents of the esophagus empty into the stomach.
Fundus	Formed by the upper curvature of the organ.
Body or Corpus	The main central region.
Pylorus	The lower section of the organ that facilitates emptying the contents into the small intestine.

3. BASIC GASTROINTESTINAL TRACT PHYSIOLOGY⁴:

Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 phases as described by Wilson and Washington.

Figure 2: "Migrating Myoelectric Cycle"⁴



Phase I (basal phase): lasts from 30 to 60 minutes with rare contractions.

Phase II (preburst phase): lasts for 20 to 40 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.

Phase III (burst phase): lasts for 10 to 20 minutes. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.

Phase IV: lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state.

4. CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEMS^{2,3,5,6}:

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

4.1 NON-EFFERVESCENT SYSTEMS^{2,7,8}:

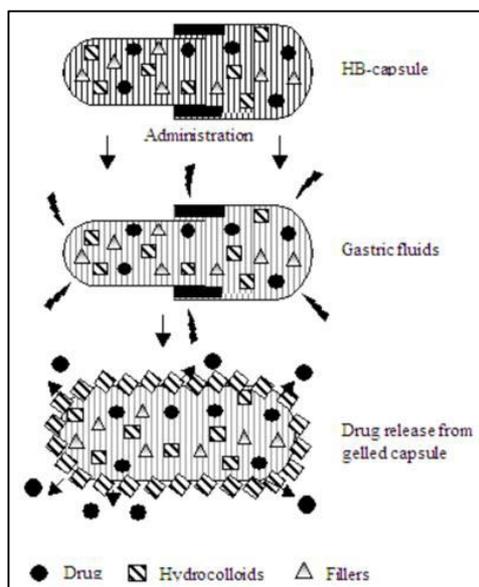
Non-effervescent floating drug delivery systems are normally prepared from gelforming or highly swellable cellulose type hydrocolloids, polysaccharides or matrix forming polymers like polyacrylate, polycarbonate, polystyrene and polymethacrylate. In one approach, intimate mixing of drug with a gel forming hydrocolloid which results in contact with gastric fluid after oral administration and maintain a relative integrity of shape and a bulk density less than unity within the gastric environment. The air trapped by the swollen polymer confers buoyancy to

these dosage forms. Excipients used most commonly in these systems include hydroxypropyl methylcellulose (HPMC) polyacrylates, polyvinyl acetate, carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates. This system can be further divided into the sub-types.

4.1.1 HYDRODYNAMICALLY BALANCED SYSTEMS (HBS):

Sheth and Tossounian first designated these 'hydrodynamically balanced systems'. These systems contains drug with gel-forming hydrocolloids meant to remain buoyant on the stomach content.

Figure 3: "Working principle of hydrodynamically balanced system"²

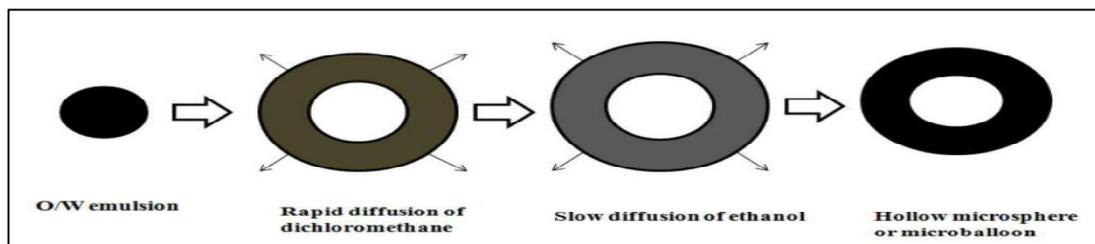


These are single-unit dosage form, containing one or more gel-forming hydrophilic polymers. Hydroxypropyl methylcellulose (HPMC), hydroxethyl cellulose (HEC), hydroxypropyl cellulose (HPC), sodium carboxymethyl cellulose (NaCMC), polycarbophil, polyacrylate, polystyrene, agar, carrageenans or alginic acid are commonly used excipients to develop these systems. The polymer is mixed with drugs and usually administered in hydrodynamically balanced system capsule. The capsule shell dissolves in contact with water and mixture swells to form a gelatinous barrier, which imparts buoyancy to dosage form in gastric juice for a long period. Because, continuous erosion of the surface allows water penetration to the inner layers maintaining surface hydration and buoyancy to dosage form. Incorporation of fatty excipients gives low-density formulations reducing the erosion.

