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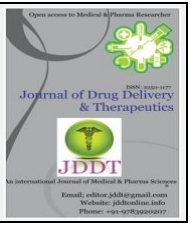

Open Access Review Article

An exhaustive overview of floating drug delivery system

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ABSTRACT

The purpose of writing this review is to narrowing down on floating drug delivery systems (FDDS) and to compile the current literature with special focus on the principal mechanism of floatation to ameliorate gastric retention. The current amelioration of FDDS including the physiological and formulation variables affecting gastric retention approaches to design single unit and multiple unit floating systems, and a plethora and formulation aspects are covered in detail. This review also summarizes the in vitro technique and in vivo studies to evaluate the performance and application of floating systems and applications of these systems. These systems are useful to several plights encountered during the amelioration of a pharmaceutical dosage form.

Keywords: FDDS: Floating Drug Delivery System, ND: Narrowing down, PD: Pharmaceutical dosage

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INTRODUCTION

In the modern era different routes of administrations having varieties of nuance but oral route administration has tremendous advancement in drug delivery system. However, oral routes have different advantages rather than any other route . This route got success because gastrointestinal physiology offers more flexibility in dosage form design than other routes. The gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms that reside in the stomach for a longer period of time than conventional dosage form. Drug absorption from gastrointestinal tract is a complexable procedure [1]. It is widely acknowledged that the extent of gastrointestinal tract drug absorption is related to contact time with the small intestine mucosa. Gastro retentive drug delivery systems are the system which are retained in the stomach for a longer period of time and thereby improve the bioavailability of drugs which are absorbed from upper gastro intestinal tract. The drug bioavailability of pharmaceutical dosage forms is influenced by various factors. However, pivotal point is that gastric residence time another factors of these dosage form. The process of gastric emptying from stomach to intestine generally lasts from a few mins to 12 hrs. This variability leads to an unpredictable bioavailability of an orally administered dosage form. FDDS have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.[2] However , the drug is released in this system very slowly after release of drugs the residual system is emptied from the stomach. This results in increased GRT and better control of fluctuations in plasma drug concentration.[3]

Basic Gastrointestinal Tract Physiology:

The digestive system are composed of the gastrointestinal tract /digestive tract/gut three pairs of salivary glands , the liver and another one is that pancreas. Different parts of the GI tract are oral cavity , pharynx , oesophagus , stomach , duodenum , jejunum , ileum , caecum , ascending colon , transverse colon , descending colon , sigmoid colon , rectum , and another pivotal component is that anal canal.

Stomach is the sac like dialated part of the gut in between oesophagus and duodenum. Its capacity may vary from 50 ml to 5 litre. The gut wall composed of four layers but it has additional muscle layer (the inner most oblique layer) . The stomach is divided into three gyners first one is fundus, second thing that is body rest pylorus. The oesophagus end of the stomach is called cardiac and is guarded by a physiological sphincter .The pylorlic sphincter is situated in between the stomach and the duodenum. The pyloric sphincter is formed by the thickening of the circular layer of

muscles. The mucous membrane of stomach is thick and is thrown into folds called gastric rugae seen only in empty stomach .This arrangmentys helps to accommodate extra volume of food without stretching the mucous membrane. The lining cells of the mucous membrane are of simple columner type which secrets mucin and arte covered by a thick layer of gastric mucin .The glands are situated within the mucous membrane in groups of 2 to 7 which together communicate with the gastric lumen through the gastric pits.[4,5]

Gastric glands:

These glands are of three types first one is cardiac second is fundic and rest body, pyloric glands. The cardiac glands are small in number , situated in the cardiac end and secrete mainly mucin .The glands in the fundus and body are highest in number and secrete the acidic juice .The pyloric glands are again of mucous types. Atypical acid secreting gland is tubular and straight .Each gland is divided into three parts neck, body and another is that base. The junction of a gland with the gastric pit is called isthmus .The cell lining the glands are of the following types isthmus cell, neck cell, oxyntic cell, another one is chief cell. The isthmus and neck cell are secrete mucin .The neck cell are common types called mother cell. These cells divided and differentiate to produce both of the surface epithelium as well as the cells of the glands proper each cells takes 2 to 3 days to mature and function and are ultimately desquamated.[6,7]

Chief cells or peptic cells:

These cells secrete pepsinogens and are the sources of rennin in calves and gelatinase in pigs. These are situated in the wall of the glands near the base and contain zymogen granules of pepsinogens.

