# Chapter-04

# GASTRO-RETENTIVE DRUG DELIVERY SYSTEM

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## INTRODUCTION

Historically, the majority of prescribed medications are delivered orally. Due to its many benefits, such as simplicity of administration, versatility in formulation, cost effectiveness, convenience of storage and transport, and high patient compliance, oral drug delivery systems have dominated alternative drug delivery methods for human administration.

However, the bioavailability of medications administered by oral route might differ significantly, particularly if the drugs are given in conventional dose form. This limitation was often ascribed to inter- and intra-subject heterogeneity in gastrointestinal tract (GIT) physiology, GIT transit duration, and in certain cases, a narrow absorption window of drugs in the GIT. Because of variations in pH, accessible surface area, degree of expression of different enzymes and transporters, and metabolism in distinct GIT areas, there may be non-uniformity in drug absorption across the alimentary canal or a region-specific absorption window. Age, gender, posture, and illness condition are biological characteristics that contribute to GIT region-specific absorption.

The development of Gastro-retentive Drug Delivery System may thus result from traditional drug delivery methods failing to keep medications in the stomach. Following are some advantages these systems provide:

Advantages of Gastro-retentive Drug Delivery System Longer stomach residence time may be beneficial for local action in the upper section of the small intestine, such as the treatment of peptic ulcer disease.

Delivery of medications with a restricted window of absorption in the small intestine area. For medications that are quickly absorbed after release in the GI tract, such as cyclosporine, ciprofloxacin, ranitidine, amoxycillin, captopril, etc., improved bioavailability is anticipated. Ensuring once-daily treatment compliance from the patient. Increased therapeutic effectiveness.

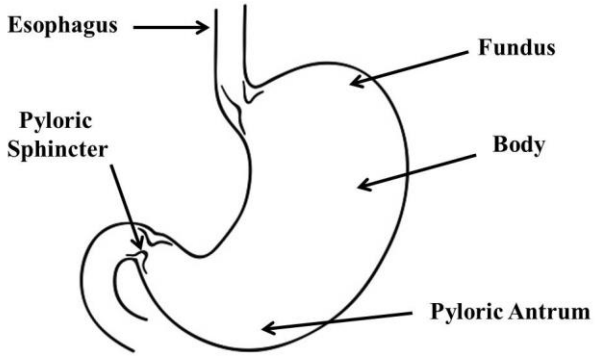


**Figure 4.1: Anatomical Parts of Stomach**

**Physiology of Stomach**

A thorough understanding of the anatomy and physiology of the stomach is a need for the effective creation of the gastroretentive dosage form since the stomach plays a significant role in the GRDDS. As depicted in **Figure 4.2**, the stomach is divided anatomically into two sections: the proximal stomach, which is made up of the fundus and body, and the distal stomach, which is made up of the antrum and the pylorus.

The Pyloric sphincter, a valve-type unit that may open to a maximum of **12.8±7 mm**, connects the beginning of the intestine and the end of the stomach, which means they are both connected to the duodenum. Therefore, larger dose forms stay in the stomach longer.

At repose, there is a minimum of **25 to 50 cc** of gastric fluid in the stomach.

The pH of stomach fluid is typically **1.5 to 2** while fasting and may rise to 2 to 6 when eaten, although it quickly drops by the release of additional gastric acid.

Stomach Retention In a fed state, GRT is raised, especially with fatty meals, but the time of any dose form is typically 1-2.5 hours.

By means of gastric motility, food is expelled from the stomach and into the intestine. In a situation known as faste, a certain pattern of motility known as the Migrating Myoelectric Complex (MMC) cycle occurs. There are four stages in MMC.

