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Gastroretentive drug delivery system: an overview

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ABSTRACT

Gastric emptying is a complex process and makes the in vivo performance of the drug delivery system uncertain. In order to avoid this fickleness, efforts have been made to increase the retention time of the dosage form, that is the development to gastroretentive drug delivery system. Gastroretentive drug delivery system (GRDDS) can remain in the stomach for prolonged period of time and there by increases gastric residence time of drugs, and also improves the bioavailability of certain drugs. These are widely used for the site specific drug delivery, for the treatment of gastrointestinal diseases and disorders. There are several approaches of Gastroretentive drug delivery system which are discussed in detail in the present review. Recent patents on (GRDDS) are also enlisted with a detailed description of evaluation parameters of the same.

Key words: Approaches of GRDDS, Evaluation parameters, Gastro-retentive drug delivery system, probable polymers used in GRDDS, recent patents on GRDDS.

Introduction

The high level of patient compliance in taking oral dosage forms is due to the ease of administration and handling of these forms. Although tremendous advances have been seen in oral controlled drug delivery system in the last two decades, this system has been of limited success in the case of drugs with a poor absorption window throughout the GIT (Gastro Intestinal Tract). In the development of oral controlled drug delivery system, one of the main challenges is to modify the GI transit time. Gastric emptying of pharmaceuticals is highly variable, which could be illustrated below in a tabular form and is dependent on the dosage form and the fed/fasted state of the stomach. Normal gastric residence time usually ranges between 5 minutes and 2 hours. In the fasted state the electrical activity in the stomach – the interdigestive myoelectric cycle or migrating myoelectric complex (MMC) governs the activity and, hence, the transit of dosage forms. It is characterized by four phases:

Phase I–Period of no contraction (40-60 minutes), phase II –Period of intermittent contractions (20-40 minutes), phase III–Period of regular contractions at the maximal frequency that travel distally also known as housekeeper wave. (10-20 minutes) and phase IV–Period of transition between phase III and phase I (0-5 minutes) [1].

If there are physiological problems and other factors like the presence of food then gastric emptying is unpredictable. Drugs having a short half-life are eliminated quickly from the blood circulation. Various oral controlled delivery systems have been designed which can overcome these problems and release the drug to maintain its plasma concentration for a longer period of time.This has led to the development of oral Gastroretentive dosage forms. Gastroretention is essential for drugs that are absorbed from the stomach, drugs that are poorly soluble or degraded by the higher pH of intestine, and drugs with an absorption which can be modified by changes in gastric emptying time. Gastroretentive dosage forms are also useful for local as well as sustained drug delivery for certain conditions, like H. pylori infection which is the cause of peptic ulcers. This dosage form improves bioavailability, therapeutic efficacy and may even also allow a possible reduction in the dose because of

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steady therapeutic levels of drug, for example furosemide and ofloxacin. The reduction in fluctuations in therapeutic levels minimizes the risk of resistance especially in case of β-lactam antibiotics (penicillins and cephalosporins) [2]

Table 1: Advantages and disadvantages of FDDS [3]

Advantages	Disadvantages
1. Improved drug absorption	1. GRDDS is not suitable for drugs with stability or solubility problems in the stomach.
2. Controlled drug delivery	2. It requires sufficiently high level of fluid in the stomach so that the system floats and thus sufficient amount of water (200–250 ml) to be taken together with the dosage form.
3. Minimizing the mucosal irritation	3. Drugs having irritant effect on gastric mucosa are not suitable for GRDDS.
4. Delivery of drug for local action in the stomach	4. Drugs which are absorbed along the entire GIT and which undergoes first pass metabolism may not be desirable e.g. nifedipine.
5. Treatment of gastrointestinal diseases.	
6. Simple and conventional equipment for manufacturing process.	
7. Site-specific drug delivery.	
8. Ease of administration and better patient compliance	

Table 2: Anatomical and physiological features of GIT [4]

Section	Average length(cm)	Diameter(cm)	Absorption mechanism	pH	Major constituents	Transit time(h)
Oral cavity	15-20	10	Passive diffusion	5.2-6.8	Amylase, maltase, mucin	Short
Stomach	20	15	Passive diffusion	1.2-3.5	Hydrochloric acid, pepsin, rennin, lipase, intrinsic factor	0.25-3.0
Duodenum	25	5	Passive diffusion, active transport, facilitated tra ir, pinocy-tosis	4.6-6.0	Bile, trypsin, chymo-trypsin, amylase, maltase, lipase, nuclease, CYP3A5	1-2
Jejunum	300	5	Passive diffusion, active transport, facilitated transport	6.3-7.3	Amylase, maltase, lactase, sucrase, CYP3A5	-
Ileum	300	2.5-5.0	Passive diffusion, active transport, facilitated transport, ion pair,pinocytosis		Lipase, nuclease, nucleotidase,	1-10
Cecum	10-30	7	Passive diffusion, active transport, pino-cytosis	7.5-8.0	-	Short
Colon	150	5	Passive diffusion	7.9-8	-	4-20
Rectum	15-19	2.5	Passive diffusion, pinocytosis	7.5-8.0	-	Variable

Factors affecting gastric retention time of the dosage form[5]

1. Density
2. Size & Shape of formulation
3. Single or multiple unit formulation
4. Fed or unfed state
5. Nature of meal
6. Caloric content
7. Frequency of feed
8. Gender
9. Age
10. Posture
11. Concomitant drug administration
12. Disease state

Approaches to achieve gastric retention

Different approaches have been pursued to increase the retention of oral dosage forms in the stomach. Some are formulated as single component whereas others are formulated as multi-component dosage forms. GRDDS can be broadly categorized into floating and non-floating system.

