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Review Article

FLOATING DRUG DELIVERY SYSTEM : An Overview

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ABSTRACT

Floating drug delivery systems (FDDS) was to organize the recently focus on the principalmechanism of floatation to achieve gastric retention time. The recent developments of FDDS including thephysiological and formulation variables affecting gastric retention, approaches to design floating systems, and their classification and formulation aspects are covered in detail. Gastric emptying ofdosage forms is an extremely variable process and ability to prolong and control the gastric emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Gastroretentive systems can remain in the gastric region for several hours for significantly prolong residence time of drugs by which improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment.. The present review addresses briefly about the floating drug delivery systems.

Keywords: Floating Drug Delivery System, Gastroretentive Drug Delivery System, It's Classification,Application.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to proper site in the body to achieve promptly and then maintain a desired drug concentration. Recent development in technology has provided viable dosage alternatives that can be administered via different routes of administration. Various routes that are used include oral, topical, nasal, rectal, vaginal and ocular, etc. but out of these routes oral route of drug delivery is considered as the most favoured and practiced way of delivery, due to following reasons :Ease of administration, Ease of production, Low cost.

Drugs which get absorbed from stomach or show local effect should spend maximum time in stomach. This however, is found very difficult to occur, In case of conventional dosage forms. The oral route is considered as the most promising route of drug delivery. Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range needed for treatment, only when taken several times a day.1 Recently, Novel drug delivery systems that could revolutionize method of medication and provide a number of therapeutic benefits.2The development of oral sustained-controlled release formulations is an attempt to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration insystemic circulation for a long time. Drugs which get absorbed from stomach or show local effect should spend maximum time in stomach. This however, is found very difficult to occur, In case of conventional dosage forms.

Gastrointestinal retention: [3,4,5].

Gastro retentive 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 patients5. To successfully modulate the gastrointestinal transit time of a drug delivery system through floating drug delivery system (FDDS) For maximal gastrointestinal absorption of drugs and site-specific delivery, one needs to have a good fundamental understanding of the anatomic and physiological characteristics of the human GIT.

These are outlined and briefly discussed[1].

1. Basic Gastrointestinal Tract Physiology:

Anatomically the stomach is divided into 3 regions: fundus, body, and antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions.

Stomach Physiology:

The stomach is an expanded section of the digestive tube between the oesophagus and small intestine. The wall of the stomach is structurally similar to the other parts of the digestive tube, with the exception that stomach has an extra, oblique layer of smooth muscle inside the circular layer, which aids in the performance of complex grinding motions. In the empty state, the stomach is contracted and its mucosa and sub mucosa are thrown up into distinct folds called rugae (Fig. 1)

There are images to four major types of secretary epithelial cells that cover the surface of the stomach and extend down into gastric pits and glands:

•Mucous cells: secrete alkaline mucus that protects the epithelium against shear stress and acid.

☐Parietal cells: secrete hydrochloric acid.

☐Chief cells: secrete pepsin, a proteolytic enzyme.

☐G cells: secrete the hormone gastrin.

The contraction of gastric smooth muscle serves two basic functions

☐Ingested food is crushed, ground, mixed and liquefying to form Chyme.

☐Chyme is forced through the pyloric canal into the small intestine, a process called gastric emptying.

Gastric motility: Gastric motility is c ontrolled by a complex set of neural and hormonal signals. Nervous control originates from the enteric nervous system as well as parasympathet ic (predominantly vagus nerve) and sympathetic systems. A large battery of hormones has been shown to influence gastric motility- for e.g. both gastrin and cholecystokinin act to relax the proximal stomach and enhance contractions in the distal stomach. The bottom line is that the patterns of gastric motility likely are a result from smooth muscle cells integrating a large number of inhibitory and stimulatory signals. Liquid readily pass through the pylorus in spurts, but solids must be reduced to a diameter of less than 1-2 mm before passing pyloric gatekeeper.

