International Journal of Pharmaceutical research and Applications
Volume 9, Issue 1, Jan.-Feb. 2024, pp:1509-1515 www.ijprajournal.com ISSN: 2456-4494

Floating Drug Delivery System

P.Sukanya[1],D.Rama Brahma Reddy[2],V.Srinivas[3],V.Vinod Kumar[4],V.Prasanna Kumar[5],A.Sai Jagadeesh Babu[6],B.S.Santhosh[7].

[1]*Assistant Professor,Pharmaceutics,Nalanda institute of pharmaceutical sciences,Guntu.*
[2]*Principal,Pharmaceutical Chemistry,Nalanda institute of pharmaceutical sciences,Gunur.*
[34567]*Student,Pharmacy,Nalanda institute of pharmaceutical sciencs,Guntur.*

Date of Submission: 08-02-2024 Date of acceptance: 23-02-2024

"ABSTRACT":
Rate controlled drug delivery systems are developed to overcome physiological adversities like short residence times and unpredictable gastric emptying times. Differences in gastric physiology such as gastric pH and motility exhibit both intra and inter subject variability demonstrating significant impact on gastric residence time and drug delivery behavior. This triggered an increased interest towards formulation of novel delivery systems which retained in the stomach for prolonged and predictable period of time. Several approaches such as floating drug delivery systems (FDDS), swelling and expanding systems, bioadhesive systems, modified shape systems, high density systems or other delayed gastric emptying devices have been discovered till now. FDDS are of particular interest for drugs that are locally active and have narrow absorption window in stomach or upper small intestine, unstable in the intestinal or colonic environment, and exhibit low solubility at high pH values. This review article is in pursuit of giving detailed information on the pharmaceutical basis of their design, classification, advantages and different types of FDDS and the future potential of FDDS.

KEYWORDS:
Floating drug delivery systems, Gastric residence time, Swelling index, Buoyancy.

I. INTRODUCTION:

Gastro retentive drug delivery is an approach to prolong gastric residence time, there by targeting site-specific drug release in the upper GIT for local or systemic effect. Oral route of drug administration is the most convenient and commonly used method of drug delivery. However, this route has several physiological problems. Including an unpredictable gastricemptying rate that varies from person to person, a brief gastrointestinal transit time (80- 12h), and the existence of an absorption window in the upper small intestine for several drugs.

These difficulties have prompted researchers to design a drug delivery system which can stay in the stomach for prolonged and predictable period. Attempts are being made to develop a drug delivery system which can provide therapeutically effective plasma drug concentration for a longer period, thereby reducing the dosing frequency and minimizing fluctuation in plasma drug concentration at steady state by delivering the drug in a controlled and reproducible manner.

One novel approach in this area is GRDDSs(gastro retentive drug delivery system).Dosage forms that can be retained in the stomach are called GRDDs. GRDDSs 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. Prolonging the gastric retention of the drugs is sometimes desirable for achieving therapeutic benefits of drug that are absorbed from the proximal part of the GIT (gastro intestinal tract) or those are less soluble in or are degraded by alkaline pH or they encounter at the lower part of the GIT.

Drugs that are easily absorbed from GIT and have short half-lives are eliminated quickly from the systemic circulation. Frequently dosing of these drugs is required to achieve suitable therapeutic activity. To avoid this limitation, the development of oral sustained controlled release formulations is an attempt to release the drug slowly into the GIT and maintain an effective drug concentration in the systemic circulation for a long time. After oral administration, such a drug delivery would be retained in the stomach and release the drug in controlled manner, so that the drug could be supplied continuously to its absorption sites in the GIT.

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PHYSIOLOGY OF STOMACH:

Anatomically the stomach is divided into three regions Fundus, Body and Antrum (pylorus)The proximal part made of fundus and body acts as a reservoir for undigested materials,whereas the antrum is the main site for mixing motions and acts as a pump for gastricemptying by propelling Anatomically the stomach is divided into three regions Fundus, Body and Antrum (pylorus). The proximal part made of fundus and body acts as a reservoir forundigested materials, whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions. Gastric emptying occurs in both the fasting and fed states.