A. Non-floating system

Non-floating system is further divided into:

1. High density (sinking) drug delivery system
2. Bioadhsive or mucoadhesive system
3. Magnetic system
4. Swelling/ Expanding Systems

B. Floating drug delivery systems (FDDS)

Floating drug delivery system can be divided into:

1. Effervescent system

1.1) Volatile liquid containing systems

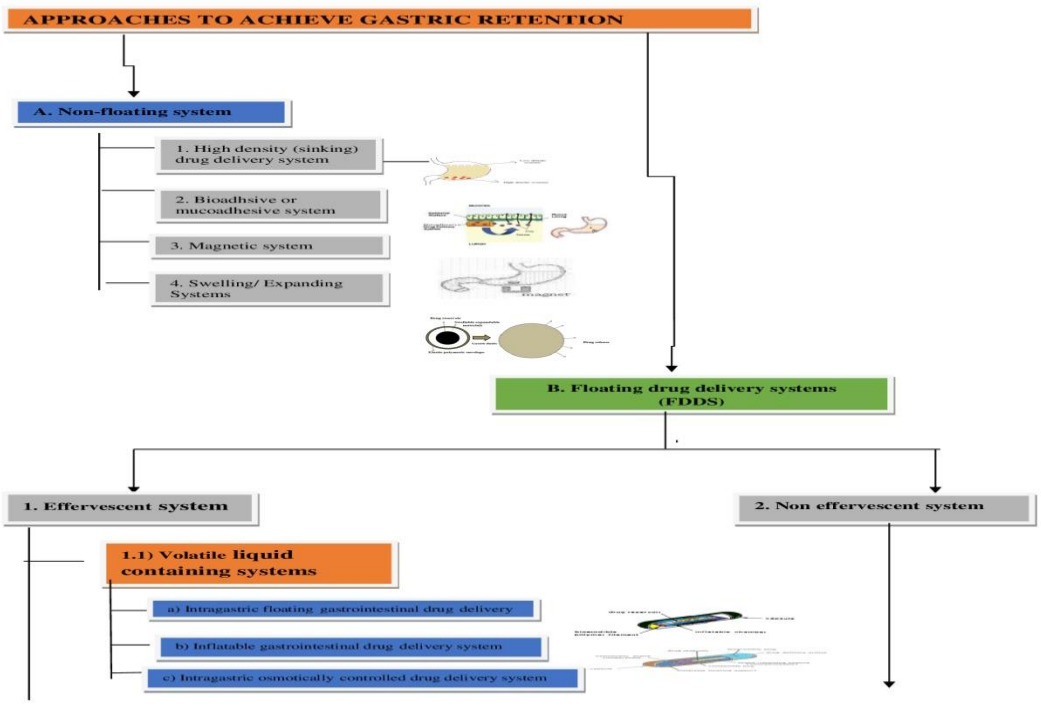
a) Intragastric floating gastrointestinal drug delivery
b) Inflatable gastrointestinal drug delivery system
c) Intragastricosmotically controlled drug delivery system

1.2) Gas generating systems

a) Floating capsules
b) Floating pills
C) Floating systems with ion exchange resins

2. Non effervescent system

2.1Hydrodynamically balanced system
2.2 Microbaloons or hollow microspheres
2.3 Alginate beads
2.4 Microporous compartment
2.5Raft systems
2.6Superporous hydrogel



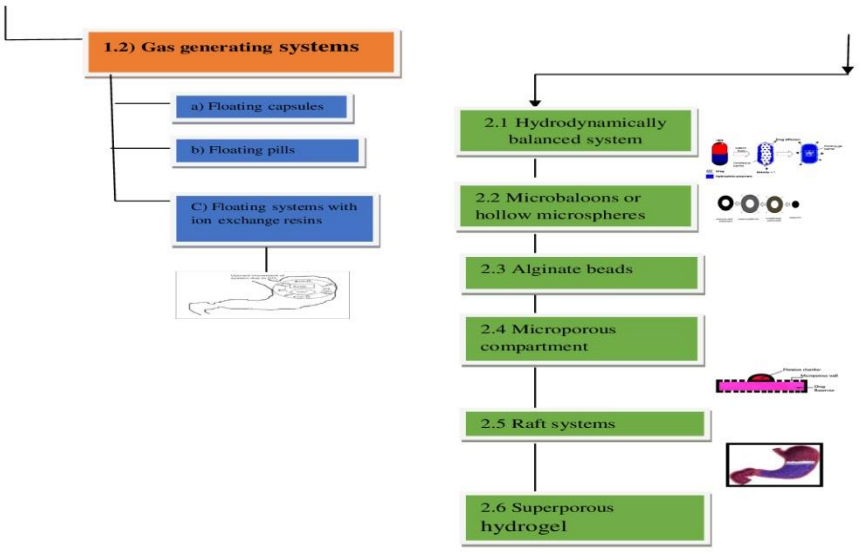


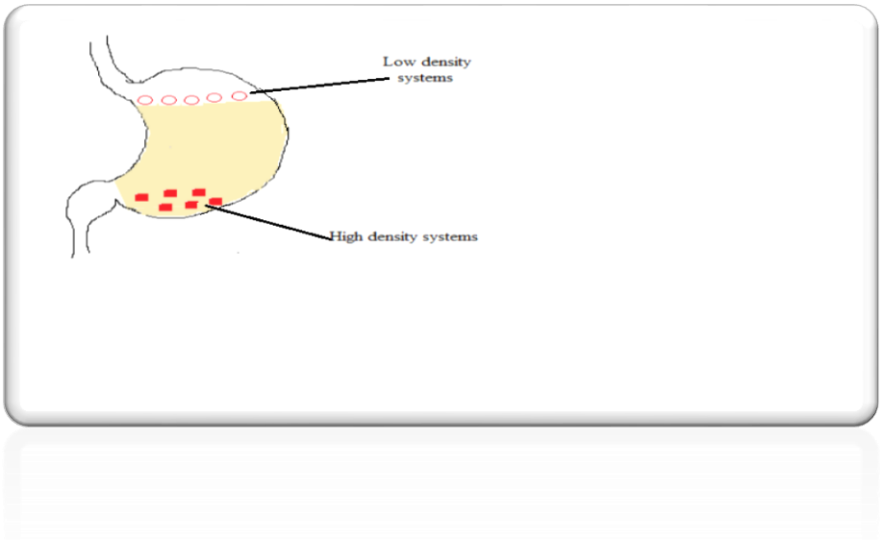
Fig 1: Showing the high density systems which are at the bottom of the stomach and low density systems which are floating

