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FLOATING BEADS AS A MAGICAL DRUG CARRIER: A REVIEW

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ABSTRACT

The development in the field of designing novel dosage form is stepping stone now a day. Thus the development like microparticulate drug delivery system has gained more attention. Microparticulate drug delivery system has the advantage like site specific drug delivery. In addition to this gastroretentive approach enhances the sustained release effect through the microparticulate drug delivery system. Drugs that have low absorption window are suitable candidate for floating drug delivery system. Beads are the ideal formulation for floating drug delivery since the polymers used are degraded easily.

Keywords: Floating drug delivery, Microparticulate drug delivery, Beads, wax, gastroretentive.

INTRODUCTION

Although there is fast development in the drug delivery, oral route of administration is more preferred as the physiology of gastrointestinal tract offer more opportunities for development of the dosage form. Hence the advancement in the field of research is continuously keeps on searching for ways to deliver rugs over an extended period of time, with a well-controlled release profile. [1] 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, which reside in the stomach for a longer period of time than conventional dosage forms. [2] The absorption of drug candidate from the GIT is predicted from position of the dosage form in the GIT. [3] Gastroretentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastroretentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs.[4]

BASIC ANATOMY OF STOMACH AND ITS PHYSIOLOGY

The stomach is an organ for storage and mixing. 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, capable of displaying a large expansion to accommodate food without much

increase in intragastric pressure. Whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions. The opening nearer to esophagus is called as cardiac end characterized by pyloric sphincter. Under fasting conditions, the stomach is collapsed bag with residual volume of 50 ml and contains a small amount of gastric fluid and air. Basic structure of gastrointestinal tract and stomach are shown in figure-1 Mucosal lining is covered throughout the stomach under this layer specialized cells are present that secret gastric juice into stomach.

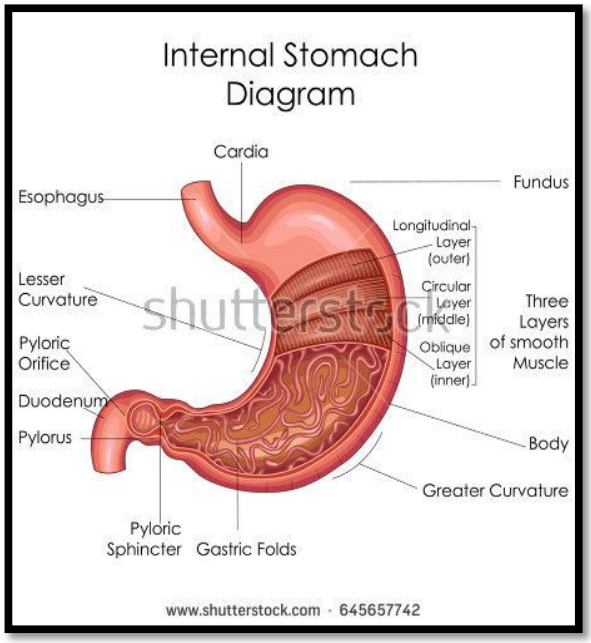

FIG. 01: ANATOMY OF STOMACH

Gastric emptying occurs during fasting as well as fed states. The passage of drug from stomach to the small intestine is called gastric emptying. It is the rate limiting step for drug absorption because the major site for absorption in intestine. Generally rapid gastric emptying increase bioavailability of the drug. Faster onset requires for drugs that degrade in gastric environment. Delayed gastric emptying promotes dissolution of the drugs, which are poorly soluble drugs and for the drugs that is majorly absorbed from stomach or proximal part of the intestine. 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 are: [5]

Phase-I (Basal phase) Lasts from 40 to 60 minutes (occurs in time between meals).

Phase-II (Pre burst phase) Lasts for 40 to 60 minutes with inter-mitten action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.

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 house-keeper wave.

