Review Article

FLOATING BEADS: A NEW TREND OF FLOATING DRUG DELIVERY SYSTEM

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ABSTRACT

A multiple unit oral floating drug delivery system was developed to prolong gastric residence time, target stomach mucosa and increase drug bioavailability. Oral sustained release gastro-retentive dosage forms offer many advantages for drugs with absorption from upper parts of the gastro intestinal tract. Gastro retentive systems such as floating systems, mucoadhesive, high-density, expandable have developed to provide controlled delivery of drugs with prolonged gastric residence time. The present study attempts to give an insight into the gastro-retentive drug delivery systems, and gastric floating dosage forms, in particular. Due to their advantages over conventional dosage forms the study has attracted the formulators. The study highlights these advantages with reference to the various types of gastro retentive drug delivery systems, as well as provides an overview of the advances that have taken place in this area. Floating dosage forms are emerging as a promising dosage forms. Various attempts have been made to develop gastro retentive systems. Several approaches are currently utilized in the prolongation of the GRT Floating dosage forms can be prepared as tablets, capsules by adding suitable ingredients as well as by adding gas generating agent. In this review various techniques used in floating dosage forms along with current and recent developments of stomach specific floating drug delivery systems are discussed.

Key Words: Floating drug delivery system, Buoyancy, Gastric residence time, Gastro retentive system.

INTRODUCTION

Gastric emptying of dosage types is a supremely variable process and ability to extend and control emptying time is a valuable benefit for dosage forms, which remain in the stomach for a longer period of time than conventional dosage forms. Oral controlled dosage forms are being originated due to their advantages. The controlled drug delivery system should basically be aimed at achieving more expectable and increased bioavailabilty of drugs. However the progressing process is challenged by several physiological obstacles, such as inability to restrain and locate drug in the particular regions of GI tract, due to the changeable gastric emptying and motility. Conventional oral dosage forms provide a certain drug concentration in systemic passage without offering any control over drug delivery. Controlled release drug delivery systems (CRDDS) produce drug release at a predetermined, expected and controlled rate. A main problem in oral CRDDS is that not whole drug candidates are absorbed uniformly throughout the gastrointestinal tract. Few drugs are absorbed uniformly throughout the gastrointestinal tract. Few drugs are absorbed in a specific portion of gastrointestinal tract only. Such drugs are said to have an “Absorption window”. After passing the absorption window, the liberated drug goes to waste with insignificant or no absorption. These discussions of CRDDS have guided to the development of oral GRDFs having gastric retention capabilities.[1]

One of the most suitable and common approaches for fulfilling a prolonged and expected drug delivery profiles in gastrointestinal tract is gastro retentive dosage forms (GRDFs) that provide a new and better choice for drug therapy. Gastro retentive systems can prevail in the gastric region for long period of time and hence significantly extend the gastric residence period of drugs. Prolonged gastric retention enhances bioavailability, reduces drug waste, and enhances solubility for drugs that are less soluble in the high pH surroundings. Gastric retention will give new therapeutic possibilities and substantial advantages for patients.[2]

The controlled gastric residing of solid dosage forms may be attained by the various efforts. Several gastro retentive drug delivery techniques being designed and improved, including: high density (sinking) systems that reside in the bottom of the stomach, low density (floating) systems that causes floatation in gastric fluids, mucoadhesive types that causes bioadhesion to stomach mucosa, unfoldable, extendible,

or swellable systems which decreases emptying of the dosage forms through the pyloric sphincter of stomach, super porous hydrogel systems, magnetic systems etc. This review deals with various gastro retentive approaches that have recently become leading approaches in the field of site-specific oral controlled release drug delivery systems.[3]

BASIC PHYSIOLOGY OF GASTROINTESTINAL TRACT

The Gastrointestinal tract is a tube of about nine meters long that runs through the middle of the body, from the mouth to the anus and involves the throat (pharynx), oesophagus, stomach, small intestine (consisting of the duodenum, jejunum and ileum) and large intestine. The wall of the gastrointestinal tract has the identical common structure throughout most of its length from the oesophagus to the anus, with some local differences for each area. The stomach is an internal organ with a capacity for storage and blending. The stomach is located in the left upper part of the abdominal cavity instantly under the diaphragm. Its size varies depending on the amount of food taken: up to 1500 ml following a meal; after food has emptied, a fallen state is obtained with resting volume of 25-50 ml.[4]

Based on fasted and fed conditions of stomach, there are two different types of gastrointestinal motility. The fasted state is related with some cyclic contractile happenings commonly called as Migrating Myoelectric Complex (MMC) or The interdigestive motility pattern is commonly known as 'migrating motor complex' ('MMC') and is arranged in cycles of activity and quiescence. MMC wave begins from the stomach down the GI tract every 90–120 minutes. A full cycle resides of four phases, starting in the lower oesophageal sphincter, continuing over the whole stomach, the duodenum and jejunum, and ends at the ileum.[5]

Phase I: (basal phase) lasts from 40 to 60 minutes with several contractions.