A. Non-floating system

1. High Density (Sinking) Drug Delivery System

Here dosage formis prepared by coating drug on a heavy core or mixed with inert materials such as iron powder, barium sulfate, zinc oxide and titanium oxide so that the density of the formulation exceeds the density of the normal gastric content [6].They increase the density up to 1.5-2.4 gm/cm^3. But effectiveness of this system in human beings was not observed [7]and no formulation has been marketed.

Fig.1Showing the high density systems which are at the bottom of the stomach and low density systems which are floating



2. Bioadhesive or mucoadhesive system

These systems bind to the gastric epithelial cell surface, or mucin, and increase the GRT by increasing the

duration of contact between the dosage form and the biological membrane. A bio mucoadhesive substance is a natural or synthetic polymer capable of adhering to a biological membrane (bio-adhesive polymer) or the mucus lining of the GIT (mucoadhesive polymer). The characteristics of these polymers are

Molecular flexibility, hydrophilic functional groups, chain length, and conformation

Furthermore, they must be

- ✓ Nontoxic and non-absorbable
- ✓ Form noncovalent bonds with the mucin–epithelial surfaces
- ✓ Have quick adherence to moist surfaces
- ✓ Easily incorporate the drug and offer no hindrance to drug release
- ✓ Have a specific site of attachment, and be economical.

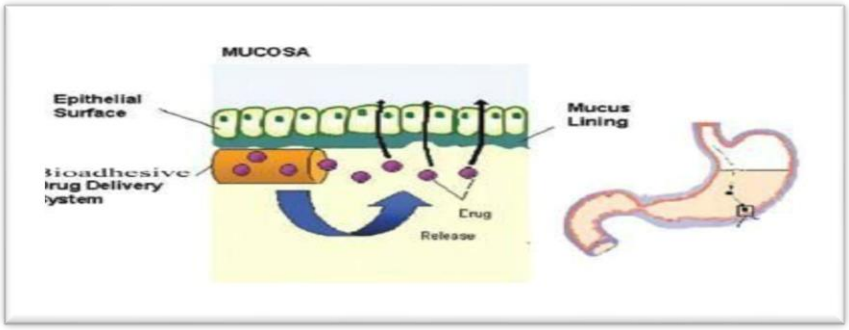


Fig.2 Bioadhesive drug delivery system

3. Magnetic systems

Here the dosage form contains a small internal magnet and a magnet placed on the abdomen over the position of the stomach. Ito et al. used this technique in rabbits with bioadhesive granules containing ultrafine ferrite (g-Fe_2O_3). They guided them to the oesophagus with an external magnet (1700 G) for the initial 2 min and almost all the granules were retained in the region after 2 hr [8].

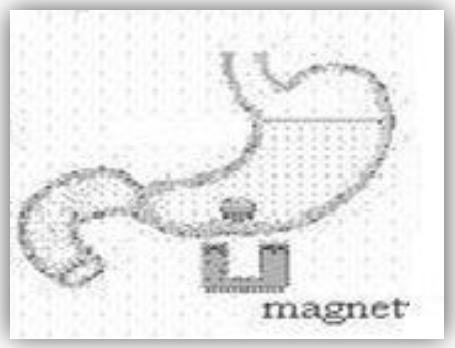


Fig 3:Magnetic systems

4. Swelling/ Expanding Systems

After being swallowed, these dosage forms swell to a size that prevents their passage through the pylorus. As a result, the dosage form is retained in the stomach for a long period of time. These systems are sometimes referred to as *plug type systems* because they tend to remain lodged at the pyloric sphincter. These polymeric matrices remain in the gastric cavity for several hours even in the fed state. Sustained and controlled drug release may be achieved by selecting a polymer with the proper molecular weight and swelling properties.

Expandable System

The extensive swelling of these polymers is due of the presence of physical-chemical crosslinking in the hydrophilic polymer network. These cross-links prevent the dissolution of the polymer and thus maintains the physical integrity of the dosage form. A balance between the extent and duration of swelling is maintained by the degree of cross linking between the polymeric chains. A high degree of crosslinking retards the swelling ability of the system and maintains its physical integrity for a prolonged period. On the other hand, a low degree of cross-linking results in extensive

swelling followed by the rapid dissolution of the polymer.

An optimum amount of cross-linking is required to maintain a balance between swelling and dissolution. The swollen system eventually will lose its integrity because of a loss of mechanical strength caused by abrasion or erosion or will burst into smaller fragments when the membrane ruptures because of continuous expansion. [9]

The expandable GRDFs are usually based on three configurations:

- A small collapsed configuration which enables sufficient oral intake
- Expanded form that is achieved in the stomach after swelling and thus prevents passage through the pyloric sphincter.
- A smaller form that is achieved in the stomach when the retention is no longer required i.e. after the GRDF has released its active ingredient, thereby enabling evacuation.