Phase-IV Lasts for 0 to 5 minutes and occurs between phase III and I of 2 consecutive cycles. [6]

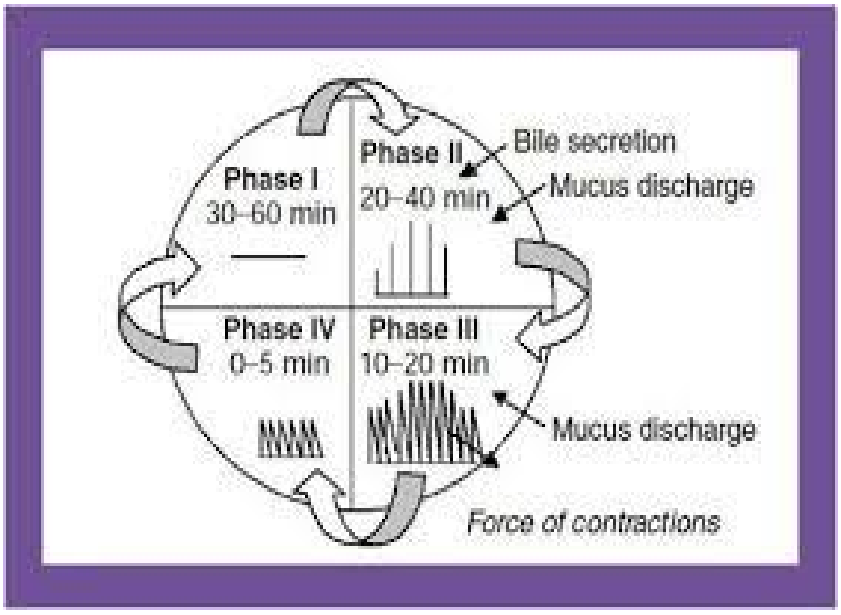

FIG.02: GASTROINTESTINAL MOTILITY PATTERN

FLOATING DRUG DELIVERY SYSTEM

Floating drug delivery systems have bulk density less than gastric fluids that have sufficient buoyancy to float over gastric contents and remain in stomach for longer duration of time without affecting gastric emptying rate and release the drug slowly at a 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 fluctuations in plasma drug concentration.

Factors to be consider for formulation of floating drug delivery: -

1. It must maintain an overall specific gravity lower than that of gastric contents (1.004 – 1.010).

2. It should dissolve slowly and release contents slowly to serve as a reservoir.

3. It must form a cohesive gel barrier.

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 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, 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. 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
GF= Gastric fluid [7]

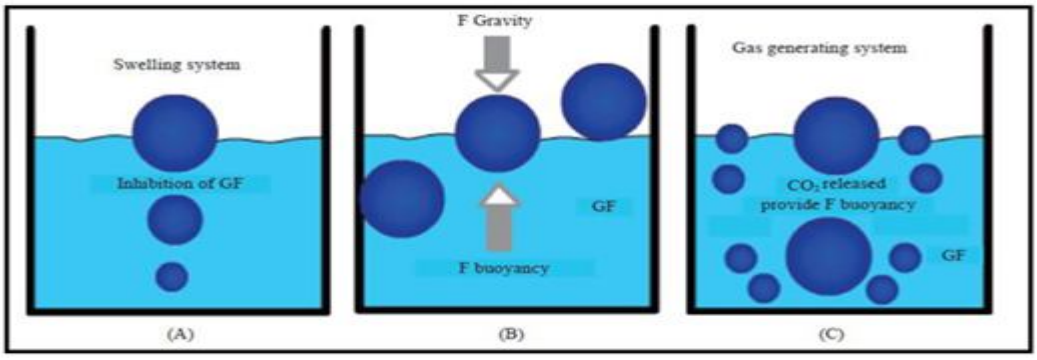

FIG. 03 MECHANISM OF DRUG RELEASE

FACTORS AFFECTING FLOATING DRUG DELIVERY SYSTEM:

1. Gender: Women have slower gastric emptying rate than men.
2. Age: Gastric emptying rate is slower in elderly patient than the younger ones.
3. Body posture: The upright position protects the faster gastric emptying of floating forms. The supine position doesn't offer protection against the early and erratic emptying.

