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FLOATING DRUG DELIVERY SYSTEMS - A REVIEW

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ABSTRACT

Technological attempts have been made in the research and development of rate-controlled oral drug delivery systems to overcome physiological adversities, such as short gastric residence times (GRT) and unpredictable gastric emptying times (GET). It is known that differences in gastric physiology, such as, gastric pH, and motility exhibit both intra-as well as inter-subject variability demonstrating significant impact on gastric retention time and drug delivery behavior. This triggered the attention towards formulation of stomach specific (gastro retentive) dosage forms. This dosage forms will be very much useful to deliver 'narrow absorption window' drugs. Several approaches are currently utilized in the prolongation of the GRT, including floating drug delivery systems (FDDS), swelling and expanding systems, polymeric bioadhesive systems, high-density systems, modified-shape systems and other delayed gastric emptying devices. In this review, current & recent developments of Stomach Specific FDDS are discussed.

Key words: floating drug delivery system, hydrodynamically balanced system, effervescent, non-effervescent, gastric residence time.

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INTRODUCTION:

The real challenge in the development of an oral controlled-release drug delivery system is not just to sustain the drug release but also to prolong the presence of the dosage form within the gastrointestinal tract (GIT) until all the drug is completely released at the desired period of time [1] Indeed, gastric drug retention has received significant interest in the past few decades. Most of the conventional oral delivery systems have shown some limitations related to fast gastric-emptying time[2].

The relatively brief gastric emptying time (GET) in humans which normally averages 2-3 h through the major absorption zone, i.e., stomach and upper part of the intestine can result in incomplete drug release from the drug delivery system leading to reduced efficacy of the administered dose. Therefore, control of placement of a drug delivery system (DDS) in a specific region of the GI tract offers advantages for a variety of important drugs characterized by a narrow absorption window in the GIT or drugs with a stability problem. Overall, the intimate contact of the DDS with the absorbing membrane has the potential to maximize drug absorption and may also influence the rate of drug absorption[3,4]. These considerations have led to the development of a unique oral controlled release dosage form with gastro-retentive properties. After oral administration, such a dosage form would be retained in the stomach and release the drug there in a controlled and prolonged manner, so that the drug could be supplied continuously to its absorption sites in the upper gastrointestinal tract[5]. Gastroretentive dosage form 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 of drugs that are less soluble in a high pH environment. It is also suitable for local drug delivery to the stomach and proximal small intestines[6]. Gastro retention helps to provide better availability of new products with suitable therapeutic activity and substantial benefits for patients. This mode of administration would best achieve the known pharmacokinetic and pharmacodynamic advantages of CR-DFs of these drugs [7].

SUITABLE DRUG CANDIDATES FOR GASTRORETENTION

(a) Drugs that act locally in the stomach e.g., antacids and misoprostol.

(b) Drugs that are primarily absorbed in the stomach.
e.g. calcium supplements, chlordiazepoxide and cinnarazine.

(c) Drugs those are poorly soluble at an alkaline pH.

(d) Drugs that have a narrow window of absorption. e.g., riboflavin and levodopa.

(e) Drugs that is unstable in the intestinal or colonic environment.
e.g. ranitidine HCl and metronidazole.

(f) Drugs with variable bioavailability. E.g. sotalol HCl [8].

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 [9]. 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 inter digestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours [10]. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phase

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 0-5 minutes and occurs between phases III and I of 2 consecutive cycles [11].

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state. 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 [12].

Scintigraphic studies determining gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically two complications, that of short gastric residence time and unpredictable gastric emptying rate.

Mechanism of floating systems[13]

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 systems, high-density systems, modified shape systems, gastric-emptying delaying devices and co-administration of gastric-

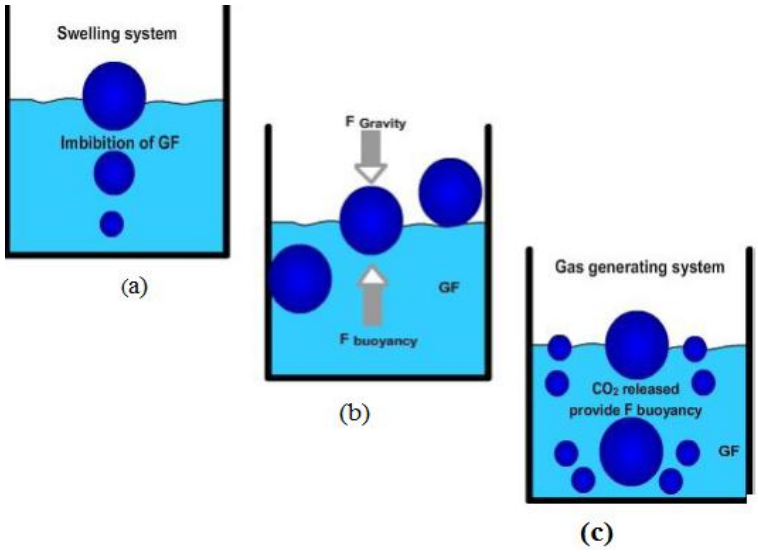

Figure 1. Mechanism of floating systems, GF= Gastric fluid.