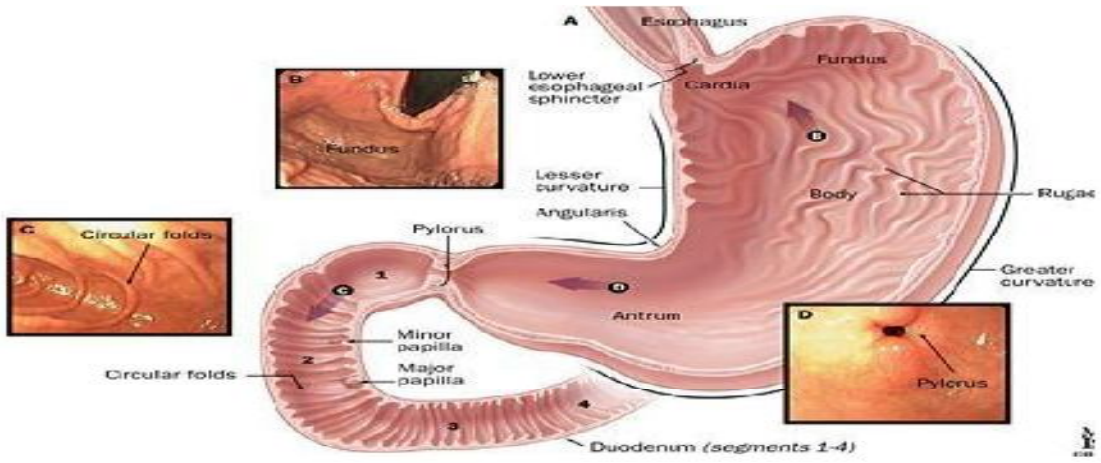

Figure 1: Physiology of stomach

The gastric volume is important for dissolution of the dosage form in vivo. The resting volume of the stomach is 25-50 ml. There is a large difference in gastric secretion of normal and achlorhydric individuals. Gastric pH also has pronounced effect of absorption of drug from delivery system. The pH of fasting stomach is 1.2-.2.0 and in fed condition 2.0-6.0.

Gastric empty rate

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 mylo electric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phases as described by Wilson and Washington.

1. Phase I (Basal phase) lasts from 40 to 60 minutes with rare contractions.
2. Phase II (Preburst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (burst phase) lasts for 4 to 6 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.
4. 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 f rom fasted to that of fed state. This is also known as diges t ive mo t i l i ty pattern and comprises continuous contractions as in Phase II of fasted state. These contractions 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. Scintigraphic studies determining gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically 2 complications, that of short gastric residence time and unpredictable gastric emptying rate.

APPROACHES TO GASTRIC RETENTION: [10]

Various types of systems have been developed to increase the GRT of dosage forms by employing range of concepts. These systems have been classified on the basis of principle of gastric retention.

1. Floating drug delivery systems (FDDS): These systems have low density and so float over the gastric contents.
2. Bioadhesive systems: They bind with stomach mucosa and hence, enable the localized retention of the system.
3. Swelling and expanding systems: Such systems absorb water and hence, enlarged size.
4. High density systems: They remain in the stomach for longer period of time, by sedimenting to the folds of stomach.