4. Concomitant intake of drug: Concurrent administration of the prokinetic agent and cholinergic agent affect the performance of the FDDS.
5. Feeding regimen: Gastric retention time increases in presence of food. [8]

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM:

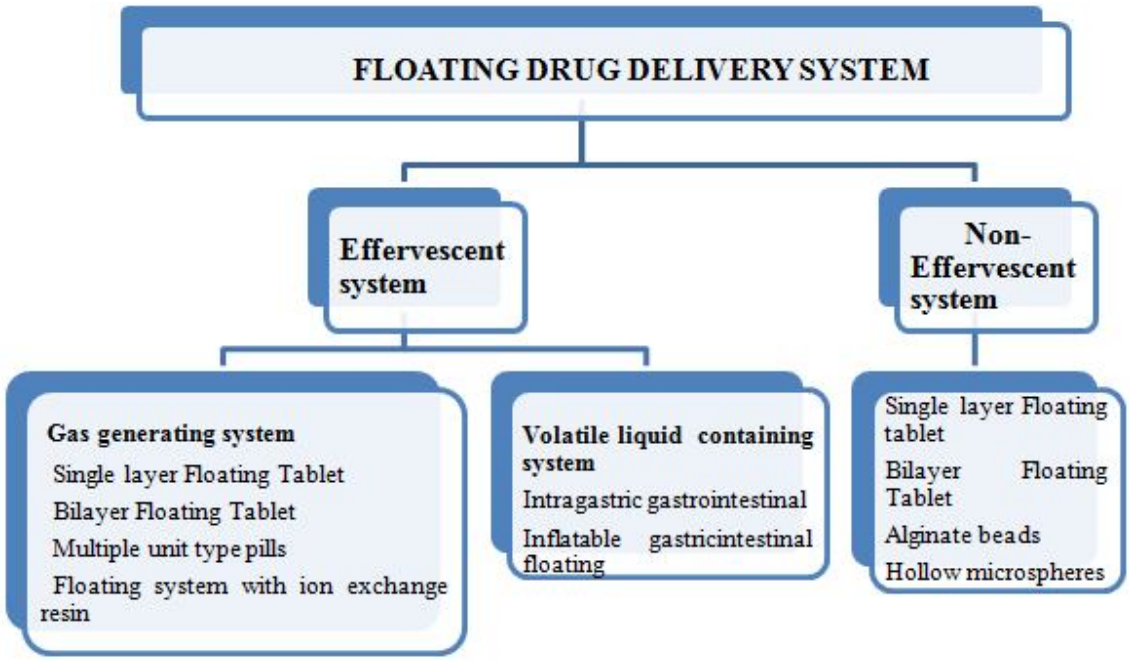

FIG. 04: CLASSIFICATION OF FLOATING DRUG DEIVERY SYSTEM

A. Effervescent system :

This are the matrix type of systems which includes gas generating systems and volatile liquid containing system. These systems are formulated using swellable materials like HPMC, methyl cellulose, and chitosan with the use of effervescent agent like sodium carbonate, citric acid and tartaric acid. The release of CO_2 causes the system to remain float on the surface of gastric fluid.

a. Gas Generating system:

1. **Single layer floating Tablet:** These systems are prepared by using the gas generating agent. The gas generating agent either reacts with the acid present in the stomach or is used along with the acids like tartaric acid or citric acid.
2. **Bilayer floating tablet:** This system is also prepared with same method as that of single layer floating tablet. One layer is immediate release and another layer is sustained release.
3. **Multiple unit type pills:** The purpose for designing multiple-unit dosage form is to develop a formulation which has all the advantages of a single-unit form.[9]

b. Volatile liquid containing system:

1. **Intragastric gastrointestinal floating system:** It consist of an osmotic pressure-controlled drug delivery device and an inflatable floating support in bio-erodible capsule.

