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A Briefreview Onfloating Drug Delivery System

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ABSTRACT:

In Recent years improvement have been made in the research and development of ratecontrolled oral drug delivery systems to defeatphysiological hardship, such as short gastric residence times (GRT) and undeterminegastric emptying period (GET). Various approaches are presently developed to extend ithe GRT, including floating drug delivery systems (FDDS), also known as hydrodynamically balanced systems (HBS), swelling and expanding systems, polymeric bioadhesive systems, modified-shape systems, high-density systems, and other delayed gastric emptying tendency. The different scheme were used in the development of FDDS by constructing the effervescent and noneffervescent type of floating tablets. FDDS is a method used to deliver the drugs that are active locally which have ia narrow absorption window in the upper ,unstable in the lower intestinal environmentgastrointestinal tract,and possess low solubility with higher pH values. . The novel methods in FDDS include approaches to design a single unit and multiple-unit floating systems, the physiological and formulation variability affecting gastric retention along with the use of recently invented and developed polymers. iIt is helpful in minimizing the dosing frequency. The density of dosage form should ibe less than the density of gastric contents (1.004 gm/ml) in FDDS. It may ibe by effervescent or non-effervescent method. iThe primary objective of writing this review article is to assemble ithe current iliterature with special focus on classification, various method of preparation, mechanism of action with its iadvantages and disadvantages.

KEYWORDS:Floating drug delivery systems (FDDS), Gastric residence time, Swelling index, Buoyancy sustaimed irelease

INTRODUCTION :

Almost icommercial idrug are delivered ithrough i oral drug delivery system due to the various iadvanatage, reduced cost ,increased patient compliance ,ease of adminstartion and various flexibility in the formulation Can be made [1] The i pure crude form of drug can be solid ,semi solid or liquid that ishould be therapeutically ieffective ,stable and harmless ienough to deliver ithe amount of the drug at the site of action i that should the target site instantly and remain ithere ifor the particular time iin ithe adpted concentrated iis represented by the drug delivery system[2] iDespite of the multiple advantages the it required increase in the dosing frequency as it get easily emptied ifrom the stomach[3] The partial idrug release ifrom the device into the absorption window due to the irapid gastro intestinal transist leads to decrease in the efficacy of the drug.To overcome such trouble iGastro retentive drug delivery systems are formulated which retain in the stomach for a longer period of time and thereby alter the bioavailability of drugs that are preferentially absorption rate ifrom upper GIT [4].

FDDS are hydro-dynamically controlled low-density systems Which are introduced ito retain the drug in the stomach widely used for the drug with low solubility and stability within the intestinal fluid. The FDDS have sufficent buoyancy ito ifloat over the gastric content without affecting the igastric emptying rate prolong the iduration of action the ibasic principle to prepare ia buoyant ipreparation ioffers practical approach to increase the gastric residence time iof dosage form to get sustained release effect[5]

BASIC GASTROINTESTINAL TRACT PHYSIOLOGY:

Basically stomach is divided into 3 regions: **fundus, body,and antrum (pylorus).**as shown in fugure 1 proximal element made from fundus and body acts as a reservoir for indigestible material, the antrum is the primary site for mixing motions and act as a pump for gastric emptying by propelling activity. Gastric emptying occurs during both ifasting and ifed condition . [6]

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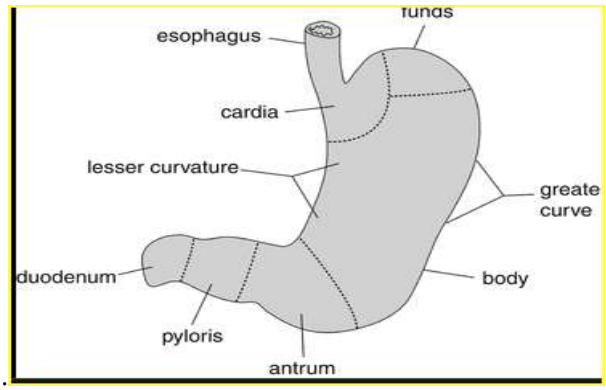

Figure 1 i iPhysiology of GIT [7]

Mucous cells: secrete alkaline fluid**,Parietal cel**ls: secretes a acid that is hydrochloric acid.,**Chief cells**: secrete pepsin, a proteolytic enzyme.,**G cells**: secrete the hormone gastrin.The pattern of motility is however defined in the secondd states. During the fasting state an interdigestive series of electricalevents take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called ias the iinter digestive myloelectric cycle or migrating myloelectric cycle (MMC) that's in additionfurther divided into following 4phases. Gastric empty rate:

Phase I (Basal section): it lasts from 40 to 60 mins with uncommon contractions.
Phase II (Preburst phase): lasts for 40to 60 mins with intermittent potential andcontractions.. Phase III (burst phase): lasts 40to 6 minutes, which incorporates extreme and regularcontractions for short time interval.
Phase IV: lasts for 0 to 5 minutes and happens among levels III and I of 2 consecutivecycle.[8]