Phase II: (pre burst phase) It includes of fragmentary contractions that adequately increase in intensity as the phase develops and it lasts about 20 to 40 minutes.

Phase III: (burst phase) lasts for 4 to 6 minutes. It considers intense and systematic contractions for small period. It is due to this wave that all the not digested material is moved out of the stomach down to the small intestine. It is also called as the housekeeper wave.

Phase IV: This is a short temporary period of about 0 to 5 minutes, and the contractions vanish between the last part of phase III and quiescence of phase I. These contractions effect in reducing the size of food particles (to less than1mm) which are moved toward the pylorus in a suspension form. During the fed state onset of MMC is detained resulting in slowdown of gastric emptying rate. The studies finding gastric emptying rates says that orally administered controlled release dosage form are subjected to basically two problems that of short gastric residence time and incalculable gastric emptying rate.[6]

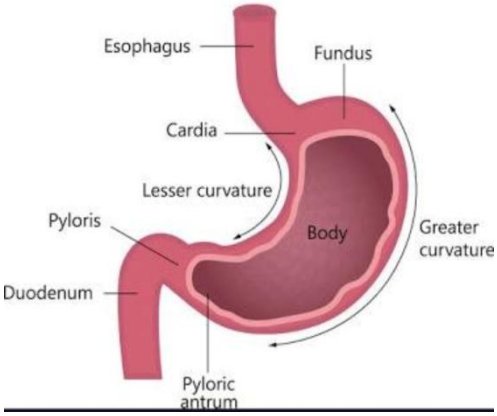


Fig. 1: **Anatomy of stomach**

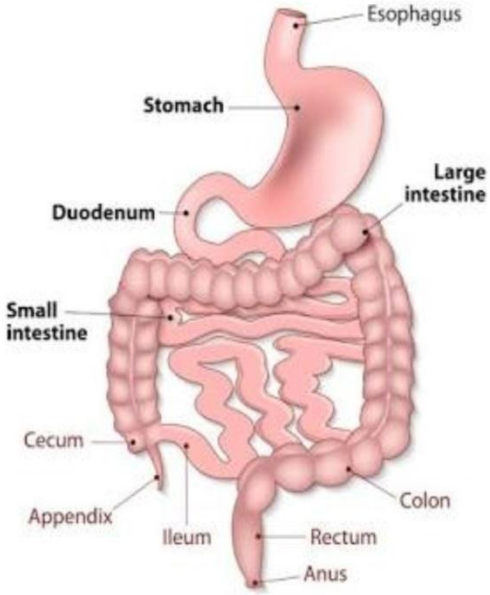
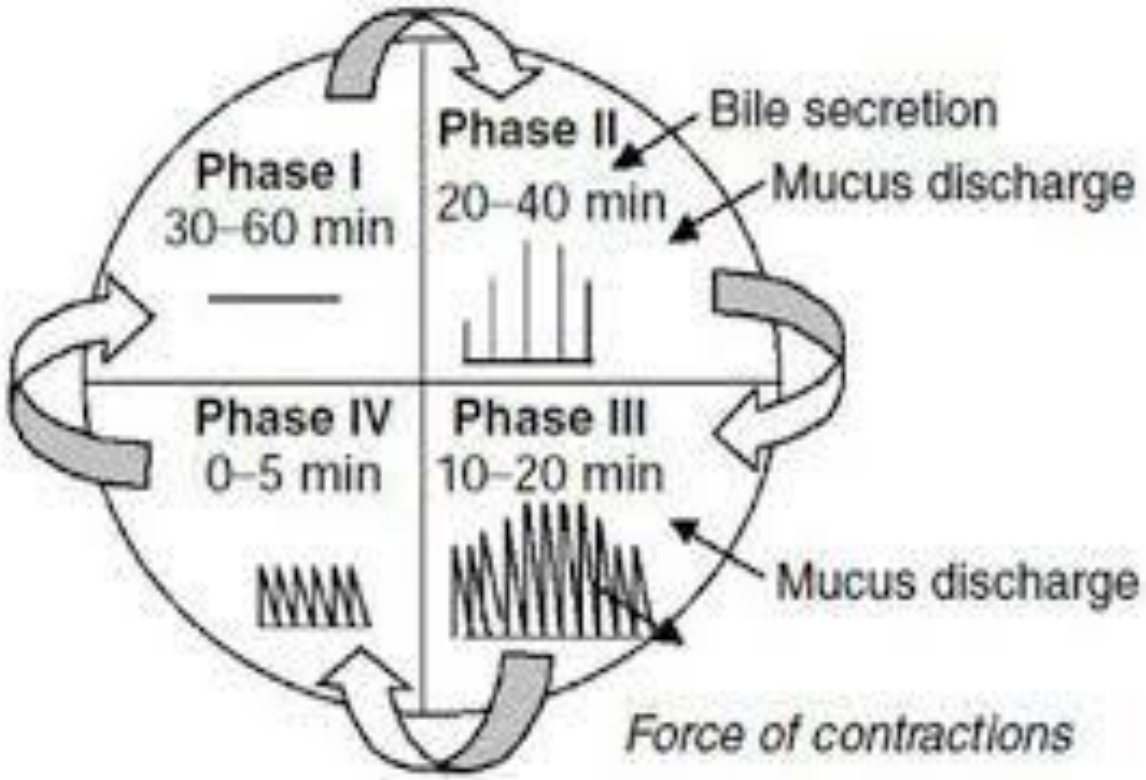


