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REVIEW ARTICLE

Gastroretentive Drug Delivery Systems: A Review

Sravya K*, Kavitha K, Rupesh Kumar M, Jagdeesh Singh SD

East Point College of Pharmacy, Bidharahalli, Bangalore, Karnataka-560049

ABSTRACT

Technological attempts have been made in the research and development of rate-controlled oral drug delivery systems to overcome physiological adversities, such as short gastric residence times (GRT) and unpredictable gastric emptying times (GET). Controlled release floating drug delivery system is a promising delivery system for a drug candidate having limited absorption window sparingly soluble and insoluble drugs, drugs those locally release in stomach and shows degradability in colon or poor colonic absorption. Floating drug delivery system comes under a gastroretentive drug delivery system that provides continuous controlled administration of sparingly soluble drugs at the absorption site. This review entitled the detailed scenario related to floating drug delivery system with their advantages over the conventional drug delivery system and also limitation, which are helpful in development of dosages form. Review focused on formulation aspect of effervescent floating drug delivery system with their evaluation techniques. The purpose of this comprehensive review is to compile the work going on this delivery system. Which provide the valuable information related to formulation aspect to achieve gastric retention and discussed the various factors affect and to overcome it.

Keywords: Floating drug delivery systems; Classification; Mechanism; Selection of polymers; Evaluations.

Corresponding author

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INTRODUCTION

The oral route is considered as the most promising and predominant route of drug delivery. Effective oral drug delivery may depend upon the factors such as gastro intestinal transit time of dosage form, gastric emptying process, drug release from the dosage form and site of absorption of drug. Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying, leading to incomplete drug release, non-uniform absorption profiles and shorter residence time of the dosage form in the stomach. This leads to incomplete absorption of drugs having absorption window especially in the upper part of the small intestine, as once the drug passes down the absorption site, the remaining quantity goes unabsorbed. The most important parameters affecting gastric emptying and, hence the gastric retention time of oral dosage forms include, Density, size, shape of the device and concomitant ingestion of food and its nature, caloric content, and frequency of intake and simultaneous administration of drugs with impact on gastrointestinal transit time, eg: drugs acting as anticholinergic agents (eg: atropine, propantheline), opiates (eg: codeine) and prokinetic agents (eg: metaclopramide, cisapride). To overcome these limitations, various approaches have been proposed to increase gastric residence of drug delivery systems in the upper part of the GIT. Dosage forms that can be retained in the stomach are called gastroretentive drug delivery systems (GRDDS). GRDDS can improve the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period of time before it reaches its absorption site, thus ensuring its optimal bioavailability. [1]

Need For Gastro Retention

- Drugs that are absorbed from the proximal part of the gastrointestinal tract (GIT).
- Drugs that are less soluble or that degrade by the alkaline pH they encounters at the lower part of GIT.
- Drugs that are absorbed due to variable gastric emptying time.
- Local or sustained drug delivery to the stomach and proximal Small intestine to treat certain conditions.
- Particularly useful for the treatment of peptic ulcers caused by H. Pylori Infections. [2]

Formulation Considerations for GRDDS

- It must be effective retention in the stomach to suit for the clinical demand.
- It must be convenient for intake to facilitate patient compliance.
- It must have sufficient drug loading capacity and control drug release profile.
- It must have full degradation and evacuation of the system once the drug release is over.
- It should not have effect on gastric motility including emptying pattern.
- It should not have other local adverse effects.

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Drugs Those Are Unsuitable for Gastro Retentive Drug Delivery Systems

•Drugs that have very limited acid solubility eg: Phenytoin etc.
•Drugs that suffer instability in the gastric environment eg: Erythromycin etc.
•Drugs intended for selective release in the colon eg: 5- amino salicylic acid and corticosteroids etc.

GASTROINTESTINAL TRACT

Anatomy of the GIT

The gastrointestinal tract is divided into three main regions namely:
•Stomach.
•Small intestine: Duodenum, Jejunum and Ileum.
•Large intestine.