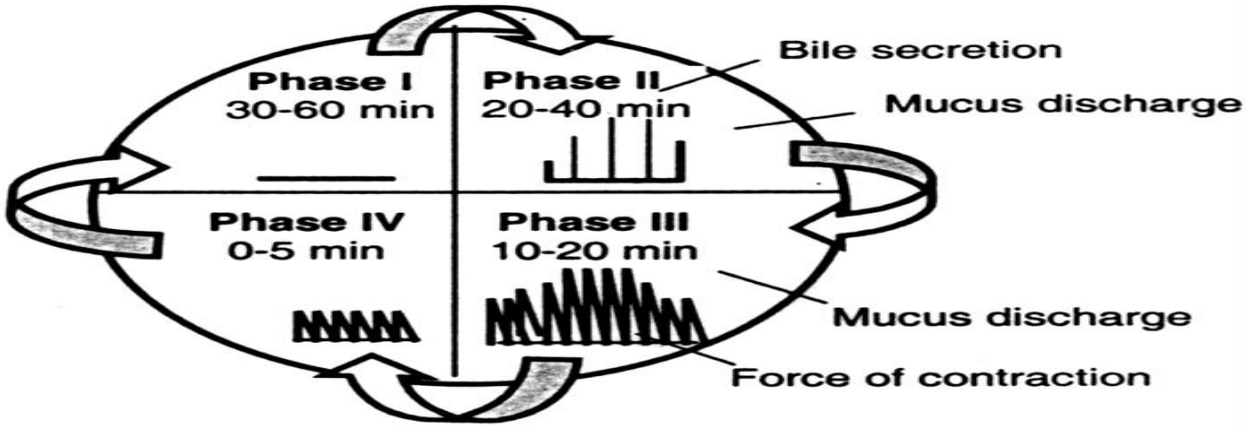

Figure 2: Motility pattern in gastrointenstinal tract.

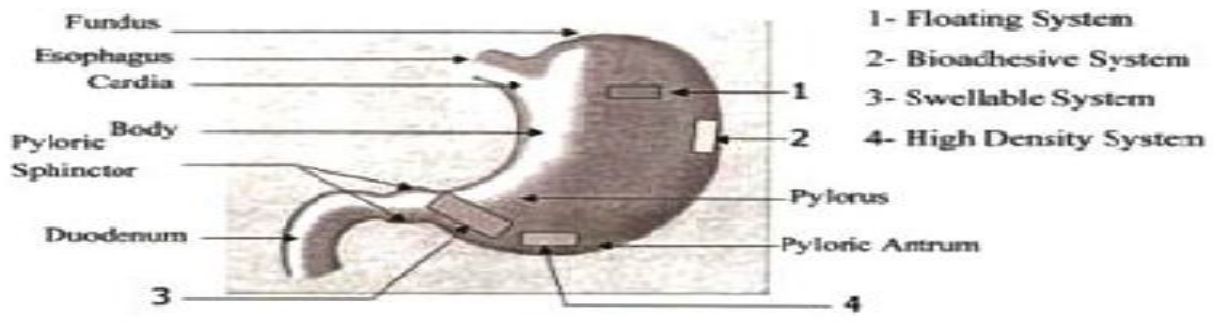

Fig 3: Various Approaches to Gastrortentive systems of system ensures no passage from gastric sphincter.

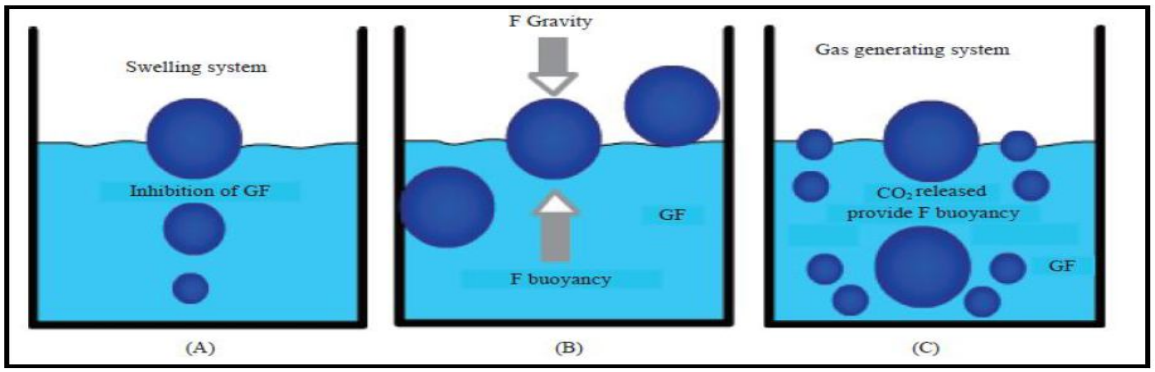

Figure 4: mechanism of floating of beads (GF=gastric fluid)