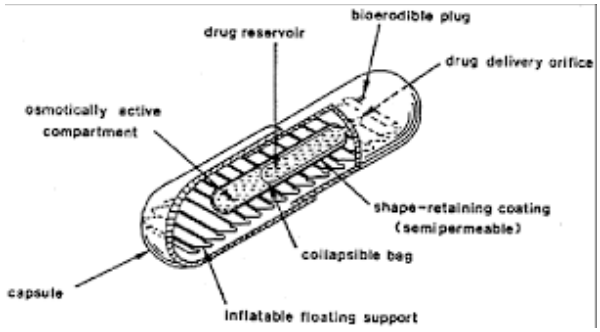

Fig. 05 Intragastric gastrointestinal floating system

2. **Inflatable gastrointestinal floating system:** The gastroretentive time of drug delivery system can be sustained by addition if inflatable chamber which contains liquid e.g., ether, cyclopentane that gasifies at body temperature to cause floatation of chamber. [10]

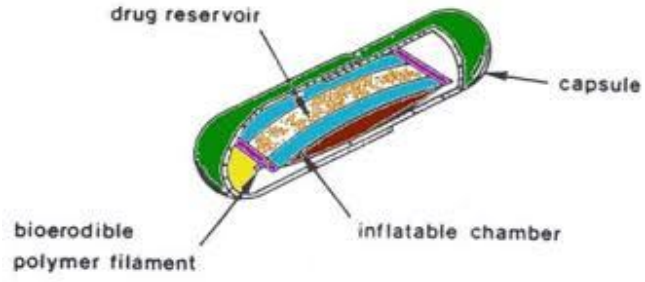

Fig.06 Inflatable gastrintestinal floating system

B. Non – effervescent system:

GEL forming or sellable hydrocolloids are used to formulate these type of systems. Polymers like polycarbonate, polymethacrylate and polystyrene are used. The swelling of polymer is responsible for floating of this system. [5]

a. Microporous compartment system:

This technology includes the encapsulation of drug reservoir within the microporous compartment with the pores on the both side of the systems. The system is coated to prevent the direct contact with gastric fluid. The air entrapped within the floatation chamber causes the floating of system.

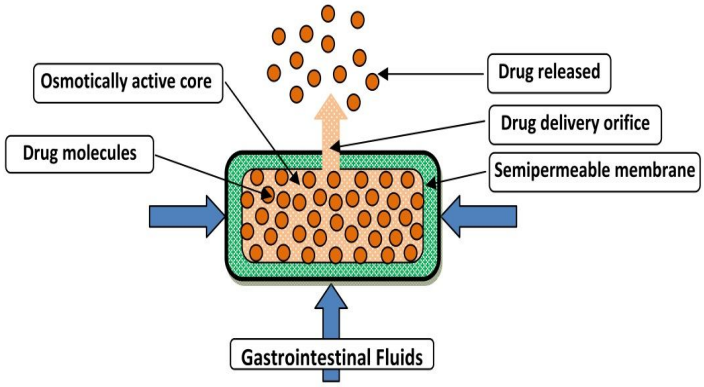

Fig. 07 Microporous compartment system

b. Alginate / wax beads:

This multi- unit system is prepared by freeze drying of calcium alginate. Generally, solution of sodium alginate is gradually dropped into the calcium chloride solution. The cross linking of the alginate with calcium results in the formation of alginate beads.

Fig.08 Beads

TYPES OF GASTRORETENTIVE BEADS [10]

1. Effervescent Beads:

I. Floating beads or porous alginate beads based on ion exchange resin: This system composed of ion exchange resin beads loaded with bicarbonate and a negatively charged drug tagged to resin. Porous alginate beads are prepared by incorporating CO2 gas generating agents like NaHCO3 and CaCO3. Bicarbonates are merged with stirring into aqueous solution of sodium alginate and then mixture is added to solution of calcium chloride with 10% acetic acid. So due to acetic acid and bicarbonate, CO2 gas is generated and simultaneously gelling of beads are occurred by calcium ions and CO2 which goes out from beads during stirring and creating porous structures in calcium alginate floating beads.