emptying delaying drugs. Among these, the floating dosage forms have been 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 (given in the Figure 1 (a)), the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats better if F is on the higher positive side (Figure 1(b)). This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intragastric buoyancy

Capability variations

F = F buoyancy - F gravity

= (Df - Ds) gv--- (1)

Where, F= total vertical force, Df = fluid density,

Ds = object density, v = volume and

g = acceleration due to gravity.

FACTORS AFFECTING GASTRIC RETENTION

There are several factors that can affect gastric emptying (and hence GRT) of an oral dosage form. These factors are as follows.

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

Size: Dosage form units with a diameter of less than 7.5 mm are reported to have an increased GRT compared with those with a diameter of 9.9 mm.

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

Single or multiple unit formulation: multiple unit formulations show a more predictable release profile and insignificant impairing of performance due to failure of units, allow co-administration 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 MMC that occurs every 1.5-2 hours. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with that of the MMC, 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 acid 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: RT can be increased by 4-10 hours with a meal that is high in proteins and fats.

Frequency of feed: RT can increase by over 400 minutes when successive meals are given, compared with a single meal due to the low frequency of MMC.

Gender : Mean ambulatory GRT in males (3.4 ± 0.6 hours) is lesser compared with their age- and race-matched female counterparts (4.6 ± 1.2 hours), regardless of the weight, height and body surface.

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

Posture: Gastric emptying is favored while standing and lying on the right side since the normal curvature of the stomach provides a downhill path, whereas lying on the left side or in supine position retards it.

Disease states : Diseases like gastroenteritis, gastric ulcer, pyloric stenosis, diabetes and hypothyroidism retard gastric emptying, while partial or total gastrectomy, duodenal ulcer and hyperthyroidism promote it.

Concomitant drug administration: rugs that retard gastric emptying include poorly soluble antacids (aluminum hydroxide), anticholinergics (atropine, propantheline), narcotic analgesics (morphine) and drugs such as tricyclic antidepressants (imipramine, amitriptyline), metoclopramide, domperidone, cisapride stimulate gastric emptying[14,15,16,17]. .

TYPES OF GASTRORETENTIVE DOSAGE FORMS

A. Floating drug delivery systems

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system.

After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

FDDS can be divided into non-effervescent and gas-generating system

***(*a) Non-effervescent systems**

This type of system, after swallowing, swells unrestrained via imbibition of gastric fluid to an extent that it prevents their exit from the stomach. One of the formulation methods of such dosage forms involves the mixing of the drug with a gel, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than one within the outer gelatinous barrier[18].The air trapped by the swollen polymer confers buoyancy to these dosage forms. Excipients used most commonly in these systems include hydroxypropyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl acetate, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates. This system can be further divided into four sub-types:

(i) Colloidal gel barrier system / hydrodynamically balanced system

Such a system 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 soluble cellulose type hydrocolloid, e.g., hydroxypropyl cellulose, hydoxyethyl cellulose, hydroxypropyl methyl cellulose (HPMC), polysacharides and matrix-forming polymer such as polycarbophil, polyacrylate and polystyrene. On coming in contact with gastric fluid, the htdrocolloid in the system hydrates and forms a colloid gel barrier around its surface[19].

(ii) Microporous compartment system

This technology is based on the encapsulation of a drug reservoir inside a microporous compartment with pores along its top and bottom walls [20]. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of gastric surface with the undissolved drug. In the stomach, the floatation chamber containing entrapped air causes the delivery system to float over the gastric content. Gastric fluid enters through the aperture, dissolves the drug and carries the dissolved drug for continuous transport across the intestine for absorption.

(iii) Alginate beads

Multi-unit floating dosage forms have been developed from freeze-dried calcium Alginate [21]. 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. These floating beads gave a prolonged residence time of more than 5.5 hours.

(iv) Hollow microspheres / Microballons

Hollow microspheres loaded with drug in their outer polymer shelf were prepared by a novel emulsion solvent diffusion method [22]. 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 40ºC. 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. The microballoon floated continuously over the surface of an acidic dissolution media containing surfactant for more than 12 h.