The expansion can be achieved by

i) Swelling system ii) Unfolding system

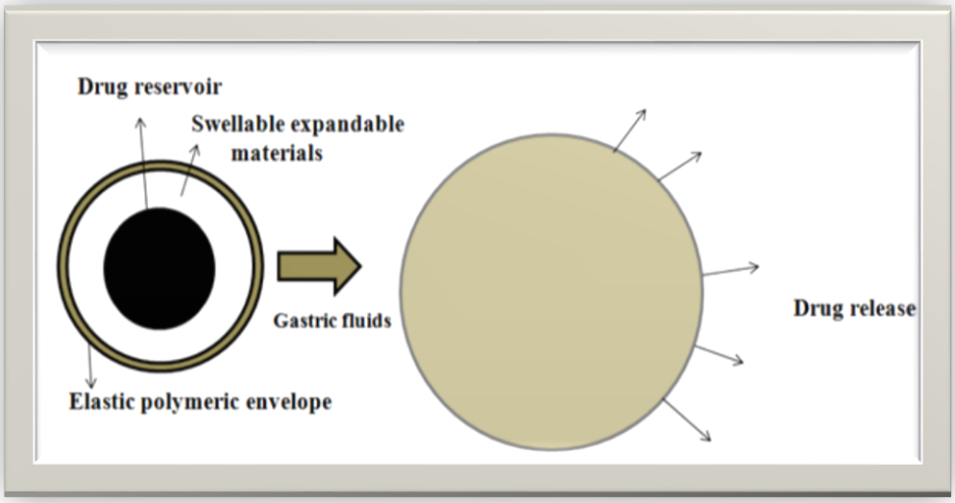


Fig 4: Swellable system

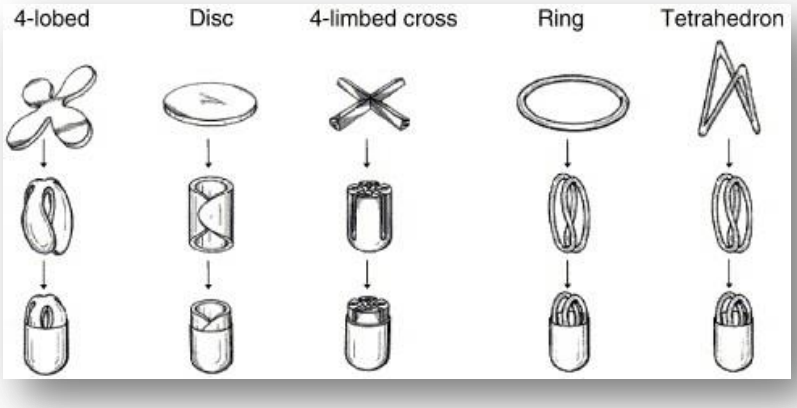


Fig 5: Various geometric forms of unfolding system

B. Floating Drug Delivery System

1. Effervescent system

These dosage forms are developed insuch a way that, when they come incontact with gastric juices in the

stomach, carbon dioxide gas is released due to the reaction between sodium bicarbonate, citric acid and tartaric acid and is trapped in the swollen hydrocolloids. This provides buoyancy to the dosage form thereby making it to float on the gastric fluid. These systems may alsocontain liquids which gasify and evaporates at body temperature bywhich the specific gravity decreases and causes the dosage form to float. These effervescent systems have been further classified into different types:

1.1) Volatile liquid containing systems[10]

These are further classified as

a) Intragastric floating gastrointestinal drug delivery systems: These systems are made tofloat in the stomach because of the floating chamber, which may be filled with air or vaccum or harmless gas, and the drug reservoir is encapsulated inside a micro porous compartment. This micro porous compartment has pores on the top and bottom surfaces, whereas the peripheral walls of the reservoir compartment were completely sealed to prevent any physical contact of the undissolved drug with the walls of the stomach.

b) Inflatable gastrointestinal drug delivery system: These systems consist of inflatable chamber with liquid ether that gasifies at body temperature making the chamber toinflate in the stomach. This inflatable chamber contains a drug reservoir which is encapsulated in a gelatin capsule. After oral administration, the capsule dissolves and releases the drug reservoir together with the inflatable.

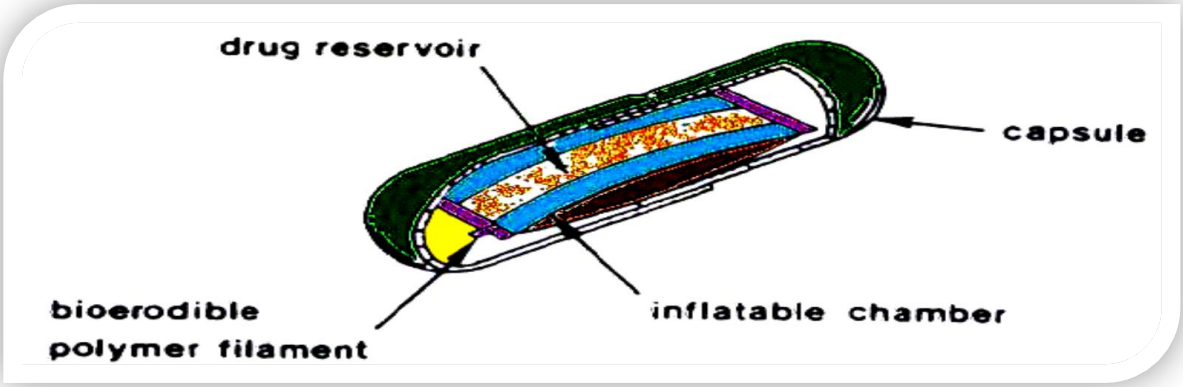


Fig 6 : Gastro inflatable drug delivery device

c) Intragastric osmotically controlled drug delivery system: It consists of osmotic pressure controlled drug delivery device and an inflatable support in a biodegradable capsule. On reaching the stomach, inflatable capsule disintegrates and releases the osmotically controlled drug delivery.