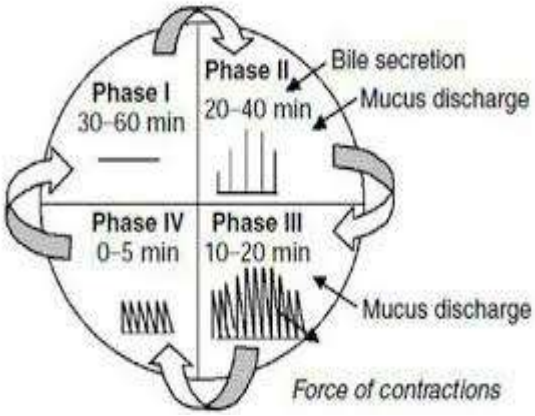

Figure 2: Motility of GIT [9]

Mechanism of Floating Systems

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retentiontime. These attempts include introducing floating dosageforms (gas-generating systems and swelling or expandingsystems), , high-density systems,mucoadhesive systems,modified shape systems, gastric-emptying delaying devices and co-administration of gastric emptying delaying drugs. Among these the floating dosage forms are the most commonly used. Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so iremain 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 drugreleased slowly at the desired rate from the system.After release of drug, the residual system is eliminated from the stomach. This results in an increased GRT and a improved control of the fluctuations in plasma drugconcentration.[10]

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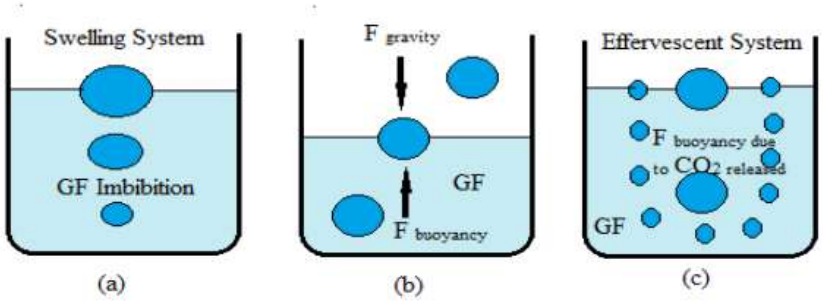

Figure3 iMechanism of FDDS [11]

SUITABLE DRUG CANDIDATES FOR GASTRO RETENTION:

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolong in a continuous, controlled manner. Drugs delivered in this manner have a lower level of side effect and provide their therapeutic effects without the need for repeated dosage with a low dosage frequency. Sustain release in the stomach is also useful for therapeutic agents that the stomach does not readily absorbed, since sustain release prolongs contact time of the agent in the stomach or in the upper part of small intestine, which is where absorption occur and contact time is limited under normal or average condition, Example. material passes through the small intestine in as little as 1-3 hrs[12]

In general, appropriated candidate are molecules that have poor colonic absorption but are characterizes by better absorption, properties at the upper part of GIT:

Narrow iabsorption window in GIT, E.g. Riboflavin iand Levodopa. i

Principally absorbed from stomach and upper part of GIT, Example: Calcium supplements, Chlordizepoxide and Cinnarazine.

Drugs that are locally acting in the stomach, Example. Antacids and Misoprostol.

Drugs that degrade in the colon, Example. Ranitidine HCl and Metronidazole. iDrugs that disturbs normal colonic bacteria, Example. Amoxicilline trihydrate.[13]

Table 1: Good candidates for gastroretentive drug delivery system[14]

Sr No	Drug and category	Bioavailabilty
1	Atenolol Antihypertesive	40-50%
2	Omeprazole Proton pump inhibitor	35-60%
3	Verapamil Antihypertensive	18-35% i
4	Propranolol Antihypertensive	4-26%
5	Nifedipine Calcium channel blocker	45-65%
6	Ramipril ACE inhibitor	28%
7	Clarithromycin Antibiotic	50%
8	.Lidocaine Local anaesthetic	35%
9	Verapamil Calcium channel blocker	20-35%

DRUGS UNSUITABLE FOR GASTRORETENTIVE DRUG DELIVERY SYSTEM:[13]

Table 2: Drug candidates unsuitable for floating Drug Delivery System[15]

Sr No.	Unsuitable Drug candidates	Example
1	Medication that are used for selective release in the colon	mesalamine and corticosteroids
2	Medication having terribly restricted acid solubility.	diphenylhydantoin
3	Medication that suffers instability among the gastric environment	Erythromycin