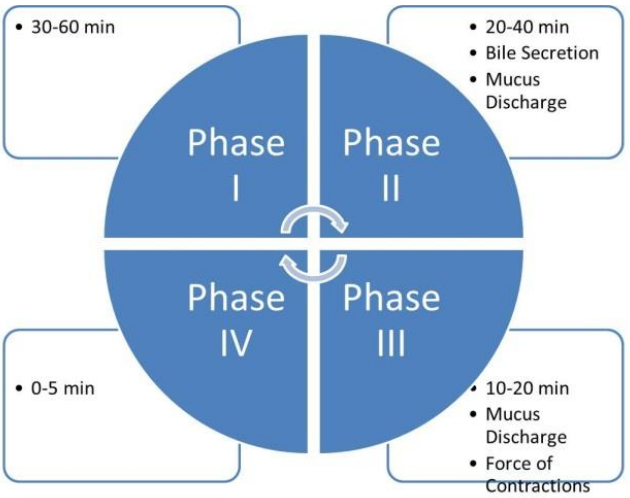


**Figure 4.2: Four Phases of The Migrating Myoelectric Complex**

**Phase I**, also known as the **basal phase**, is a quiet period lasting 30 to 60 minutes that is devoid of secretory, electrical, and contractile activity. There are also no contractions during this phase.

**Pre-burst phase**, or **Phase II**, is characterised by sporadic activity lasting 20 to 40 minutes. The frequency of contractile movements has increased as some bile secretion has begun. Phase II's latter stages are when mucus discharge begins.

**Burst phase,** or **phase III**, is marked by powerful, sporadic contractions known as "house keeper waves." By increasing the pyloric aperture, these waves remove undigested food for 10 to 20 minutes. Therefore, these stages make the evacuation of the stomach's contents effective.

Phase IV is the up to five minute gap between phases III and I.

Every two to three hours, the MMC cycle is completed again.

In the feed condition, motor activity is triggered 5–10 min after mealtime and lasts as long as food is still in the stomach.

The duration of fed activity increases with meal intake, often lasting between 2 and 6 hours, albeit more frequently 3 or 4 hours. Its contractions are phasic and resemble those of phase II of the MMC.

**Table 4.1: Salient Features of Upper Gastrointestinal Tract**

| Section | Length (m) | Transit Time (h) | pH | Microbial Count | Absorbing Surface Area ($m^2$) | Absorption Pathway |
|---|---|---|---|---|---|---|
| **Stomach** | 0.2 | Variable | 1-4 | $<10^3$ | 0.1 | P,C,A |
| **Small Intestine** | 6-10 | 3±1 | 5-7.5 | $10^3$-$10^{10}$ | 120-200 | P,C,A,F,I,E,CM |

P = Passive diffusion; C = Aqueous channel transport; A = Active transport; F = Facilitated transport; I = Ion-pair transport; E = Entero-or pinocytosis; CM = Carrier mediated transport

Drug requirements for gastric retention

Localised effects of drugs in the stomach. For instance, antacids with misoprostol, a medication for *H. Pylori*

The majority of a drug's absorption occurs in the stomach Example: Amoxycillin

Drugs with low solubility at alkaline pH For instance, furosemide, zolpidem, verapamil, etc.

Drugs with a limited absorption window Levodopa, methotrexate, and others come to mind.

Drugs that are quickly absorbed from the GI tract. such as tetracycline and metronidazole.

Medicines that break down in the gut. Including ranitidine and metformin HCl.

Factors influencing the dosage form's stomach retention time

**Density:** GRT depends on density since dosage form buoyancy is a function of density.

**Size:** It has been noted that dosage form units with a diameter of more than 7.5mm have a higher GRT than those with a diameter of 9.9mm.

**Tetrahedron and ring-shaped dosage forms** are found to have improved GRT 90 to 100% retention at 24 hours compared to other shapes. These shapes have flexural moduli of 48 and 22.5 kilo pounds per square inch (KSI).

**Single or multiple unit formulation:** Compared to single unit dosage forms, multiple unit dosage forms have a higher margin of safety against dosage form failure, a more

predictable release profile, and minimal performance impairment from unit failure. They also allow co-administration of units with different release profiles or containing incompatible substances.

**In a fed or unfed state, when fasting:** Periods of vigorous motor activity, or the migrating myoelectric complex (MMC), which happens every 1.5 to 2 hours, are characteristics of GI motility. The MMC removes undigested matter from the stomach, therefore if the formulation is administered at the same time as the MMC, the unit's GRT should be extremely brief.

**Meal type:** consuming indigestible polymers or fatty acid salts might cause the stomach to enter a state of feeding, slowing down gastric emptying and delaying the release of drugs.