Oxynntic cells or parietal cells:

These are situated mainly towords the neck of the glands and secrete hydrochloric acids and the intrinsic factors .These cells have an extensive microcanalicular system which communicates with the lumen of the glands by a canaliculus . In resting state of the cell part of this microcanalicular system is converted into innumerable tubulovesicular structures formed of smooth membrane .These vesicles are fused with the microcanalicular system when the cell is stimulated to secrete HCL.

Gastric glands:

Gastric glands also contain many other types of cells .The amine precursor uptake and decarboxylation cells (APUD cells) form the important group which secrete different GIA hormones .Mast cells secrete histamine .Argentaffin cells are yhere to secrete serotonin . There are also cells which secrete various local hormones like bombesin , somatostatin , glucagon etc.

G cells:

The G cells of the stomach are present in the pyloric glands and secrete gastrin .These cells are triangular or conical in shape with the narrow apex towords the lumen. Several microvilli project from the apex .Gastrin is stored in the granules inside the cells .The cells release gastrin through the basal side when they receive stimuli from the apical side through the microvilli.

Mechanism of action of HCL Secretion:

In the microcanalicular system of the oxyntic cells there are proton pumps H+K+ATPase. On stimulation of the cell the tubulovesicles fuse with the microcanaliculi to increase surface area along with the number of proton pumps in it. These proton pumps actively transport H+ into the microcanaliculi from the cytoplasm of the oxyntic cell in exchange of K+ after consumption of ATP. Chloride ions are transported through the chloride channels in the micro canalicular membrane and K+ follows. These H+ and CL- secreted into the microcanaliculi now form the HCL. The CL comes from the plasma through the basal side of the cell via CL- HCO3- exchange . H+ is produced in the cytoplasm from ionisation of water ($H_2O \rightarrow H^+ + OH^-$) For each H+ ,one OH- is produced which is highly toxic and is neutralised by H+ produced within the cells from hydration of CO_2 in presence of carbonic anhydrase.[8]

Intestinal secretion :

It is the secretion produced by the glands in the small intestine. It is more a transduate than a secretion by the glands .The glands involved are called crypts of Lieberkuhn .These glands are produced by outward extension of the surface mucous membrane or as depressions in between the intestinal villi. These are simple tubular glands lined by columner cells. The villi are finger like projections situated all over the mucous membrane of the small intestine but are more in jejunum than in ileum .The villi are lined externally by a layer of columnar cells also called enterocytes., the, main lining epithelium of the intestine .Each villus is about 0.5 to1 mm in length .The core of the villus contains connective tissue, blood vessels, smooth muscles fibres and a lymphatic channel. The blood vessels form loops through which the arterial blood goes towards the tip and then returns as venous blood .The lacteal joins the lymphatic system .This types of arrangements in lymph and blood flow in the villi is very much helpful for absorption .The enterocytes have microvilli (brush border) on the luminal side which is covered by a layer of glycocalyx . The cell membrane in the brush border contains various enzymes needed for digestion. The villi and microvilli both of them increase the surface area of the mucous membrane of the small intestine and thus aid the process of absorption. The cells lining the crypts of Lieberkuhn which elaborate the succus entericus, differentiate into enterocytes and gradually move up the villi .One such cell is the goblet cell which secretes mucus. The paneth cells secrete bacteriolytic enzymes. Enterochromaffin cells secrete serotonin which probably cause intestinal secretion and movement.Another types of cells are present that is M cells or microfold cells. It is an antigen presenting cell and present antigens to the lymphoid cells in the gut to cause secretory immunity.[9]

Gastric empty rate :

A gastric empty rate occurs during fasting condition as well as fed states. The pattern of motility distinct in the 2 states. During the fasting in condition indigestive series of electrical events takes place which cycles both through stomach intestine every 2 to 3 hours . This is called indigestive mylo electric cycle. This cycle is divided into 4 gyners .