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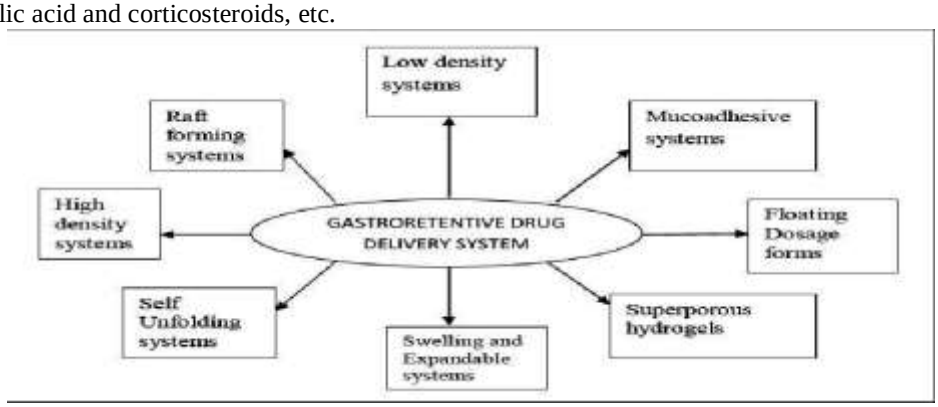
Drugs which have very limited solubility in the acid medium e.g. Phenytoin, etc.

- iDrugs enduring instability in the gastric environmental conditions e.g. Erythromycin, etc

.• iThe Drugs which are primarily employed for their selective release in the colon e.g. 5-aminosalicylic acid and corticosteroids, etc.

CLASSIFICATION OF GRDDS:

Dosage forms that can be retained in the stomach are called as Gastroretentive Dosage Forms (GRDF).



High Density System: These GRDF type have a density of -3g / cm3, and are retained in the stomach rugae. These systems can be retained in the lower part of the stomach above a maximal threshold density of 2.4-2.8g / cm3. The major disadvantage of it is that they are technically difficult deal iwith a large amount of drug product.

Swelling and Expandable System: The expandable GRDF is typically based on three designs, a small configuration that allows for easy oral intake; an expanded form that is complete in the stomach and thus preventing its transition through the pyloric sphincter and eventually another small form that is achieved in the stomach when retention is no longer essential. Swelling commonly occurs due to osmosis and the unfolding is because of mechanical shape memory.

Mucoadhesive or Bioadhesive System: these systems allow the include ithe bioadhesive agents that allow the system to adhere to the walls of the stomach, thus prevent gastric emptying. Bio/Mucoadhesive systems binds to the surface of the gastric epithelial cell, or mucin, and extend the GRT by increasing the intimacy and contact duration between the dosage type and the biological membrane.

Superporous Hydrogel: These are the swellable systems with an ordinary pore size of > 100µm, within a minute they swell to equilibrium due to a speedy absorption of water through capillary wetting through multiple interconnected open pores. They swell to a larger size and expect owo to iprovide enough mechanical strength to bear the pressure by the gastric muscular contraction.

Magnetic System: The magnetic dosage types contain an extra-corporal magnet and a small internal magnet that relats the gastrointestinal transit of the dosage form.

From the formulation and technical ipoint of view Floating Drug Delivery System (FDDS) is considerably easy and logical approach in the development of GRDF.[17-18]

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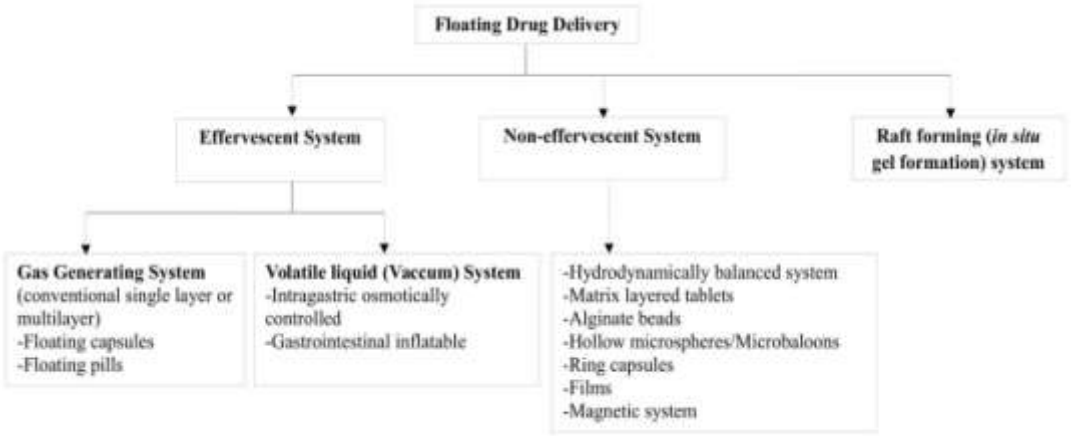
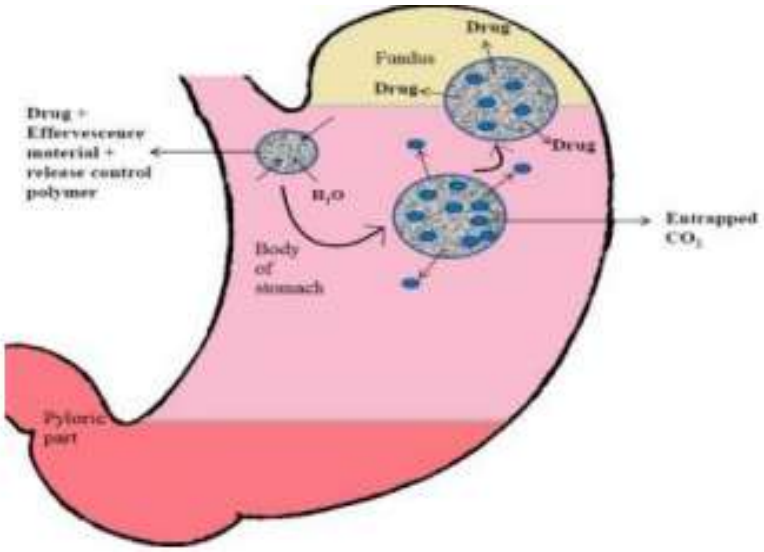
CLASSIFICATION OF FDDS