Fig. 2: Gastro intestinal tract



Need for Gastro retentive drug delivery system (GRDDs)

- ✓ Usually oral delivery is commonly utilized in pharmaceutical field to treat or prevent diseases. Although, conventional delivery had many obstacles and the major obstacle is non-site specificity.
- ✓ Gastro retentive delivery is a site-specific delivery for the confinement of drugs either at stomach or at intestine. It is obtained by residing dosage form in the stomach and the drug is delivered in a controlled manner to the specific site either in stomach or other parts of GI tract.
- ✓ Some drugs are absorbed at particular site. They need to be delivered at specific site or to be delivered such that maximum amount of drug reaches the specific site.
- ✓ Pharmaceutical field is now concentrating more towards such drugs which require particular site.[7]

Factors affecting gastric retention

1. **Nature of the meal of:** Fats, particularly fatty acids retard gastric secretion and have a particular reductive effect on the rate of emptying. Proteins and starch are known to have inhibitory effect on gastric emptying, though to a less extent. As the viscosity of the gastric fluids is increased, there is a corresponding reduction in the rate of emptying.[8]

2. **Caloric content:** Gastric residence time can be enhanced by 4-10 hours with a food that is rich in proteins and fats.[9]
3. **Density of dosage form:** The density of a dosage form also affects the gastric emptying time and effects the location of the system in the stomach.
4. **Frequency of the food:** The GRT can be enhanced by over 400 minutes, when consecutive meals are given, due to the reduced frequency of MMC.
5. **Size of dosage form:** The mean gastric retention time of nonfloating dosage forms are highly variable and much more dependent on their size, which may be large, medium and small units. In most cases, the larger the dosage form the greater will be the gastric residence. In broad it is known that indigestible food particles > 1-2mm are retained in the stomach throughout the postprandial period, after which they are removed by cyclical recurring burst of interdigestive gastric contractions.10
6. **Single or multiple unit formulation:** Multiple unit dosage forms show a more predictable release profile and unimportant impairing of performance due to failure of units allow co- administration of units with different release patterns or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.
7. **Sex**: Mean ambulatory GRT in males (3.4±0.6 hours) is less when measured with their age and race matched female counter parts (4.6±1.2 hours), nonetheless of the weight, height and body surface.
8. **Emotional state of subject:** The influence of psychological factors on gastric motility depending upon whether the emotional experience is of an aggressive or a depressive type.
9. **Body posture:** Gastric emptying is ideal while standing and by lying on the right side since the normal curvature of the stomach provides a hanging path whereas lying on the left side or in supine position reduces it.[11]
10. **Effect of drugs:** Drugs that reduce gastric retention includes poorly soluble Antacids (Aluminium hydroxide), Anticholinergics (Atropine, Propantheline), Narcotic analgesics (Morphine) and Tricyclic antidepressants (Imipramine, amitryptiline).Drugs such as Metoclopramide, Domperidone and Cisapride (Anti emetics) stimulates gastric emptying.
11. **Exercise:** Heavy physical activity retards gastric emptying.
12. **Disease states:** Diseases like gastric ulcer, pyloric stenosis, gastroenteritis, diabetes and hypothyroidism retard gastric emptying. Diseases like duodenal ulcer and hyperthyroidism promote gastric emptying rate.[12]

