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Floating type drug delivery system: A review

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ABSTRACT

Floating Type drug delivery system retains the dosage form for a long span. They provide local delivery to specific region like stomach and proximal small intestine and shows better bioavailability and improve therapeutic activity and substantial benefit to patients. FDDS is one of the novel drug delivery system to prolong gastric retention time. Various forms of gastro retentive drug delivery system, such as floating and non-floating.

Keywords: Floating Drug Delivery System, Classification effervescent, non-effervescent, and Factors affecting FDDS.

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INTRODUCTION

The high level of patient compliance in taking oral dosage form is due to the ease of administration, patient compliance, flexibility in formulation and handling of this form. Although tremendous advances have been seen in oral controlled drug delivery system during last two decades .This system has been of limited success. This approach is bailed with several physiological difficulties such as inability to restrain and locate the controlled drug delivery system within the desired region of the gastrointestinal tract (GIT) due to variable gastric emptying and mobility. Normal gastric residence times usually range between 5 minutes and 2 hours .Migrating myoelctric complex is characterized by four phases: Phase1-Period of no contraction (40-60 minutes), phase 2-Period of intermittent contraction (20-40 minutes), Phase 3-period of regular contraction at the maximal frequency 20 minutes and phase4-Period of transition between phase 3 And Phase 1 (0.5minutes) [1] (figure 1)[1]

Gastro retentive system 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.[2]Slowed mobility of the gastrointestinal tract by concomitant administration of drugs or pharmaceutical excipient also increases gastric retention of drug. These efforts resulted in GRDSs that where designed, in large part, based on the following approaches. (Figure: 2)[3]

Low density form of the DF that causes buoyancy in gastric fluid.

High density DF that is retained in the bottom of the stomach.

Bio adhesion to the stomach mucosa.

Expansion by swelling or unfolding to a large size which limits passage of dosage form through the pyloric sphincter.[3]

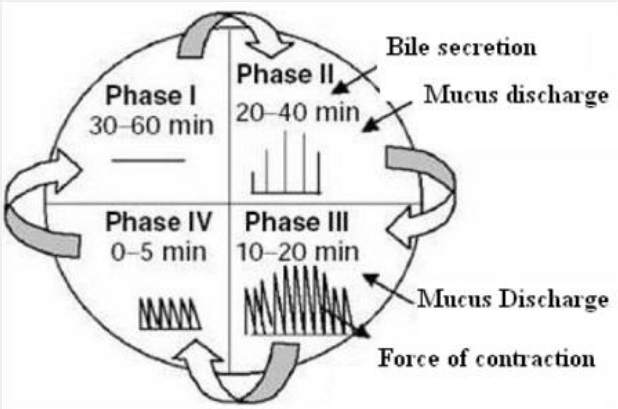

Figure 1: Schematic Representation of Interdigestive Motility

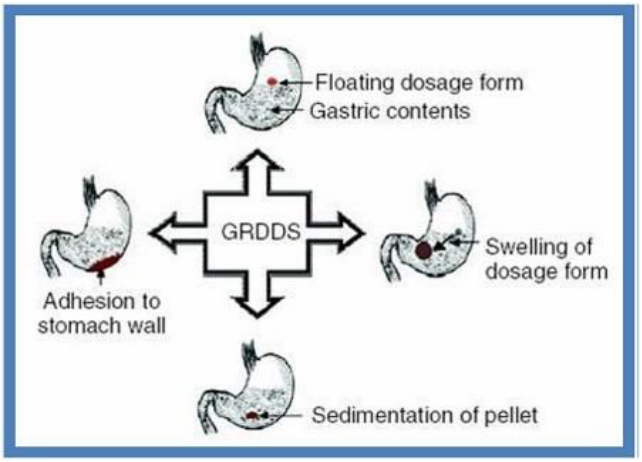

Figure 2:Types of Gastro - retentive drug delivery system

CLASSIFICATION OF FLOATING TYPE DRUG DELIVERY SYSTEM

A.Single Unit Floating Dosage System

a. Effervescent System (Gas Generating System)

b. Non-effervescent Systems

B.Multiple Unit Floating Dosage Systems

a. Non- effervescent systems

b. Effervescent System (Gas- Generating System)

c. Hollow Microsphere

d. Raft Forming Systems[4]

A. Single Unit Dosage Form

a. Effervescent System (Gas-Generating System)

effervescent system are matrix type of systems this are prepared with the help of swell able polymers such as methylcellulose and chitosan and various effervescent components like sodium bicarbonate, citric acid and tartaric acid or chamber containing a liquid that gaffes at body temperature.(Fig:3)[1] The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1. The common approach for preparing these system involves resin beads loaded with bicarbonate and coated with ethylcellulose.Excipient used most commonly in these system include HPMC, polyacrylate polymers, polyvinyl acetate, carbopol ,agar sodium alginate, calcium chloride, polyethylene oxide and polycarbonates[4] .