(A) Effervescent FDDS :1. Gas generating system i2. Volatile liquid containing system
(B)Non- Effervescent FDDS :1. Colloidal gel barrier system, 2. Micro porous compartment system3. Floating microsphere i,4. Alginate floating beads.
(C) Raft forming system

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEMS

[**A] Effervescent system** floating drug delivery systemThese are specific drug delivery system made up of matrix type and a swellable polymer such as chitosan and imethylcellulose along with effervescent compounds viz. sodium bicarbonate, tartaric acid, citric acid. These are formulated in such a peculiar way as once it comes in connected iwith gastric juice; co2 gets liberated with entrapment in swollen hydrocolloid to provide buoyancy for dosage form. The basis of the delivery system is on swellable asymmetric triple layer tablet approach design [19,21].



ifigure 5 GRDDS ibased on effervesent i[22]

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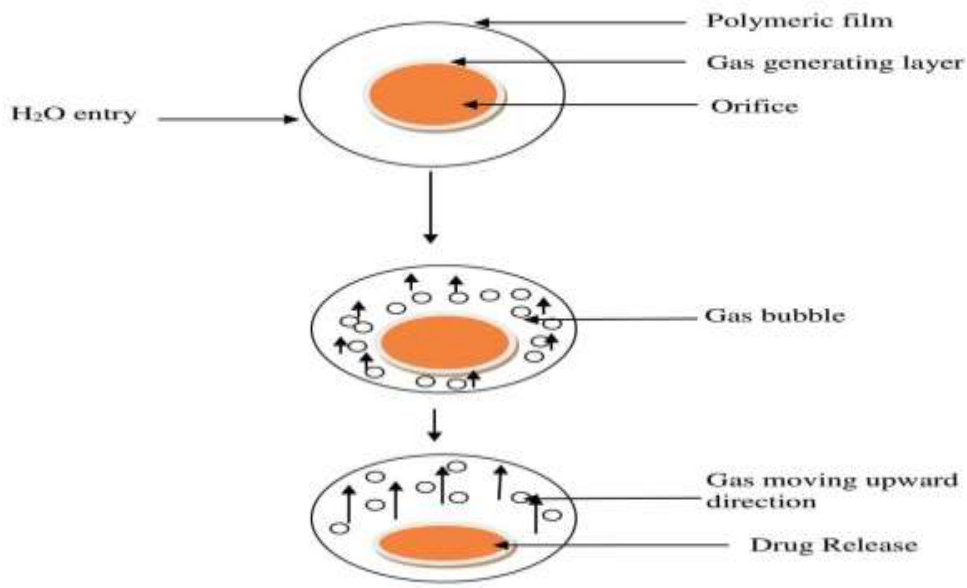
[I]Gas generating systems

Low-density FDDS is based on the release of co2 upon contact with gastric fluids after oral administration. The materials are formulated in such a way that after entering in the stomach, co2 is librated due to reaction with acidic gastric content and which get entrapped in the gel-based hydrocolloid (fig. 2). It produces an upward motion of the dosage form and maintains its buoyancy. Ultimately it causes a decrease in specific gravity of dosage form and hence resulting into a float on the chime. The co2 generating components are mixed within the tablet matrix in a single layer or multi-layered form to produce gas generating mechanism in hydrocolloid layer, and the drug iin the other layer results into a sustained release effect [19,21].

(II) Volatile liquid containing systems (Osmotically i controlled drug delivery system)

This is an osmotically controlled floating system that incorporate a device hollow deformable unit in convertible collapsed form. Housing would be connected to its deformable unit and internally divided into a first and second chamber separated by an impermeable, pressure sensitive movable unit. The first chamber usually contains an active drug, while the second a volatile liquid, such as cyclo pentane or ether get vaporized at a physiological temperature to produce a gas, enabling the drug reservoir to float. The unit gets expelled from the stomach, with the help of bioerodible plug that allowed the vapour to=escape[19,21].