Phase 1: it's also called basal phase .However lasts from 40 to 60 mins with rare contraction.

Phase 2: This phase is also called preburst phase. However lasts for 40 to 60 mins with intermittent action potential and contractions In this phase progresses the intensity and frequency are also increase gradually.

Phase 3: This is also called burst phase. However lasts for 4 to 6 mins . It includes intense and regular contraction for short period of time.

Approaches to gastric retention:

In the modern era different types of system have been developed to increase the gastric retention time of dosage forms by employing range of concepts. The basic classification of this system has been explaned briefly under.

1. Floating drug delivery system: This system have low density and so float over the gastric contents.
2. Bioadhesive system : This system is very important because they bind with stomach mucosa and hence enable to localize retention of the system
3. Swelling and expanding: Such system absorbs water and hence enlarged size.
4. High density system: They remain in the stomach for longer period of time by sedimenting to the folds of the stomach.

Floating drug delivery system:

Floating drug delivery system (FDDS) or hydrodynamically controlled system which have a bulk density less than gastric fluids and because of this these systems remains buoyant (3-4hrs) for a prolonged of time in the stomach without affecting the gastric emptying rate.

Advantages of floating drug delivery system:

1.Floating dosage forms such as tablets or capsules will remains in the solution for prolonged time event alkaline PH of the intestine.

2. FDDS are advantageous for drugs meant for local action in the stomach. eg: Antacids.

3. 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.

4. Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence FDDS formulations may be useful for the administration of aspirin and other similar drugs.

5. The FDDS are advantageous for drugs absorbed through the stomach . eg: Ferrous salts , antacids.
6. Slow release of the drug into the body minimizes the counter activity leading to higher drug efficacy.
7. FDDS reduces the drug concentration fluctuation over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes.
8. Retention of drug in GRDF at stomach minimizes the amount of drugs that reaches the colon and hence prevents the degradation of drug that degraded in the colon.
9. A floating dosage form is a widely accepted approach especially for drugs which have limited absorption sites in upper small intestine.[10]

Disadvantages of Floating drug delivery system:

1. These systems require a high level of fluid in the stomach for drug delivery to float and work efficient – coat.
2. Not suitable for drugs that have solubility or stability problem in GIT.
3. Drugs such as Nifedipine (calcium channel blocker) which is well absorbed along the entire GIT and which undergoes first pas metabolism , may not be desirable.
4. Drugs which are irritant to gastric mucosa are also not desirable or suitable.
5. The drug substance that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the systems.
6. The dosage form should be administered with a full glass of water(200- 250 ml)
7. These system do not offer significant advantages over the conventional dosage forms for drugs , which are absorbed throughout the gastrointestinal tract.[11]

Drug Candidates Suitable for Floating drug delivery systems:

In general, appropriate candidates for CR-GRDF are molecule that have poor colonic absorption but are characterized by better absorption properties at the upper part of the GIT :

- Narrow absorption window in GI tract , e.g , riboflavin and levodopa
- Primarily absorbed from stomach and upper part of GI tract , e.g: calcium supplement , cholrdiazepoxide and cinnarazine.
- Drugs that act locally in the stomach , e.g : H2 receptor antagonists , antacids and misoprostol.
- Drugs that degrade in the colon, e.g : ranitidine HCL and metronidazole.
- Drugs that disturb normal colonic bacteria , e.g : amoxicillin trihydrate.[12,13]