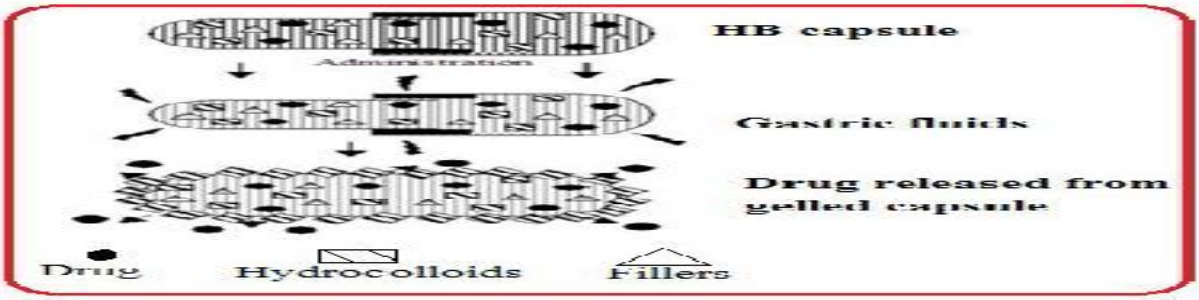

Fig.No.5: Schematic diagram shows the mode of action for HBs.

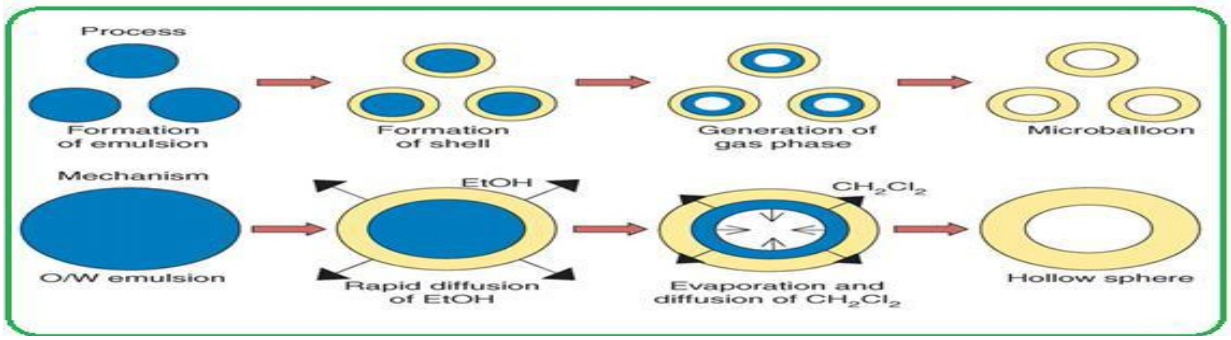

Fig.No.6: Preparation technique (emulsion-solvent diffusion method) and mechanism of 'microballoon'.

Floating drug Delivery System:

Floating drug delivery systems (FDDS) or hydro dynamically 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 Gastric retention time 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 Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres.

Classification of Floating Drug Delivery System: [11,12,13].

A. Effervescent system

• Gas generating system

• Volatile liquid containing system

B. Non-effervescent System:

• Colloidal gel barrier system.

• Alginate beds.

• Hollow microspheres / Microballons.