2. Non- Effervescent system:

I. Calcium alginate / pectinate beads: Freeze dried spherical beads of calcium alginate approximately 2.5 mm in diameter are formed by dropping sodium alginate solution into aqueous solution of calcium chloride, causing a precipitation of calcium alginate. So due to chemical reaction gelation take place and forms solid spherical gel beads. These beads were then separated; snap frozen in liquid nitrogen and freeze dried at 40oC for 24 h leading to formation of porous system. The resultant weight of beads is less giving buoyancy up to 12 h. Similar to alginate, pectin can also be used for preparing gel beads. Combination of both means calcium-alginate-pectinate gel beads, which make fasten drug release as compare to only calcium pectinate beads. Calcium alginate beads are also prepared with incorporation of chitosan polymer so that it can include air in beads.

II. Alginate beads with air compartment: These are also calcium alginate beads but the difference is that the calcium alginate core is separated by air compartment from a coating membrane calcium alginate or mixture of calcium alginate and Poly Vinyl Alcohol (PVA). During the preparation of calcium alginate beads before drying process the beads are coated with the coating solution which may be the mixture of calcium alginate and PVA, and then they are dried. During the process of drying it makes the air compartment which creates buoyancy. PVA is incorporated in coating mixture for improving membrane permeability as PVA is water soluble additive cause the leaching from membrane and making pores in membrane.

III. Oil entrapped gel beads: Vegetable oil is utilized as floating carrier as they are light in weight and hydrophobic in nature and is used for floating by including it into gel matrix of beads. Oil entrapped beads are prepared by both calcium alginate bead and calcium pectinate beads. Pectin has some emulsification property, so aqueous solution of pectin is mixed with edible oil. Emulsion is obtained by homogenization. This emulsion is extruded into calcium chloride solution to form beads which are kept for further process of separation, washing and drying.

IV. Casein-gelatin floating beads: Casein has emulsifying property and thus cause air bubble incorporation that behave as air reservoir for floating system. Beads are prepared by adding solution of casein and gelatin in deionized water at 60°C to the preheated mineral oil. The dispersion stirred to obtain emulsion and temperature is reduced to 5°C by rapid cooling and previously cooled acetone is added to get solid beads which dried under vacuum. Floating is due to air entrapments demonstrate by preparing non floating beads which are prepared similarly from a solution mixture of casein and gelatin previously treated at decrease pressure to completely remove air bubbles.

c. Hollow microsphere / microballons:

These are prepared by either solvent diffusion or solvent evaporation method. The gas phase generated during the preparation leads to the floating of the system.

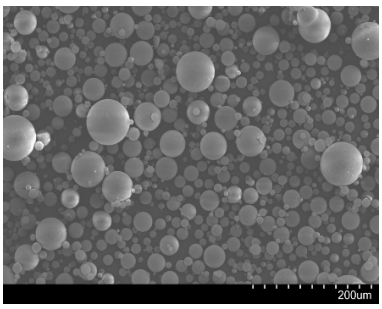

Fig. 09 Microballons

SUITABLE DRUG CANDIDATES FOR GASTRO RETENTIVE DELIVERY SYSTEMS

1. Drugs those are used in the treatment of local diseases e.g. peptic ulcers caused by H. pylori infections.
2. Drugs those are poor soluble in intestinal media and unstable in the intestinal pH. e.g. diazepam, verapamil HCl, captropril, ranitidine HCl.
3. Drugs that are having maximum absorption in stomach and upper part of GIT.
4. Drugs that disturb normal colonic microbial environment e.g. antibiotics against Helicobacter pylori.[7]

DRUGS THOSE ARE UNSUITABLE FOR GASTRORETENTIVE DRUG DELIVERY SYSTEM

1) Drugs that have very limited acid solubility e.g. phenytoin etc.
2) Drugs that suffer instability in the gastric environment e.g. erythromycin etc.
3) Drugs intended for selective release in the colon e.g. 5- amino salicylic acid and corticosteroids etc.[4]

METHODS OF PREPARATION OF GASTRO-RETENTIVE MULTIPARTICULATE SYSTEM

1. Solvent Evaporation Method
2. Ionotropic Gelation Method
3. Emulsion Solvent Diffusion Method

1. Solvent evaporation method:

This system leads to the formation of hollow inner core. The drug is either dissolved or dispersed in the solution of organic solvent containing polymer. This organic solution containing polymer is emulsified in the aqueous phase containing surfactant. The solvent is evaporated by increasing the temperature under pressure or by continuous stirring. The solvent removal leads deposition of polymer at oil-water interface which leads to the formation of hollow cavity that results in the floatation of system. Generally, polymers like cellulose acetate, chitosan, eudrgit, carbopol, agar are used in this system.