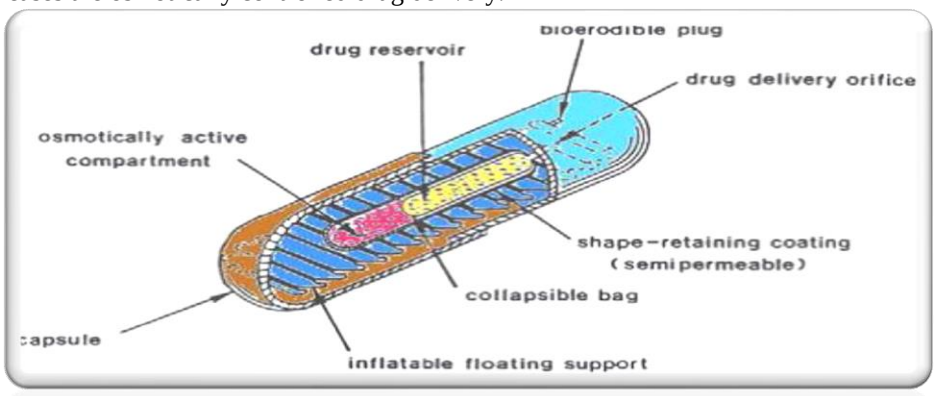


Fig 7: Intragastric osmotically controlled drug delivery system

1.2. Gas generating systems [11]

In these systems floatability is achieved by generation of gas bubbles. Carbon dioxide is generated in situ by incorporation of carbonates or bicarbonates, which react with acid, either the natural gastric acid or co-formulated as citric or tartaric acid. The gas generated makes the system to float on the gastric fluid and releases the drug ata predetermined rate. These are of different types

a. Floating capsules

b.Floating pills

C. Floating systems with ion exchange resins

These systems are formulated by using ion exchange resins that are loaded with bicarbonate by mixing the beads with sodium bicarbonate solution.

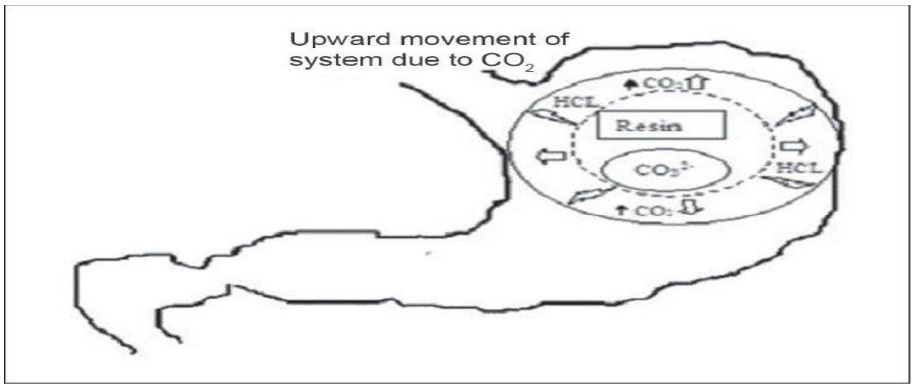


Fig 8: Floating system with ion exchange resins

2) Non effervescent systems

Non effervescent systems incorporate a high level (20–75% w/w) of one or more gel-forming, highly swellable, cellulosic hydrocolloids .Upon coming into contact with gastric fluid, these gel formers, polysaccharides, and polymers hydrate and forms a colloidal gel barrier that controls the rate of fluid penetration into the device and consequent drug release.

2.1) Hydrodynamically balanced system: The hydrodynamically balanced system (HBS) was first designed by [12]. They are meant to remain buoyant on the stomach content. This system contains one or more gel forming cellulose type hydrocolloid e.g., hydroxypropyl methyl cellulose, ethyl cellulose, hydroxypropyl cellulose, agar, carrageen or alginic acid. It also contains matrix forming polymers such as polycarbophil, polyacrylate and polystyrene. When such system comes in contact with gastric fluid, the hydrocolloid in the system hydrates and forms a colloid gel barrier around its surface.

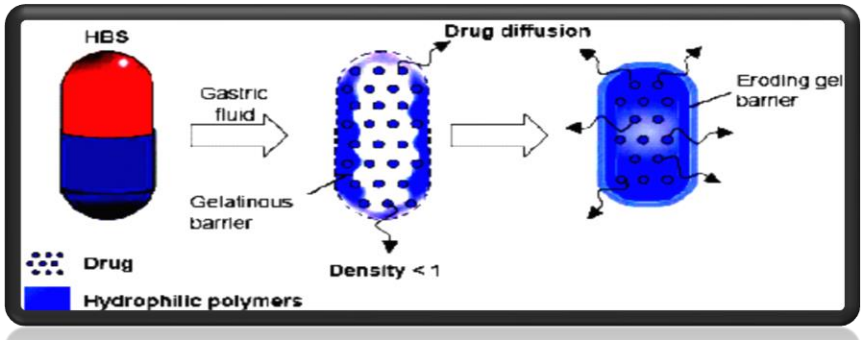


Fig 9:Hydrodynamically balanced system (HBS)

2.2 Microballoons / Hollow microspheres:

Microballoons / hollow microspheres loaded with drugs in their outer polymeric shell were prepared by simple solvent evaporation or solvent diffusion / evaporation methods to prolong the gastric retention time (GRT) of the dosage form.

Commonly used polymers to develop these systems are polycarbonate, cellulose acetate, calcium alginate, Eudragit S, agar and low methoxylated pectin etc. Buoyancy and drug release from dosage forms are dependent on

- Quantity of polymers
- The plasticizer polymer ratio and
- The solvent used for formulation.

At present hollow microspheres are considered to be one of the most promising buoyant systems because they combine the advantages of multiple-unit system and good floating.