• Intragastric Floating Drug Delivery Device / Microporous compartment system

A. Effervescent Systems:

These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, eg, sodium bicarbonate, tartaric acid, and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, C02 is liberate and gas entrapped in swollen hydrocolloids which provides buoyancy to the dosage forms.

a. Volatile liquid containing systems:

The GRT of a drug delivery system can be sustained by incorporating an inflatable chamber, which contains a liquid (like ether, cyclopentane), that gasifies at body temperature to cause the inflatation of the chamber in the stomach. The device may also consist of a bio-erodible plug made up of PVA, Polyethylene, etc. that gradually dissolves and causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable systems from the stomach.

b. Gas-generating Systems:

These buoyant delivery systems utilize effervescent reactions between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO2, which gets entrapped in the gellified hydrocolloid layer of the systems thus decreasing its specific gravity and making it to float over chyme. How the dosage form float is shown in the figure 4.

B. Non-effervescent systems:

Non-effervescent floating dosage forms use a gel forming or swellable cellulose type hydrocolloids, polysaccharides, and matrix-forming polymers like polycarbonate, polyacrylate, polymethacrylate, and polystyrene. The formulation method includes a simple approach of thoroughly mixing the drug and the gel-forming hydrocolloid. After oral administration this dosage form swells in contact with gastric fluids and attains a bulk density of < 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir and allow sustained release of drug through the gelatinous mass.

a. Colloidal gel barrier systems:[11]

Hydrodymamically balance system (HBSTM) was first design by Sheth and Tossounian in 1975.Such systems contains drug with gel forming hydrocolloids meant to remain buoyant on stomach contents. This system incorporate a high level of one or more gel forming highly swellable cellulose type hydrocolloids.e.g.HEC, HPMC, NaCMC, Polysacchacarides and matrix forming polymer such as polycarbophil, polyacrylates and polystyrene, incorporated either in tablets or in capsule. On coming in contact with gastric fluid, the hydrocolloid in the system hydrates and forms a colloidal gel barrier around the gel surface. The air trapped by the swollen polymer maintains a density less than unity and confers buoyancy to these dosage form.

b. Alginate beads:

Multi-unit floating dosage forms have been developed from freeze-dried calcium alginate. Spherical beads of approximately 2.5 mm in diameter can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride, causing the precipitation of calcium alginate. The beads are then separated, snap-frozen in

liquid nitrogen, and freeze-dried at -40ºC for 24 hours, leading to the formation of a porous system, which can maintain a floating force for over 12 hours.

c. Hollow microspheres :[12]

Hollow microspheres (microballons), loaded with ibuprofen in their outer polymer shells were prepared by a novel emulsion-solvent diffusion method. The ehanol: dichloromethane solution of the drug and an enteric acrylic polymer was poured in to an agitated aqueous solution of PVA that was thermally controlled at 40°C.The gas phase generated in dispersed polymer droplet by evaporation of dichloromethane formed in internal cavity in microspheres of the polymer with drug. The microballons floated continuously over the surface of acidic dissolution media containing surfactant for greater than 12 hours in vitro.

d. Intragastric / Microporous compartment system:[13] The system composed of a drug reservoir encapsulated in a microporous compartment having pores on top and bottom surfaces. The peripheral walls of the reservoir compartment were completely sealed to prevent any physical contact of the undissolved drug with walls of the stomach.17. 18 Novel levodopa gastro retentive dosage form based on unfolding polymeric membranes which combines extended dimensions with high rigidity. It was folded into a large size gelatin capsules. In vitro studies showed that unfolded form reached within 15 minutes after administration and it was confirmed in vivo in beagle dogs. The unfolded form was maintained for at least 2 hours. It was concluded that this dosage form could improve therapy of different narrow absorption window drugs. However, there are possibilities of the polymeric films to get stuck in the esophagus causing extreme discomfort to the patient or drug related injuries and repeated administration of rigid dosage form may result in gastric obstruction.