2. Ionotropic gelation method:

This system is based on the capability of polyelectrolytes to cross link in the presence of counter ions to form beads. These anions forms meshwork structure by combining with the polyvalent cations and induce gelation by binding mainly to the anion blocks. The hydrogel beads are produced by dropping a drug-loaded polymeric solution into the aqueous solution of polyvalent cations.

3. Emulsion solvent diffusion method :

In this method the affinity between the drug and organic solvent is stronger than that of organic solvent and aqueous solvent. The solution of drug in organic solvent is dispersed in the aqueous solution to produce emulsion droplets. The drug is crystallized by the diffusion of organic solvent out of the emulsion droplet into the surrounding aqueous solution. [11]

ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM

1. It increases the bioavailability of the drug.
2. Chances of first pass metabolism are minimized.
3. Useful for sustained drug delivery with reduced frequency of dose administration.
4. Targeted therapy for local ailments in the upper GIT can be achieved.
5. Site specific drug delivery can be accomplished.
6. Reduces the adverse activity at the colon.

LIMITATIONS / DISADVANTAGES

1. These systems require a high level of fluid in the stomach for drug delivery to float and work efficiently-coat.
2. Not suitable for drugs that have solubility or stability problem in GIT.
3. Drugs such as Nifedipine which is well absorbed along the entire GIT and which undergoes first pass metabolism, may not be desirable.
4. Drugs which are irritant to gastric mucosa are also not desirable or suitable.
5. The drug substances 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 systems do not offer significant advantages over the conventional dosage forms for drugs, which are absorbed throughout the gastrointestinal tract. [1]

INNOVATIVE TECHNOLOGIES FOR GASTRORETENTIVE TECHNOLOGY

1. **Oleotec™ and Soctec™ :** Oleotec™ and Soctec™ gastro-retentive technology are invented by Skyepharma. Oleotac™ technique is designed for the developed for the drugs having high therapeutic doses but are not compatible for the conventional dosage form. Drugs that show effect primarily in the upper part of the GIT are designed by this technique. Oleotec system is basically a gel supplied in the form of stick pack that forms a continuous layer at surface of the stomach. Soctec™ system is designed for the drugs that should be delivered as sustained release and should be absorbed in the upper part of intestine i.e. duodenum and jejunam for absorption and increases the bioavailability. Soctec is provided as elongated capsule.

Soctec™ can be used with a range of drugs that have a narrow absorption window and are preferably absorbed in the upper intestine segments. It can also improve the bioavailability of drugs that are degraded by the alkaline pH of the lower gastrointestinal tract. Soctec™ is very adaptable and can be used with drugs having different physicochemical and therapeutic characteristics.

2. **Accordion Pill™ Technology:** This is versatile gastroretentive formulation composed of the biodegradable polymers. It is a multi-layer, planar structure, folded to an accordion shape into a standard size, regular capsule. Upon reaching the stomach, the capsule dissolves, the Accordion Pill™ unfolds and is retained in the stomach for up to 12 hours, under regular calorie diets. While in the stomach, the Accordion Pill™ releases the drug in a controlled manner towards the upper part of the gastrointestinal tract which enables prolonged and continuous absorption phase of the drug in the upper part of the gastrointestinal tract, resulting in improved efficacy and safety profile, as well as reducing frequent daily dosing. The drug release mechanism is independent of the Accordion pill™ retention mechanism Once the Accordion Pill™ is expelled from the stomach, it is fully degraded in the intestine. It can combine immediate as well as controlled release profile and is suitable for more than one API with high drug loading efficiency upto 550mg. Drugs belonging to the BCS Class II and BCS Class IV are more suitable candidate 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. During the cycle of intense gastric movements, GRID retains its shape and form so as to release medication in a controlled fashion. 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:** Cetapin XR the Sanofi formulation of Metformin XR uses a patented multiple polymer hydrophilic matrix technology as a gastroretentive delivery system, to achieve prolonged release of Metformin hydrochloride. The polymers are a novel combination of non-ionic and ionic hydrophilic polymers. Metformin hydrochloride granules are compressed into tablets along