During the fasting state an inter digestive series of electrical events take place which cycle both through stomach and intestine every 2-3 hrs, which is called as inter digestive myloelectric cycle or migrating myoelectric cycle (MMC).
Migrating myoelectric cycle (MMC) is further divided in to four phases. They are:

1. Phase I (basal phase)
2. Phase II (preburst phase)
3. Phase III (burst phase)
4. Phase IV

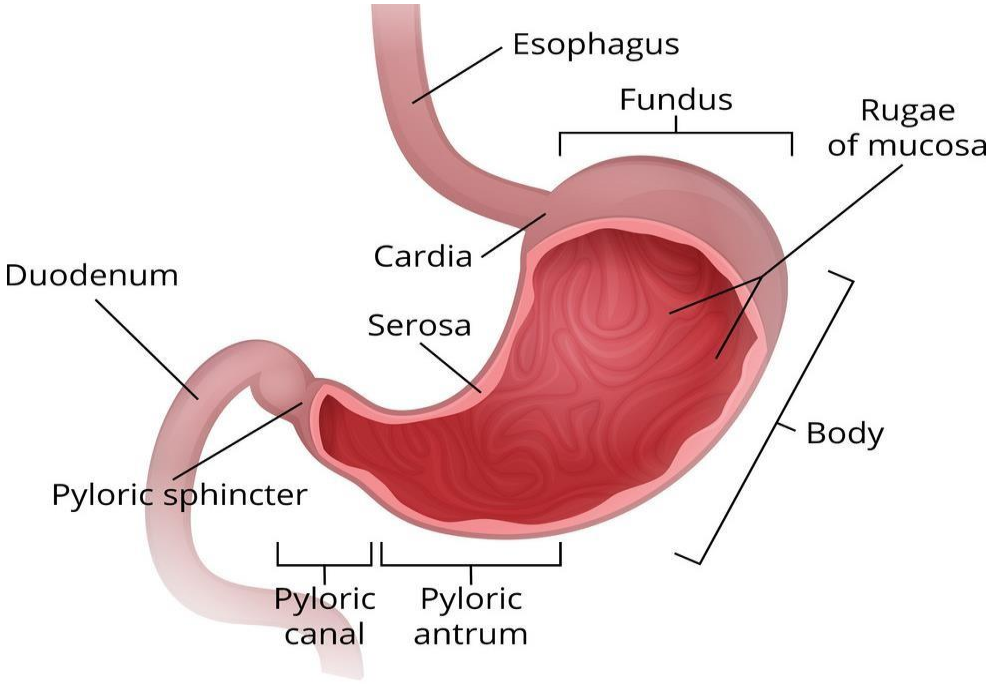

FIGURE 1: INTERNAL STUCTURE OF STOMACH

Phase I: It is a quiescent period lasting from 30 to 60minutes with no contractions.

Phase II: It consists of intermittent contractions that gradually increase in intensity as the phase progresses, and it lasts about 20 to 40minutes. 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 - 5contractions 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 to5 minutes, and the contractions dissipate between the last part of phase III and quiescence of phase I.

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises continuous contractions as in phase 2 of fasted state. These contractions result in reducing the size of food particles (to less than 1 mm), which are propelled towards the pylorus in a suspension from. During the fed state onset of MMC

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is delayed resulting in slow down of gastric emptying rate.13 Scintigraphic studies determining gastric emptying rate revealed that orally administered controlled released dosage forms are subjected to complications that of short gastric residence time and unpredictable gastric empting rate.

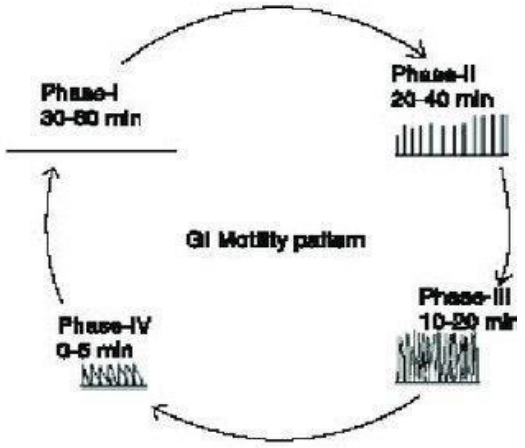

FIGURE 2:Schematic respresentation of inter digestive motility. Advantages:

1. Enhanced bioavailability :
The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act concomitantly to influence the magnitude of drug absorption.

2. Enhanced first-pass biotransformation :
In a similar fashion to the increased efficacy of active transporters exhibiting capacity limited activity, the pre-systemic metabolism of the tested compound may be considerably increased when the drug is presented to the metabolic enzymes (cyto chrome P450, in particularCYP3A4) in a sustained manner, rather than by a bolus input.