Mechanism of Floating Systems:

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introducing floating dosage forms (gas generating systems and swelling or expanding systems) , mucoadhesive system , high density 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 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 eliminated from the stomach . This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However , besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention effect , a minimal level of floating force (F) is also required to maintain the buoyancy of the dosage form on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature.[14,15]

$F = F_{buoyancy} - F_{gravity} = (D_f - D_s)\, g\, v$

Where , F = total vertical force
DF = fluid density
Ds = object density
V= volume
G = acceleration due to gravity

Drugs Unsuitable for Gastric Retention:

1. Drugs that have very limited acid solubility e.g . phenytoin
2. Drugs that suffer instability in the gastric environment e.g erythromycin .

3. Drugs intended for selective release in the colon e.g 5 amino salicylic acids and corticosteroids .

Factors Affecting Gastric Retention:

The gastric retention time (GRT) of dosage form is controlled by several factors that affect their efficacy as a gastroretentive system .

Density: GRT is a function of dosage form buoyancy that is dependent on the density.

Size: Dosage form units with a diameter of more than 9.5 mm are reported to have an increased GRT.

Shape of Dosage form : Tetrahedron and ring- shaped devices with a flexural modulus of 48 and 22.5 kilopounds per square inch (KSI) are reported to have better GRT . 90 % to 100 % retention at 24 hrs compared with other shapes.

Single or Multiple Unit Formulation : Multiple unit formulation shows a more predictable release profile and insignificant impairing of performace due to failure of units , allow coadministration of units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.

Fed or Unfed State: Under fasting conditions , the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hrs . The MMC sweeps undigested material from the stomach and if the timing of administration of the formulation coincides with that of the MNC , the GRT of the unit can be expected to be very short. However , in the fed state , MMC is delayed and GRT is considerably longer .

Nature of Meal: Feeding of indigestible polymers or fatty acids salts can change the motility pattern of the stomach to a fed state , thus decreasing the gastric emptying rate and prolonging drug release.

Caloric Content: GRT can be increased by four to 10 hours with a meal that is high in proteins and fats .

Frequency of Feed: The GRT can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MNC.

Gender : Mean ambulatory GRT in meals (3.4 ± 0.6 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 .

Age: Aged people, especially those over 70, have a significantly longer GRT.

Posture: GRT can vary between supine and upright ambulatory states of the patients.

Concomitant Drug Administration: Anticholinergics like Atropine and propantheline , opiates like codeine and prokinetic agent like Metoclopramide and Cisapride.

Biological Factors: Diabetes and Crohn's disease . 1.Single unit 2 . Multiple unit[16,17,18]

Approaches to Design Floating Dosage:

Single Unit Dosage Form

In low density: Approach the globular shells apparently having lower density than that of gastric fluids 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 24 popcorn , poprice and polystyrol have been used 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 ethyl cellulose or hydroxypropyl cellulose depending on the type of release desired .[19] Finally the product floats on the gastric while releasing the drug gradually over a prolonged duration .

Fluid Filled Floating Chamber:

Type of dosage forms includes incorporation of a gas filled floatation chamber into a microporus component that houses a drug reservoir . Apertures or openings are present along the top and bottom walls through which the gastrointestinal tract fluid enters to dissolve the drug .The other two walls in contact with the fluid are sealed so that the undissolved drug remains therein. The fluid present could be air , under partial vacuum or any other suitable gas , liquid or solid having an appropriate specific gravity and an inert behaviour . The device is of swallowable size , remains afloat within the stomach for a prolonged time , and after the complete release the shell disintegrates passes off to the intestine and is eliminated.[20]

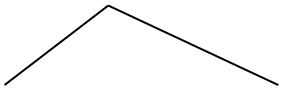
Hydrodynamic Balanced System:

