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## A REVIEW OF GASTRO RETENTIVE DRUG DELIVERY SYSTEM

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### Abstract

Currently receiving a lot of interest, Gastro Retentive Drug Delivery Systems (GRDDS) are a unique technique that improve the performance of oral controlled release dosage forms. It is the methods used in the pharmaceutical business to provide improved therapeutic outcomes, like flexible formulations, simple dosage administration, and patient compliance. Its foundations include controlled release drug delivery systems (GRDDS) and oral drug delivery systems, which serve as drug reservoirs and release drugs in a predetermined amount of time under controlled conditions. The present review primarily focuses on the requirements for formulating the GRDDS, various approaches involved in formulation, and factors affecting gastric residence time. Alternative approaches to formulate GRDDS include floating drug delivery systems, non-effervescent drug delivery systems, high density drug delivery systems, bio adhesive systems, magnetic systems, and expandable systems. Enhancing the medicine's bioavailability is the primary goal of the gastro-retentive drug delivery method. Basic Anatomy and Physiology of the Gastrointestinal Track, Requirements for Gastro Retentive Drug, Need for Gastro Retention, Factors Affecting Gastro Retentive Time, Benefits and Drawbacks of GRDDS, and Recent Approaches to Gastro-Retentive Drug Delivery System are all covered in this overview. prescription drugs.

**Keywords:** Gastroretention, Approaches, Anatomy and physiology, Oral Administration.

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### Introduction

Historically oral drug administration/delivery is the primary choice for drug delivery system. It is also based on such oral drug delivery system i.e., controlled release drug delivery system, Gastro retentive drug delivery system which act as a drug reservoir and release drug in controlled manner in defined period of time (prolong time).(1) Drug bioavailability of oral dosage forms is subjective by various factors. One of the significant factors is a gastric residence time (GRT) of these dosage forms. Truly, gastric retention has received important interest in the past few years as many of the conventional oral delivery systems have some limits related to fast gastric emptying time. Gastro retentive dosage form is a type of novel drug delivery system which can persist in the stomach for prolonged period of time and thus increases the GRT of drugs. Gastro-retention helps to improve bioavailability of drugs. The classification of different modes of gastric retention:

- High-density (Sinking) systems
- Low-density (Floating) systems

- Expandable systems
- Super porous hydrogel systems
- Mucoadhesive systems
- Magnetic systems

However, in following condition gastro retention is considered undesirable: low density system, raft systems incorporating alginate gels, mucoadhesive or bio adhesive systems, high density systems, super porous hydrogels and magnetic systems(2). Current progress in technology has provided feasible dosage alternatives which can administered by different routes of administration like oral, topical, parenteral, rectal, nasal, ocular, vaginal, etc. But out of all these routes, oral route is considered as the best preferred and practiced way of drug delivery.

Due to the following reasons:

- Ease of administration
- Ease of production
- More flexibility in designing
- Low cost

Many drugs given by oral route are subjected to absorption through the GIT, with major absorption from the stomach and intestine. A drug which is absorbed from the stomach or show local effect should spend extreme time in stomach. Gastric emptying of dosage form

depends on several factors like temperature and viscosity of the meal, volume and composition of the meal, emotional state of the individual, the pH of the stomach, body posture, etc. (3) Prolonged gastric retention of the drug is required in the following conditions:

- The drug is best absorbed from the stomach. Example: Aspirin, Phenylbutazone, etc.
- Slow dissolving drugs.
- Dissolution and absorption of drug is stimulated by the food. Example: Griseofulvin.
- Drug show local effects in the stomach.
- Gastric fluids facilitate and increase the disintegration and dissolution of the drug.

Ideal properties of GRDDS

1. Drug should act locally in stomach
  2. Drug should not unstable the intestinal environment
  3. Absorption window in GIT should be narrow
  4. Drug should be low soluble in GIT in high pH region
2. Basic Anatomy and physiology of gastrointestinal Tract (4).

Basically, GIT is divided in three main regions they are: -

1. Stomach
2. Small intestine
3. Large intestine

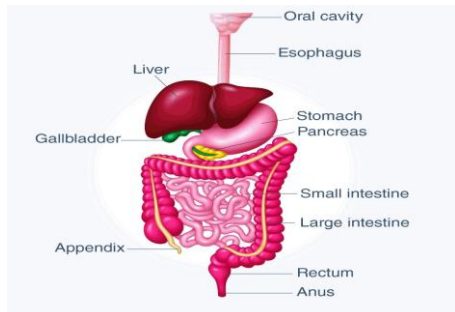


Figure 1: Anatomy of gastrointestinal track

The internal structure of GIT consists of muscles tube. The size of muscles tube is about 9 meter which extends from mouth to anus. (5) The main purpose of GIT is to store food, grind it, utilized its nutrients, and release slowly in duodenum and discards body waste material. The proper understanding of anatomy and physiology of stomach is required for better development of Gastro retentive drug delivery system. (5)

Stomach contain approximately 50ml of liquid (Gastric fluid), which is known as HCL having pH 1-3, it is also called as stomach gastric fluid. The production of HCL is done by parietal cells (epithelium cell) of the stomach. The parietal cell is responsible for the control of gastric acid or gastric fluid. Whereas pepsins are release by Zymogenic cell which are necessary for nutrient absorption (8).