(B) Non-effervescent FDDS

Non-Effervescent Floating Drug Delivery Systems comprises agel-forming (or) swellable cellulose type of hydrocolloids made up of polysaccharide along with matrix forming polymers like polycarbonate, polymethacrylate, and polystyrene. The routineformulation method relate the mixing of the drug with gel forming hydrocolloids that swell in contact with gastric fluidon oral administration and maintains its integrity of shape and a bulk density barrier, the air trapped by swollen polymer confer buoyancy to the dosage forms[19,21].

(I) Colloidal gel barrier systems (Hydrodynamic balancedsystems)

This system extend gastric retention time and maximizes the amount of drug that reaches its absorption site in the solution form. It basically contains drug with gel-forminghydrocolloids to remain buoyant on the stomach content. Such a system incorporates one or more gel-formingcellulose type hydrocolloid e.g. hydroxypropyl i methylcellulose (HPMC), polysaccharides and matrix forming polymers such as polycarbophil, polystyrene, and polyacrylate. Upon contact with gastro-Intestinal (GI) fluid,the hydrocolloid in the system hydrates to generate a colloid gel barrier to itssurrounding [20].

(II) Micro porous compartment systems

This technology include the encapsulation technique of a drug reservoir inside a micro porous

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compartmental on with pores at top and bottom walls. The peripheral wall of the drug reservoir compartment is entirely sealed to prevent any direct contact of the gastric surface with the undissolved drug. In the stomach, the floatation chamber composed of entrapped air causes the delivery system to float over the gastric content. Gastric fluid enters through the aperture, to the level that it prevents theirs exist from the drug and carrier the dissolved drug forcontinuous transport across the intestine for absorption[20].

(III) Floating Microspheres/Micro balloons

Hallow microspheres also are known as micro balloons are considered as a most efficient buoyant system. It is composed of central hallow space inside the microsphere. Hallow microsphere is loaded with a drug in their outer polymer shelf are fabricated by a novel solvent Diffusion method for emulsion [19].

(IV) Alginate beads/Floating beads Multi-unit floating dosage forms have been developed from calcium alginate spherical beads of about 2.5 mm in diameter and can be fabricated by adding sodium alginate solution into aqueous solution of calcium chloride, resulting in the precipitation of calcium alginate, the beadsare further separated, snap-frozen in liquid nitrogen and freeze-dried at 400 °C for 24 h, leads to generation of a porous system. This fabricated system would maintain a floating force for over 12 h and these floating beads provide a longer residence time of more than 5.5 h [20].

(C) Raft-forming systems

Raft-forming systems are in much attention for the delivery of antacid and drug delivery for gastro infection and disorders. On contact with gastric fluid, a gel-forming solution swells and forms a viscous cohesive gel entrapped with co2 bubbles which generate raft layer on top of gastric fluid, thus facilitates releases drug slowly in the stomach [19].

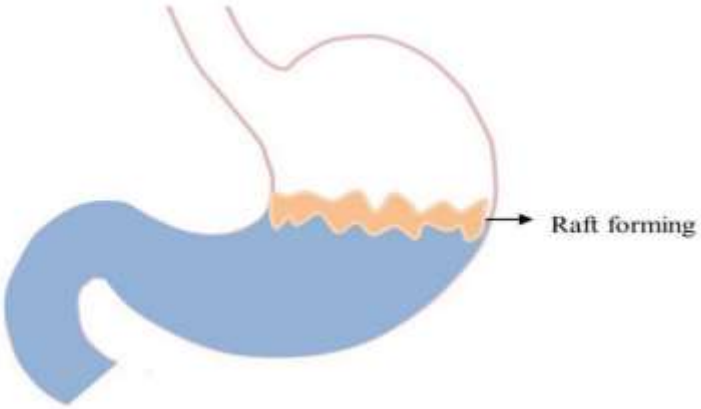

Figure 7: GRDDS based on Raft Forming System.[23]

FACTORS CONTROLLING FDDS:

Factors affecting gastric residence time of the floating drug delivery system:

1. Density of dosage form Floating is a function of dosage form buoyancy that is dependent on the density. Density of the dosage form should be less than the gastric contents (1.004gm/ml). A density of less than 1.0 gm/cm3 is required to exhibit floating property [25]. Hence dosage forms having a density lower than the gastric contents can float to the surface while high density systems sink to bottom of the stomach.

2. Shape and size of dosage form The shape and size of the dosage form are other factors that affect gastric retention. Dosage form unit with adiameter of more than 7.5 mm are reported to increaseGRT as compared to those with a diameter of 9.9 mm. Thedosage form having tetrahedron and ring shape deviseswith a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to exhibit better GIT for 90to 100 % retention at 24 hours compared with othershapes [26].