The GIT is a muscular tube, from the mouth to the anus, which functions to take in nutrients and eliminate waste by secretion, motility, digestion, absorption and excretion, which are known as physiological processes. The stomach is a J-shaped enlargement of the GIT which is divided into 4 anatomical regions: cardia, fundus, body and antrum. The main function of the stomach is to store and mix food with gastric secretions before emptying its load (chyme) through the pyloric sphincter and into the small intestine at a controlled rate suitable for digestion and absorption. During empty state, the stomach occupies a volume of about 50 ml, but this may increase to as much as 1 liter when full. The walls of the GIT, from stomach to large intestine, have the same basic arrangement of tissues, the different layers, from outside to inside, comprising serosa, intermuscular plane, longitudinal muscle, submucosa, circular muscle, lamina propria, muscular is mucosae, and epithelium. In addition to longitudinal and circular muscle, the stomach has a third muscle layer known as the "oblique muscle layer", which is situated in the proximal stomach, branching over the fundus and higher regions of the gastric body. The different smooth muscle layers are responsible for performing the motor functions of the GIT, i.e. gastric emptying and intestinal transit.

GI Tract Physiology

The stomach is divided into 3 regions anatomically: fundus, body, and antrum pylorus. The proximal part is the fundus and the body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states but the pattern of motility is distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle through both stomach and intestine every 2 to 3 hours. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is divided into following 4 phases, seen in figure.1.

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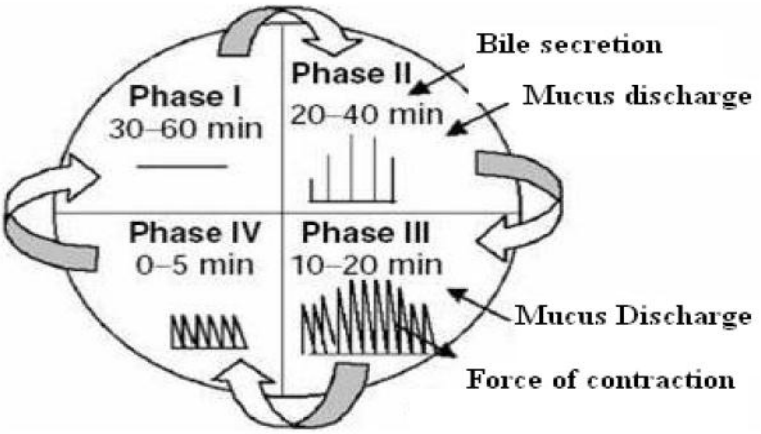

Figure1: Schematic representation of interdigestive motility

• **Phase I**: This period lasts about 30 to 60 minutes with no contractions.
• **Phase II**: This period consists of intermittent contractions that increase gradually in intensity as the phase progresses, and it lasts about 20 to 40 minutes. Gastric discharge of fluid and very small particles begins later in this phase.
• **Phase III**: This is a short period of intense distal and proximal gastric contractions (4-5 contractions per minute) lasting about 10 to 20 minutes these Contractions, also known as ‘‘house-keeper wave,’’ sweep gastric contents down the small Intestine
• **Phase IV:** This is a short transitory period of about 0 to 5 minutes, and the contractions dissipate between the last part of phase III and quiescence of phase I. [3]

Approaches to Gastric Retention

Various approaches have been pursued to increase the retention of an oral dosage form in the stomach. These systems include:

A. Floating systems
B. Bioadhesive systems
C. Raft – forming systems
D. Swelling and expanding systems
E .Super porous Hydrogels
F. Magnetic systems and
G. High density systems

A. Floating drug delivery systems:

Floating drug delivery system is also called the hydrodynamically balanced system (HBS). Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time shown figure 2. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from

the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.[4]