4.1.2 MICROBALLOONS OR HOLLOW MICROSPHERES:

Microballoons or hollow microspheres loaded with drugs in their other polymer shell were prepared by simple solvent evaporation or solvent diffusion / evaporation methods to prolong the gastric retention time (GRT) of the dosage form.

Figure 4: "Formulation of floating hollow microsphere or microballoon"⁷



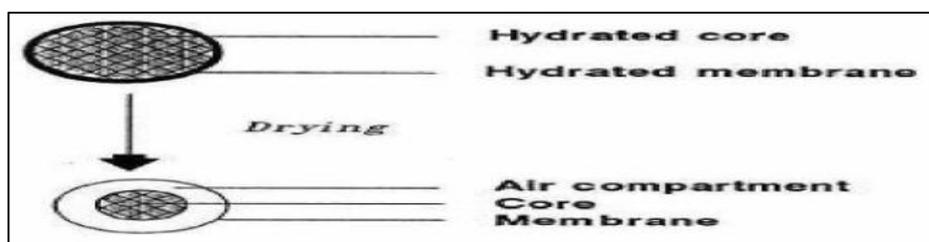
Commonly used polymers to develop these systems are polycarbonate, cellulose acetate, calcium alginate, Eudragit S, agar and low methoxylated pectin etc.

Buoyancy and drug release from dosage form are dependent on quantity of polymers, the plasticizer polymer ratio and the solvent used for formulation. The microballoons floated continuously over the surface of an acidic dissolution media containing surfactant for greater than 12 hours. At present hollow microspheres are considered to be one of the most promising buoyant systems because they combine the advantages of multiple-unit system and good floating.

4.1.3 ALGINATE BEADS:

Talukdar and Fassihi recently developed a multiple-unit floating system based on cross-linked beads. They were made by using Ca²⁺ and low methoxylated pectin (anionic polysaccharide) or Ca²⁺ low methoxylated pectin and sodium alginate.

Figure 5: "Alginate Bead with Air Compartment"⁸



In this approach, generally sodium alginate solution is dropped into aqueous solution of calcium chloride and causes the precipitation of calcium alginate. These beads are then separated and

dried by air convection and freeze drying, leading to the formulation of a porous system, which can maintain a floating force for over 12 hrs. These beads improve gastric retention time (GRT) more than 5.5 hrs.

4.1.4 MICROPOROUS COMPARTMENT SYSTEM:

This approach is based on the principle of the encapsulation of a drug reservoir inside a microporous compartment with pores along its top and bottom walls. The peripheral walls of the device were completely sealed to present any direct contact of the gastric surface with the undissolved drug. In the stomach the floatation chamber containing entrapped air causes the delivery system to float in the gastric fluid. Gastric fluid enters through the aperture, dissolves the drug and causes the dissolved drug for continuous transport across the intestine for drug absorption.

4.2 EFFERVESCENT (GAS GENERATING) SYSTEMS:

Floatability can be achieved by generation of gas bubbles. These buoyant systems utilize matrices prepared with swellable polymers such as polysaccharides (e.g. chitosan), effervescent components (e.g. sodium bicarbonate, citric acid or tartaric acid). The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76: 1. In this system carbon dioxide is released and causes the formulation to float in the stomach.

Figure 6: "Effervescent (gas generating) systems"⁸

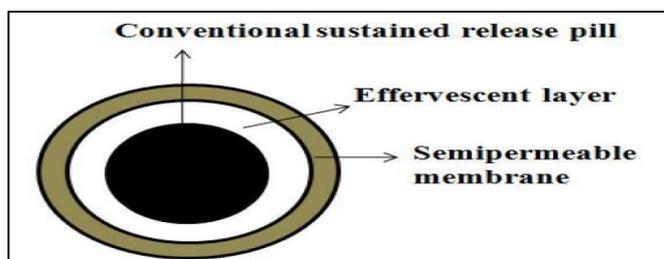
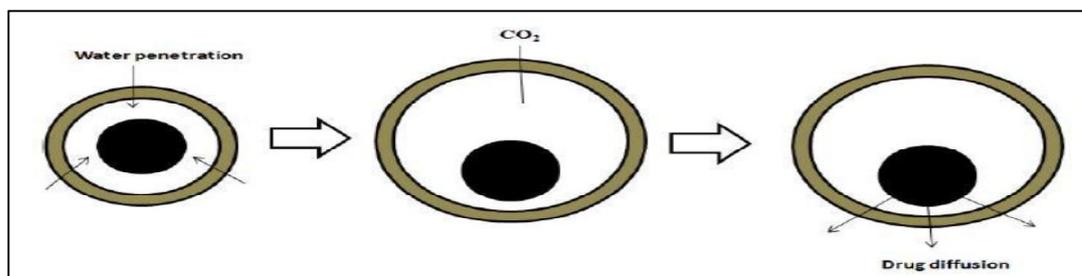