3. Sustained drug delivery/reduced frequency of dosing:
For drugs with relatively short biological half-life, sustained and slow input from CR-GRDF may result in a flip-flop pharmacokinetics and enable reduced dosing frequency. This feature is associated with improved patient compliance, and thereby improves therapy.

4. Targeted therapy for local ailments in the upper GIT:
The prolonged and sustained administration of the drug from GRDF to the stomach may be advantageous for local therapy in the stomach and small intestine. By this mode ofadministration, therapeutic drug concentrations may be attained locally while systemic concentrations, following drug absorption and distribution, are minimal.

5. Reduced fluctuations of drug concentration:
Continuous input of the drug following CRGRDF administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index24.

6. Extended time over critical (effective) concentration :
For certain drugs that have non-concentration dependent pharmacodynamics, such as beta lactam antibiotics, the clinical response is not associated with peak concentration, but rather with the duration of time over a critical therapeutic concentration. The sustained mode of administration enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes.

7. Minimized adverse activity at the colon:
Retention of the drug in the GRDF at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This pharmacodynamic aspect provides the rationale for GRDF formulation for beta-lactam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism‟s resistance.

8. Site specific drug delivery :
A floating dosage form is a feasible approach especially for drugs which have limited absorption sites in upper small intestine25. The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also uce the dosing

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frequency.

Disadvantages :

1. Unsuitable for drugs with limited acid solubility. Eg.phenytoin.
2. Unsuitable for drugs those are unstable in acidic environment. Eg. Erythromycin
3. Drugs that irritates or causes gastric lesions on slow release. E.g. Aspirin & NSAID¨s
4. Drugs that absorb selectively in colon .E.g. Corticosteroid
5. Drugs that absorb equally well through GIT. E.g. Isosorbidedinitrate, Nifidipine.
6. Floating drug delivery systems require high fluid level in stomach to float and effect .

Factors controlling gastricretention of dosage forms:

The stomach anatomy and physiology contain parameters to be considered in the development of gastro retentive dosage forms. To pass through the pyloric valve in to the small intestine the particle size should be in the range of 1 to 2 mm. the most important parameters controlling the gastric retention time (GRT) of oral dosage forms include: density, size and shape of the dosage form, food intake and its nature, caloric content and frequency of intake, posture, gender, age, sex, sleep, body mass index, physical activity and diseased states of the individual (e.g. chronic metclopramide, cisapride). The molecular weight and lipophilicity of the drug depending on its ionization state are also important parameters.

Density of dosage forms:

The density of a dosage form also affects the gastric emptying rate and determines the location of the system in the stomach. Dosage forms having a density lower than the gastric contents can float to the surface, while high density systems sink to bottom of the stomach Both positions may isolate the dosage system from the pylorus. A density of < 1.0 gm/ cm is required to exhibit floating property.

Shape and size of the dosage form:

Shape and size of the dosage forms are important in designing indigestible single unit solid dosage forms. The mean gastric residence times of non- floating dosage forms are highly variable and greatly dependent on their size, which may be large, medium and small units. In most cases, the larger the dosage form the greater will be the gastric retention time (GRT) due to the larger size of the dosage form would not allow this to quickly pass through the pyloric antrum into the intestine.

Gender:

Mean ambulatory GRT in male (3.4hrs) is less compared with the age and race matched female counterparts (4.6hrs) regardless of height, weight and body surface.

Age:

People with age more than 70 have a significant longer GRT. Concomitant drug administration- anticholinergic like atropine and propetheline, opiates like codeine can prolong GRT.

Types of gastro retentive drug delivery system:

1. Floating systems:

Floating systems are described by Davis in 1968. FDDS have a bulk density less than gastric fluid and sore main buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. 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.