These are designed to prolong the stay of the dosage form in the gastrointestinal tract and aid in enhancing the absorption . Such systems are best suited for drugs having a better solubility in acidic environment and also for the drugs having specific site of absorption in the upper part of the small intestine . To remain in the stomach for a prolonged period of time the dosage form must have a bulk density of less than 1. It should stay in the stomach , maintain its structural integrity and release drug constantly from the dosage form .[21]

Multiple Unit Dosage Form:

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 drawback of single unit formulations. Single unit formulations are associated with problems such as sticking together or being obstructed in gastrointestinal tract , which may have a potential danger of producing irritation .Multiple unit systems avoid the all or none gastric emptying nature of single unit systems. It reduces the intersubject variability in absorption and the probability for dose damping is lower .Microspheres have high loading capacity and many polymers have been used such as albumin , gelatine , starch , polymethacrylate, polyacrylamine, and polyalkylcyano-acrylate. Spherical polymeric microsponges , also referred to as microballoons have been prepared .Microspheres have a characteristic internal hollow structure and show an excellent in vitro floatability .[22]

Classification of Floating Drug Delivery System



Effervescent system	Non effervescent system
Gas generating system	Colloidal gel barrier system
Volatile liquid containing system	Alginate beds
	Hollow microspheres/ Microballoons
	Intragastric Floating Drug Delivery
	Device / Microporous compartment system

Effervescent Floating Dosage Forms:

These are matrix types of systems prepared with the help of swellable polymers (methyl cellulose and chitason) and various effervescent compounds (sodium bicarbonate , tartaric acids , and citric acid) .They are formulated in such a way that when come in contact with acidic gastric contents , CO2 liberate and gas entrapped in swollen hydrocolloids which provides buoyancy to the dosage forms .

Gas Generating Systems:

These buoyant delivery systems utilize effervescent reactions between carbonate /bicarbonate salts and citric / tartaric acids to liberate CO2 which gas entrapped in the gellified hydrocolloid layer of the systems thus decreasing its specific gravity and making it to float over chime.

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 inflation 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 .[23]

Non –effervescent Floating Dosage Forms:

The non-effervescent FDDS works on the mechanism of polymer swelling , bioadhesion of the polymer to mucosal layer of GI tract .The most common used excipients for the preparations of non-effervescent FDDS are gel forming or swellable cellulose type hydrocolloids , polysaccharides and matrix forming polymers like polycarbonate, , polyacrylate , polymethacrylate and polystyrene . The formulation method includes simple approach of thoroughly mixing of the drug and the gel –forming hydrocolloid . After oral administration this dosage form swells in contact with gastric fluids and attains bulk density of less than 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form ,so formed swollen gel- like structure release of drug through the gelatinous mass.[24]

Colloidal Gel Barrier Systems:

A system that contains drug with gel – forming hydrocolloids meant to remain buoyant on the stomach content. This prolongs GRT and maximizes the amount of drug that reaches its absorption sites in the solution form for ready absorption. This system incorporates a high level of one or more gel forming highly swellable cellulose type hydrochlorides , e.g : HEC , HPMC, NaCMC , polysacchacaries 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 this dosage forms.[25]

Alginate beads:

Multi –unit floating dosage forms have been ameliorates 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 -40 degree C for 24 hrs ., leading to the formation of a porous system , which can maintain a floating force for over 12 hours.[26]

Hollow microspheres / Microballoons:

It is prepared by a novel emulsion solvent diffusion method . The ethanol / dichloromethane solution of the drug and an enteric acrylic polymer was poured into an agitated solution of poly Vinyl Alcohol(PVA) that was thermally controlled at 40 degree C . The gas phase is generated in the dispersed polymer droplet by the evaporation of dichloromethane formed and internal cavity in the microsphere of the polymer with drug.[27]

Intragastric / Microporous Compartment System:

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. Novel levodopa gastro retentive dosage form based on unfolding polymeric members 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 narrow absorption window drugs. However , there are possibilities of the polymeric films to get stuck in the oesophagus causing extreme discomfort to the patient or drug related injuries and repeated administration of rigid dosage form may result in gastric obstruction.[28]

Application of Floating Drug Delivery System:

Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal

tract . It remains the dosage form at the site of absorption and thus enhances the bioavailability . These are summarized as follows:

1. **Sustained Drug Delivery:**

HBS system can remain in the stomach for long periods and hence can release the drug over a prolonged period of time . The problem of short gastric residence time encountered with an oral CR formulation hence can be overcome with these systems . These systems have a bulk density of < 1 as a result of which they can float on the gastric contents .These systems are relatively large in size and passing from the pyloric opening is prohibited . Recently sustained release floating capsules of nicardipine hydrochloride were developed and were evaluated in vivo. The formulation compared with commercially available MICARD capsules using rabbits. Plasma concentration time curves showed a longer duration for administration (16 hours) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hours)

2. Site Specific Drug Delivery:

These systems are particularly advantages for drugs that are specifically absorbed from stomach or the proximal part of the small intestine e.g : riboflavin and furosemide (K+ sparing diuretics) . However the pivotal point is that furosemide is primarily absorbed from the stomach followed by the duodenum. It has been reported that a monolithic floating dosage from with prolonged gastric residence time was developed and the bioavailability was increased .AUC obtained with the floating tablets was approximately 1.8 times those of conventional furosemide tablets. A bilayer – floating capsule was developed for local delivery of misoprostol , which is a synthetic analog of prostaglandin used as a protectant of gastric ulcers caused by administration of NSAIDs by targeting slow delivery of misoprostol to the stomach , desired therapeutic levels could be achieved and drug waste could be reduced.

3. **Absorption Enhancement:**

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

4. **Enhanced Bioavailability:**

The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non –CR-GRDF 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.

5. **Enhanced first –pass biotransformation:**

In a similar fashion to the increased efficacy of active transporters exhibiting capacity limited activity , the pre-systemic metabolism of the tested compound may be considerably increased when the drug is presented to the metabolic enzymes (cytochrome p450, in particular CYP3A4) in a sustained manner ,rather than by a bolus input.

6. Sustained drug delivery/reduced frequency of dosing:

For drugs with relatively short biological half-life ,sustained and slow input from CR-GRDF may result in a flip –flop pharmacokinetics and enable reduced dosing frequency .This features is associated with improved patient compliance ,and thereby improves therapy.

7. Targeted therapy for local ailments in the upper GIT:

The prolonged and sustained administration of the drug from GRDF to the stomach may be advantageous for local therapy in the stomach and small intestine . By this mode of administration ,therapeutic drug concentrations may be attained locally while systemic concentration ,following drug absorption and distribution , are minimal.

8. Reduced fluctuations of drug concentration:

Continuous input of the drug following CR-GRDF administration produces blood drug concentration 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.

9. Imporved selectivity in receptor activation:

Minimization of fluctuations in drug concentration also makes it possible to obtain certain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations.

10. Reduced counter –activity of the body:

In many cases , the pharmacological response which intervenes with the natural physiological process provokes a rebound activity of the body that minimizes drug activity .Slow input of the drug into the body was shown to minimize the counter activity leading to higher drug efficacy.[29,30]

CONCLUSION

From this review we opined that drug absorption in gastro intestinal tract is highly variable procedure and prolonging the gastric retention of the dosage form. FDDS is better approach rather than any other drug delivery system to achieve gastric retention. This article give a lacunae overview of the FDDS as well as the main concept used to design the drug delivery system to achieve the prolong gastric retention.