Figure 7: "Drug release from effervescent (gas generating) systems"⁸



Other approaches and materials that have been reported are a mixture of sodium alginate and sodium bicarbonate, multiple unit floating dosage forms that generate gas (carbon dioxide) when ingested, floating mini capsules with a core of sodium bicarbonate, lactose and polyvinyl pyrrolidone (PVP) coated with hydroxypropyl methylcellulose (HPMC), and floating system based on ion exchange resin technology etc. Bilayer or multilayer system has also been designed. Drugs and excipients can be formulated independently and the gas generating material can be incorporated in to any of the layers. Further modifications involve coating of the matrix with a polymer which is permeable to water, but not to carbon dioxide. The main difficulty of these formulations is finding a good compromise between elasticity, plasticity and permeability of the polymers.

4.3 HIGH DENSITY SYSTEMS:

High density formulations include coated pellets that have density greater than that of stomach contents (~1.004g/cm³). This is accomplished by coating the drug with heavy inert materials such as barium sulfate, titanium dioxide, iron powder or oxide. The weighted pellet can then be covered with a diffusion controlling polymer membrane.

4.4 SWELLING AND EXPANDING SYSTEMS:

Swelling type dosage forms are such that after swallowing, these products swell to an extent that prevents their exit from the stomach through the pylorus. As a result, the dosage form is retained in the stomach for a long period of time. These systems may be referred to as "plug type" systems since they exhibit tendency to remain lodged at the pyloric sphincter.

4.5 BIOADHESIVE SYSTEMS:

They are used to localize a delivery device within the lumen and cavity of the body to enhance the drug absorption process in a site-specific manner. It makes use of bioadhesive polymers. These polymers tend to form hydrogen and electrostatic bonds at the mucus polymer boundary.

5. APPROACHES TO DESIGN FDDS^{9,10}:

Approaches to design the various floating dosage form: Two types of floating Dosage systems i.e. Single- and multiple-unit floating dosage systems.

5.1 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

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. single-unit dosage forms are associated with problems such as sticking together or being obstructed in the gastrointestinal tract (GIT) which may produce irritation.

5.2 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. The multiple dosage forms have the following advantages over single unit dosage forms.

- Uniform drug release
- Reduced intersubject variability
- Reduced dose dumping

6. FACTORS AFFECTING FLOATING DRUG DELIVERY SYSTEM^{7,8}:

6.1 BIOLOGICAL FACTORS

- a) **Gastric pH:** Gastric emptying is retarded at low stomach pH and promoted at higher pH. The pH of stomach in fasted condition is about 1.5-2 and in fed conditions it is usually 2 to 6.
- b) **Gastric secretions:** Acids, pepsin, gastrin, mucus and some other enzymes are the secretions of the stomach. Other potent stimulators of gastric acid are the hormone gastrin, peptides and amino acids.
- c) **Volume of gastric secretions:** The resting volume of stomach is about 25-52 ml. Gastric volume is important for dissolution of the dosage forms *in vivo*.
- d) **Age:** In the case of elderly persons, gastric emptying is slowed down.
- e) **Gender:** In males, mean ambulatory GRT (3.4 ± 0.4 h) is less compared with their age and race-matched female counterparts (4.6 ± 1.2 h) regardless of the weight, height and body surface.

- f) **Emotional state:** Stress increases gastric emptying rates while depression slows it down.
- g) **Disease states:** Diseases like gastroenteritis, gastric ulcer, pyloric stenosis, diabetes and hypothyroidism promote gastric retention. Partial or total gastrectomy, duodenal ulcer and hyperthyroidism promote gastric emptying rate.