APPROACHES FOR GASTRIC RETENTION

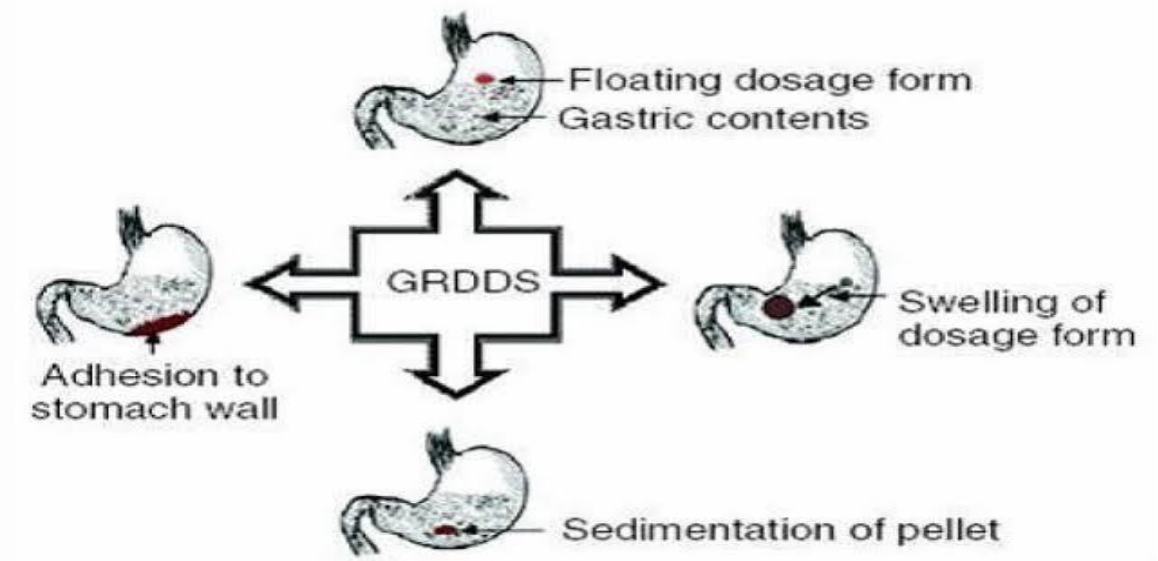


Fig. 3: Figure showing various approaches for gastro retentive drug delivery system.

A) High Density Systems: It is also known as Sedimentation system. These systems with a density of about 3 g/cm3 will reside in the antrum part of the stomach and are capable of withstanding its peristaltic movements. This system is made by covering the drug or mixed with heavy inert substances such as titanium dioxide, barium sulfate, iron and zinc oxide powder. In the system, the formulation density exceeds the density of common stomach content (1.004 g/mL). The only major problem with such systems is that it is technically very difficult to manufacture such formulations with high amount of drug (>50%) and to achieve a density of about 2.8g/cm3.[13]

B) Swelling and expanding system: One way to reside a dosage form in the stomach is by increasing its size. These are the dosage forms, which after engulfing, swells to an level that prevents their departure from the pylorus. As a outcome, the dosage form is retained in the stomach for extended or long period of time. These systems are also named as 'plug type systems'. In this system, polymers are used with ideal molecular mass and swelling properties, which (in addition to imparting floatation) also helps in controlled and sustained drug release. This system undergoes contact with gastric media; the polymer absorbs water and swells.
Eg: Developed swelling systems of Losartan tablets using sodium bicarbonate, sodium carboxy methyl cellulose (Na CMC), and hydroxyl ethyl cellulose (HEC).[14]

C) Bioadhesive Systems: These systems are based on bioadhesive polymers, which adhere or bind to the mucin and / or epithelial surface. A bio/muco-adhesive substance is a natural or synthetic polymer, which is capable of developing an adhesive interaction based on hydration–mediated, bonding mediated or receptor mediated adhesion with a mucus lining of GI mucosa.[15]

D) Floating Drug Delivery systems and its mechanism: Floating drug delivery systems (FDDS) or hydro-dynamically balanced systems have a bulk density lesser than gastric fluids and thus survive buoyant in the stomach without affecting the gastric emptying rate for a long period of time. The system floats in the gastric fluid and the drug is slowly liberated at the required rate. This causes an increased GRT and a improved control of the fluctuations in plasma drug concentration. Several approaches or systems were used to develop an ideal FDDS. These buoyant formulations include hollow microsphere (micro balloons), granules, powders, tablets, pills, laminated film.

To determine the floating force kinetics, ideal apparatus for determination of resultant weight has been mentioned in the literature. The apparatus works by measuring continuously the force equivalent to F (as a function of time) that is essential to maintain the submerged object or dosage form. The object floats better if F is on the greater positive side as shown in figure. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the disadvantages of unforeseeable intragastric buoyancy capability imbalances.[16]

F = F buoyancy – F gravity = (Df – Ds) gv

Where, **F**= total vertical force, **Df** = fluid density,
Ds= object density, **v** = volume and **g** =acceleration due to gravity.
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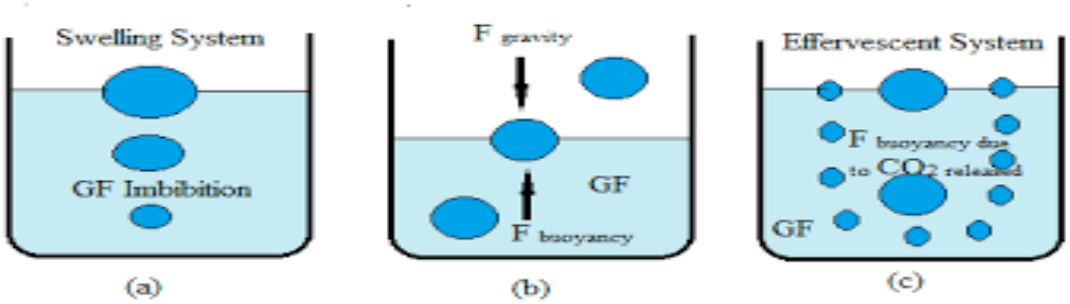