2.3 Alginate beads: Freeze dried calcium alginates have been used to develop multiunit floating dosage forms .By dropping sodium alginate solution into aqueous solution of calcium chloride ,spherical beads of about 2.5 mm diameter can be prepared. These beads are separated and air dried. This results in the formation of aporous system which remains buoyant in the stomach.

2.4Microporous compartment: In this system, drug reservoir is encapsulated inside a microporous compartment having pores along its top and bottom walls. 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 releases it for absorption.

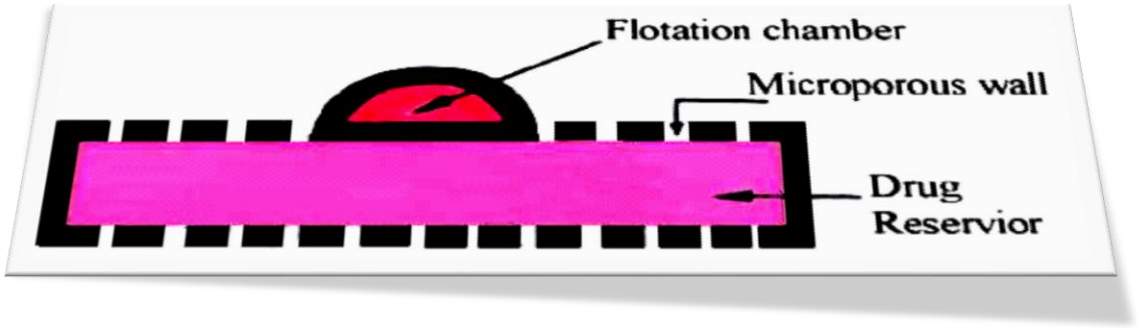


Fig 10: Floating drug delivery device with microporous membrane and floatation chamber

2.5 Raft systems

This incorporates alginate gel and a carbonate component and, upon reaction with gastric acid, bubbles form in the gel, enabling floating. Raft forming systems produce a layer on the top of gastric fluid. Here, a gel forming solution (e.g. sodium alginate solution containing carbonates or bicarbonates)swells and forms a viscous cohesive gel containing entrapped CO2 bubbles on contact with gastric fluid.

A patent assigned to Reckitt and Colman Products Ltd., describes a raft forming formulation for the treatment of *Helicobacterpylori (H. Pylori)* infections in the GIT [13]. The composition contained drug, alginic acid, sodium bicarbonate, calcium carbonate, mannitol and a sweetener. These ingredients were granulated, and citric acid was added to the granules. The formulation produces effervescence and aerates the raft formed, making it to float.

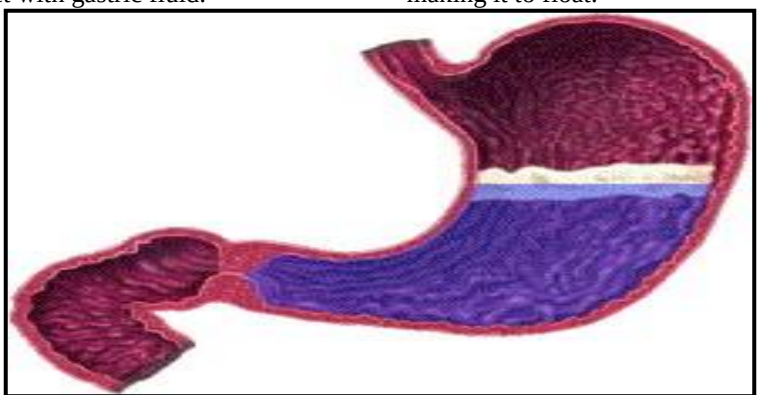


Fig 11:Schematic illustration of the barrier formed by a raft-forming system

2.6 Superporous hydrogels

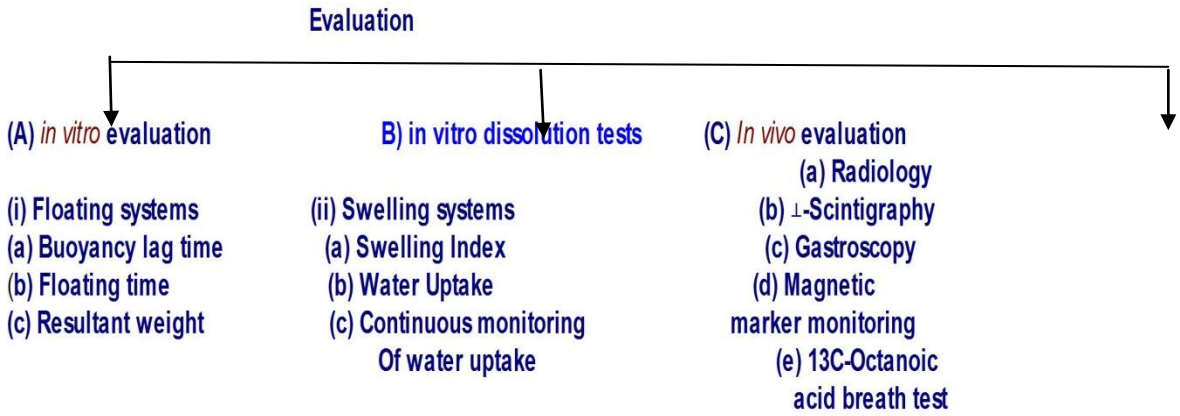
These are swellable systems that differ from conventional types. Absorption of water by conventional hydrogel is very slow process and several hours may be required to reach the equilibrium states [14] during which the premature evacuation of the dosage form may occur. Superporous hydrogel have a pore size >100µm which swell to equilibrium size within a minute, due to rapid intake of water by capillary wetting through inter connected open pores. They swell to a larger size and have sufficient mechanical strength to withstand the pressure by gastric contraction. This is achieved by coformulation of a hydrophilic particulate material, Ac-Di-Sol[15].