6.2 FOOD RELATED FACTORS

- a) **Fasting or fed state:** Under fasting conditions, migrating myoelectric complexes (MMC) sweeps undigested material from the stomach and so the GRT is very short. However, in the fed state, MMC is delayed and GRT is considerably longer. Gastric emptying of a dosage form in the fed state can be increased by decreasing the size.
- b) **Nature of the meal:** The rate of gastric emptying for various food materials is in the following order: *carbohydrate* > *proteins* > *fats*. Fat promotes the secretion of bile which too has an inhibitory effect on gastric emptying. The rate of gastric emptying depends mainly on viscosity, volume and caloric content of meals.
- c) **Physical state and viscosity of meal:** Liquid meal takes less than an hour to empty whereas a solid meal may take as long as 6-7 h. Viscous material empty at slow rate in comparison to less viscous materials.
- d) **Frequency of food:** The gastroretention time can be increased by over 400 minutes, when successive meals are given compared with a single meal due to the low frequency of MMC.
- e) **Volume of meals:** Volume of meal affects gastric emptying of liquids. Solids/liquids taken in meal, empty exponentially (i.e. the larger the volume the faster is the gastric emptying). Fluids taken at body temperature leave the stomach faster than colder or warmer fluids.

6.3 FACTORS RELATED TO DRUG DELIVERY SYSTEMS

- a) **Effects of drugs:** Drugs that promote gastric retention include poorly soluble antacids (e.g. Al(OH)₃), anticholinergics (atropine, propantheline), narcotic analgesics (morphine) and tricyclic anti-depressants (imipramine, amitriptyline), metoclopramide, domperidone and cisapride (antiemetic) stimulate gastric emptying.
- b) **Size of dosage form:** Dosage form unit with a diameter of more than 7.5 mm are reported to have an increased GRT.
- c) **Shape of dosage form:** The dosage form with a shape tetrahedron and ring shape have better GIT (≈ 90 to 100 %) retention at 24 h compared with other shapes.

d) **Density of dosage form:** A buoyant dosage form having a density less than that of gastric fluids (≈ 1.004 gm/ml) floats in the stomach for a prolonged period.

Table 1: "Polymers and other ingredients used in preparations Of floating drugs"^{1,2,3}

Polymer & Ingredients	Examples
Polymers	HPMC K4M, Eudragit RL and RS, HPMC 100, HPMC 4000, CMC, PVA, Calcium alginate, carbopol, ethyle cellulose, acrylic polymer
Inert fatty materials	Bees wax, fatty acids, Gelucires 39/01 and 43/01
Effervescent agents	Sodium bicarbonate, citric acid, tartaric acid, citroglycine
Release rate accelerants	Lactose, Mannitol
Release rate retardants	Dicalcium phosphate, Magnesium stearate, talc
Buoyancy increasing agents	Ethyl cellulose
Low density material	Polypropylene foam powder (Accurel MP 1000)

7. ADVANTAGS OF FDDS¹¹:

- Drugs with considerably short half life can be administered in this manner to get an appreciable therapeutic activity.
- Enhancement of the bioavailability for drugs which can be metabolized in the upper GIT.
- They also have an advantage over the conventional system as it can be used to overcome the adversities of gastric retention time as well as the gastric emptying time.
- The duration of treatment through a single dose, which releases the an active ingredient over an extended period of time
- The active entity is delivered specifically to the site of action, thus minimizing or eliminating the side effects.

8. DISADVANTAGE OF FDDS¹¹:

- a) The major disadvantage of floating systems is requirement of a sufficiently high level of fluids in the stomach for the drug delivery. However this limitation can be overcome by coating the dosage form with the help of bioadhesive polymers that easily adhere to the mucosal lining of the stomach.
- b) The dosage form should be administered with a minimum of glass full of water (200-250ml).
- c) Floating system is not feasible for those drugs that have solubility or stability problems in gastric fluids.
- d) The drugs, which are absorbed through out gastro intestinal tract, which undergo significant first pass metabolism, are not desirable candidate.
- e) Some drugs present in the floating system causes irritation to gastric mucosa.

Table 2: "Commonly used drugs in formulation of FDDS"^{21,22}

Capsule	Tablet	Microspheres	Films	Granules
L-DOPA and Benserazide	Ampicillin	Aspirin	Cinnarizine	Diclofenac sodium
Nicardipine	Atenolol	Griseofulvin		Indomethacin
Misoprostol	Ciprofloxacin	Ibuprofen		Prednisolone
Pepstatin	Flurouracil	Terfenadine		

9. EVALUATION TECHNIQUES^{12,13,14}:

In-vitro evaluation of floating tablets

Evaluation was performed to determine the physicochemical properties and release characteristics of the developed formulations.