(b) Gas-generating (Effervescent) systems

These buoyant systems utilize matrices prepared with swellable polymers such as methocel, polysaccharides (e.g., chitosan), effervescent components (e.g., sodium bicarbonate, citric acid or

tartaric acid) [23]. The system is so prepared that upon arrival in the stomach; carbon dioxide is released, causing the formulation to float in the stomach. Other approaches and materials that have been reported are a mixture of sodium alginate and sodium bicarbonate [24], multiple unit floating pills that generate carbon dioxide when ingested, floating minicapsules with a core of sodium bicarbonate, lactose and polyvinylpyrrolidone coated with hydroxypropyl methylcellulose (HPMC), and floating systems based on ion exchange resin technology, etc.

B. Expandable systems

Expandable gastroretentive dosage forms (GRDFs) have been designed over the past 3 decades. They were originally created for possible veterinary use but later the design was modified for enhanced drug therapy in humans. These GRDFs are easily swallowed and reach a significantly larger size in the stomach due to swelling or unfolding processes that prolong their GRT. After drug release, their dimensions are minimized with subsequent evacuation from the stomach [25]. Gastroretentivity is enhanced by the combination of substantial dimensions with high rigidity of the dosage form to withstand the peristalsis and mechanical contractility of the stomach. Positive results were obtained in preclinical and clinical studies evaluating the GRT of expandable GRDFs. Narrow absorption window drugs compounded in such systems have improved *in vivo* absorption properties.

C. Bio/Muco-adhesive systems

Bioadhesive drug delivery systems (BDDS) are used as a delivery device within the lumen to enhance drug absorption in a site specific manner. This approach involves the use of bioadhesive polymers, which can adhere to the epithelial surface in the stomach [26]. Gastric mucoadhesion does not tend to be strong enough to impart to dosage forms the ability to resist the strong propulsion forces of the stomach wall. The continuous production of mucous by the gastric mucosa to replace the mucous that is lost through peristaltic contractions and the dilution of the stomach content also seem to limit the potential of mucoadhesion as a gastro retentive force. Some of the most promising excipients that have been used commonly in these systems include polycarbophil, carbopol, lectins, chitosan and gliadin, etc.

D. High-density systems

Sedimentation has been employed as a retention mechanism for pellets that are small enough to be retained in the rugae or folds of the stomach body near the pyloric region, which is the part of the organ with the lowest position in an upright posture. Dense pellets (approximately 3g/cm-3)

trapped in rugae also tend to withstand the peristaltic movements of the stomach wall. With pellets, the GI transit time can be extended from an average of 5.8–25 hours, depending more on density than on the diameter of the pellets [27]. Commonly used excipients are barium sulphate, zinc oxide, titanium dioxide and iron powder, etc. These materials increase density by up to 1.5–2.4g/cm3.

OTHER TECHNIQUES:

Two patents on FDDS issued to the Alza Corporation disclosed drug delivery devices for the controlled and continuous administration of medicinal agents.

Inflatable gastrointestinal drug delivery system

The residence time of the drug delivery device in the stomach can also be sustained by incorporation of an inflatable chamber which contains a liquid, e.g., ether, which gasifies at body temperature to cause the chamber to inflate in the stomach.

Intragastric osmotically controlled drug delivery system

It is composed of an osmotic pressure controlled drug delivery and an inflatable floating support in a bio erodible capsule. When the drug delivery device reaches the site of drug administration, e.g., the stomach, the capsule quickly disintegrates to release the intragastric osmotically controlled drug delivery device. The inflatable floating support is made from a deformable hollow polymeric bag that contains a liquid which gasifies at body temperature to inflate the bag [28].