with the polymers in a ratio that is optimized to provide pH independent drug release from the tablet. The unique release-controlling properties of the polymer compounds allows for a gradual and complete release of Metformin hydrochloride from stomach to jejunum, unaffected by gastric pH fluctuations [Figure 4]. When the tablet comes in contact with the gastrointestinal fluids (fig A), Metformin imbibes water hydrates and forms a gelatinous swellable matrix (fig B). The drug release from the matrix occurs via a process of dissolution of the drug and subsequent diffusion through the gel matrix in a controlled manner (fig C). The matrix controls the rate and extent of release of Metformin XR (fig D). As the tablet swells, it is retained in the stomach and upper intestines for a longer time, thereby providing maximum drug available at the site of absorption (fig D). This technology has given consistent and reproducible results providing: Optimal absorption; Less irritation; Improved plasma levels; and better bioavailability.

5. **Acuform® technology:** Acuform® is Depomed's patented, polymer-based technology designed to optimize drug delivery. This technology allows for targeted, controlled delivery of pharmaceutical ingredients to the upper gastrointestinal (GI) tract, the preferential absorption site for many oral drugs. Unlike immediate release and some extended release formulations that pass through the upper GI tract within approximately three hours following ingestion, Acuform technology's unique swelling polymers allow the tablet to be retained in the stomach for approximately eight to ten hours. During this time, the tablet's active ingredient is steadily delivered to the upper GI tract at the desired rate and time. This gradual, extended release allows for more of the drug to be absorbed in the upper GI tract, offering the potential for greater treatment efficacy and increased treatment tolerability with the convenience of once- or twice-daily dosing. In particular, this technology may prove to be an effective delivery solution for compounds that are absorbed in the upper GI region, Insoluble in water, Available through active transport mechanisms, irritating to the mucosa of the small intestines, imbalancing, irritating, or unsafe in the lower GI region and More effective when plasma levels have less fluctuation.

6. **Gastrointestinal Permeation Enhancement Technology:** Merrion Pharmaceutical's Gastrointestinal Permeation Enhancement Technology (GIPET) is a unique approach allows drugs that currently can only be given parenterally (injectable) to be converted into oral (tablet/capsule) forms, as well as improving the absorption of current oral drugs [Figure 5]. GIPET uses specifically designed oral formulations of patented absorption enhancers which activate micelle formation facilitating transport of drug and substantially increasing absorption with good reproducibility and a strong safety profile.
7. **Gastrointestinal Retention System (GIRES) :** GIRES™ is a gastro-retentive technology that gives 16-24hour retention times in the stomach, without food having a detrimental effect. GIRES comprises a controlled-re lease dosage form inside an inflatable pouch, which is placed in a drug capsule for oral administration. Upon dissolution of the capsule, a gas generating system inflates the pouch in the stomach

where it is retained for 16-24 hours, all the time releasing agents described herein. Merrion's developed another GIRES technology that consists of a controlled-release dosage form inside an inflatable pouch, which is placed in a drug capsule for oral administration. Upon dissolution of the capsule, a gas generating system inflates the pouch in the stomach. In clinical trials the pouch has been shown to be retained in the stomach for 16-24 hours.