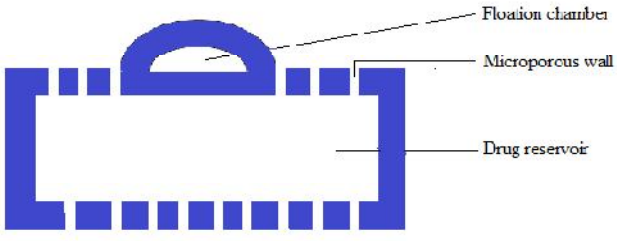

Fig.No.7: Intra-gastric floating drug delivery device.

Advantages:[14]

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery.

These advantages include:

1. Floating dosage forms such as tablets or capsules will remains in the solution for prolonged time even at the alkaline pH of the intestine.
2. FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhoea to keep the drug in floating condition in stomach to get a relatively better response.
3. Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
4. The FDDS are advantageous for drugs absorbed through the stomach eg: Ferrous salts, Antacids. Improved drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site .
5. Controlled delivery of drugs. It minimizes the mucosal irritation by releasing drug slowly.
6. Treatment of gastrointestinal disorders such as gastro esophageal reflux.

Disadvantages of floating drug delivery system:[15]

1.Floating system is not feasible for those drugs that have solubility or stability problem in GI tract.

2.These systems require a high level of fluid in the stomach for drug delivery to float and work efficientlycoat, water

3.The drugs that are significantly absorbed throughout gastrointestinal tract, which undergo significant first pass metabolism, may not be desirable candidate. E.g. Nifedipine.

4.The ability of drug to remain in the stomach depends upon the subject being positioned upright.

5.The residence time in the stomach depends upon the digestive state. Hence, FDDS should be administered after the meal.

6.Not suitable for drugs that cause gastric lesions e.g. Non steroidalanti inflammatory drugs. Drugs that are unstable in the strong acidic environment, these systems do not offer significant advantages over the conventional dosage forms

for drugs, which are absorbed throughout the gastro intestinal tract.

7.The mucus on the walls of the stomach is in the state of constant renewal, resulting in the unpredictable adherence.

8.Faster swelling properties are required and complete swelling of the system should be achieved well before the gastric emptying time.

9.The ability to float relies in the hydration state of dosage form.

10.In all the above, the most important and primary requirement for the success is the physical integrity of the system.

FACTORS AFFECTING GASTRIC RESIDENCE TIME OF FDDS:[9-14]

a) Formulation factors

Size of tablets

Retention of floating dosage forms in stomach depends on the size of tablets. Small tablets are emptied from the stomach during the digestive phase, but large ones are expelled during the house keeping waves 9. Floating and nonfloating 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 floating dosage units remained buoyant regardless of their sizes on the gastric contents throughout theirresidence in the gastrointestinal tract, while the nonfloating dosageunits sank and remained in the lower part of the stomach. Floatingunits away from the gastro-duodenal junction were protected fromthe peristaltic waves during digestive phase while the nonfloatingforms stayed close to the pylorus and were subjected to propellingand retropelling waves of the digestive phase.[9]

Density of tablets

Density is the main factor affecting the gastric residence time of dosage form. A buoyant dosage form having a density less than that of the gastric fluids floats, since it is away from the pyloric sphincter, 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.[10]

Shape of tablets

The shape of dosage form is one of the factors that affect its gastric residence time. Six shapes (ring tetrahedron, 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 [12,11]

Viscosity grade of polymer

Drug release and floating properties of FDDS are greatly affected by viscosity of polymers and their interaction. Low viscosity 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.[12]

b) Idiosyncratic factors

Gender

Women have slower gastric emptying time than do men. Mean ambulatory GRT in meals (3.4±0.4 hours) is less compared with their age and race-matched female counterparts (4.6±1.2 hours), regardless of the weight, height and body surface.[13]

Age

Low gastric emptying time is observed in elderly than do in younger subjects. Intrasubject and intersubject variations also are observed in gastric and intestinal transit time. Elderly people, especially those over 70 years have a significantly longer GRT.[14]