1.3 PATENTS ON GRDDS

Table 3: List of some patented gastro retentive drug delivery systems

US patent No.	Patent title	Pub. Date
US6710126 B1	Hydrogel composites and superporous hydrogel composites having fast swelling, high mechanical strength, and superabsorbent properties	Aug. 7, 2001
US 6,488,962 B1	Tablet shapes to enhance gastric retention of swellable controlled release oral dosage Forms	Dec. 3, 2002
WO 2002102415 A1	Gastric floating system	27 Dec 2002
US 2008/0220060 A1	Gastroretentive formulations and manufacturing process there of	Sep. 1 1, 2008
WO 2011048494 A2	Novel gastroretentive dosage forms of poorly soluble drugs	Apr 1, 2010
WO 2011151708 A1	Gastroretentive dosage forms of gaba analogs	8 Dec 2011
US 8808669 B2	Gastroretentive, extended release composition of therapeutic agent	19 Aug 2014

Evaluation[16]



(A) *In vitro* evaluation

(i)Floating systems

(a) Buoyancy lag time: It is the time taken up by the dosage form to float on the top of the dissolution medium after being placed in the medium.

(b) Floating time: Test for buoyancy is usually performed in SGF-Simulated Gastric Fluid maintained at 37^0 C.The time for which the dosage form continuously floats on the dissolution media istermed as floating time.

(c) Resultant weight: Now, we know that bulk density and floating time are the main parameters for describing buoyancy. But only single determination of density is not sufficient to describe the buoyancy because density changes with change in resultant weight as a function of time. For example a matrix tabletwith bicarbonate and matrixing polymer floats initially by gas generation and entrapment but after sometime, some drug is released and simultaneously some outer part of matrixing polymer may erode out leading to change in resultant weight of dosageform.The magnitude and direction of force/resultant weight (up or down) is corresponding to its buoyancy force (Fbuoy) and gravity force (Fgrav) acting on dosage form (Fig. 14).

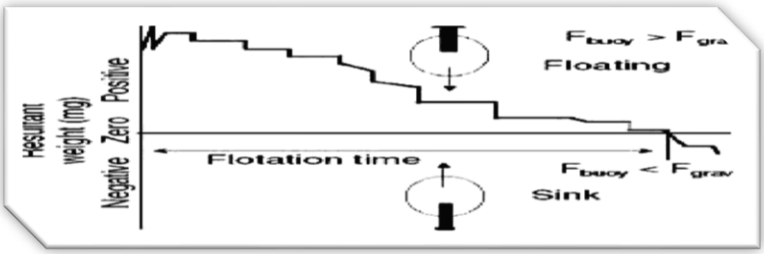


Fig 12 : Floating time and Resultant weight

F = Fbuoy–Fgrav, F = Df g V – Ds g V, F = (Df– Ds) g V, F = (Df– M/V) g V

Where,

F = Resultant weight of object

Df = Density of fluid

Ds = Density of solid object

g = Gravitational force

M = Mass of dosage form

V = Volume of dosage form

So when Ds, density of dosage form is lower, F force is positive gives buoyancy and when it is Ds ishigher, F will be negative shows sinking.

Plot of F vs. Time is drawn and floating time is time when F approaches to zero from positive values.

(ii) Swelling systems

(a) Swelling Index: After immersion of swelling dosage form into SGF at 37 ^{0}C, dosage form isremoved out at a regular intervals of time and dimensional changes are measured in terms of increase in tabletthickness/diameter with time.

(b) Water Uptake [17]**:** It is an indirect measurement of swelling property of swellable matrix. Here dosage form is removed out at a regular intervals of time and weight changes are determined with respect to time. So it is also termed as Weight Gain.

Water uptake = WU = (Wt – Wo) * 100 / Wo

Where, Wt = Weight of dosage form at time t

Wo = Initial weight of dosage form

In this assembly concentric circles with various diameters are drawn in computer and print out islaminated to make hydrophobic. This laminated piece is attached with some system which can facilitate up and down movement of assembly.

This assembly is placed in beaker and tablet is placed exactly at center and then there is no disturbance given to tablet.

Tablet is allowed to swell on laminated paper and diameter can be easily noted without removing of a tablet.

To determine water uptake/weight gain, whole assembly can bring out. Weighing of assembly done after wiping off water droplets adhered at surface of assembly and then can be placed back as it is without touching to tablet.

(c) Continuous monitoring of water uptake[18]**:** Although previous method has advantage ofun-disturbance of swollen tablet, but for measuring water uptake one has to remove whole assembly outof beaker, so process in not continuous.

Continuous monitoring of water uptake is possible by following apparatus.

In this apparatus, swelling tablet is placed on a glass filter as support in one hollow cylinder with smooth surface inside, and one light weight punch is placed on it to prevent floating. This cylinder is placed pre-heated in dissolution medium. Another beaker containing dissolution medium reservoir is placed on digital balance and both are connected with media filled U tube and medium level is kept equal. As tablet swells, it absorbs water and water level in outer part of cylinder goes down.The decrease in water level is maintained by importing extra medium via U tube from reservoir beaker.As medium is transfered from reservoir, amount of water transfer can be determined by observing lossof weight by digital balance.

B) I*n vitro* dissolution tests[19]

A. *In vitro* dissolution test is generally done by using USP apparatus with paddle and GRDDS isplaced normally as for other conventional tablets. But sometimes as the vessel is large and paddles are atbottom, there is much lesser paddle force acts on floating dosage form which generally floats on surface. Asfloating dosage form not rotates may not give proper result and also not reproducible results. Similar problem occurs with swellable dosage form, as they are hydrogel may stick to surface of vessel or paddle and gives irreproducible results.

In order to prevent such problems, various types of modifications in dissolution assembly made are as follows.

B. To prevent sticking at vessel or paddle and to improve movement of dosage form, method suggested is to keep paddle at surface and not too deep inside dissolution medium.