8. **Micropump Technology:** Flamel's Micropump® platform permits either extended, or both delayed and extended, delivery of small molecule drugs via the oral route. Micropump consists of a multiple-particulate system containing 5,000 to 10,000 microparticles per capsule or tablet. The 200-500 microns diameter-sized microparticles release the drug at an adjustable rate and over an extended period of time. Micropump's key attributes includes extended release in the GI tract allowing mean plasma residence times to be extended for up to 24 hours, potentially improved efficacy (by extending therapeutic coverage), potentially reduced toxicity and/or side effects (by reducing Cmax or peak drug concentration in the plasma, or by reducing intra- and inter-patient variability), improved patient compliance (by reducing frequency of administration), applicable to poorly soluble (< 0.01mg/L) as well as highly soluble (> 500g/L) and to low dose (e.g. 4 mg) or high dose (e.g. 1,000 mg) drugs, excellent mouth feel, taste masking properties.
9. **Gastro Dose Technology:** Gastrodose is retained in the stomach for extended periods of time used for the treatment of disorders of the stomach or upper gastrointestinal tract. It is also suited for drugs that are readily absorbed into the circulation from the stomach or upper small intestine. For instance, Alza Corporation has developed a gastro-retentive platform for the OROS™ system, which showed prolonged gastric residence time in a dog model as the product remained in the canine stomach at 12 hours post dose and was frequently present at 24 hours. In humans, in the fasted state, the average gastric residence time for the same system was 33 minutes. DepoMed has developed technology that consists of a swellable tablet. After ingestion of the tablet, it swells and achieves sufficient size to resist gastric emptying, while simultaneously providing controlled release of the drug. Two of the products that DepoMed is developing include Metformin GR™ and Ciprofloxacin GR™.[13]

EVALUATION OF GASTRORETENTIVE DRUG DELIVERY SYSTEM

1. **Size and Shape Evaluation**:

The particle size and shape plays a major role in determining solubility rate of the drugs and thus potentially its bioavailability. The particle size of the formulation can be determined using Sieve analysis, Air elutriation analysis, Photo analysis, Optical microscope, Electro résistance counting methods (Coulter counter), Sedimentation techniques, Laser diffraction methods, ultrasound attenuation spectroscopy, Air Pollution Emissions Measurements etc.

2. **Surface Topography**:

   The surface topography and structures were determined using scanning electron microscope operated with an acceleration voltage of 10k.v, Contact angle meter, Atomic Force Microscopy (AFM), Contact profilio-meter.

3. **Swelling Studies:**

   Swelling studies were performed to calculate molecular parameters of swollen polymers. Swelling studies was determined by using Dissolution apparatus, optical microscopy and other sophisticated techniques which include 1HNMR imaging, Confocal laser scanning micro- and fats scopy (CLSM), Cryogenic Scanning Electron Microscopy (Cryo-SEM), Light scattering imaging (LSI) etc. The swelling studies by using Dissolution apparatus was calculated as per the following formula.

Swelling ratio = Weight of wet formulation / Weight of formulations

4. Determination of the Drug Content: Percentage drug content provides how much amount of the drug that was present in the formulation. [1] Beads from each formulation were powdered. Equivalent weight of beads was weighed and dissolved in 5ml of water in 50ml standard flask. Shake them and make up with phosphate buffer and then centrifuge it. From that take 5ml of solution in 50 ml standard flask make up with phosphate buffer. Generally, the drug content in any formulation should fall within the limit of 90 – 110%.[12]

5.Floating lag time and floating time determination:

This test is performed using 0.1N HCl. The time required by the dosage form to come upon the surface of the dissolution medium is called as floating lag time. The time period for which the dosage form remains buoyant on the surface of the dissolution medium is called as floating time.

APPLICATIONS OF MICROPARTICULATE GASTRORETENTIVE DRUG DELIVERY SYSTEM

1. Sustained Drug Delivery Hollow microspheres of non-steroidal anti-inflammatory drugs are very effective for controlled release as well as it reduces the major side effect of gastric irritation; for example, floating microspheres of indomethacin are quiet beneficial for rheumatic patients
2. Site-Specific Drug Delivery These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, e.g., Riboflavin, furosemide. Bilayer-floating capsule was developed for local delivery of misoprostol, which is a synthetic analog of prostaglandin E1 used as a protectant of gastric ulcers caused by administration of NSAIDs.
3. Absorption Enhancement Drugs that 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 systems, thereby maximizing their absorption. [12]

4. Absorption Enhancement Drugs which are having poor bioavailability because of site specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, there by maximizing their absorption.
5. Minimized Adverse Activity at the Colon Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented.
6. 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. [15]

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