Posture

i) Upright position: An upright position protects floating forms against postprandial emptying because the floating form remains above the gastric contents irrespective of its size14. Floating dosage forms show prolonged and more reproducible GRTs while the conventional dosage form sink to the lower part of the distal stomach from where they are expelled through the pylorus by antral peristaltic movements.[14]

ii) Supine position: This position offers no reliable protection against early and erratic emptying. In supine subjects large dosage forms (both conventional and floating) experience prolonged retention. The gastric retention of floating forms appear to remain buoyant anywhere between the lesser and greater curvature of the stomach. On moving distally, these

units may be swept away by the peristaltic movements that propel the gastric contents towards the pylorus, leading to significant reduction in GRT compared with upright subjects.[14]

Concomitant intake of drugs

Drugs such as prokinetic agents (e.g., metoclopramide and cisapride), anti Cholinergics (e.g., atropine or propantheline), opiates (e.g., codeine) may affect the performance of FDDS. The coadministration of GI-motility decreasing drugs can increase gastric emptying time.[14]

Feeding regimen

Gastric residence time increases in the presence of food, leading to increased drug dissolution of the dosage form at the most favorable site of absorption. A GRT of 4-10 h has been reported after a meal of fats and proteins.[14]

EVALUATION PARAMETERS OF GASTRORETENTIVE SYSTEM:[16,17].

Different studies reported in the literature indicate that pharmaceutical dosage forms exhibiting gastric residence in vitro floating behavior show prolonged gastric residence in vivo.

1) Hardness, friability, assay, content uniformity (Tablets):

These tests are performed as per described in specified monographs.

2) Floating lag time and total floating time determination: It is noted by the time between the introduction of the tablet into the medium and its rise to upper one third of the dissolution vessel is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time.These tests are usually performed in gastric fluid or 0.1 mole.lit-1 HCl maintained at 37o C, by using USP dissolution apparatus containing 900 ml of 0.1 molar HCl as the dissolution medium.

3) Drug release:

It is important test for in vitro drug release study and carried out in gastric fluids and intestinal fluidsmaintained at 370 C. Dissolution tests are performed using the USP dissolution apparatus. Recent methodology as described in USP XXIII states that the dosage unit is allowed to sink to the bottom of the vessel before rotation of blade is started and standard dissolution methods based on the USP or British Pharmacopoeia (BP) have been shown to be poor predictors.

4) Floating microspheres and beads: Drug loading by crushing accurately weighed sample of beads or microspheres in a mortar and added to the appropriate dissolution medium and centrifuged, filtered and analyzed by various analytical methods like spectrophotometry. The percentage drug loading is calculated in beads or microspheres and the size and shape calculate by optical microscopy method. The external and cross-sectional morphology which is surface characterization is done by scanning electron microscope (SEM). The measured weight of prepared microspheres was divided by total amount of all non-volatile components used for the preparation of microspheres, which will give the total percentage yield of floating microspheres [23].

5) Resultant weight determination:

Bulk density and floating duration have been the main parameters of a dosage form's buoyancy. Although single density determination does not predict the floating force evolution the dosage forms. It operates by force equivalent to the force F required to keep the object totally submerged in the fluid. The magnitude, direction of the force and the resultant weight corresponds to theVictoria sum of buoyancy (Fbuoy) and gravity (Fgrav) forces acting on the objects as shown in the equal- $F = Fbuoy – Fgra$

$$F = dfgV – dsgV = (df-ds)\, gV$$

$$F = (df – M/V)\, gV$$

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

7) X Ray/Gamma scintigraphy:

For in vivo studies, X-Ray/Gamma Scintigraphy is the main evaluation parameter for floating system. In each experiment, the animals are allowed to fast overnight with free access to water, in a formulation allows indirect external observation using a γ-camera or scintiscanner. But the main drawback of γ- scintigraphy are the associated ionizing radiation for the patient, the limited topographic information, low resolution inherent to the technique and the complicated and expensive preparation of radiopharmaceutical.