REFERENCES

1. Kandwal M, Gnanarajan G, Kothiyal P; Floating Drug Delivery System: A Novel Approach , Volume 3 , No : 3 ,2014, page no : 57-69

2. Narang N: An updated on : Floating drug delivery system(FDDS); International journal of applied pharmaceutics , 2010; 3(30:1-7

3. Abhishek Chandel , Kapil Chauhan , Bharat Parashar , Hitesh Kumar , Sonia Arora ; Floating drug delivery systems : A better approach , Vol : 1 , International Current Pharmaceutical Journal , 2012 1 (5) : 110 -118

4. Juhi Dubey , Navneet Verma ; Floating drug delivery system : A review , International Journal of Pharmaceutical Science and Research , , Vol : 4 , No :8 , 2013 ,Page no : 2893 -2899

5. Purnima Tripathi , U.Ubaidulla , Roop kishan khar , Vishwavibhuti ; Floating drug delivery system, International Journal of Research and Development in Pharmacy and Life Sciences , Volume : 1 , No :1 , 2012 , Page no : 1-10

6. Bhavjit kaur , Shivani Sharma , Geetika Sharma , Rupinder Saini , Sukhdev Singh ; A Review of Floating Drug Delivery System ; Asian Journal of Biomedical and Pharmaceutical Sciences , Volume : 3 , No : 24 , 2013 , Page no : 1-6

7. Prajapati ST, Patel LD , Patel CN ; Polymers for Floating Drug Delivery System ; Systematic Reviews in Pharmacy , Volume :2 , No :1 , 2011 January – June

8. Azhar Danish Khan , Meenakshi Bajpai ; Floating Drug Delivery System : An Overview ; International Journal of Pharma Tech Research , Volume : 2 , No :4 ,2010, Page no : 2497-2505

9. P.G Yeole , Shagufta Khan , V.F .Patel ; Floating Drug Delivery System : Need and Development ; Indian Journal of Pharmaceutical Science , 2005 , (3) : 265-272

10. Singh Amit Kumar , Arora Vandana ; Formulation and In vitro Evaluation of Glipizide as Floating Drug Delivery system with Natural Polymer (Gur –Gum) ; Journal of Pharmaceutical and Scientific Innovation ;Volume 1 , , 2012 July –August , Page no : 24-28

11. Kataria Sahil , Middha Akanksha , Bhardwaj Sudeep , Sandhu Premjeet ;Floating Drug Delivery System : A Review ; International Research Journal of Pharmacy ; 2011 ,2(9) , 18-24

12. P.S.Dongare , A.B.Darekar , Gondkar S.B , R.B.Saudagar ; Floating Drug Delivery System : A Better Approach ; International Journal of Pharmacy and Biological Sciences , Volume :3 , No:4 ,2013 , October - December , Page no : 72-85

13. Hetangi Rathod , Vishnu Patel , Moin Modasia ; Floating Drug Delivery System : Innovative Approach of Gastroretention ; International Journal of Pharmaceutical Sciences Review and Research ; Volume : 4 , No: 3 , 2010 September – October , Page no 183 -192

14. Abdul Hafeez , Arun Maurya , Jagpal Singh , Ankit Mittal , Lakhan Rana ;An Overview on Floating Microsphere : Gastro Retention Floating Drug Delivery System (FDDS) ; The Journal of Phytopharmacology ; 2013 ;2(3) :1-12

15. Srujana Katta , Mettu Srikanth Reddy , N.G.Raghavendra Rao ; Ovierview on Floating Drug Delivery System ; American Journal of PharmTech Research; 2018 , Volume 3, No: 6

16. Jagdale S, Shinde M ; Development of Floating Delivery for Solid Self Micro –Emulsifying Drug Delivery System of Prochlorperazine Maleate ; Recent Pat Drug Deliv Formul , 2017 ; 11(3) : 198-210

17. Mahmoud DB , Shukr MH , EIMeshad AN ; Gastroretentive Cosolvent –Based in Situ Gel as a Promising Approach for Simultaneous Extended Delivery and Enhanced Bioavailability of Mitiglinide Calcium International Journal of Pharmaceutical Sciences , 2018 Sep 26 , Volume :3 , No: 2 , Page no 257-298