Fig. 4: Mechanism of floating systems, GF=Gastric fluid

Approaches to design floating dosage forms
The following approaches have been used for the design of floating dosage forms of single and multiple unit systems.
Single-Unit Dosage Forms: In low density systems, the globular shells, having lower density than that of gastric content or fluid can be used as a carrier for drug for its controlled rate release. A floating dosage form can also be derived by using a fluid-filled system that remains buoyant in the stomach. In coated shells or beads popcorn, poprice, and polystyrol have been used as drug carriers. Sugar polymeric materials such as methacrylic polymer and cellulose acetate phthalate have been utilized to undercoat these shells. These are additionally coated with a drug-polymer combination. The polymer of possible can be either ethylcellulose or hydroxypropyl cellulose, which depends on the type of released rate. Finally, the product remains buoyant on the gastric fluid while liberating the drug gradually over a prolonged period of time. Fluid filled floating chamber type of dosage forms includes incorporation of a gas filled floatation chamber in to a micro porous component that houses as a reservoir having apertures present at top and bottom walls through which the gastrointestinal tract fluid enters to dissolve the drug.[17]
Hydrodynamically balanced systems (HBS) are designed to prolong the stay of the dosage form in the gastro intestinal tract and help in enhancing the absorption. Such systems are best acceptable for drugs having a ideal solubility in acidic environment and also for the drugs having particular site of absorption in the upper region of the small intestine. To exist in the stomach for a long period of time the dosage system must have a bulk density of less than 1. It should remain in the stomach, sustain its structural integrity, and release drug regularly from the dosage form. The outcome of HBS capsule as a better system is best explained with Chlordiazeopoxide hydrochloride. This drug is classical example of a solubility issue, wherein it exhibits a 4000-fold distinctness in solubility going from pH 3 to 6. But Single-unit formulations systems are associated with issues such as sticking together or being blocked in the gastrointestinal tract, which may have a possible danger of producing irritation. These forms are also unreliable in prolonging GRT in stomach when orally delivered, owing to their fortuitous (all or nothing) emptying process.[18]

Multiple-Unit Dosage Forms: Multi particulate dosage forms are obtaining much favour over single-unit dosage forms. The potential advantages includes increased bioavailability; predictable, reproducible and normally short gastric residence time, no risk of dose dumping; reduced risk of local irritation, and the flexibility to mix pellets with different compositions or release models. In chasing of this endeavour many multiple unit floatable dosage systems have been designed. Microspheres have high storing capacity and numerous polymers have been used such as albumin, gelatin, starch, polymethacrylate, polyacrylamine, and poly alkyl cyanoacrylate. Spherical polymeric microsponges also called as “microballoons” have been

prepared. Microspheres have internal hollow structure and show an excellent in vitro floatability or buoyancy.[19]

CLASSIFICATION OF FLOATING SYSTEM

Based on the mechanism of floating, the floating drug delivery systems are of following types:

A) Non effervescent floating dosage form: These dosage forms or systems use a gel forming or swellable cellulose type of hydrocolloids, polysaccharides and matrix forming polymers like polycarbonates, polymethacrylate and polystyrene. The formulation is done by blending the drug and the gel-forming hydrocolloid, after oral delivery of this dosage form swells while comes in contact with gastric fluids gains bulk density of <1. The air entrapped by the swollen polymer causes buoyancy to these dosage forms. Excipients used most frequently in these systems include hydroxypropyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl acetate, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates.[20]

They are classified as:

a. Colloidal gel barrier systems
b. Micro porous compartment systems
c. Alginate beads

B) Effervescent floating dosage forms: These are the matrix type of floating dosage forms which are prepared by using swellable polymers like methyl cellulose, HPMC and chitosan based polymers as well as different effervescent compounds like Sodium carbonate, Calcium carbonate, Tartaric acid and Citric acid. They are developed in such a way that when in contact with the acidic gastric contents, $C0_2$ is liberated and gas entrapped in swollen hydrocolloids which provides buoyancy to the dosage forms.[21]

They are classified as:

a. Volatile liquid containing systems
b. Gas generating systems

Drugs suitable for GRDDS:

1. Drugs acting locally in the stomach E.g. Antacids and drugs for H. Pylori viz., Misoprostol
2. Drugs that are primarily absorbed in the stomach E.g. Amoxicillin
3. Drugs that is poorly soluble at alkaline pH E.g. Furosemide, Diazepam, Verapamil
4. Drugs with a narrow window of absorption E.g. Cyclosporine, Methotrexate, Levodopa, etc.
5. Drugs which are absorbed rapidly from the GI tract. E.g. Metronidazole, tetracycline.
6. Drugs that degrade in the colon. E.g. Ranitidine, Metformin HCl.
7. Drugs that disturb normal colonic microbes E.g. antibiotics against Helicobacter pylori.