9.1 PRE-COMPRESSION PARAMETERS:

a) Angle of Repose:

The angle of repose of API powder was determined by the fixed height funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The

powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

$$\tan \phi = h/r$$

Where, h and r are the height and radius of the powder cone respectively.

Table 3: "Effect of angle of repose (ϕ) on flow property"¹²

Angle of repose (ϕ)	Type of flow
<20	Excellent
20-30	Good
30-34	Passable
>35	Very poor

b) Bulk Density:

Accurately weighed 10 g of drug (M), which was previously passed through 20 # sieve was transferred in 100 ml graduated cylinder. Carefully level the powder without compacting, and read the unsettled apparent volume (V0). Calculate the apparent bulk density in gm/ml by the following formula:

$$\text{Bulk density} = \text{Weight of powder} / \text{Bulk volume}$$

c) Tapped Bulk Density:

Accurately weighed 10 g of drug (M), which, Then mechanically tap the cylinder containing the sample by raising the cylinder and allowing it to drop under its own rop of 14 ± 2 mm at a nominal rate of 300 drops per minute. Tap the cylinder for 500 times initially and measure the tapped volume (V1) to the nearest graduated units, repeat the tapping an additional 750 times and measure the tapped volume (V2) to the nearest graduated units.

$$\text{Tapped Density} = \text{Weight of powder} / \text{Tapped volume}$$

d) Carr’s Index:

The compressibility index of the powder blend was determined by Carr’s compressibility index. It is a simple test to evaluate the BD and TD of a powder and the rate at which it packed down. The formula for Carr’s Index is as below:

$$\text{Carr's Index (\%)} = \frac{[(TD-BD)*100]}{TD}$$

e) Hausner’s Ratio:

The Hausner’s ratio is a number that is correlated to the flowability of a powder or granular material. The formula for hausner’s ratio is as below:

$$\text{Hausner's Ratio} = \frac{TD}{BD}$$

Table 4: “Effect of Carr’s index and Hausner’s ratio on flow property”¹³

Carr’s index	Flow Characteristic	Hausner’s Ratio
<10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
>38	Very very poor	>1.60

9.2 POST-COMPRESSION PARAMETERS:

a) In-vitro floating studies:

The time of duration of tablet floatation was observed visually. The time taken for dosage form to emerge on surface of medium called Floating Lag time and total duration of time by which dosage form remain buoyant is called total floating time.

b) Swelling study:

The floating tablets were weighed individually (designated as W_0) and placed separately in glass beaker containing 200 ml of 0.1 N HCl and incubated at $37^\circ\text{C} \pm 1^\circ\text{C}$. At regular 1-hr time intervals until 12 hrs, the floating tablets were removed from beaker, and the excess surface liquid was removed carefully using the tissue paper. The swollen floating tablets were then re-weighed (W_t), and % swelling index (SI) was calculated using the following formula:

$$\text{SI (\%)} = (W_t - W_0 / W_0) * 100$$

c) Weight variation test:

Twenty tablets were selected at random, weighed and the average weight was calculated. Not more than two of the individual weights should deviate from the average weight by more than 10 %.

Table 5: "percentage deviation in weight variation test"¹⁴

Average weight of Tablet	Percent deviation
130 mg or less	10
>130 mg and <324 mg	7.5
324 mg or more	5

d) Friability:

For each formulation, pre weighed tablet sample (20 tablets) were placed in the Roche friabilator (Electro lab, Mumbai, India) which is then operated for 100 revolutions. The tablets were deducted and reweighed. Conventional compressed tablets that loose less than 0.5 to 1% of their weight are considered acceptable.

$$\% \text{ of Friability} = 100 (1 - W_0 / W)$$

e) Hardness:

Hardness of tablet was determined using Pfizer hardness tester.

f) Content uniformity:

Twenty tablets were weighed and powdered in a glass mortar. Quantity of powder equivalent to 100 mg of Ferrous fumarate was accurately weighed and transferred in a 100 ml volumetric flask, add 10 ml 0.1N H₂SO₄ and shake well for 5 min. Adjust the final volume with distilled water. The solution was filtered through a 0.45 µm Millipore filter and the drug content was determined by UV spectroscopy after a suitable dilution with reference to the calibration curve by using 2,2 Bipyridine reagent and hydroxylamine HCL as reducing agent by comparison method.

g) *In vitro* dissolution study:

The release rate of Ferrous fumarate from floating matrix tablets were determined using USP dissolution testing apparatus II (paddle type) at 75 rpm. The dissolution test was performed using 900 ml of 0.1 N HCL (pH 1.2) for 24 h at 37 ± 0.5 °C. Five ml of the sample was withdrawn at regular intervals and replaced with the same volume pre-warmed with fresh dissolution medium. After filtration, the amount of drug release was determined from the standard calibration curve of pure drug.