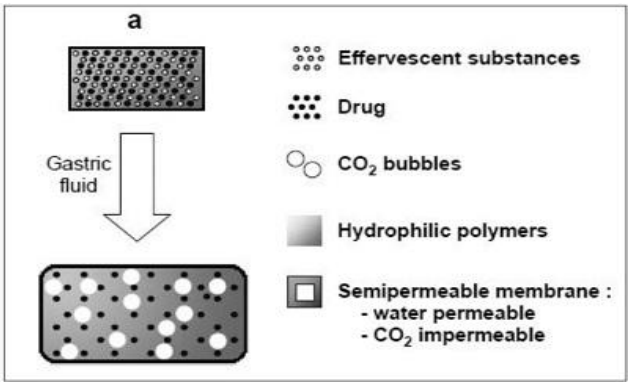

Figure: 3 Gas-Generating System

b. Non-effervescent System

One or more gel forming, highly swell able, cellulosic hydrocolloids (e.g. hydroxyl ethyl cellulose, hydroxyl propy l cellulose and sodium carboxyl methyl cellulose), polysaccharides, or matrix forming polymers(e.g., polycarbophil, polyacrylate, and polystyrene) are inc orporated in high level (20 75% w/w) to tablets or capsules. For the preparation of these types of systems, the drug and t he gel-forming hydrocolloid are mixed thoroughly. After oral administration this dosage form swells in contact with gastri c fluids and attains a bulk density of <1.[5]

B. Multiple Unit Floating Dosage Form

a. Non-effervescent system

Alginate Beads

They were made using a combination and low methoxylated pectin. Spherical beads of approximately 2.5 mm in diameter can be prepared by dropping a sodium alginate solution in to aqueous solutions of calcium chloride, causing precipitation of calcium alginate. The beads are then separated snap and frozen in liquid nitrogen, and freeze dried at -40° for 24 h, leading to the formation of porous system, which can maintain a floating force over 12 h. Yong-Dan Tang et. Al prepared alginate beads based on the above method for the sustained release of both hydrophobic and hydrophilic drugs. They added sunflower oil in the beads and found the beads floating for 24 hours. The hydrophobic drug ibuprofen was released from this system for 24 hours due to oil partitioning.[6]

b. Effervescent System

Floating pills

These systems consist of sustained release pills as 'seeds' surrounded by double layers. The inner layer consists of effervescent agents like sodium carbonate while the outer layer is of swell able polymer like polyvinyl acetate. When this system is immersed in to dissolution medium at body temp, it sinks at once and then forms swollen pills like balloons which then float as they have lower density. This lower density is due to generation and entrapment of CO2 within the system[7] (Fig. 4)[7]

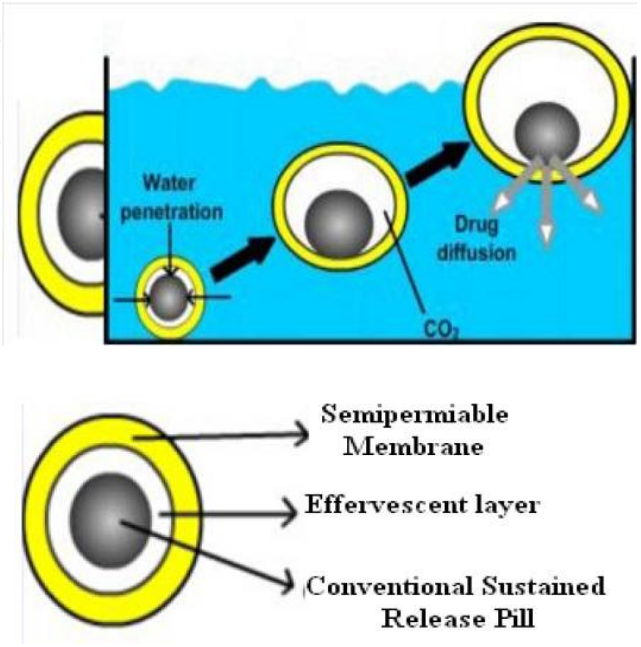

Figure 4:

(A) Multiple-unit oral floating drug delivery system.