Drugs unsuitable for GRDDS:

1. Drugs that suffer instability in the gastric environment. E.g. Erythromycin etc.
2. Drugs intended for selective release in the colon. E.g. Amino salicylic acid and corticosteroids etc.[22]

Merits of Floating Drug Delivery System

1. The floating drug delivery systems are advantageous for drugs absorbed through the stomach or proximal part of the small intestine. E.g. Ferrous salts, furosemide.
2. The ability of the medicaments administered utilizing the sustained release principle of floating formulation has been found to be independent of the site of particular medicaments.
3. The floating drug delivery systems are advantageous for drugs meant for local action in the stomach. E.g. antacids
4. Acidic substances like aspirin cause irritation on the stomach wall when come in contact with it. Hence HBS formulation may be useful for the administration of aspirin and other similar drugs.
5. Complete absorption of the drug from the floating dosage form is expected even at the alkaline pH of the intestine. The dissolution of the drug in gastric fluid occurs and then the dissolved drug is available for absorption in the small intestine after emptying of the stomach contents.
6. Enhanced bioavailability.
7. Sustained drug delivery/reduced frequency of dosing. 8. Reduced counter-activity of the body.[23]

Demerits of Floating Drug Delivery System:

1. Floating system is not suitable for those drugs that have solubility or stability problem in GI tract.
2. These systems require a high level of fluid in the stomach for drug delivery to float and work effectively.
3. Drugs such as nifedipine, which under goes first pass metabolism may not be suitable for the production of these types of systems.
4. Drugs which are annoyance to Gastric mucosa are also not suitable.
5. The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be included in the systems.[23]

POLYMERS USED IN FDDS

Polymers are used in floating system so as to target the drug delivery at specific region in the GI tract i.e. stomach. Both synthetic and natural polymers are used in the floating drug delivery. Polymers are classified based on their source as follows.

- Natural polymers used in floating system are Guar gum, Chitosan, Xanthan gum, Gellan gum, Sodium alginate, etc.
- Synthetic polymers used for the floating drug delivery are HPMC, Eudragit, ethyl cellulose, etc.

Natural polymers

The use of natural polymers is ideal based on proven biocompatibility and safety margin. Natural gums are among the popular hydrophilic polymers since of their cost-effectiveness and regulatory approval. Polymers are generally used in floating drug delivery systems so as to target the drugs to a specific site in the gastro intestinal tract i.e. stomach. Moreover, these polymers are safe, nontoxic and capable of chemical moderation and gel forming nature.

Natural polymer has advantages over synthetic polymer. They are as follows:

1. Biodegradable.
2. Biocompatible and non-toxic.
3. Low cost.
4. Environment friendly.
5. Local availability.

Natural polymer has some disadvantages. They are as follows

1. Microbial contamination.
2. Batch to batch variation.
3. Uncontrolled rate of hydration.
4. Reduced viscosity on storage.[24]

Synthetic polymers

Synthetic polymers are important in pharmaceuticals. Use of synthetic polymers ranges from binder, film coating agent, etc. Synthetic polymers are either purely synthetic or they are modified form of natural polymers which are known as semi-synthetic.

List of synthetic polymer used is as follows:

1. Hydroxy propyl methyl cellulose.
2. Eudragit.
3. Ethyl cellulose.

Disadvantages of synthetic polymers are as follows:

1. High cost toxicity environmental pollution.
2. Acute and chronic adverse effect.
3. Poor biocompatible.
4. Inflammatory response and local reaction.[25]

Polymers used in GRDDS

Polymers	HPMC 4000, HPMC 100, HPMC K4M, CMC, PVA, Calcium alginate, Carbopol, Ethyl cellulose,Eudragit RS and RL, acrylic polymer
Buoyancy increasing agents	Ethyl cellulose
Release rate accelerants	Mannitol, Lactose
Release rate retardants	Magnesium Stearate, Dicalcium phosphate, Talc
Low density materials	Polypropylene foam powder
Inert fatty materials	Fatty acids, Bees wax.
Effervescent agents	Tartaric acid, Citric acid, Sodium bicarbonate, Citroglycine

METHODS OF PREPARATION OF FLOATING BEADS

1. **Solvent evaporation method.**
2. **Emulsion gelation method.**
3. **Ionotrophic Gelation method.**

1. **Solvent evaporation method:** Preparation of floating beads by solvent evaporation technique has been applied greatly in pharmaceutical industries for different purposes such as FDDS. This method includes the emulsification of an organic solvent which contains dissolved polymer and dissolved or dispersed drug in more amount of continuous phase, with the assist of an agitator or mixer. The concentration of the emulsifier exists in the aqueous phase will affect the particle size and its shape. When the desired or ideal droplet size is formed, the stirring or mixing rate is minimized and evaporation of the organic solvent is undertaken under atmospheric or reduced pressure at an ideal temperature. Subsequent evaporation of the solvent yields solid polymeric micro beads entrapping the drug. The solid beads are separated from the suspension by filtration, centrifugation, or lyophilisation.