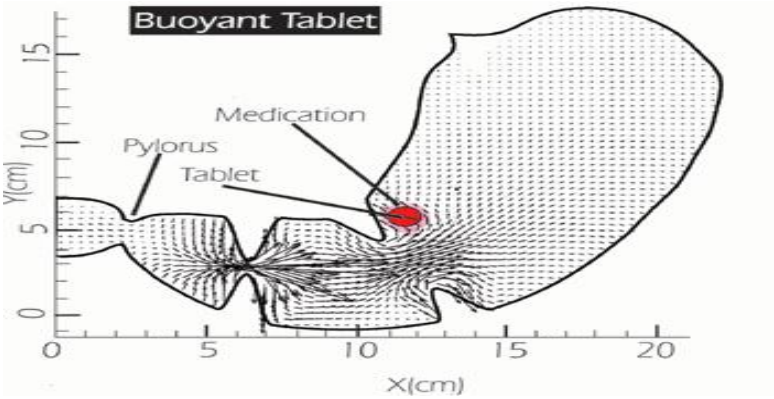

Figure 2: Graphic of Buoyant tablet which is less dense than the stomach fluid and therefore remains in the fundus.

This delivery system is further divided into in to noneffervescent and effervescent gas-generating system.

MECHANISM OF FLOATING SYSTEMS [5]

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introducing floating dosage forms (gas-generating systems and swelling or expanding systems), mucoadhesive systems, high-density systems, modified shape systems, gastric-emptying delaying devices and co-administration of gastric-emptying delaying drugs. Among these, the floating dosage forms have been most commonly used. FDDS have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents (given in the Figure 3 (a)), the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. These results in an increased GRT besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats better if F is on the higher positive side (Figure 3(b)). This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intragastric buoyancy capability variations

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F = F buoyancy - F gravity

= (Df - Ds) gv--- (1)

Where, F= total vertical force, Df = fluid density,
Ds = object density, v = volume and
g = acceleration due to gravity and a better control of the fluctuations in plasma drug concentration.

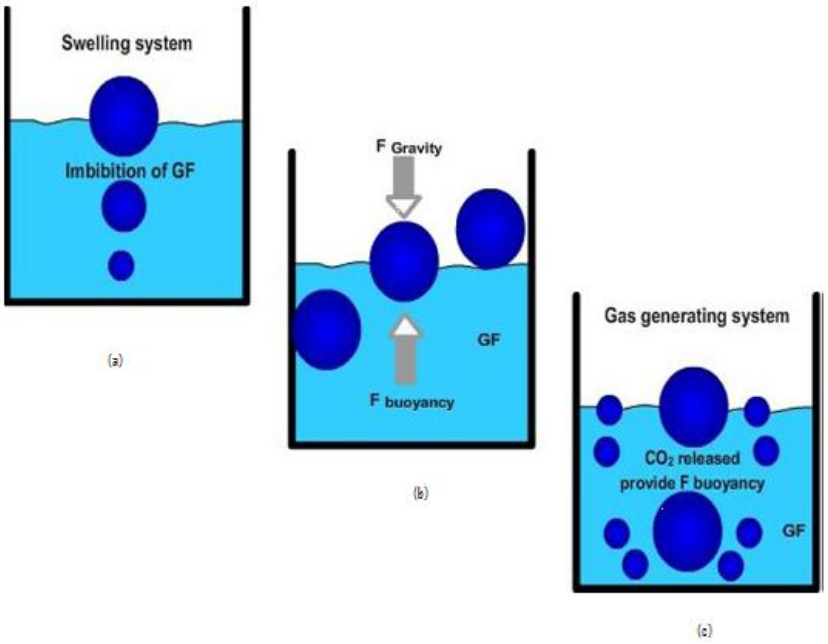

Figure 3: Mechanism of floating systems, GF= Gastric fluid

(a) Non-effervescent systems

i. Colloidal gel barrier systems

Hydrodynamically balanced system, which contains drugs with gel forming hydrocolloids. These systems incorporate a high level (20- 75%w/w) of one or more gel forming, highly swellable, cellulose type hydrocolloids, polysaccharides and matrix forming polymers. On coming in contact with gastric fluid, the hydrocolloids in the system hydrate and form a colloidal gel barrier around its surface. This gel barrier controls the rate of fluid penetration into the device and consequent release of the drug.