8) Pharmacokinetic studies:

Pharmacokinetic studies include AUC (Area under Curve), C max, and time to reach maximum and a radiograph is made just before the administration of the floating tablet to ensure the absence of radio-opaque material. Visualization of

dosage form by X-ray is due to the inclusion of a radio-opaque material. The formulation is administered by natural swallowing followed by 50 mL of water. Gastric radiography was done at 30-min time intervals for a period of 5 h using an X-ray machine. The inclusion of a γ-emitting radionucleide plasma concentration (T max) were estimated using a computer. Statistical analyses were performed using a Student t test with p, 0.05 as the minimal level of significance.

9) Specific Gravity:

The displacement method is used to determine the specific gravity of floating system using compound benzene as a displacing medium .

LIST OF DRUGS EXPLORED FOR VARIOUS FLOATING DOSAGE FORMS:

1. Microspheres Tablets /Pills: Chlorpheniramine maleate, Aspirin, griseofulvin, Acetaminophen, p-nitroaniline, Acetylsalicylic acid, Ibuprofen, Amox-ycillin trihydrate, Terfenadine, Ampicillin, Trani-last,Atenolol, Theophylline, Captopril, Isosorbide di nitrate, Sotalol, Isosorbide mononitrate.
2. Films: P-Aminobenzoic acid, Cinnarizine, Pireta-nide, Prednisolone, Quinidine gluconate.
3. Granules: Cinnarizine, Diclofenac sodium , Diltia-zem, Indomethacin ,Fluorouracil ,Prednisolone , Isosorbide mononitrate ,Isosorbide dinitrate.
4. Powders: Riboflavin,phosphate, Sotalol, Theophyl-line.
5. Capsules: Verapamil HCl, Chlordiazepoxide HCl, Diazepam, Furosemide, L-,opa and benserazide Misoprostol, Propranolol HCl, Ursodeoxycholic ac-id, Nicardipine .

Table 1: Marketed products of FDDS

Sr.No.	PRODUCT	Active Ingredient
1.	Madopar	Levodopa & Benserzide
2.	Valrelease	Diazepam
3.	Topalkan	Aluminium Magnesium Antacid
4.	Almagate	Flatcoat Antacid
5.	Liquid gavi-son	Alginic acid & Sodium bicarbonate

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS: [18,19].

• Enhance bioavailability:

The bioavailability of CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption.

• Sustained drug delivery:

In this systems dose large in size and passing from the pyloric opening is prohibited. New sustained release floating capsules of nicardipine hydrochloride were developed and were evaluated in vivo. 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). Similarly a comparative study between the Madopar HBS and Madopar standard formulation was done it shown the drug was released up to 8 hours in vitro in the former case and the release completed in less than 30 minutes in the latter case.

• Site–specific drug delivery systems: These systems are particularly advantageous for drugs those are specifically absorbed from the stomach or the proximal part of the small intestine.55 The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. It reduces the side effects which 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.

• 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 absorption.

• Minimize adverse activity at the colon:

Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This pharmacodynamic aspect provides the rationale for GRDF formulation for beta-lactam antibiotics that are

absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance.

• Reduce fluctuations of drug concentration:

Continuous input of the drug following controlled release gastro-retentive dosage form administration 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 effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.

CONCLUSION:

Recently many drugs have been formulated as floating drug delivery systems with an objective of sustained release and restricting the region of drug release to stomach. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release. The currently available polymer-mediated non effervescent and effervescent FDDS, designed on the basis of delayed gastric emptying and buoyancy principles, appear to be a very much effective approach to the modulation of controlled oral drug delivery. The most important criteria which has to be looked into for the productions of a floating drug delivery system is that the density of the dosage form should be less than that of gastric fluid. And hence, it can be concluded that these dosage forms serve the best in the treatment of diseases related to the GIT and for extracting a prolonged action from a drug with a short half life.

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