(B) Working principle of effervescent floating drug delivery system.

c. Microballoons / Hollow microspheres

These are loaded with drugs in their other polymer shelf were prepared by simple solvent evaporation. (Figure 5)[1] to prolong the gastric retention time (GRT) of the dosage form. . Polycarbonate,Eudrgit S, Cellulose acetate, calcium alginte agar and low methoxylted pectin re commonly used s polymers in preperation of hollow microsphere. Buoyancy and drug release are dependent on quantity of etc. Buoyancy and drug release from dosage form are dependent on quantity of polymers, the plasticizer polymer ratio and the solvent used for formulation. The micro balloons floated continuously over the surface of an acidic dissolution media containing surfactant for >12 hours.[8]Buoyancy and drug release are dependent on quantity of polymer the plasticizer- polymer rtio and the solvent used.[1,8]

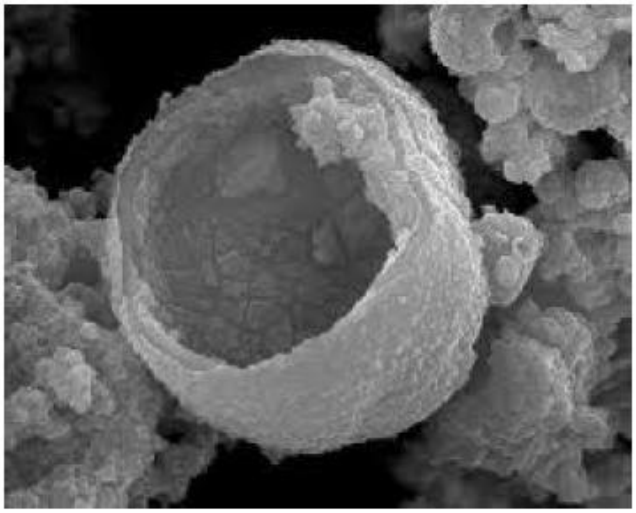

Figure: 5 Micro ballons

D. Raft Forming System

On contact with gastrict fluid A gel- forming solution (sodium alginate solutn containing carbonate or bicarbonate) swells and forms a viscous cohesive gel containing entrapped CO2 bubbles.[1] Which forms raft layer on top of gastric fluid which release drugs slowly in stomach . such formation typically contains antacids such as aluminium hydroxide or calcium carbonate to reduce gastric acidity . They are often used for gastro esophageal reflux treatment as with liquid gaviscon[9] (GlasxoSmithline) (FIG.6)[10]

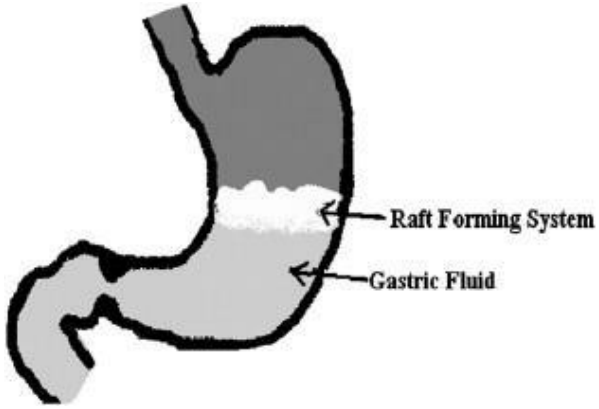

Figure: 6 Barrier formed by a raft-forming system

MECHANISM OF FDDS

There are various attempts have been made to reatain the dosage form in the stomach as a way of increaseing the retention time. These attempts include introdusing the floating dosage form as gas generating system and swelling system modified shape system . Gastric emptying delaying devices and co- administration of gastric-emptying delaying drugs. Among these, thefloating dosage form have been most commonly used.Floating drug delivery systems have a bulk density less than gastric fluid and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolong period of time. While the system is floating on the gastric content , (fig.7a)[11] the drug is released slowly at the desired rate from the system. This result in an increased GRT, better control of the fluctuation in plasma drug concentration . After the Release Of Drug, The Residual System Is emptied from the stomach .However ,beside a minimal gastric content needed to allow the proper acheivement of the buoancy retention principle ,a minimal level of floating force(F) is also requred to keep the dosage form reliably buoyant on the surface of the meal. To meaure the floating force kinetic, a novel apparatus fr determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuosly the force equivalent to F is on the higher positive side (fig.7b)[11] . apparatus help in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawback of unforeseeable intragastric buoyancy capability variations.[11]