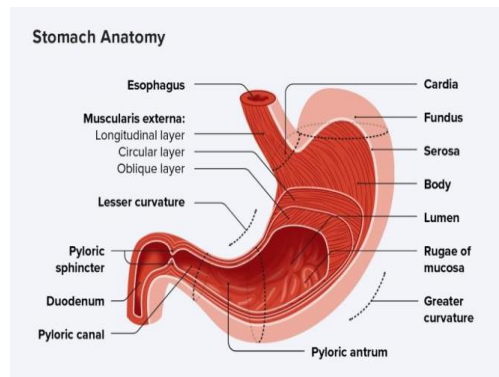


Figure2: Anatomy of gastrointestinal track

Phase	Duration
Phase 1 (Basal phase)	30-60 min with infrequent contractions.
Phase 2 (Preburst)	20-40 min with the irregular action potential and contractions as the phase developments, the intensity and the frequency also rises gradually
Phase 3 (Burstphase)	10-20 min, it contains intense and regular contractions for short periods. It's due to this wave that all the undigested material is swept

#### Phases of Migrating Myoelectric Complex.

After the digestion of mixed meal, the pattern of contractions changes from fasted to feed state. This is also recognized as digestive motility pattern and contains endless contractions as in phase II of fasted state. The contractions result in decreasing the size of food particles (<1 mm), which are propelled towards the pylorus in the suspension form. Throughout the fed state onset of mmc is postponed resulting in a slowdown of the gastric emptying rate. Scrintigraphic studies including the measurements of the gastric emptying rate in healthy human subjects have discovered that an orally administered controlled release dosage form is primarily subject to two physiological difficulties:

1. Short GRT
2. Unpredictable gastric emptying rate

Yet additional major difficulty encountered through the oral route is first pass effect that leads to decreased systemic bioavailability of numerous drugs.

6. Disadvantages of Gastro retentive drug delivery system (8)

1. These are not suitable candidates for drug which have stability or solubility problem in stomach.
2. Floating system has limitation that it requires high fluid level in stomach for floating and absorption efficiently.
3. The mucoadhesive system has the limitation of high turnover of the mucus layer, thick mucus layer and limitation associated with soluble mucus.
4. Gastric retention is affected by many factors such as gastric motility, pH, and food presence. Buoyancy cannot be predicted because these factors are not constant.
5. The swelling formulation can be swelled in the system before reaching the site of the stomach.
6. Longer time required to swell for hydrogel based swelling system.
7. Need of gastro retentive drug delivery system

Oral dosage forms pose low bioavailability problems because of their fast gastric transition from the stomach, particularly in case of drugs that are less soluble at an alkaline pH of the intestine. Also the drugs that produce their local action in the stomach get quickly emptied and do not get sufficient residence time in the stomach. Therefore, frequency of dose administration in such condition is increased. To avoid such problem floating drug delivery system has been developed.

#### 8. Approaches of gastro retentive drug delivery system (8).

There has been a large development of oral control release and sustain release drug delivery system for gastrointestinal diseases, for prolong absorption of drug. This system improve the bioavailability in Gastro retentive track and maintain an effective drug concentration for prolong time in stomach (GIT). As oral drug (Tablet, Capsule and Pellets) administered orally in stomach there is retention of drug in stomach and release drug in controlled manner. Due to controlled and sustained release the drug will supplied continuously to its absorption site or targeted site.

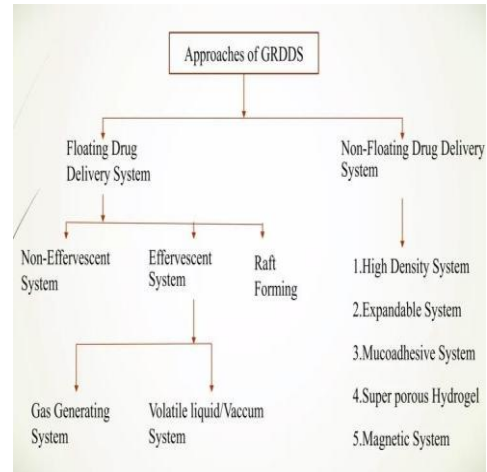


Figure 4: Approaches of GRDDS

#### 8.1 Floating drug delivery system

Initially the floating drug delivery system was introduced by Sir Davis in year 1968. In floating drug delivery system, the bulk density is lower than that of gastric fluid hence remain prolong time in stomach or targeted site, it releases it drug in control manner(9).

The floating drug delivery does not affect the rate of gastric emptying over a prolong time. The gastric emptying of residual system is followed by drug release in stomach. Thus, improve bioavailability and control over plasma drug concentration and increases its gastric retention time.