The floating system is divided in to two types

A) Non- effervescent systems
B) Effervescent systems

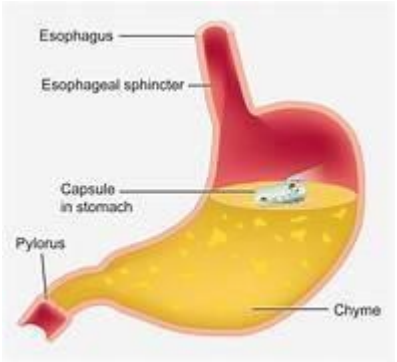

FIGURE 3: FLOATING SYSTEMS

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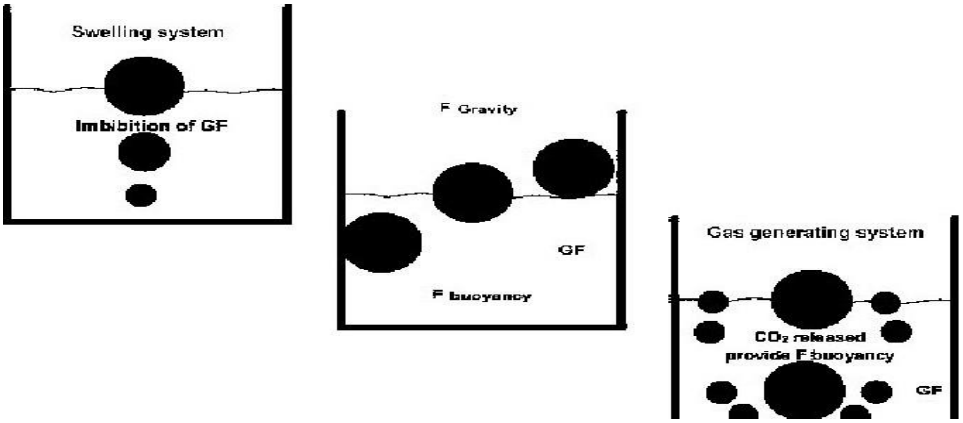

FIGURE 4: MECHANISAM OF FLOATING TABLETS

A) Non- effervescent systems:

This type of system, after swallowing swells unretrained via inhibition of gastric fluid to an extent that it prevents their exit from the stomach. Excipients used most commonly in these systems include Hydroxy propyl methyl cellulose (HPMC), Polyacrylate polymers, Polyvinyl acetate, Carbopol, agar, Sodium alginate, Polyethylene oxide and Polycarbonates.

This System can be further divided into four sub- types:

- **Colloidal- gel barrier systems:**

Sheath and Tossounian first designated this "Hydro dynamically Balanced Systems". Such a system contain drug with gel forming hydrocolloids meant to remain buoyant the stomach content. This prolongs GRT and maximizes the amount of drug that reaches its absorption sites in the solution form for ready absorption. This system incorporates a high level of one or more gel- forming highly soluble Cellulose type hydrocolloid.

These materials are commonly used as Hydroxy propyl methyl cellulose, Hydroxy propyl methyl cellulose, Hydroxyl ethyl cellulose, Hydroxy propyl cellulose, Polysaccharide and matrix forming Polymer, such as Polyacrylate and Polystyrene.

On coming in contact with gastric fluid, the hydrocolloid in the system hydrates and forms a colloid- gel barrier around its surface.

- **Microporous compartment systems:**

This technology is based on the encapsulation of a drug reservoir inside a microporous 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 dissolved drug. In the stomach the floatation chamber containing entrapped air cause 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.

- **Micro balloons\ hallow microspheres:**

Hallow microspheres loaded with drug in their outer polymer shelf were prepared by an novel emulsion solvent diffusion method. The ethanol\ dichloromethane solution of the drug and an enteric acryclic polymer was poured in to an agitated solution polyvinyl alcohol, that was thermally controlled at 40^0C.

The gas phase is generated in the dispressed polymer droplet by the evaporation of dichloromethane formed and internal cavity the microsphere of the polymer with the drug. The micro balloon floated continuously over the surface of an acidic dissolution media containing surfactant for more than 12 hours.

B) Effervescent systems:

These buoyant systems utilize matrices prepared with swellable polymers such as methocel, polysaccharides (e.g., chitosan), effervescent components (e.g., sodium bicarbonate, citric acid or tartaric acid).

The system is so prepared that upon arrival in the stomach, carbon dioxide is released, causing the formulation to float in the stomach. Other approaches and materials that have been reported are a mixture of sodium alginate and sodium

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bicarbonate multiple unit floating pills that generate carbon dioxide when ingested, floating minicapsules with a core of sodium bicarbonate, lactose and polyvinyl pyrrolidone coated with hydroxyl propyl methylcellulose (HPMC), and floating systems based on ion exchange resin technology, etc.

2. Bio/muco–adhesive systems :

Bio adhesive drug delivery systems (BDDS) are used as a delivery device within the lumen to enhance drug absorption in a sitespecific manner. This approach involves the use of bioadhesive polymers, which can adhere to the epithelial surface in the stomach. Gastric mucoadhesion does not tend to be strong enough to impart to dosage forms the ability to resist the strong propulsion forces of the stomach wall. The continuous production of mucous by the gastric mucosa to replace the mucous that is lost through peristaltic contractions and the dilution of the stomach content also seem to limit the potential of muco-adhesion as a gastroretentive force. Some of the most promising excipients that have been used commonly in these systems include polycarbophil, carbopol, lectins, chitosan and gliadin, etc.