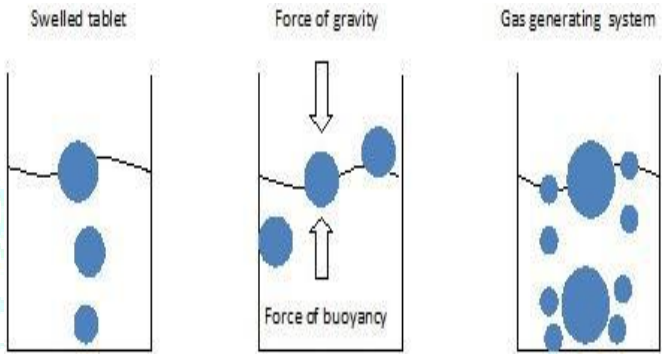

Figure: 7 Different mechanisms of floating systems.

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 o gravity

FACTORS AFFECTING FDDS

Density: Floating is a function of dosage form buoyancy that is dependent on the density.

Shape of the dosage form: ring haped and Tetrahedron device with flexural modules of48 and 22.5 kilo pounds per squares inch (KSI) are reported to have better floating, 90% to100% retention at 24hours as compared with other shapes.[12]

Concomitant drug administration: Anticholinergic like atropine and propantheline, prokinetic agens like metoclopramide and cisapride;can affect floating time

Fed or Unfed State: Under fasting conditions,the gi mobility is characterized by periods of strng motor activty or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours.

Nature of meal: Feeding of indigistible plymers or fatty acid salts can change the motolity pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release.

Caloric content and feeding frequency: Floating can be incresed by four to 10hours with ameal that is high in protein and fats. The floating can increase by over 400minutes when successive meals are given compared with a singal meal dueti low frequency of MMC

Age: Elderly people, especially those over 70, have a significanly longer; floting, Disease condition such as dabetes and crohn`s disease etc also affect drug delivery.

Posture: Floating can vry between supine and upright ambulatory states of the patents.[13]

ADVANTAGES OF FDDS

Sustained drug delivery: A floating drug delivery system can remain in the stomach for several hours and the assumed prolongation in the gastric retention is postulated to cause sustained drug release behaviour.

Site-specific drug delivery: Targeting of drug[14] to stomach appears to be useful for all substances intended to produce a lasting local action on the gastro duodenal wall.

Pharmacokinetic advantage: In addition, with the total gastrointestinal transit duration is increased, a greater amount of drug may be delivered and thus the relative bioavailability will consequently be increased.

Reduced counter-activity of the body: Slow input of the drug into the body was shown to minimize the counter activity leading to higher drug efficiency.[11]

Improves patient compliance.

Freedom from incompatibilities between drug and excipients especially with buffers.

Better therapeutic effect of short half life drugs can be achieved.

Gastric retention time is increased because of buoyancy.

Site specific drug delivery to the stomach can be achieved.[15,16]

DISADVANTAGES OF FDDS

These systems require a high level of fluid in the stomach for drug delivery to float and work efficiently-coat, water.

The drugs that are significantly absorbed through out gastrointestinal tract, which undergo significant first pass metabolism, are only desirable candidate.

Gastric Irritation due to the presence of some drug in the Floating Type Drug Delivery System.

These systems require a high level of fluid in the stomach for drug delivery to float however this can be overcome by using low density polymers.[11]

The release rate of the controlled release dosage form varies from a variety of factors like rate of food transit through the drug. 3) Potential toxicity due to loss of integrity of drugs.

The dosage forms should be administered with more amount of water (200-250ml).

These dosage forms should not be crushed or chewed.[15]

PROBABLE CANDIDATES FOR FDDS

Following are the probable candidates, but not limited to, for gastro retentive drug delivery system:

Drugs required exerting local therapeutic action in the stomach: antacids, anti-H.pylori agents, misoprostol

Drugs that have narrow absorption window in stomach or upper parts of the small intestine, e.g., furosemide, riboflavine-5-phosphate[17]

EVALUATION PARAMETER OF FDDS

A . In Vitro Methods

1. Floating Lag Time And Floating Time

It is the time taken by the tablet to emerge on to the surface of dissolution medium and is expressed in seconds or minutes.[18] In (fig 8)[17,18]

