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FLOATING DRUG DELIVERY SYSTEM: A REVIEW

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Abstract
In recent years scientific and technological advancements have been made in the research and development of rate-controlled oral drug delivery systems by overcoming physiological adversities, such as short gastric residence times (GRT) and unpredictable gastric emptying times (GET). Several approaches are currently utilized in the prolongation of the 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 devices. The different strategies used in the development of FDDS by constructing the effervescent and noneffervescent type of floating tablets basis of which is buoyancy mechanism. FDDS is a method to deliver the drugs that are active locally with a narrow absorption window in the upper gastrointestinal tract, unstable in the lower intestinal environment, and possess low solubility with higher pH values. The recent developments in floating drug delivery systems are containing the physiological and formulation variables impacting on gastric retention time, approaches to formulating of single-unit and multiple-unit floating systems, and their classification and formulation aspects are discussed in detail. This review also summarizes evaluation parameters and application of floating drug delivery systems.
Keywords: Floating drug delivery systems (FDDS), Gastric residence time, Swelling index, Buoyancy.

Introduction

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, low cost of therapy, patient compliance and flexibility in formulation etc.[1] Oral sustained drug delivery formulations show some limitations connected with the gastric emptying time. Variable and too rapid gastrointestinal transit could result in incomplete drug release from the device into the absorption window leading to diminished efficacy of the administered dose. Gastro retentive drug delivery systems are the systems which are retained in the stomach for a longer period of time and thereby improve the bioavailability of drugs that are preferentially absorbed from upper GIT [2]. The drug bioavailability of pharmaceutical dosage forms is influenced by various factors. One of the important factors is the gastric residence time (GRT) of these dosage forms. The gastric emptying process from the stomach to small intestine generally lasts from a few minutes to 12 h. This variability leads to an unpredictable bioavailability of an orally administered dosage form [3]. The relatively brief gastric emptying time in humans, which normally averages 2–3 h through the major absorption zone (stomach or upper part of the intestine), can result in incomplete drug release from the drug delivery system leading to diminished efficacy of the administered dose.

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines.

Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patient. The identification of new diseases and the resistance shown towards the existing drugs called for the introduction of new therapeutic molecules. In response, a large number of chemical entities have been introduced, of which some have absorption all over the gastrointestinal tract (GIT), some have absorption windows (i.e. absorption sites, especially the upper part of the small intestine) and some drugs have poor solubility in intestinal media. The drugs belonging to the second and third categories and the drugs which are required for local action in the stomach, require a specialized delivery system. All the above requirements can be met and effective delivery of the drugs to the absorption window, for local action and for the treatment of gastric disorders such as gastro-oesophageal reflux, can be achieved by floating drug delivery systems (FDDS).

Floating drug delivery systems (FDDS) are invented to retain the drug in the stomach and applicable for drugs with poor solubility and low stability in intestinal fluids. The basis behind FDDS is making the dosage form less dense than the gastric fluids to make it float on them.

FDDS are hydro-dynamically controlled low-density systems with sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. The residual system is emptied from the stomach with the release of the drug. This results in enhanced gastric residence time and good control over plasma drug concentration fluctuations. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release [4]. Prolonging the gastric retention of a delivery system is desirable for achieving the greater therapeutic efficacy of the drug substance under certain circumstances. For example, drugs which show better absorption at the proximal part of the gastrointestinal tract and drugs with low solubility and get degraded in alkaline pH found efficient in prolonging gastric retention. In addition, for sustained drug delivery to the stomach and proximal small intestine in treating certain ulcerative conditions, prolong gastric retention of the therapeutic moiety and hence offer numerous advantages including improved bioavailability and therapeutic efficacy with reduction of dosing frequency [4]

Basic Gastrointestinal Tract Physiology

Basically stomach is divided into 3 regions: fundus, body, and antrum (pylorus). proximal part made of fundus and body acts as a reservoir for undigested material, the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC) which is further divided into following 4 phases.

a) Phase 1: In this phase, the gastric emptying rate is slow as the onset of MMC is delayed. This phase usually lasts for 30 to 60 min. Contraction does not occur in this phase. It is also known as the basal phase.

b) Phase 2: In this phase bile secretion and mucus discharge take place and intermediate contraction occurs. It lasts for 20 to 40 min. It is also known as the pre-burst phase. The intensity and frequency increase gradually as the phase progresses.

c) Phase 3: In this phase, regular and intense contraction takes place for a short time. It last usually for 10 to 20 min. This phase is also called a housekeeper wave as it tends to empty the fasting contents of the stomach. Large objectives remain in the stomach in the fed state but passed down to the small intestine during this phase.

d) Phase 4: lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles. After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase II of fasted state. 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[5]

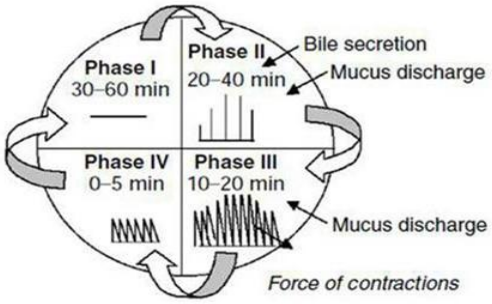

Figure 1: GIT Motility Pattern.