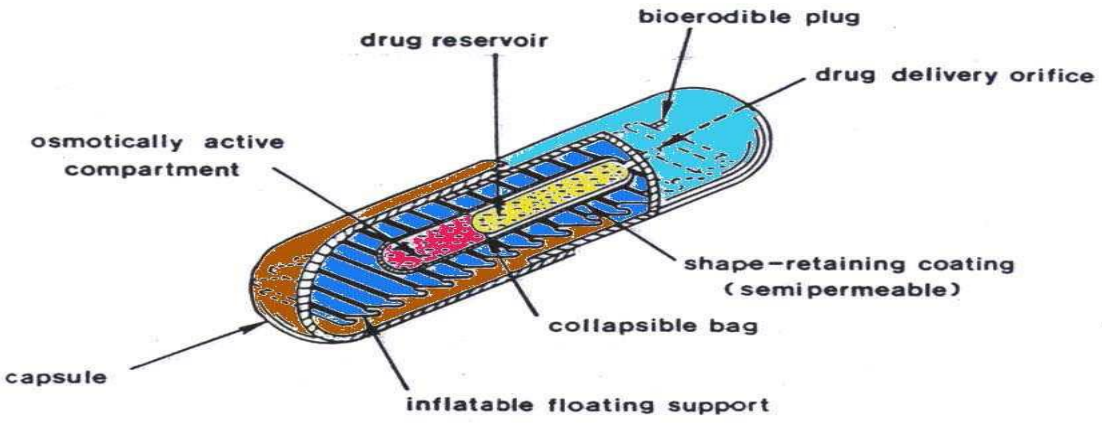

Figure 2 Intragastric osmotically controlled drug delivery system

ADVANTAGES OF GASTRORETENTIVE DRUG DELIVERY SYSTEMS

Enhanced bioavailability

The bioavailability of riboflavin 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[29].

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.

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 feature is associated with improved patient compliance, and thereby improves therapy.

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 concentrations, following drug absorption and distribution, are minimal.

Reduced fluctuations of drug concentration

Continuous input of the drug following CRGRDF 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 [30].

Improved 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.

Reduced counter-activity of the body

In many cases, the pharmacological response which intervenes with the natural physiologic processes 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 efficiency.

Extended time over critical (effective) concentration

For certain drugs that have non-concentration dependent pharmacodynamic, such as beta-lactam antibiotics, the clinical response is not associated with peak concentration, but rather with the duration of time over a critical therapeutic concentration. The sustained mode of administration enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes.

Minimized adverse activity at the colon

Retention of the drug in the GRDF 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.

Site specific drug delivery

A floating dosage form is a feasible approach especially for drugs which have limited absorption sites in upper small intestine [31].. The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that 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.

POLYMERS AND OTHER INGREDIENTS

Following types of ingredients can be incorporated into HBS dosage form in addition to the drugs:

Hydrocolloids (20%-75%): They can be synthetics, anionic or non-ionic like hydrophilic gums, modified cellulose derivatives. Eg. Acacia, pectin, Chitosan,agar, casein, bentonite, veegum, HPMC(K4M, K100M and K15M),Gellan gum(Gelrite®), Sodium CMC, MC, HPC.

Inert fatty materials(5%-75%): Edible, inert fatty materials having a specific gravity of less than one can be used to decrease the hydrophilic property of formulation and hence increase buoyancy. Eg. Beeswax, fatty acids, long chain fatty alcohols, Gelucires® 39/01 and 43/01.

Effervescent agents: Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di-Sodium Glycine Carbonate, CG (Citroglycine), calcium carbonate.

Release rate accelerants (5%-60%): eg lactose, mannitol

Release rate retardants (5%-60%): eg Dicalcium phosphate, ethylcellulose, sodium carboxy methul cellulose.

Buoyancy increasing agents (upto80%): eg. Ethyl cellulose

Low density material: Polypropylene foam powder (Accurel MP 1000®).

DRUGS USED IN THE FORMULATIONS OF STOMACH SPECIFIC FLOATING DOSAGE FORMS

Floating microspheres – Aspirin, Griseofulvin, p-nitroaniline, Ibuprofen, Ketoprofen , Piroxicam, Verapamil, Cholestyramine, Theophylline, Nifedipine, Nicardipine, Dipyridamol , Tranilast and Terfinadine

Floating granules - Diclofenac sodium, Indomethacin and Prednisolone

Films – Cinnarizine , Albendazole

Floating tablets and Pills - Acetaminophen, Acetylsalicylic acid, Ampicillin, Amoxycillin trihydrate, Atenolol, Fluorouracil, Isosorbide mononitrate, Para- aminobenzoic acid, Piretanide, Theophylline, Verapamil hydrochloride, Chlorpheniramine maleate, Aspirin, Calcium Carbonate, Fluorouracil, Prednisolone, Sotalol , pentoxyfilline and Diltiazem HCl, Atenolol, ciprofloxacin.

Floating Capsules - Chlordiazepoxide hydrogen chloride, Diazepam , Furosemide, Misoprostol, L-Dopa, Benserazide, Ursodeoxycholic acid and Pepstatin, and Propranolol [32.]

EVALUATION OF FLOATING DOSAGE FORMS [33]

A. FOR SINGLE UNIT DOSAGE FORMS (EX: TABLETS)

(i) **Floating lag time**: The buoyancy lag time is determine in the U.S.P. dissolution test apparatus II in a acid environment. The time interval between the introduction of the tablet into the dissolution medium and its buoyancy to the top of the dissolution medium is buoyancy lag time or floating lag time.