3. Swelling systems :

These are the dosage forms, which after swallowing, swell t an extent that prevents their exit from the pylorus. As a result, the dosage form is retained in the stomach for a long period of time.These systems may be named as “plug type systems”,since they exhibit the tendency to remain lodged at the pyloric sphincter. The formulation is designed for gastric retention and controlled delivery of the drug into the gastric cavity. Such polymeric matrices remain in the gastric cavity for several hours even in the fed stat e. Sustained and controlled drug release may be achieved by selection of proper molecular weight polymer, and swelling of the polymer retards the drug release. On coming in contact with gastric fluid, the polymer imbibes water and swells. The extensive of these polymers is due to the presence of physical/chemical cross-links in the hydrophilic polymer network. These cross links prevents the dissolution of the polymer and hence maintain the physical integrity of the dosage form. An optimum cross linking which maintains a balance between the swelling and dissolution should be maintained.

4. High density system:

Sedimentation has been employed as a retention mechanism for pellets that are small enough to be retained in the rugae or folds of the stomach body near the pyloric region, which is the part of the organ with the lowest position in an upright posture. Dense pellets (approximately 3g/cm-3) trapped in rugae also tend to withstand the peristaltic movements of the stomach wall. With pellets, the GI transit time can be extended from an average of 5.8–25 hours, depending more on density than on the diameter of the pellets27. Commonly used excipients are barium sulphate, zinc oxide, titanium dioxide and iron powder, etc. These materials increase density by up to 1.5–2.4g/cm^3.

5. Magnetic system:

This approach to enhance the gastric retention time (GRT) 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. Although magnetic system seems to work, the external magnet must be positioned with a degree of precision that might compromise patient compliance.

II. CONCLUSION:

Dosage forms with a prolonged GRT will bring about new and important therapeutic options. They will significantly extend the period of time over which drugs may be released and thus prolonged dosing intervals and increase patient compliance beyond the compliance level of existing CRDFs.Many of the “once-a-day “ formulatins will be replaced by products with release and absorption phases of approximately 24 hrs. Also, GRDFs will greatly improve the pharmacotherapy of the stomach itself through local drug release leading to high drug concentrations at gastric mucosa which are sustained over a large period. Finally, GRDFs will be used as carriers of drug with the”absorption window”.Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing towards commercializing this technique.

REFERENCES:

[1]. Roshan vilas ahire, Gauri bhaivshet, et., al.The quick review on floating drug delivery systems: International journal of all

research education and scientific methods. June 2023:11(7);320-882

[2]. Manikandan Palanivelu, Senthil Rajan Dharmalingam, A comprehensive review on gastro retentive drug delivery systems: International journal of pharmaceutical sciences review and research. Nov 2020:65(1);143-149

[3]. Chanchal Choudhary, Vikas Jain, Yogendra Malviya. International of pharmaceutical sciences &medicine: Apr 2023:8(4);18-30

[4]. Meenakshi Jassa, Ujjawal Nautiyal, Jyotsanakundlas, D.Singh. A review: Gastro retentive drug delivery system. International jouranal of pharmaceutical and biological research, 2015; 3(1): 82-92.

[5]. Devkant Sharma, Anjali Sharma. Gastroretentive drug delivery system –A mini review. Smt. Tarawati institute of biomedical and allied sciences, 2014; 1(2): 86.

[6]. Nautiyalet al./Indian journal of pharmaceutical and biological reaserch, 2015; 3(1): 82-92.

[7]. Deepak Sharma, Sanjay Kumar Sharma Jaiminiand Amit Kumar. Floating drug delivery system.International journal of pharmaceutical, chemical and biological sciences,2014;4(1): 201-207.

[8]. Sanap Sunil A, Mahale N.B, Salunkhe K.S, Chaudhari. S.R. A review on: Floating drug delivery system. Journal of advanced drug delivery, 2014; 1(2): 96-113.

[9]. HemantMaheta, MR Patel, KR Patel, MS Patel. An overview on: floating drug delivery system. ISSN. 2014; 2(3): 61-71.

[10]. Devkant Sharma, and Anjali Sharma. Gastroretentive drug delivery system.Gastroretentive drug delivery system: A mini review, 2014; 1(2): 80-89.