The polymers used for the development of such systems include, Cellulose acetate, Chitosan, Eudragit, Acrycoat, Methocil, Polyacrylates, Polyvinyl acetate, Carbopol, Agar, Polyethylene oxide and Polycarbonates.[26]

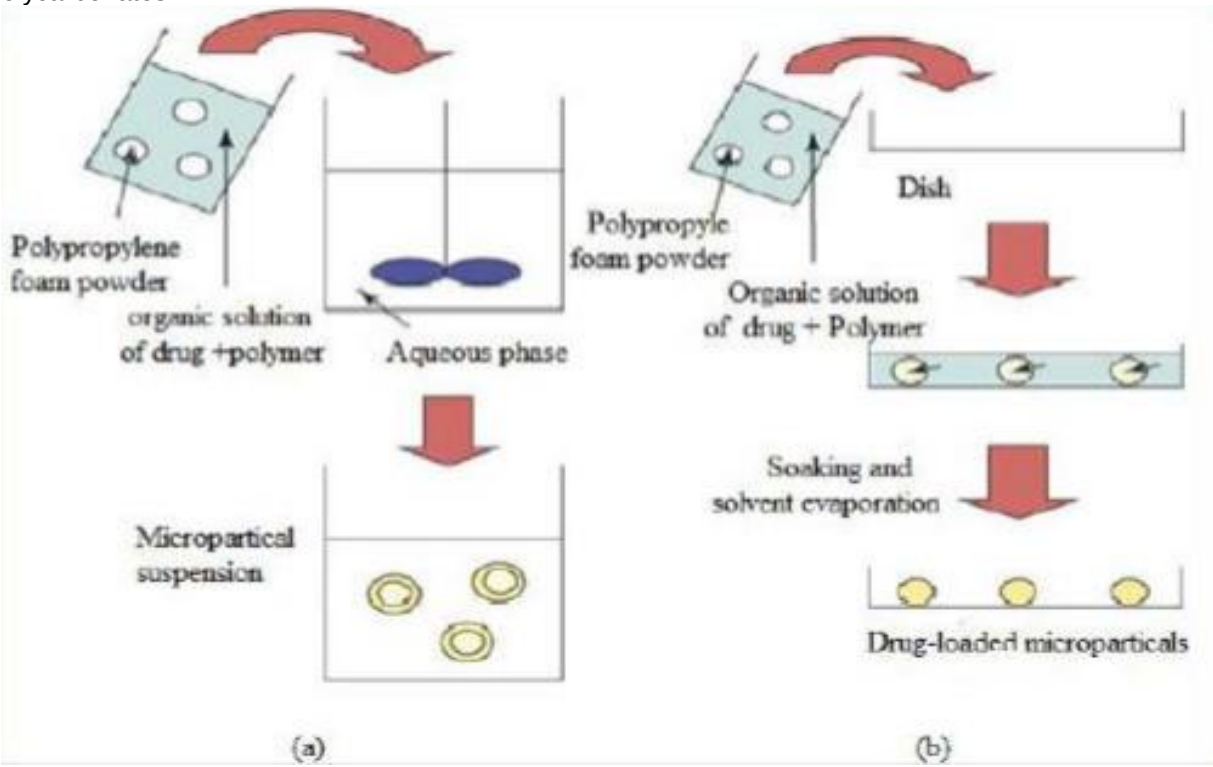

Fig. 5: Schematic presentation of the preparation of floating micro-particles based on low-density foam powder, using (a) The solvent evaporation method or (b) The soaking method

2. **Emulsion gelation method:** In this method the polymer is added in to distilled/ demineralised water with stirring or mixing. Drug and different quantity of oil are then added to the polymeric solution. This solution containing drug and oil is dropped through 21G needle in to 5% calcium chloride solution and left at room temperature for 2h. The obtained hydrogel beads are washed twice with distilled/demineralised water and kept for dehydration at room temperature up to 12 hours.[27]
3. **Ionotrophic gelation method:** Ionotropic gelation is a technique based on the capability of polyelectrolytes to cross link in the existence of counter ions to form hydrogel beads also known as gelispheres. Gelispheres are round crosslinked hydrophilic polymeric body that has ability of gelation and swelling in simulated biological fluid contents and thus the liberation of drug through it is managed by polymer relaxation. The hydrogel beads are formulated by dropping a drug-containing polymeric solution into the aqueous solvent of polyvalent cations. The cations try to diffuse into the drug-loaded polymeric drop of beads, which results in the formation of a three dimensional lattice of ionically crosslinked moiety. Biomolecules can also be loaded into these gelispheres under ideal conditions to retain their three dimensional structure.[28]