18. Gong L , Sun Y , Yu M , Gao Y , Zou M , Cheng G ; Development and Evaluation of Compression Coating Gastro Floating Tablet of Alfuzosin Hydrochloride for Zero Order Controlled Releases, AAPS PharmSci Tech , 2018 Oct ; 19 (7) : 3277 -3286

19. Zhang C, Tang J , LiuD , Cheng L , Tang X ; Design and evaluation of an innovative floating and bioadhesive multiparticulate drug delivery system based on hollow structure; International Journal of Pharmaceutical Science and Research ; 2016 , April 30, 503 (1-2) : 41-55

20. Huanbutta K , Limmatvapirat S , Sungthongjeen S , Sriamornsak P; Novel Strategy to Fabricate Floating Drug Delivery System Based on Sublimation Technique ; International Journal of Pharmaceutical Sciences and Research ; Volume :3 , No:3 , 2016 , Page no :526-540

21. Darbasizadeh B , Motasadizadeh H , Foroughi –Nia B , Farhadnejad H ; Triphosphate- crosslinked chitasan /poly (ethylene oxide) electrospun nanofibrous mats as a floating gastro retentive delivery system for ranitidine hydrochloride ;J Pharm Biomed Anal ; 2018 May 10 , 53 : 63 -75

22. Kim JI , Park SW , Lim JJ , Sohn SI , Shin JS , Park SC , Jang YP , Chung EK , Lee HW , Lee KT ;Gastroprotective effects of the isopropanol extract of Artimisia princeps and its gastroretentive floating tablets on gastric mucosal injury ; Acta Pharma ;2017 Dec 20,67 (4) : 479-494

23. Chen R , Guo X, Liu X , Cui H , Wang R , Han j ;Formulation and statistical optimization of gastric floating alginate /oil /chitosan capsuleas loading procyanidins : in vitro and in vivo evaluations ;International Journal of Biological Macromol , 2018 March ; 108: 1082 -1091

24. Bera H , Kumar S ; Diethanolamine –modified pectin based core-shell composites as dual working gastroretentive drug –cargo; International Journal of Biological Macromol ,2018 March ; 108: 1053 -1062

25. Li Q , Guan X , Cui M , Zhu Z , Chen K , Wen H , Jia D , Hou J , Xu W, Yang X, Pan W, International Journal of Pharm ,2018 Jan 15 ; 535 (1-2) : 325 – 332

26 .Chen K ,Wen H , Yang F , Yu Y , Gai X , Wang H , Li P , Pan W , Yang X ; Study of controlled –release floating tablets of dipyridamole using the dry –coated method ; Drug Dev Ind Pharm , 2018 Jan ; 44 (1) : 116 – 124

27. Wang JF, Wang F , Zhao N , Yang CY , Wang GY , Wei Y , Zhang WY; Preparation and release mechanism of tectorigenin intragastric floating sustained release tablets ; Zhongguo Zhong Yao Za Zhi , 2017 January ;42(2) : 298 -302

28. He YL , Li Y , Yang DD , Zhu CY ; Preparation and evaluation of gastric adhesive – floating pellets for Bolo leaf phenols ; Zhongguo Zhong Yao Za Zhi , 2017 January , 42(1) : 107 -112

29.Zhang LP , Wang XL , Pang QQ , Humang YP , Tang L , Chen M, Liu ZS; Solvent –responsive floating liquid crystalline molecularly imprinted polymers for gastroretentive controlled drug release system ; Int J Pharm . 2017 Oct 30, 532(1): 365-373

30. Zhang X , Zhang Y , Han H , Yang J , Xu B , Wang B , Zhang T ; Formulation Optimization of Gastro –Retention Tablets of Paeonol Treatment of Experimental Gastric Ulcer; Chem Pharm Bull . 2017 Aug 1; 65 (8): 706 -713.