C. Floating unit can be made fully submerged, by attaching some small, loose, non-reacting material,such as few turns of wire helix, around dosage form. However this method can inhibit three dimensional swelling of some dosage form and also affects drug release.

D. Other modification is to make floating unit fully submerged under ring or mesh assembly andpaddle is just over ring that gives better force for movement of unit.

E. Other method suggests placing dosage form between 2 ring/meshes.

F. In previous methods unit have very small area, which can inhibit 3D swelling of swellable units,another method suggests the change in dissolution vessel that is indented at some above place from bottomand mesh is placed on indented protrusions, this gives more area for dosage form.

G. Inspite of the various modifications done to get the reproducible results, none of them showed correlation with the *in vivo* conditions. So a novel dissolution test apparatus with modification of Rossett-Ricetest Apparatus was proposed.

Rossett-Rice test is used for predicting in-vitro evaluation of directly acting antacid (action bychemical neutralization of acid), where HClis added gradually to mimic the secretion rate of acid from the stomach.

In this modified apparatus, it has side arm from bottom of beaker such that it maintains volume of 70 mL in beaker and fresh SGF is added from burette at 2 mL/min rate. Thus sinkcondition is maintained. Stirring is done by magnetic stirrer at 70-75 RPM.

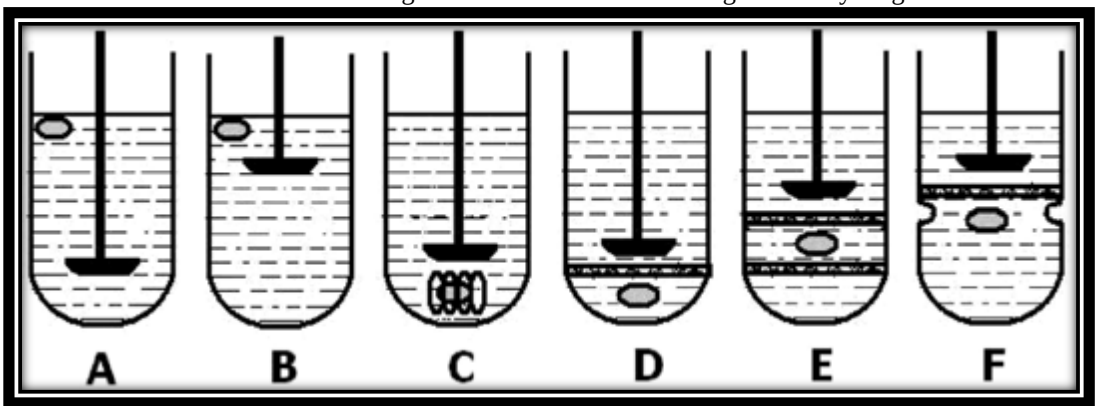


Fig 13: *In vitro* dissolution tests

(C) *In vivo* evaluation

(a) Radiology: X-ray is widely used for examination of internal body systems. Barium Sulphate iswidely used Radio Opaque Marker. So, BaSO4 is incorporated inside dosage form and X-ray images aretaken at various intervals to view GR.

(b) ⊥-Scintigraphy: Similar to X-ray, ⊥-emitting materials are incorporated into dosage form and then images are taken by scintigraphy. Widely used ⊥-emitting material is 99Tc.

(c) Gastroscopy: Gastroscopy is peroral endoscopy used with fiber optics or video systems. Gastroscopy is used to inspect visually the effect of prolongation in stomach. It can also give the detailedevaluation of GRDDS.

(d) Magnetic marker monitoring: In this technique, dosage form is magnetically marked with incorporating iron powder inside, and images can be taken by very sensitive bio-magnetic measurementequipment. Advantage of this method is that it is radiation less and so not hazardous.

(e) ^{13}C Octanoic acid breath test: ^{13}C Octanoic acid is incorporated into GRDDS. In stomach due to chemical reaction, octanoic acid liberates CO_2 gas which comes out in breath. The important Carbon atom which will come out in CO_2 is replaced with ^{13}C isotope. So time upto which $^{13}CO_2$ gas is observed in breath can be considered as gastric retention time of dosage form. As the dosage form moves to intestine, there is no reaction and no CO_2 release. So this method is cheaper than other.[20]

1.5 Different gastroretentive approaches and probable polymers used in them

Different gastroretentive approaches	Probable polymers
1)high density (sinking) drug delivery system	Iron powder, barium sulfate, zinc oxide and titanium oxide.
2)bioadhesive drug delivery system	Anionic polymers: carboxy methylcellulose, poly acrylic acid, chitosan, alginic acid.Cationic polymers: polylysine Neutral polymers: polyethylene glycol, dextran.[21]
3)swelling/ expanding systems	All grades of hpmc, polyethylene oxide, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose, sodium carboxymethyl cellulose, calcium carboxymethyl cellulose, methyl cellulose, polyacrylic acid, xanthan gum, and polyvinyl alcohol.
4)effervescent systems	Sodium bicarbonate, citric acid andtartaric acid.
5)non effervescent systems	High levels (20–75% w/w) of one or more gel-forming highly swellable cellulosic hydrocolloids.

Conclusion

Above literature concludes that GRDDS is one of the efficient technique to maintain the sustained release of drug in gastric environment and there by increases its absorption and bioavailability. All these GRDDS approaches are convenient and more feasible when compared to other drug delivery systems and have their own advantages and disadvantages. Now a lot of research program is going on to develop new formulation using different polymers or copolymers which are discussed in various patents of this review. GRDDS have systemic, localized as well as site specific action. GRDDS helps in the treatment of various gastrointestinal diseases, and also reduces dose frequency thereby minimizing contra indication, systemic toxicity, drug dependence. Ultimately GRDDS is a simple yet effective drug delivery system.

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