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Research Article

GASTRO RETENTIVE – FLOATING DRUG DELIVERY SYSTEM AN OVERVIEW

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ABSTRACT

Drug efficacy, minimal frequency of administration and bioavailability are the major concern of every new drug development and formulation, the research is going on for existing drug novelty for above said. To achieve the novelty of formulation, researches applying various techniques to modify site specific drug release. The recent technological research has been focusing on site specific retardation of drug delivery system. Orally administered drug reaches to stomach, which plays an important fate of drug release for further process. Some narrow absorption window drug not able to release the medicament significantly in the specific part of stomach due course of time, thus leads to poor therapeutic effect. Drug bioavailability may impair due to lesser contact time with the specific stomach part. To overcome this problem several technical approaches are applied in formulation. Gastro retentive dosage forms (GRDFs) is one of the novel technique will facilitate the continuous prolong release of the drug at the upper part of gastro intestinal tract. This is significantly extend the duration of drug release thus enhance the bioavailability of narrow therapeutic absorption drugs. The prolongation of drug release reduce the frequency of dosing and better patient compliance. This review briefly discuss about various floating dosage of gastro retentive drug delivery system, advantages, disadvantages and limitation of floating system.

Key words: *Bioavailability, Floating tablets, Gastro retentive dosage forms, Gastric emptying.*

INTRODUCTION

Floating drug delivery system improves bioavailability, reduces drug waste, and better patient's compliance. Nowadays several gastro retentive drug delivery approaches being designed and formulate. Floating systems or hydro dynamically controlled systems that have sufficient buoyancy to float the tablet over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.[1]

System is floating on the gastric contents, the drug is released slowly at the desired rate from the system, after the drug release the residual system is emptied from the stomach. This results in an increased gastro retardation time (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. Prolonged gastric retention time in the stomach could be advantageous for local action in the upper part of the stomach e.g. treatment of peptic ulcer.

Many narrow absorption window drugs categorized as once a day dosage form, however to make this formulation is challenging and need to come across many factors including an unpredictable gastric emptying rate (that varies from person to person), gastrointestinal transit time, and absorption. The current review brief about various floating gastroretentive approaches, principles, advantages that have recently become leading.

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FLOATING DRUG DELIVERY SYSTEMS

Floating drug delivery systems (FDDS) or hydro dynamically balanced systems [HBS]. The system is floating on the gastric contents, the drug is released slowly at a desired rate from it to the stomach. After the release of the drug, the residual system is emptied from the stomach. This system provides more gastric retentive drug release time and a better control of the fluctuations in plasma drug concentration.

The test for floating behavior and drug release are generally performed in simulated gastric fluids at 37°C. Timmermans and Andre characterized the buoyancy capability of floating forms and sinking of non-floating dosage forms using an apparatus to quantitatively measure the total floating force acting vertically on the immersed object (FDDS). The apparatus operates by measuring continuously the force equivalent to F (as a function of time), which is required to maintain the submerged object. The object floats better if F is on the higher positive side.

F = f (buoyancy) – f (gravity) F = (Db - Ds) gV

F – Total vertical force; Ds – Object density; Db – fluid density; V- Volume of fluid; g- Acceleration due to gravity.[2,3]

Mechanism of floating systems

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids so it buoyant in the stomach without affecting the gastric emptying rate in prolonged period of time. The tablet will require minimum gastric contents for the proper achievement of 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.[3,4] Floating drug delivery system can be divided into effervescent (gas generating) non-effervescent system.

Gas-generating (Effervescent) systems

INTRA GASTRIC SINGLE LAYER FLOATING TABLETS

These buoyant systems prepared with swellable polymers such as methocel (hydroxyl propyl methyl cellulose), polysaccharides (e.g., chitosan), and effervescent components (e.g., sodium bicarbonate, citric acid or tartaric acid). The system has reach to stomach carbon dioxide is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms.[5,6]

Stages of floating mechanism: (A) penetration of water; (B) generation of CO and floating; (C) dissolution of drug.

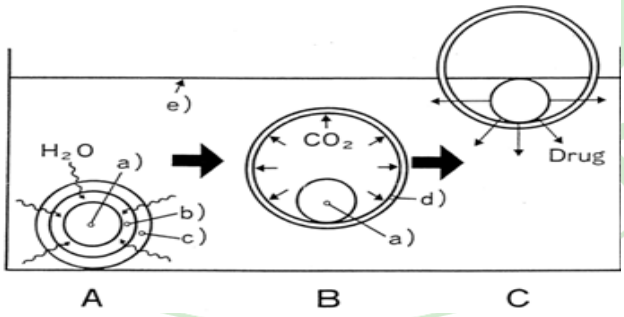

Fig.1 Mechanism of floating

Key: (a) conventional SR pills; (b) effervescent layer; (c) swellable layer; (d) expanded swellable membrane layer; (e) surface of water in the beaker (37^0C).