ii. Microporous compartment systems

This technology is based on the encapsulation of a drug reservoir inside a micro porous compartment with apertures along its top and bottom walls. The peripheral walls of the drug

reservoir compartment are completely sealed to prevent any direct contact of the gastric mucosal surface with the undissolved drug.

iii. Multiparticulate system

Floating Beads Multi-particulate drug delivery systems are mainly oral dosage forms consisting of a multiplicity of small discrete units, each exhibiting some desired characteristics. In these systems, the dosage of the drug substances is divided on a plurality of subunit, typically consisting of thousands of spherical particles with diameter of 0.05-2.00mm. Thus multi-particulate dosage forms are pharmaceutical formulations in which the active substance is present as a number of small independent subunits. To deliver the recommended total dose, these subunits are filled into a sachet.

iv. Microballoons

There are various approaches in delivering substances to the target site in a controlled release fashion. One such approach is using polymeric microballoons as carrier for drugs. Hollow microspheres are known as the microballoons. Microballoons were floatable in vitro for 12 hrs, when immersed in aqueous media. Radio graphical studies proved that microballoons orally administered to human were dispersed in the upper part of stomach and retained there for 3 hr against peristaltic movements.

(b) Effervescent systems

A drug delivery system can be made to float in the stomach by incorporating a floating chamber, which may be filled with vacuum, air or inert gas.

i. Volatile liquid containing systems

These have an inflatable chamber which contains liquid example ether, cyclopentane that gasifies at body temperature to cause the inflation of the chamber in the stomach. These systems are osmotically controlled floating systems containing a hollow deformable unit. There are two chambers in the system first contains the drug and the second chamber contains the volatile liquid.

ii. Gas generating systems

These buoyant delivery systems utilizes effervescent reaction between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO_2 , which gets entrapped in the jellified hydrocolloid layer of the system, thus decreasing its specific gravity and making it float over chime. A multiple unit type of floating pills, which generate CO_2, have also been developed. The system consists of a sustained release pill as seed, surrounded by double layers. The inner layer is an effervescent layer containing sodium bicarbonate and tartaric acid. The outer layer is of a swellable membrane layer containing PVA, shellac etc. Another effervescent

system consisting of a collapsible spring, which controls the release of drug from the polymer matrix, has also been developed. The common approach for preparing these systems involves resin beads loaded with bicarbonate and coated with ethyl cellulose. The coating which is insoluble but permeable, allows permeation of water. Thus, carbon-dioxide is released, causing the beads to float in the stomach. [6]

B. Bio/Muco-adhesive Systems

Bioadhesive drug delivery systems are used as a delivery device within the human to enhance drug absorption in a site-specific manner. In this approach, bio adhesive polymers are used and they can adhere to the epithelial surface in the stomach. Thus, they improve the prolongation of gastric retention. The basis of adhesion in that a dosage form can stick to the mucosal surface by different mechanism.

These mechanisms are:
•The wetting theory, which is based on the ability of bioadhesive polymers to spread and develop intimate contact with the mucous layers.
•The diffusion theory, which proposes physical entanglement of mucin strands the flexible polymer chains, or an interpenetration of mucin strands into the porous structure of the polymer substrate.
•The absorption theory, suggests that bioadhesion is due to secondary forces such as Vander Waal forces and hydrogen bonding.