Properties for Gastro retentive drug delivery system

- Slow drug release
- Act as drug reservoir
- Bulk density should be lower than gastric fluid (Approximately 1.004 – 1.0 g/cm).
- Must form a cohesive gel barrier [21]

##### I. Non Effervescent system

##### II. Effervescent system

##### a. Gas generating system

The main mechanism is involved in this system is the production of CO<sub>2</sub> gas due to reaction between sodium bicarbonate, citric acid and tartaric acid(9). The gas produced results in the reduction of density of the system, thereby making it float on the gastric fluids.

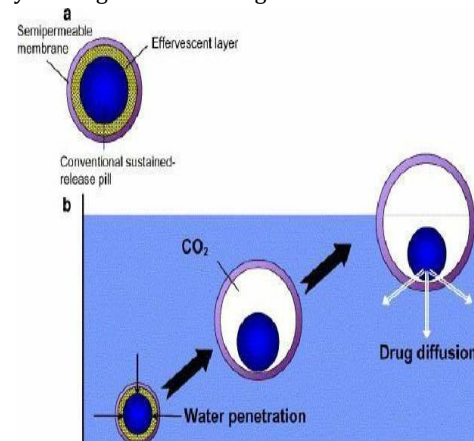


Figure 5: Gas Generating System.

a. Volatile liquid containing system([10])

The volatile liquid and vacuum system is the recent approaches in gastro retentive drug delivery system.

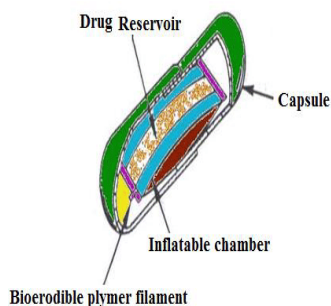


Figure 6: Volatile Liquid Containing System.

I. Raft forming [25]

The raft forming system is mainly used for the treatment of GERD – gastric oesophageal reflux diseases.

7.2 Non Floating Drug Delivery System

In non – floating drug delivery system the dosage form of gastro retentive drug delivery system does not float in the stomach but stays remain in the stomach by different mechanism. The drug may settle down in stomach showing bio adhesive and mucoadhesive properties, in this system dosage form release drug in sustain manner it also releases it drug at targeted site it is also pH dependent drug delivery system it gets dissolve at a certain ph. (11)

➤ Further approaches of non-floating drug delivery system

- High density system
  - Expandable system
  - Mucho adhesive system
  - Super pores hydrogel system
  - Magnetic system
- a. High density system

The inert material increases the density up to 1.5 – 2.4 g/cm<sup>3</sup>, according to the density present in the stomach GI transit time of pellet can be extent from 6 – 24 hours (as they are small in size), its rate of dispersion decreases. The product of high density system is not marketed because it ineffective in humans till, research and development are ben working on it (11).

b. Expandable system

These systems are capable of expanding and retain in the stomach for longer periods. These are usually formulated as a capsule containing dosage form folded and compact form. After being exposed to stomach environment, capsule shell disintegrates and dosage form expands preventing its exit through the stomach. By using a suitable polymer, sustained and controlled drug delivery can be achieved(12).

c. Mucho adhesive system

The adherence of the delivery system to the gastric wall increases residence time thereby improving bioavailability(13). The chemicals used for the

mucoadhesion purpose include polycarbophil, carpool, lecithin, chitosan, carboxy methylcellulose, gliadin etc. Novel adhesive material derived from fimbriae of bacteria or its synthetic analogues have also been tried for the attachment to the gut.

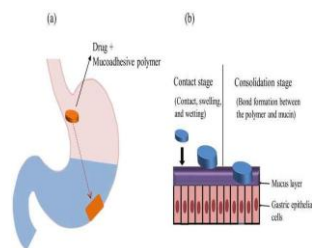


Figure 7: Mucho adhesive system

d. Super pores hydrogel system

The super pores hydrogel system contains interconnected microscopic pores those pores are responsible for absorption of water in short period of time; the water absorption capacity should be high due to limitation of time(14). The super pores hydrogel system is the interconnected network of hydrophilic polymer and due to presence of super-size pores capillary action occurs and swelling o dosage form is observed.

e. Magnetic system

In this system, the dosage form contains a small magnet and another magnet is placed on the abdomen over the position of the stomach. The external magnet should be placed with a degree of precision which may decrease the patient compliance. The gastric residence time of dosage form can be enhanced by extra incorporated of magnet (15).

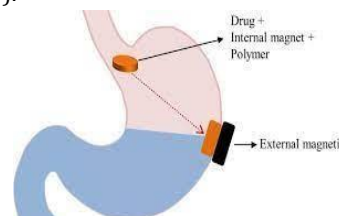


Figure 8: Magnetic System

Conclusion

Drug delivery systems that are gastro-retentive can help increase a drug's bioavailability. There will be the added benefit of better drug absorption in the jejunum, upper portion of the stomach, and duodenum (19). Therefore Researchers were trying to come up with novel methods for creating gastro-retentive drug delivery formulations with a variety of polymers and excipients for distinct medication classes.(20) As a result, it's possible that gastro-retentive drug delivery systems work better at getting medications into the bloodstream. prescription drugs delivered with a retentive system.

Author contributions

All authors are contributed equally.

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### Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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