INTRA GASTRIC BILAYER FLOATING TABLETS

These are compressed tablet which have two layer, one is immediate release layer and another one is sustained release layer. After the ingestion of drug the immediate layer disintegrate immediately and produce instant drug release and starts pharmacological effect as early as possible. The second will produce prolong release to maintain constant drug level. The principle of buoyancy is similar as floating tablet.[5]

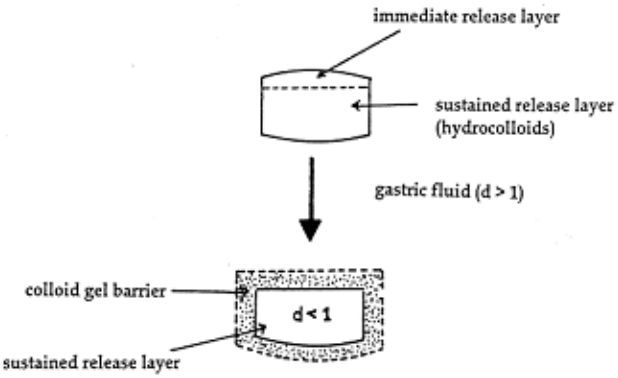

Fig.2 Bilayer floating tablet

INTRA GASTRIC MULTI-LAYER FLOATING TABLETS

These systems consist of sustained release pills as 'seeds' surrounded by double layers. The inner layer consists of effervescent agents while the outer layer is of swellable membrane layer. When the system is immersed in dissolution medium at body temperature, it sinks and then forms swollen like balloons, which float as they have lower density. This lower density is due to generation and entrapment of Carbon di oxide within the systems.[5,7,8]

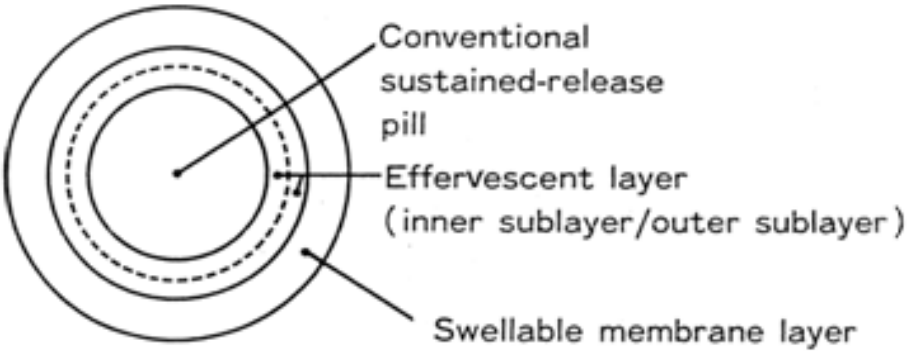

Fig.3 Multilayer floating tablet

Non-effervescent systems **[9]**

After swallowing the tablet get contact with gastric fluid it will swells in stomach. The formulation methods of such dosage forms involves the mixing of the drug with a gel, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than one within the outer gelatinous barrier.

The air trapped by the swollen polymer confers buoyancy to these dosage forms. Excipients used in these systems include hydroxyl propyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl acetate, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates. This system is further divided into following sub-types:

VACUUM CONTAINING SYSTEM

These systems can be made to float in the stomach because of floatation chamber, which may be a vacuum or filled with air or a harmless gas, while drug reservoir is encapsulated inside a micro porous compartment.[8]

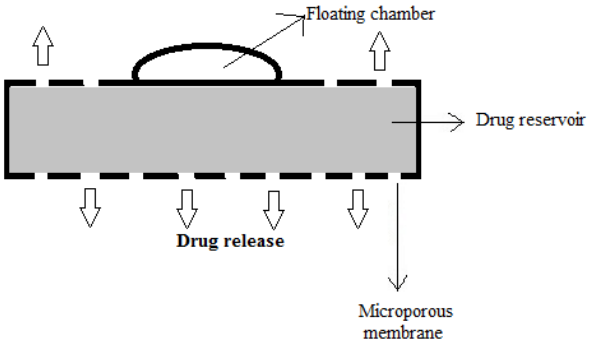

Fig.4 Vacuum containing system

INFLATABLE GASTROINTESTINAL DELIVERY SYSTEMS (CONTAINS VOLATILE LIQUIDS)