The electron theory, which proposes attractive electrostatic forces between the glycoprotein mucin net work and the bio adhesive material. Materials commonly used for bioadhesion are poly acrylic acid, chitosan, cholestyramine, sodium alginate, hydroxypropyl methylcellulose (HPMC), sucralfate, tragacanth, dextrin, polyethylene glycol (PEG) and polylactic acids etc. Even though some of these polymers are effective at producing bioadhesive, it is very difficult to maintain it effectively because of the rapid turnover of mucus in the GIT. [7]

C. Raft-forming systems

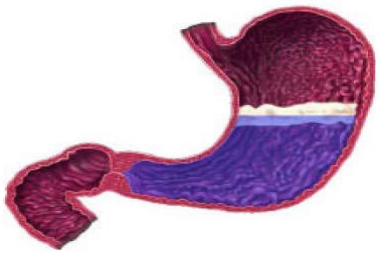

Figure 4: Barrier formed by a raft-forming system

These systems contain gel-forming solution (e.g. sodium alginate solution containing carbonates or bicarbonates), which on contact with the gastric contents, swells and forms a viscous cohesive gel containing entrapped CO_2 bubbles, releases drug slowly in stomach by

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forming the raft layer on the top of gastric fluid shown in figure 4. These formulations contain antacids such as calcium carbonate or aluminum hydroxide to reduce gastric acidity.[8]

D. Swelling/Expanding/Unfoldable Systems:

A dosage form in the stomach will withstand gastric transit if it is bigger than the pyloric sphincter, also the dosage form must be small enough to be swallowed, and must not cause gastric obstruction either singly or by accumulation. Thus, their configurations are required to develop an expandable system in order to prolong the GRT:

1) A small configuration for oral intake,
2) An expanded gastro retentive form, and
3) A final small form enabling evacuation following drug release from the device.

Thus, gastro-retentivity is improved by the combination of substantial dimension with high rigidity of dosage form to withstand peristalsis and mechanical contractility of the stomach. Unfoldable and swellable systems have been investigated and recently tried to develop an effective gastroretentive drug delivery.

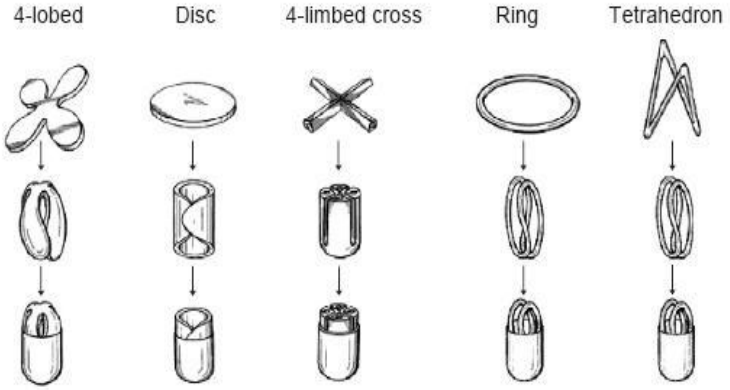

Figure 5: Different geometric forms of unfoldable systems

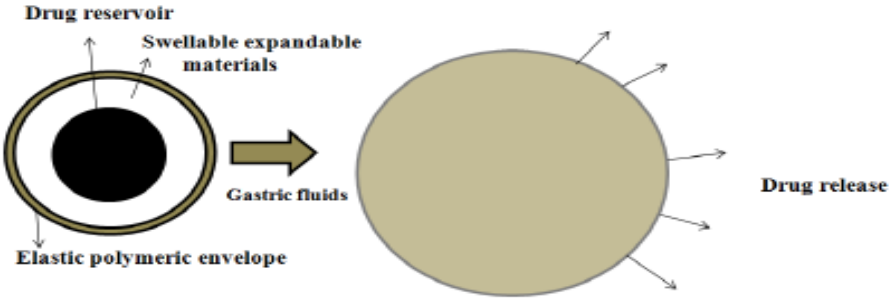

Figure 6: Drug release from swellable systems

•Unfoldable systems are made of biodegradable polymers. They are available in different geometric forms like tetrahedron, ring or planner membrane (4 - label disc or 4 - limbed cross form) of bioerodible polymer compressed within a capsule which extends in the stomach can be seen in figure 5.