(ii**) In vitro drug release and duration of floating**: This is determined by using USP II apparatus (paddle) stirring at a speed of 50 or 100 rpm at 37 ± 0.2 °c in simulated gastric fluid (pH 1.2 without pepsin). Aliquots of the samples are collected and analysed for the drug content. The time (hrs) for which the tablets remain buoyant on the surface of the dissolution medium is the duration of floating and is visually observed.

(iii)**Tablet swelling indices**

Tablet was weighed (W1) and placed in a glass beaker, containing 200 mL of 0.1 N HCl, maintained in a water bath at 37 ± 0.5° C. At regular time intervals, the tablet were removed and the excess surface liquid was carefully removed by a filter paper. The swollen tablet was then reweighed (W2). The swelling index (SI) was calculated using the formula:

$$SI = W_2 – W_1 / W_1$$

(iii) **In vivo evaluation for gastro-retention**: This is carried out by means of X-ray or Gamma scintigraphic monitoring of the dosage form transition in the GIT.

The tablets are also evaluated for hardness, weight variation, etc.

B. FOR MULTIPLE UNIT DOSAGE FORMS (EX: MICROSPHERES) [33]

Apart from the In vitro release, duration of floating and in vivo gastro-retention tests, the multiple unit dosage forms are also evaluated for –

(i) **Morphological and dimensional analysis** with the aid of scanning electron microscopy (SEM). The size can also be measured using an optical microscope.

(ii) **% yield of microsphere**s: This is calculated from weight of microspheres obtained ×100 total weight of drug and polymer

(iii) **Entrapment efficiency**: The drug is extracted by a suitable method, analyzed and is calculated from:

$$\frac{\text{Practical amount of drug present}}{\text{Theoretical drug content}} \times 100$$

(iv**) In vitro floating ability (Buoyancy %**): A known quantity of microspheres are spread over the surface of a USP (Type II) dissolution apparatus filled with 900 ml of 0.1 N HCl containing 0.002% v/v Tween 80 and agitated at 100 rpm for 12 hours. After 12 hours, the floating and settled layers are separated, dried in a dessicator and weighed. The buoyancy is calculated from the following formula.

$$\text{Buoyancy (\%)} = Wf / (Wf + Ws) * 100$$

Where Wf and Ws are the weights of floating and settled microspheres respectively.

(v) **Drug-excipient (DE) interactions**: This is done using FTIR. Appearance of a new peak, and/or disappearance of original drug or excipient peak indicates the DE interaction. Apart from the above mentioned evaluation parameters, granules (ex:Gelucire 43/01) are also evaluated for the effect of ageing with the help of Differential Scanning Calorimeter or Hot stage polarizing microscopy.

Table 1: Commercially available floating products [34]

Brand name	Drug	Dosage form	Polymers used	Manufacturers
Cifran O.D	Ciprofloxacin	Tablet	Xanthan gum and sodium alginate	Ranbaxy
Liquid Gavison	Mixture of Alginates	Liquid	Alginates	GlaxoSmithKline
Madopar HBS	Levodopa and Benserazide	Capsule	HPMC	Roche
Glumetza	Metformin Hydrochloride	Tablet	HPMC	Depomed

FUTURE POTENTIAL

FDDS approach may be used for various potential active agents with narrow absorption window, e.g. antiviral, antifungal and antibiotic agents (sulphonamides, quinolones, penicillins, cephalosporins, aminoglycosides and tetracyclines) which are absorbed from very specific regions of GI tract and whose development has been halted due to the lack of appropriate pharmaceutical technologies. In addition, by continual supplying the drug to its most efficient site of absorption, the dosage form may allow for more effective oral use of peptide and protein drugs such as calcitonin, erythropoetin, vasopressin, insulin, low molecular weight heparin, and LHRH. Some of the unresolved critical issues related to the rational development of FDDS include, the quantitative efficiency of floating delivery systems in the fasted and fed states and the correlation between prolonged GRT and SR/PK characteristics. However, we are as close as we have ever been to see a greater transition of gastric retention devices from developmental level to the manufacturing and commercial level.

CONCLUSION

Growing understanding of impact of GIT physiology on drug delivery and increasing sophistication of drug delivery technology will ensure development of an increasing number of GRDDs to optimize drug delivery of molecules exhibiting regional variability in drug absorption. The research in this area is ongoing and it will not be long before an improved system is developed. .

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