An inflatable chamber is incorporated in this system, which contains liquid ether that gasifies at body temperature to cause the chamber to inflate in the stomach. These systems are prepared by loading the inflatable chamber with a drug reservoir, which can be a drug, impregnated polymeric matrix, then encapsulated in a gelatin capsule. After oral administration, the capsule dissolves to release the drug reservoir together with the inflatable chamber. The inflatable chamber automatically inflates and retains the drug reservoir into the gastric fluid.[4,5]

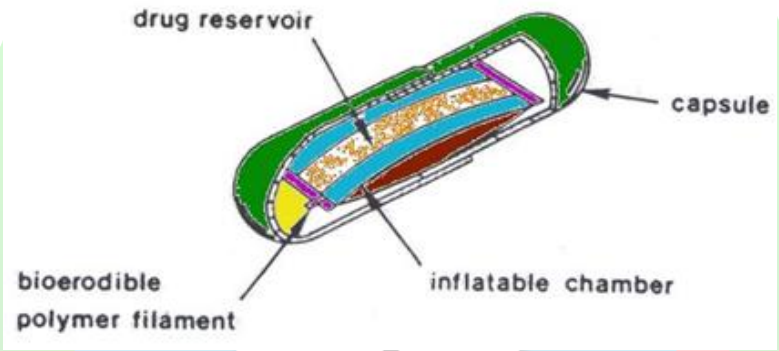

Fig.5 Volatile liquid containing system

INTRAGASTRIC OSMOTICALLY CONTROLLED DRUG DELIVERY SYSTEM

The osmotic pressure controlled drug delivery device consists of two components, drug reservoir compartment and an osmotically active compartment. The drug reservoir compartment is enclosed by a pressure responsive collapsible bag, which is impermeable to vapour and liquid and has a drug delivery orifice.

The osmotically active compartment contains an osmotically active salt and is enclosed within a semipermeable housing. In the stomach, the water in the GI fluid is continuously absorbed through the semi-permeable membrane into osmotically active compartment to dissolve the osmotically salt. An osmotic pressure is then created which acts on the collapsible bag and in turn forces the bag reservoir compartment to reduce its volume and activate the drug release of a drug solution formulation through the delivery orifice. The floating support is also made to contain a bio-erodible plug that erodes after a predetermined time to deflate the support. The deflated drug delivery system is then emptied from the stomach.[5]

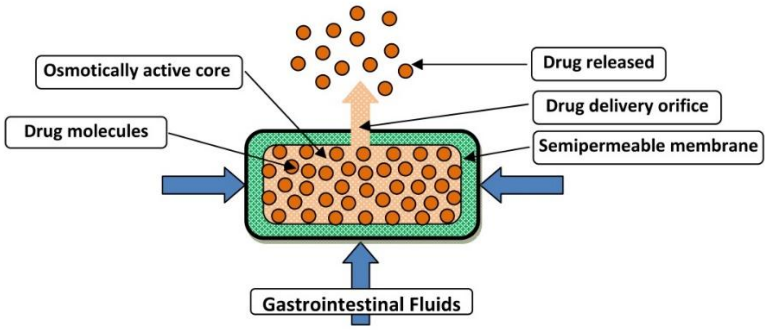

Fig.6 Osmotically controlled drug delivery system

MICRO POROUS COMPARTMENT SYSTEM

This technology is based on the encapsulation of a drug reservoir inside a micro porous compartment with pores along its top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of gastric surface with the undissolved drug. In the stomach, the floatation chamber containing entrapped air causes the delivery system to float over the gastric content. Gastric fluid enters through the aperture, dissolves the drug and carries the dissolved drug for continuous transport across the intestine for absorption.[4]

COLLOIDAL GEL BARRIER SYSTEM

This system contains drug with gel-forming hydrocolloids meant to remain buoyant on the stomach content. This prolongs gastro retardation and maximizes the amount of drug that reaches its absorption site. This system incorporates a high level of one or more gel-forming highly soluble cellulose type hydrocolloid, e.g., hydroxypropyl cellulose, hydoxyethyl cellulose, hydroxypropyl methyl cellulose (HPMC), polysaccharides and matrix-forming polymer such as polycarbophil, polyacrylate and polystyrene. On coming in contact with gastric fluid, the hydro colloid in the system hydrates and forms a colloid gel barrier around its surface.[4]