• Swellable systems are also retained in the gastro intestinal tract (GIT) due to their mechanical properties. The swelling is usually results from osmotic absorption of water and the dosage form is small enough to be swallowed by the gastric fluid, drug release is explained pictorially in figure 6.

• Expandable systems have some drawbacks like problematical storage of much easily hydrolysable, biodegradable polymers relatively short-lived mechanical shape memory for the unfolding system most difficult to industrialize and not cost effective. Again, permanent retention of rigid, large single-unit expandable drug delivery dosage forms may cause brief obstruction, intestinal adhesion and gastropathy. [9]

E. Superporous Hydrogels

Conventional hydrogels, with pore size ranging between 10 nm and 10 µm has very slow process of water absorption and require several hours to reach an equilibrium state during which premature evacuation of the dosage form may occur while the Superporous hydrogel, having average pore size (>100 µm), swell to equilibrium size within a minute, due to rapid water uptake by capillary wetting through numerous interconnected open pores. Moreover they swell to a large size (swelling ratio 100 or more) and are intended to have sufficient mechanical strength to withstand pressure by gastric contractions, shown in figure 7. This is achieved by a co- formulation of a hydrophilic particulate material, Ac-Di-Sol (crosscarmellose sodium). [10]

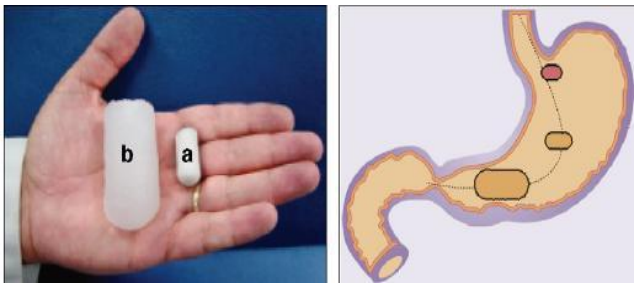

Figure 7: On the left, Superporous Hydrogels in its dry (a) and water-swollen state (b) On the right, schematic illustration of the transit of Superporous Hydrogels.

F. Magnetic Systems:

This approach is based on the simple principle that the dosage form contains a small internal magnet, and a magnet placed on the abdomen over the position of the stomach to enhance the GRT. The external magnet must be positioned with a degree of precision that might compromise patient compliance. [11]

G. High Density (sinking) system or non- floating drug delivery system [12]

This approach involves formulation of dosage forms with the density that must exceed density of normal stomach content (~ 1.004 gm/cm3). These formulations are prepared by coating drug on a heavy core or mixed with inert materials such as iron powder, barium sulphate, zinc oxide and titanium oxide etc. The materials increase density by up to 1.5- 2.4

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gm/cm3. A density close to 2.5 gm/cm^3 seems necessary for significant prolongation of gastric residence time, shown in figure 8.

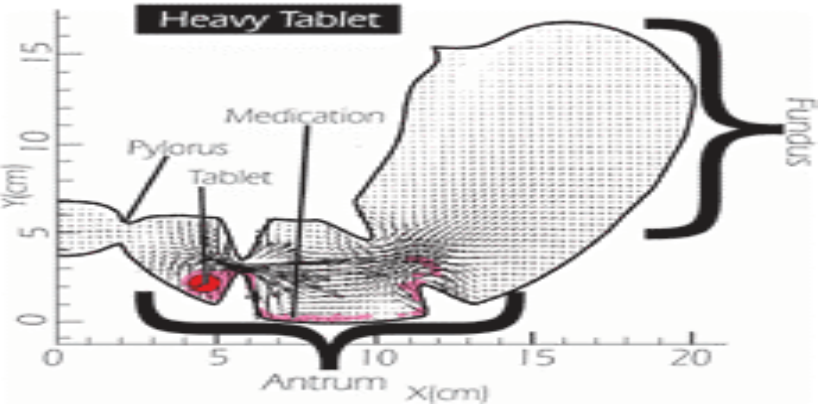

Figure 8: Graphic of heavy tablet which is denser than the stomach fluid and therefore sinks to the antrum