3. Food intake and its Nature Food intake, viscosity and volume of food, caloric value and frequency of feeding have a great influence on the gastric retention of dosage forms. The presence or absence of food in the gastrointestinal tract (GIT) affects the gastric iretention time (GRT) of the dosage form. Feeding of iindigestible polymers or fatty acid salts can alter the motility pattern of the stomach to a fed state thus leads to decreased gastric emptying rate and prolonging drug release.

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4. Caloric content i The gastric retention time (GRT) can be increased by 4 to10 hours with a meal that is high in proteins and fats [27]. Floating can increase by over 400 minutes when successive imeals are given as compared with a single meal due to the ilow frequency of migrating myoelectric complexes (MMC).

5. **Effect of gender, posture and age i**Females have slower gastric emptying rates than male. The effect of posture does not have much more difference in the mean gastric retention time (GRT). In case of elderly ipersons, especially those over 70, have a significantly longer GRT so gastric emptying is slowed down. Disease icondition such as diabetes and crohn's disease etc also affect drug delivery.

6. Fed or Unfed State During fasting conditions the gastric motility is characterized by periods of strong motor activity or the imigrating myoelectric complexes (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and if the timing of administration of the i formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However in thefed state, MMC is delayed and GRT is considerably longer [28].

7. Concomitant drug administration Anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramideand cisapride can affect floating time [29].

8. Single or multiple unit formulation i Multiple unit formulations are more predictable due to failure of units, allow co administration of units with different release profiles or containing incompatiblesubstances and permit a larger margin of safety against dosage form failure compared with single unit dosageforms.

ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM:[30]

I

FDDS can remain in the stomach for several hours and thereby prolonging the gastric retention time of various drugs. Advantageous for drugs which are meant for local action in the stomach E.g. Antacids.

Formulation of FDDS are useful in intestinal movement and in diarrhoea to hold the drug in floating state in the stomach in order to get comparatively better response. iBy decreasing the dosing frequency FDDS improves patient compliance.

Treatment of gastrointestinal disorders such as gastroesophageal reflux. Despite of first pass effect the bioavailability since the plasma drug concentration are avoided.

HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs since these drugs are acidic and causes irritation on the stomach wall

Advantageous for drugs which are absorbed through the stomach E.g. Ferrous salts, Antacids.

Delivery of the drug to the specific site.

DISADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM:[30]

The drug substances which are unstable in the acidic environment of the stomach are not suitable candidates for integration into the systems.

In these systems the presence of food is usually required to prolong their gastric emptying.

It is not suitable for drugs which are having stability or solubility problem in GIT.

he drugs which undergo first pass effect and the drugs which are significantly absorbed throughout gastrointestinal tract are only desirable candidate.

The tendency to float depends on the hydration state of the dosage form. Intermittent water administration is useful in order to keep these tablets floating.

METHODS OF DEVELOPING FLOATING DRUG DELIVERY SYSTEM:[31-34]

• **Direct compression technique**: It means compressing tablets directly from powder content without altering the substance's physical structure itself. Dicalcium itrihydrate phosphate, tricalcium phosphate, etc. are the most widely used carriers.

• **Effervescent Technique**: An effervescent reaction between organic acid (citric acid) and bicarbonate salts will fill the floating chamber of the drug delivery system with inert gas (CO2).

Wet granulation technique: Involves wet powder massaging, milling or drying. Wet granulation shapes the granules by binding the powders together with an adhesive rather than compacting them.

• **Ionotropic Gelation Technique**: Gelation of anionic polysaccharide sodium alginate, the primary polymer of natural origin, was accomplished with opposite charged calcium ions (counter-ions) with the objective of forming instantaneous micro particles.

• **Solvent evaporation technique**: Continuous phase ability is inadequate to remove the entire amount of liquid dispersal solvent. Solvent

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evaporates from the dispersal surface to receive hardened microspheres.

• **Spray Drying Technique**:Involves dispersing the core layer into the liquefied coating content and spraying the core coating mixture into the environment so that the coating is solidified by rapidly evaporating in which the coating material is solubilized. • Melt Solidification Technique: This method involves emulsifying the molten mass in the aqueous phase followed by cooling it to solidify. Lipids, waxes, polyethylene glycol, etc. are the carriers used for this technique. • Melt Granulation Technique: This is the method that agglomerates the pharmaceutical powders using a meltable binder and does not use water or organic solvents for granulation

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS

Enhanced Bioavailability In contrast to the administration of non-GRDF CR polymeric formulations, riboflavin CR-GRDF has a considerably greater bioavailability. There are numerous mechanisms that function in design to affect the degree of drug absorption, including drug absorption and transit in the gastrointestinal tract.