10. CHARACTERIZATION PARAMETERS:

a) Size and shape evaluation¹⁵:

The particle size and shape plays a major role. The particle size determined by Sieve analysis, Air elutriation analysis, Photo analysis, Optical microscope ,Coulter counter, Sedimentation techniques, Laser diffraction methods, ultrasound attenuation spectroscopy, Air Pollution Emissions Measurements etc.

b) Floating properties¹⁶:

Floating properties can determine by continuous floating monitoring system.

c) Surface topography¹⁷:

The surface topography and structures were determined using scanning electron microscope (SEM), Contact angle meter, Atomic force microscopy (AFM).

d) Determination of moisture content¹⁸:

Moisture content of the prepared formulations was determined by Karl fisher titration, vacuum drying, Thermo gravimetric methods.

e) Determination of the drug content¹⁹:

Percentage drug content given how much amount of the drug that was present in the formulation. Drug content was determined by using HPLC, HPTLC methods, Near infrared spectroscopy (NIRS).

f) Powder X-ray diffraction²⁰:

X-ray powder diffraction is the predominant tool for the study of polycrystalline materials and is eminently suited for the routine characterization of pharmaceutical solids. Samples were irradiated with α - radiation and analyzed between 2 °C and 60 °C .The voltage and current used were 30KV and 30mA respectively.

g) Fourier transform infrared analysis²⁰:

Fourier transform infrared spectroscopy 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 FTIR. 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.

h) Differential Scanning Calorimetry (DSC)²⁰ :

DSC 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 calibrate the DSC temperature and enthalpy scale. The sample preparations were hermitically sealed in an aluminum 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.

Table 6: "Gastroretentive products available in the market"^{21,22}

Brand Name	Active Ingredient(s)	Company Name
Cifran OD [®]	Ciprofloxacin	Ranbaxy
Madopar [®]	L-DOPA and Benserazide	Roche Pharma
Valrelease [®]	Diazepam	Roche Pharma
Almagate FlatCoat [®]	Aluminium-magnesium antacid	Pierre fabre

Liquid Gavison®

Aluminium hydroxide

Glaxo Smith Kline

Pharmaceuticals

Cytotec®

Misoprostal

G.D. Searle and Co.

11. APPLICATION OF FLOATING DRUG DELIVERY SYSTEM^{9,10,11}:

- a) Sustained drug delivery
- b) Site-specific drug delivery
- c) Local action in stomach
- d) Reduce irritation of acidic drugs
- e) Advantageous to drugs which are unstable in intestine environment
- f) Beneficial to drugs that show low solubility at high Ph
- g) Ease of administration and better patient compliance
- h) Site-specific drug delivery

12. PHARMACEUTICAL ASPECTS:

In development of FDDS, following characteristics should be sought:

- Retention in the stomach according to the clinical demand.
- Lag time
- Optimization between the buoyancy time and release rate (Buoyancy time increases by increasing drug: polymer ratio but release retards by increasing polymer level).
- Inexpensive industrial manufacture
- Complete matrix integrity of the SR formulation in the stomach.
- Ability to load substantial amount of drug with different physicochemical properties and release them in a controlled manners.
- Convenient intake.

13. FUTURE POTENTIAL:

FDDS approach is suitable for potential active agents with narrow absorption window, e.g. antiviral, antifungal and antibiotic agents (sulphonamides, quinolones), which require specific region for their absorption. Release the drug continuously in controlled manner. Reduced the fluctuations in the plasma level of the drug. Also enhancing the bio-availability and release the drug in controlled manner. And large numbers of companies are focusing on this type technique. And recent publication says Floating dosage form offers various future potential.

14. CONCLUSION:

Drug absorption in GIT is variable procedure and prolong the gastric retention of dosage form extends time for drug absorption. FDDS has ability to dosage form remain in the stomach. Floating drug delivery systems enhancing the bio-availability and release the drug in controlled manner. FDDS developed on the requirements such as, buoyancy principle and gastric emptying, for the release in controlled manner. This approach is suitable for those drugs whose absorption window is narrow. This approach is suitable for the gastric retention. And large numbers of companies are focusing on this type technique.

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