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 systems, 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 (Fig. 2), 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

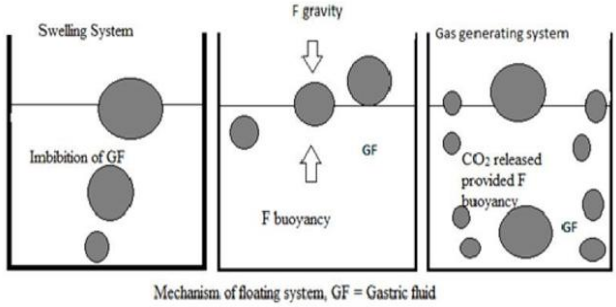

Figure 2: Mechanism of floating system.

CLASSIFICATION OF FDDS

(A) Effervescent FDDS

1. Gas generating system
2. Volatile liquid containing system

(B) Non- Effervescent FDDS

1. Colloidal gel barrier system
2. Microporous compartment system
3. Floating microsphere
4. Alginate floating beads.

(C) Raft forming system

Classification of Floating Drug Delivery Systems

[A] Effervescent system floating drug delivery system

These are particular drug delivery system made up of matrix type and a swellable polymer such as methylcellulose and chitosan along with effervescent compounds *viz.* sodium bicarbonate, tartaric acid, citric acid. These are formulated in such a specific way as once it comes in contact with gastric juice; co_2 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 [6-8].

[I]Gas generating systems

Low-density FDDS is based on the release of co_2 upon contact with gastric fluids after oral administration. The materials are formulated in such a way that after entering in the stomach, co_2 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 co_2 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 in the other layer results into a sustained release effect [6, 9].

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

This is an osmotically controlled floating system in which a device comprised of a hollow deformable unit in convertible collapsed form. Housing would be attached 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 cyclopentane 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 [6, 9].

(B) Non-effervescent FDDS

Non-Effervescent Floating Drug Delivery Systems comprises a gel-forming (or) swellable cellulose type of hydrocolloids made up of polysaccharide along with matrix forming polymers like polycarbonate, polymethacrylate, and polystyrene. The routine formulation method involves the mixing of the drug with gel forming hydrocolloids that swell in contact with gastric fluid upon oral administration and maintains the integrity of shape and a bulk density barrier, the air trapped by swollen polymer confer buoyancy to the dosage forms [6, 9].

(I) Colloidal gel barrier systems (Hydrodynamic balanced systems)

This system prolongs gastric retention time and maximizes the amount of drug that reaches its absorption site in the solution form. It essentially contains drug with gel-forming hydrocolloids to remain buoyant on the stomach content. Such a system incorporates one or more gel-forming cellulose type hydrocolloid e. g. hydroxypropyl 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 its surrounding [6, 9].

(II) Microporous compartment systems

This technology incorporates the encapsulation technique of a drug reservoir inside a microporous compartment along with pores at top and bottom walls. The peripheral wall of the drug reservoir compartment is completely 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 extent that it prevents theirs exist from the drug and carrier the dissolved drug for continuous transport across the intestine for absorption [9].

(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 [8].

(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 beads are 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 [9].

(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 co_2 bubbles which generate raft layer on top of gastric fluid, thus facilitates releases drug slowly in the stomach [9].

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 Controlled-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]

Factors Affecting 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/cm^3 is required to exhibit floating property [14]. 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 influence gastric retention. Dosage form unit with a diameter of more than 7.5 mm are reported to increase GRT as compared to those with a diameter of 9.9 mm. The dosage form having tetrahedron and ring shape devises with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to exhibit better GIT for 90 to 100 % retention at 24 hours compared with other shapes [15].

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 retention time (GRT) of the dosage form. Feeding of indigestible 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.

4. Caloric content

The gastric retention time (GRT) can be increased by 4 to 10 hours with a meal that is high in proteins and fats [16]. Floating can increase by over 400 minutes when successive meals are given as compared with a single meal due to the low frequency of migrating myoelectric complexes (MMC).