Absorption Enhancement Drugs having reduced bioavailability due to site-specific absorption from the upper part of the GIT may be formulated as FDDS to get better absorption

Sustained Drug Delivery Problems with gastric residence duration in the Gastrointestinal Tract (GIT) have been obtain with oral controlled release formulations. These issues can be resolved by HBS systems, that can retain in the stomach for prolonged timeperiod and increase in bulk density.

Reduced Fluctuations Of Drug Concentration In contrast to immediate release dosage types, continuous input of the medication after controlled release gastroretentive dosage form (CRGRDF) administration induces blood drug concentrations within a narrower range. Thus, Drug effect variations are reduced, and concentrationdependent adverse effects associated with peak doses can be avoided.

Minimized Adverse Activity At The Colon The amount of drug that enters the colon is reduced when the drug is stored in the Hydrodynamically Balanced system (HBS) systems at the stomach. Hence, the drug's unenviable effects in the colon can be avoided. ThGastro-retentive dosage form (GRDF) formulation for betalactam antibiotics that get absorbed only from the small intestine and whose presence in the colon contributes to the production of microorganism resistance is based on this pharmacodynamic aspect.

Site –Specific Drug Delivery Systems These systems are particularly useful for medications that are absorbed predominantly via stomach or the proximal small intestine. The monitored, gradual delivery of the medication to the stomach assure sufficient local therapeutic levels while limiting the drug's systemic exposure. The drug's side effects in the blood supply are minimised as a result. Furthermore, a site guided delivery system's prolonged gastric availability can cut down dosing frequency. For instance, furosemide and riboflavin.

EVALUATION OF FLOATING TABLET

Tablet density Tablet density is considered as an important parameter for floating tablets. The tablet will float only when its density ispeutic[35]

Tablet dimension A calibrated vernier calliper was used to measure thickness and diameter. Three tablets of each formulation were chosen randomly, and their thicknesses were measured individually[36]

Weight variation test Twenty tablets were selected randomly from each batch and measured separately to see if there was any weight variation. The USP allows for small variation in the weight of a tablet. The percentage deviation in weight variance allowed is as follows. The tablet weight was greater than 324 mg in all formulations, allowing for a maximum difference of 5%.

Hardness test The hardness of a tablet determines its ability to tolerate mechanical shocks while being observed . The Monsanto tester was used to measure the hardness (kg/cm2) tablet. The mean of five replication determinations was used in all cases.

Friability test This was determined by weighing 26 pills after dusting, placing them in the Roche friabilator, and rotating the plastic cylinder vertically at 25 rpm for four minutes, according to Indian Pharmacopoeia (IP). The total remaining weight of the tablets was reported after dusting, and the percentage friability was calculated using the equation below. % Friability = Initial wt. of tablets – Final wt. of tablets / Initial wt. of tablets × 100 % The acceptable Friability of tablets= < 1%.

In vitro buoyancy study The time period between the introduction of the dosage form and its buoyancy on the SGF, as well as the time the dosage form stays buoyant, were all determined. The time it takes for the dosage form to appear on the medium's surface is known as Floating Lag Time (FLT) or Buoyancy Lag Time (BLT), and the

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total time it takes for the dosage form to stay buoyant is known as Total Floating Time (TFT). Floating behaviour study were carried out in a USP XXIII dissolution Apparatus type II (Paddle) at a speed 50 RPM in 900 ml SGF at 37±0.50C for 12 hr to mimic in vivo conditions[37]

X-Ray method Nowadays, X-Ray has become a very common evaluation parameter for floating dosage forms. It aids in the location of dosage forms in the GIT, as well as the prediction and correlation of gastric emptying time and dosage form passage in the GIT. The incorporation of a radio-opaque substance into a solid dosage shape allows for X-ray visualisation[38.]

Swelling index: The weight determines the swelling activity of the measurement device. When using a pH 6.8 buffer dissolution medium at 370.5 °C, the tablet swelling index correlates to the tablet site in the dissolution tool basket (type 1). At each time point, the trials were repeated three times[38].

INNOVATIVE TECHNOLOGIES FOR FDDS[39]

Oleotec™ and Soctec™ : Oleotec™ and Soctec™ gastroretentive capsule technology are innovated by Skyepharma company. For Drugs having high therapeutic doses, Oleotac TM technique is designed but it is unsuitable for the conventional dosage form. Drugs that show effect primarily in the proximal part of the gastro intestinal tract are developed by this technique. Oleotec system is basically a gel incorporated in the form of stick pack that forms a continuous layer at walls of the stomach. Soctec TM system is designed for the drugs that should be administered as controlled release and should be absorbed in the proximal part of intestine for increasing the bioavailability of drug. Soctec is an elongated capsule fill with drug. It can be used with a range of drugs that have a short absorption window and are preferably absorbed in the proximal intestine fragment. It can also improve the bioavailability of drugs that are degraded by the basic pH of the distal part of GIT.