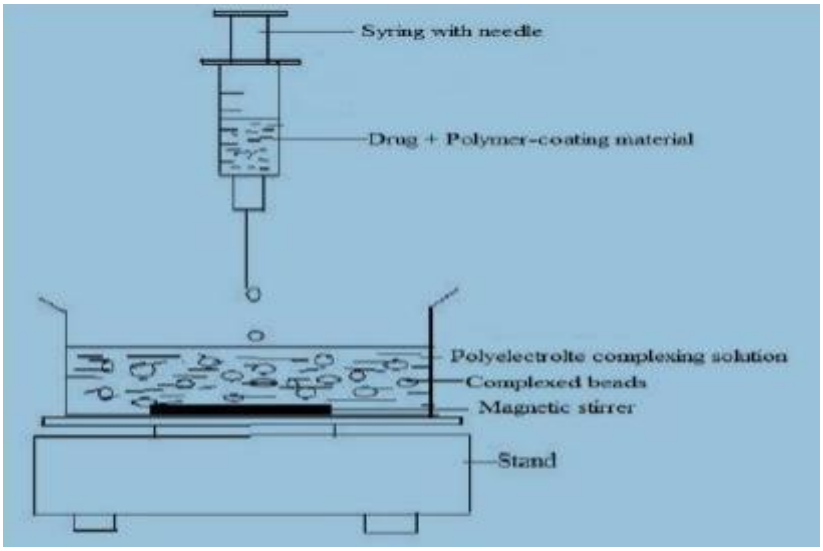

Fig. 6: Ionotropic gelation method

Characterization of floating gel beads include:

a) Percentage Yield

The prepared floating gel beads with given size range will be collected and weighed. The measured weight divided by total amount of non-volatile component which are used in the formulation gives percentage yield.[29]

$$\textbf{Percentage yield} = \frac{\textbf{Actual weight of the produt}}{\textbf{Total weight of drug and excipients}} \times 100$$

b) Size analysis of floating gel beads: The particle size of drug containing beads were measured by an optical microscope, with calibrated ocular and stage micrometer and particle size distribution was calculated. Around 50 particles or beads in five unlike areas were examined.[29]

c) Drug Content and Drug Entrapment Efficiency:

100mg equivalent drug loaded polymer beads will be dissolved in suitable solvent. It will be stirred using magnetic stirrer. The resulting solution will be then filtered and filtrate will be suitably diluted with suitable solvent. Drug content can be determined spectrophotometrically.[30]

Drug content and entrapment efficiency determined using equation:

$$\textbf{Drug content} = \frac{\textbf{Concentration} \times \textbf{Dilution factor}}{1000} \times 100$$

$$\textbf{Entrapment efficiency} = \frac{\textbf{Actual yield}}{\textbf{T heoretical yield}} \times 100$$

d) In vitro buoyancy study:

Beads (300mg) were scattered over the USP XXIV dissolution apparatus type II containing 900 ml of 0.1 N HCl and 0.02% Tween 80. The medium was disturbed with a paddle revolving at 100 rpm for 12 hr. The floating and the immersed portions of beads were collected separately. The beads were dehydrated and weighed. Buoyancy percentage was measured as the ratio of the mass of the beads that remained buoyant and the total mass/weight of the beads.[31]

$$\%\text{of buoyancy} = \frac{Qf}{Qf + Qs}$$

Where,

Qf = Weight of the floating Beads

Qs = Weight of settled Beads

e) Scanning electron microscopy (SEM):

Morphological examination of the surface and internal structure of the dried beads can be performed by using a scanning electron microscope (SEM).[31]

f) In-vitro drug release study:

The drug release analysis from beads is conducted by using USP dissolution apparatus Type I containing 900 ml of 0.1 N HCl as dissolution media (pH- 1.2) at 100 rpm and 37°C. 2 ml sample was taken at 1 hr. time interval for 12 hr. and same volume of fresh medium was replaced to maintain sink condition. Taken samples were assayed spectrophotometrically at suitable wavelength. The drug release was analyzed by UV spectrophotometer.[32]

g) Stability studies:

As per ICH guidelines, the beads filled in hard gelatin capsule shells, stability studies are performed on the formulations as short time stability study at $40^0C \pm 2^0C$ and 70±5% RH for 3 months to assess their stability.[32]

CONCLUSION

Gastro retentive drug delivery systems have been extensively investigated in recent years. Gastro retentive drug delivery techniques are the most selected systems in order to target the drugs which have a narrow absorption site near the gastric region. Recently number of drug delivery systems are being developed which aim at liberating the drug at gastric region. A number of FDDS have been emerged, such as single and multiple unit HBS, single and multiple unit gas generating systems, hollow microspheres and raft forming systems. Development of sustained release dosage forms is advantageous in providing prolonged gastric retention and increased efficacy of the dosage forms. The floating ability of the low density drug delivery dosage forms could successfully be joined with valid control of the drug release manners in order to boast accurate bioavailability. Hence further more studies are required in this view in order to improve effective drug delivery systems.

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