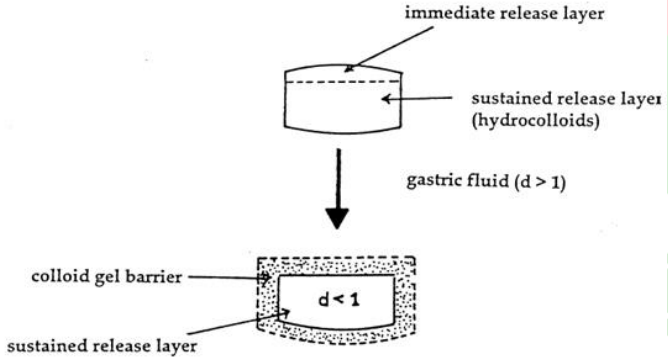

Fig.7 Colloidal gel barrier system

ALGINATE BEADS

Multi-unit floating dosage forms have been developed from freeze-dried calcium Alginate. Spherical beads of approximately 2.5 mm in diameter can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride, causing the precipitation of calcium alginate. The beads are then separated, snap-frozen in liquid nitrogen, and freeze-dried at -40ºC for 24 hours, leading to the formation of a porous system, which can maintain a floating force for over 12 hours. These floating beads gave a prolonged residence time.[4,9,10]

HOLLOW MICROSPHERES / MICROBALLONS

Hollow microspheres loaded with drug in their outer polymer shelf were prepared by a novel emulsion solvent diffusion method.

The ethanol/dichloromethane solution of the drug and an enteric acrylic polymer was poured into an agitated solution of Poly Vinyl Alcohol (PVA) that was thermally controlled at 40ºC. The gas phase is generated in the

dispersed polymer droplet by the evaporation of dichloromethane formed and internal cavity in the microsphere of the polymer with drug. The microballoon floated continuously over the surface of an acidic dissolution media containing surfactant for more than 12 hours.[4]

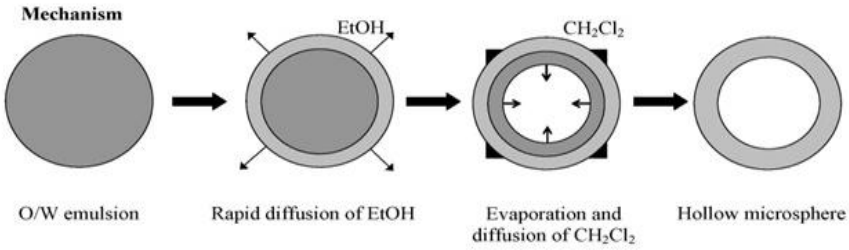

Fig.8 Hollow Microspheres

RAFT FORMING

This system is used for delivery of antacids and drug delivery for treatment of gastrointestinal infections and disorders. The mechanism involved in this system includes the formation of a viscous cohesive gel in contact with gastric fluids, forming a continuous layer called raft. This raft floats on gastric fluids because of a low density created by the formation of CO_2. Usually this contains a gel-forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO_2 to make the system less dense to float on the gastric fluids.[11]

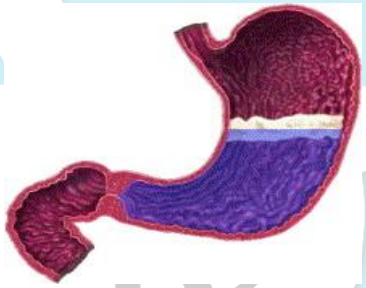

Fig.9 Raft forming

ADVANTAGES OF FLOATING DOSAGE FORM [12]

- Advantageous for drugs that are specifically absorbed in stomach or the proximal part of the small intestine, e.g., riboflavin and furosemide.
- Complete absorption of the drug.
- The fluctuations in plasma drug concentration are minimized, and concentration-dependent adverse effects can be prevented.
- Poor absorption due there is vigorous intestinal movement and a shorted transit time as might occur incertain type of diarrhea, Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.
- A significant increase in the bioavailability of drug.

DISADVANTAGES OF FLOATING TABLETS [1,7]

- Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
- They require a sufficiently high level of fluids in the stomach, so that the drug dosages form float therein and work efficiently.
- High variability in gastric emptying time due to its all or non-emptying process.
- Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diameter and size. Therefore patients should not be dosed with floating forms just before going to bed.

LIMITATIONS OF FLOATING DRUG DELIVERY SYSTEMS

- A high level of fluid in the stomach is required for drug delivery to float and work efficiently.
- Drugs which have stability and solubility problems in gastro intestinal tract are not

suitable candidates for floating drug delivery system.

- Drugs such as nifedipine, which under goes first pass metabolism may not be desirable for the preparation of these types of systems.
- Drugs which are irritant to Gastric mucosa are also not desirable.
- The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the systems.[4]

DISCUSSION

Floating drug delivery system is a better technique to enhance bioavailability of narrow absorption drug. The several float technique is an added advantage for choice to fit a drug as per its physiochemical property. The gastro retentive floating system reduce the frequency of administration, thus makes better patient compliance. However the patient counselling is important for these type of formulation prescribed to patient. The success of floating is sufficient amount of fluid / water presence in stomach, so advice the patient to consume sufficient amount of water and important and special care to be taken for night time dosage.

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