Accordion Pill™ Technology: This is a versatile gastro adhesive formulation composed of the biodegradable polymers. It is a multi-layer, planar structure, folded to an accordion shape into regular standard size capsule. When capsule reaches to the stomach, it dissolves, the folded pill unfolds and is sustained in the stomach last up to 12 hours. During it is in the stomach, the pill releases the drug in a controlled manner towards the proximal part of the GI tract which gives extended and continuous absorption phase of the drug in the upper part of the GI tract, resulting in increased efficacy and safety profiling, as well as reducing frequency dosing. The drug release mechanism is not dependent on the Accordion pill™ retention mechanism. After the Accordion Pill™ is expelled from the stomach, it is get degraded in the intestinal media. Drugs which are belonging to the BCS Class II and BCS Class IV are more preferable for this system.

Gastro Retentive Innovative Device (GRID): Gastro Retentive Innovative Device (GRID) is an ideal once-a- day system for drugs that are otherwise absorbed only in stomach or small intestine. GRID is designed so that drug is retained in the stomach for over an eight-hour span. Longer retention in stomach improves the drug absorption. The tablet offers a combination of instant and sustained drug release profiles, and being once a day improves patient compliance. This innovative system is a dosage form with specialized multiple coatings. On ingestion of the dosage form along with food, it floats instantaneously on the gastric contents. GRID's coatings are activated by gastrointestinal fluid, eventually leading to swelling, to about eight to eleven times its initial volume. Plasma concentrations for medicines are thus maintained in the therapeutic range for a prolonged period; hence this dosage form can be used as a "Once-a- day" system. Specific release profiles for drugs can be customised to achieve combination of immediate and slow release using this innovative dosage form. Retention of the dosage form close to its site of absorption may help in reducing the dose and thus the side effects.

Multiple Polymers Hydrophilic Matrix Technology: Multiple polymer hydrophilic matrix technology is a sustained gastro drug delivery system. Cetapin XR is a formulation of this system patented by Sanofi which contain Metformin XR as a drug , to achieve extended release of Metformin hydrochloride. The polymers are made by combining non-ionic and ionic hydrophilic polymers. The drug release from the matrix pore occurs through a process of dissolution of the drug and undergoing diffusion through the gel matrix in a sustained manner. This technology gives consistent and reproducible results with good optimal absorption, minimum irritation, increased plasma drug levels and good bioavailability.

Acuform® technology: Acuform® is formulated patented by Depomed's. it is a polymer-based technology formulated to optimize drug delivery in GIT. This technology permit targeted and controlled delivery of drug to the proximal (upper)

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GIT which is the preferable absorption site for many oral drugs. In particular, for drugs that are absorbed in the upper GI region this technology is an effective delivery solution. It is also valuable for drugs insoluble in water, irritating for mucosa of the small intestines or not safe in the distal GIT region and it is more effective when plasma drug levels have less fluctuation. . Gastrointestinal Permeation Enhancement Technology: Gastrointestinal Permeation Enhancement Technology (GIPET) is formed by Merrion Pharmaceutical's and it is specific approach which allows drugs that now can only be injected by parenterally (injectable). For to converted into oral solid forms e.g. tablet/capsule, as well as enhance the absorption of oral drugs. Gastrointestinal Permeation Enhancement Technology uses selectively formulated oral formulations absorption enhancers which activate micelle formation undergoing transport of drug and increasing absorption with good reproducibility and a strong safety profile.[39]

LIST OF DRUGS FORMULATED AS SINGLE AND MULTIPLE UNIT FORMS OF FLOATING DRUG DELIVERY SYSTEM (40)

Tablet	Acetylsalicylic acid, Prednisolone, Acetaminophen, Ampicillin, Cinnarazine,Ciprofloxacin, Chlorpheniramine maleate, Theophylline, Furosemide, Captopril, Acetylsalicylic acid, Sotalol, Nimodipine, Amoxycillintrihydrate
Powder	Several basic drugs
Capsule	Furosemide, Nicardipine, Misoprostol, Diazepam, Propranolol,L Dopa, Benserazide, Urodeoxycholic acid, Chlordiazepoxide HCl,
Microspheres	Aspirin, Griseofulvin, iTerfenadine, Tranilast, Ibuprofen.Verapamil, p-Niroaniline, Ketoprofen.,
Films	Drug Delivery Device, Cinnarizine.
Granules	Diclofenac sodium, Prednisolone, Indomethacin

THE MARKETED PRODUCTS OF FLOATING DRUG DELIVERY SYSTEM.(41)

Drug	**Brand Name**	**Delivery System**
Ferrous sulphate	Conviron®	Colloidal gel forming FDDS
Aluminium hydroxide,	Gaviscon®	Effervescent floating liquid
Misoprostol	Cytotech®	Bilayer floating capsule
Diazepam	Valrelease®	Floating Capsule
Ciprofloxacin	Cifran OD®	Gas-generating floating form
Mg Carbonate	Gaviscon® i	alginate beads

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