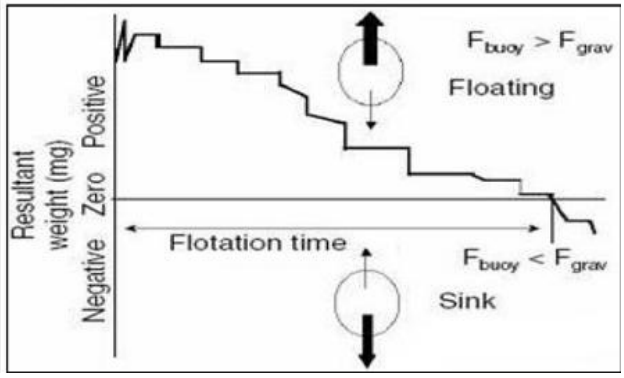

Figure 8:

2. Dissolution Study

Gohel et al proposed a more relevent in vitro dissolution method to evaluate a floating drug delivery systems.[1]The in vitro release study for all the formulations were carried out by USP Dissolution Test Apparatus Type-II. The temperature of the dissolution medium (0.1 M HCl, 900 ml) was maintained at 370C with a stirring rate of 50 rpm ,then 5ml of dissolution medium was taken out at intervals of 1,2,3&4 hours. Exactly 5ml of fresh buffer was added to the dissolution vessel after each withdrawal, to maintain a constant volume. Then the withdrawal samples were analyzed by using a U.V [19, 20,21](fig:9)[1]

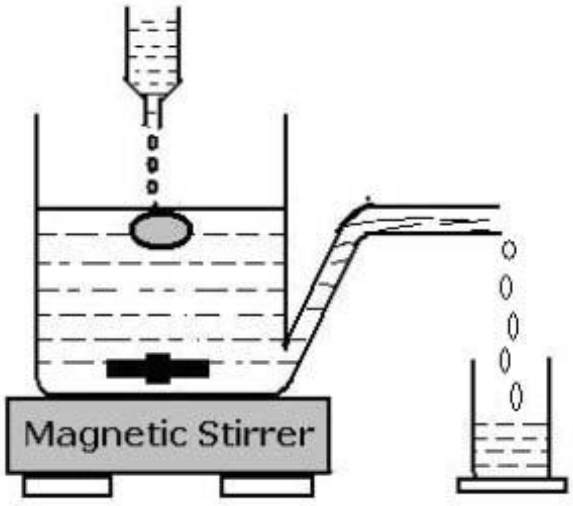

Figure 9: In vitro dissolution method

3. Resultant Weight Test

An in Vitro measurng apparatus has been conceived to determine the real floating capabilities of buoyant dosage forms as a funtion of time. It operates by measuring the force equivalent to the force F required to keep the object totally submerged in the fluid.(fig:10)[1]

The following equation by which weight are tested,

F = F buoy – F grav

F = d f Gv – d s Gv = (d f – d s) Gv

F = (df – M / V) Gv[20]

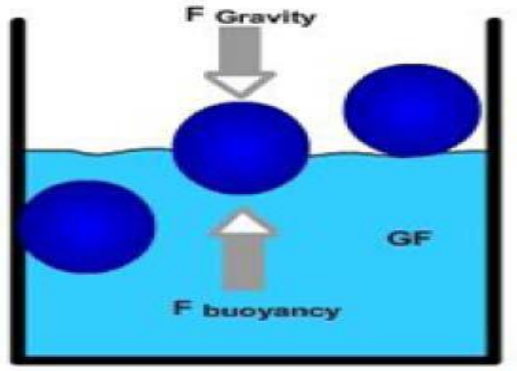

Figure 10: Effect of various forces on floating

B. In Vivo Method

1. X-Ray Method

X- Ray is a very polular evaluation parameter for floating dosage form now a day. It help to locate dosage form in the G.I.T and by which one can predict ane crrelate the gastrict emptying time and the passge of dosage form in the GIT.[1,4,23]

2. Gastroscopy

It comprises of peroral endoscopy, used with a fibereoptic and video system. It is suggested that gastroscopy may be used to inspect visually the effect of prolonged stay in stomach milieu ion the FDDS.[1,23]

3. Utrasonography

Ultrasonic waves reflected substantially different acoustic impedances across interface enables the imaging of some abdominal organs. Most DFs not have sharp acoustic mismatches result across their interface with the physiological milieu. Therefore, This is not routingly used for the evaluation of Floating Type Drug Delivery System.[1,23]

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