FACTORS AFFECTING GASTRIC RETENTION

The gastric retention time (GRT) of dosage form is controlled by several factors that affect their efficacy as a gastroretentive system.

- ✓ **Density** – GRT is a function of dosage form buoyancy that is dependent on the density.[13]
- ✓ **Size** – Dosage form units with a diameter of more than 9.5mm are reported to have an increased GRT.[14]
- ✓ **Shape of dosage form** – Tetrahedron and ring-shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better GRT. 90% to 100% retention at 24 hours compared with other shapes.
- ✓ **Single or multiple unit formulation** – Multiple unit formulations show a more predictable release profile and insignificant impairing of performance due to failure of units, allow coadministration of units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.
- ✓ **Fed or unfed state** – Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.
- ✓ **Nature of meal** – Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release.[15]
- ✓ **Caloric content** – GRT can be increased by four to 10 hours with a meal that is high in proteins and fats.

- ✓ **Frequency of feed** – The GRT can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC.
- ✓ **Gender** – Mean ambulatory GRT in males (3.4-0.6 hours) is less compared with their age and race-matched female counterparts (4.6-1.2 hours), regardless of the weight, height and body surface.
- ✓ **Age** – Elderly people, especially those over 70, have a significantly longer GRT.
- ✓ **Posture** – GRT can vary between supine and upright ambulatory states of the patient.[16]
- ✓ **Concomitant drug administration**– Anticholinergics like Atropine and Propantheline, Opiates like Codeine and Prokinetic agents like Metoclopramide and Cisapride.
- ✓ **Biological factors** – Diabetes and Crohn's disease.

SELECTION OF POLYMERES [17], [18], [19]

A. GAS GENERATING AGENTS

Alkalinizing agents and acidulent Sodium bicarbonate, Calcium carbonates, Citric acid, Tartaric acid, Adipic acid.

Rational behind the selection

Effervescent compound generally use for this purpose. Sodium bicarbonate, calcium carbon with citric acid and tartaric acid. When these compounds come in contact with the acidic gastric contents, carbon dioxide is liberated and gets entrapped in swelled hydrocolloids, which provide buoyancy to the dosage forms. Sodium bicarbonate induced CO_2 generation in the presence of dissolution medium (0.1 N HCL). The gas generated trapped and protected within the gel, formed by the hydration of polymer, thus decreasing the density of the tablet as the density of the tablet falls below 1, the tablet become buoyant. Acidulent is used; since the pH of the stomach is elevated under fed condition (~3.5). Acidulent (Citric acid, Tartaric acid, Adipic acid) was incorporate in the formulation to provide an acidic medium for sodium bicarbonate.

B. Viscolyzing agent

Sodium alginate, Carbopol 934

Rational behind the selection

They are used to increase the viscosity in the system. Carbopol is being used in the controlled release solid dosage formulations since last four decades. The numbers of manufacturers commercializing controlled release tablets using carbomers are increasing considerably in recent period of development. Tablet formulations using Carbopol polymers have demonstrated zero-order and near zero-order release kinetics. These polymers are effective at low concentrations (less than 10%). Still they show extremely rapid and efficient

swelling characteristics in both simulated gastric fluid (SGF) and simulated intestinal fluid (SIF). The Carbopol polymers produce tablets of excellent hardness and low friability. These polymers can be successfully formulated into a variety of different tablet forms, including the traditional swallowable tablets, chewable tablets, buccal tablets, sublingual tablets, effervescent tablets, and suppositories; providing controlled-release properties as well as good binding characteristics. Carbomers show larger dissolution times at lower concentrations than other excipients. Because of these factors Carbopol polymers have greater extent in formulating dosage forms. Because Carbopol polymers swell rapidly in water and absorb great quantities, to avoid the use of flammable solvents, roller compaction is being used as the method to prepare a new form of Carbopol polymer 71GNF.