5. Effect of gender, posture and age

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 persons, especially those over 70, have a significantly longer GRT so gastric emptying is slowed down. Disease condition 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 migrating 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 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 [17].

7. Concomitant drug administration

Anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramide and cisapride can affect floating time [18].

8. Single or multiple unit formulation

Multiple unit formulations are more predictable 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.

Application of Floating Drug Delivery System: [19,20]

1. 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.

2. 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 (cyto chrome P450, in particularCYP3A4) in a sustained manner, rather than by a bolus input.

3. 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.

4. 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.

5. 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 index24.

6. Minimization of fluctuations in drug concentration

It makes it possible to obtain certain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations.

7. 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.

8. Extended time over critical (effective) concentration

For certain drugs that have non-concentration dependent pharmacodynamics, 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.

9. 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.

10 Site specific drug delivery

A floating dosage form is a feasible approach especially for drugs which have limited absorption sites in upper small intestine25. 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.

Evaluation of Floating Drug Delivery System

Shape of Tablets

Compressed tablets designed for FDDS are examined under the magnifying lens for the determination of its shape consistency.

Tablet Dimensions

As per official compendia, the thickness and diameter of tablets in FDDS form are measured using a calibrated Vernier callipers same with that of conventional tablets. Three tablets of each formulation are picked randomly, and thickness is measured individually.

Hardness of the Tablet

Randomly sampled twenty tablets in each batch of formulations should be used for the determination of hardness with the help of Monsanto type hardness tester.

Weight Variation

Twenty tablets selected at random are weighed accurately, and the average weight of the tablet is calculated. Then the deviation of individual weight from the average weight is calculated.

Thickness of the Tablet

The individual crown to crown thickness of ten tablets is determined using slide calipers for each batch

Measurement of Floating Capacity

Three individual tablets are put in an individual flask containing 400 ml of 0.1(N) HCL solutions. Then the time in minutes for each tablets to go from the bottom to the top of the flask (floating lag time) and the time for which tablets constantly float on the water surface (duration of floating) are measured. The sample mean and standard deviation are then calculated

Density of the formulation

The apparent densities of the tablets are calculated from their volumes and masses in triplicate. The volume V of the cylindrical tablets are calculated from their height h and radius r (both determined with a micrometer gauge) using the mathematical equation for a cylinder

$(V = A \times r^2 \times h)$.

Drug Content in Tablets

Ten tablets from each batch are selected randomly and transferred to a 100 ml volumetric flask filled up with 0.1(N) HCL. Stir and Keep it aside for 2 h then take 1 ml from the volumetric flask and transfer it to the test tube. Samples are then filtered, suitably diluted and analyzed spectrophotometrically at a suitable wavelength [21,22].

***In vitro* dissolution study**

The tablet was placed inside the dissolution vessel. 5 ml of sample is withdrawn at time intervals of 1h, 2h, 3h, 4h, 5h, 6h, 8h, 10 h, and 12h or any other time intervals as needed. The volume of dissolution fluid adjusted to 900 ml by replacing fresh 5 ml of dissolution medium after each sampling. The release studies were conducted with "n" tablets, and the mean values are plotted versus time. Each sample is analyzed at maximum wavelength using UV visible spectrophotometer against a reagent blank and the corresponding concentration is determined from the respective calibration curve [23].

Buoyancy/Floating test

The time between introduction of the dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant are measured. The time taken for the dosage form to emerge on the surface of a medium called floating lag time (FLT) or buoyancy lag time (BLT) and total duration of time by which dosage form remain buoyant is called total floating time (TFT) [24].

Swelling study

The swelling behavior of a dosage form is measured by studying its weight gain or water uptake. The dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake can be measured in terms of percent weight gain, as given by the equation.

$WU = (Wt - Wo) \times 100$

Where,

WU= Water uptake

Wt = Weight of dosage form at time t. Wo = Initial weight of dosage form [24].

INNOVATIVE TECHNOLOGIES FOR FDDS[25]

1. Oleotec™ and Soctec™ : Oleotec™ and Soctec™ gastro-retentive capsule technology are innovated by Skyepharma company. For Drugs having high therapeutic doses, Oleotac TM technique is designed but it is not suitable 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.

2. 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 prolonged 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.

3. 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 tailored 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.

4. 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.

5. 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) 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.

6. Gastrointestinal Permeation Enhancement Technology: Gastrointestinal Permeation Enhancement Technology (GIPET) is developed by Merrion Pharmaceutical's and it is unique 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.

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