C. Swelling agent/Gel forming polymer

Hydroxy propylmethylcellulose (HPMC)

Rational behind the selection

Hypermellose powder is stable material, although it is hygroscopic after drying. Solution is stable at pH 3-11. Increasing temperature reduces the viscosity of solutions. Hypermellose undergoes a reversible sol-gel transformation upon heating and cooling, respectively. The gel point 50-90°C, depending upon grade and concentration of material. Grade which are highly viscous in nature like HPMC K100, HPMC K 4, HPMC K 15.

D. Disintegrating agent

Povidone, Polyplasdone XL and XL-10

Rational behind the selection

PVP belongs to a class of compounds known as superdisintegrantes. When they comes in contact with the fluid media they provide the swelling properties to the system they used as highly active explosive agent and as an accelerating agent for disintegration of solid medications. In tabletting, povidone solutions are used as binder in the wet granulation processes.

EVALUATION TECHNIQUES

In vitro evaluation of floating tablets evaluation was performed to assess the physicochemical properties and release characteristics of the developed formulations.

I. Pre-compression parameters[23]

a) Angle of Repose (θ)
b) Compressibility Index

II Post-compression parameters[20],[21],[22]

a) Shape of Tablets
b) Tablet Dimensions
c) Hardness
d) Friability test
e) Tablet Density
f) Weight Variation Test
g) Buoyancy / Floating Test
h) Swelling Study
j) *In vitro* drug release studies

ADVANTAGES OF GASTRORETENTIVE DRUG DELIVERY SYSTEMS

1) The bioavailability of therapeutic agents can be significantly enhanced especially for those which get metabolized in the upper GIT by this gastroretentive drug delivery approach in comparison to the administration of non-gastroretentive drug delivery. There are several different factors related to absorption and transit of the drug in the GIT that act concomitantly to influence the magnitude of drug absorption.
2) For drugs with relatively short half life, sustained release may result in a flip- flop pharmacokinetics and also enable reduced frequency of dosing with improved patient compliance.
3) They also have an advantage over their conventional system as it can be used to overcome the adversities of the GRT as well as the gastric emptying time (GET). As these systems are expected to remain buoyant on the gastric fluid without affecting the intrinsic rate of employing because their bulk density is lower than that of the gastric fluids.
4) Gastroretentive drug delivery can produce prolong and sustain release of drugs from dosage forms which avail local therapy in the stomach and small intestine. Hence they are useful in the treatment of disorders related to stomach and small intestine.[24]
5) The controlled, slow delivery of drug form gastroretentive dosage form provides sufficient local action at the diseased site, thus minimizing or eliminating systemic exposure of drugs. This site-specific drug delivery reduces undesirable effects of side effects.
6) Gastroretentive dosage forms minimize the fluctuation of drug concentrations and effects. Therefore, concentration dependent adverse effects that are associated with peak concentrations can be presented. This feature is of special importance for drug with a narrow therapeutic index.
7) Gastroretentive drug delivery can minimize the counter activity of the body leading to higher drug efficiency.
8) Reduction of fluctuation in drug concentration makes it possible to obtain improved selectivity in receptor activation.
9) The sustained mode of drug release from Gastroretentive doses form enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the chemical outcomes. [25]

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DISADVANTAGES OF GASTRORETENTIVE DRUG DELIVERY SYSTEMS [26]

1) Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.
2) Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
3) High variability in gastric emptying time due to its all or non-emptying process.
4) 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

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

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