**Caloric content:** A meal strong in proteins and lipids can extend GRT by 4 to 10 hours.

**Feeding frequency:** Due to the low frequency of MMC, the GRT can increase by almost 400 minutes when many meals are given in succession as opposed to a single meal.

**Gender:** Regardless of weight, height, or body surface, the mean ambulatory GRT in men (3.40.6 hours) is shorter than that in their age- and race-matched female counterparts (4.61.2 hours).

**Age:** The GRT is noticeably longer in older adults, particularly those over 70.

GRT might differ between the patient's supine and upright ambulatory phases.

Diabetes and Crohn's disease are biological causes.

**Limitations of GRDDS**

In all of the severe stomach circumstances, more repeatable and predictable floating qualities should be attained. However, this system still suffer from following limitations.

In the case of swellable systems, the floating systems in patients with achlorhydria may be in doubt; quicker swelling qualities are necessary, and the system's entire swelling should be attained well before the stomach emptying time.

High mucus turnover and bioadhesion in an acidic environment might cast doubt on this method's efficacy. The conservation of high density networks in the antrum portion under the stomach's migratory waves is also under doubt.

Not suited for medications that might lead to stomach lesions, such as medicines that are non-steroidal anti-inflammatory. These methods do not significantly outperform traditional dose forms for medications that are absorbed throughout the gastrointestinal tract for those pharmaceuticals that are unstable in the very acidic environment.

Unpredictable adhesion is caused by the stomach's mucus, which is constantly renewing itself.

The physical integrity of the system is a crucial component and the main condition for the success of all the systems mentioned above.

**Various Gastro-retentive Drug Delivery Systems Technologies**

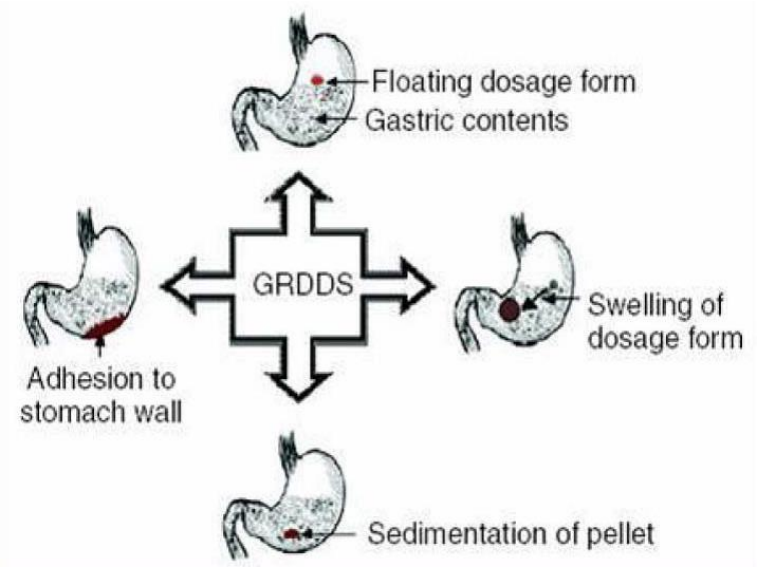


**Figure 4.3: Floating Systems – A Low Density Approach**

Hydro-dynamically balanced systems (HDBS) or floating drug delivery systems (FDDS) float in the stomach without slowing down the gastric emptying rate since their bulk density is lower than that of gastric fluids.

The medicine is released from the stomach slowly and at the desired pace while the system is floating on the gastric contents. After the release of the drug, the residual system is emptied from the stomach. In certain situations, this causes an increase in stomach retention duration and improves control over variations in plasma drug concentration.

The hydrophilic matrices, also known as hydro-dynamically balanced systems, which are hydrated and create a gelled barrier at the outer surface, are this system's most crucial feature. Progressive drug release occurs from the enlarged matrix. Because their bulk density is smaller than that of the gastric contents, these forms are anticipated to float on the contents of the stomach for three to four hours without changing the intrinsic rate of emptying. The results also show that the buoyancy retention principle cannot be properly achieved without the presence of stomach content.

The most often used hydrocolloids among those suggested for floating form formulations are cellulose ether polymers, particularly hydroxypropyl methylcelluloses. To reduce the water intake rate and boost buoyancy, the formulation may include fatty material having a bulk density lower than one.

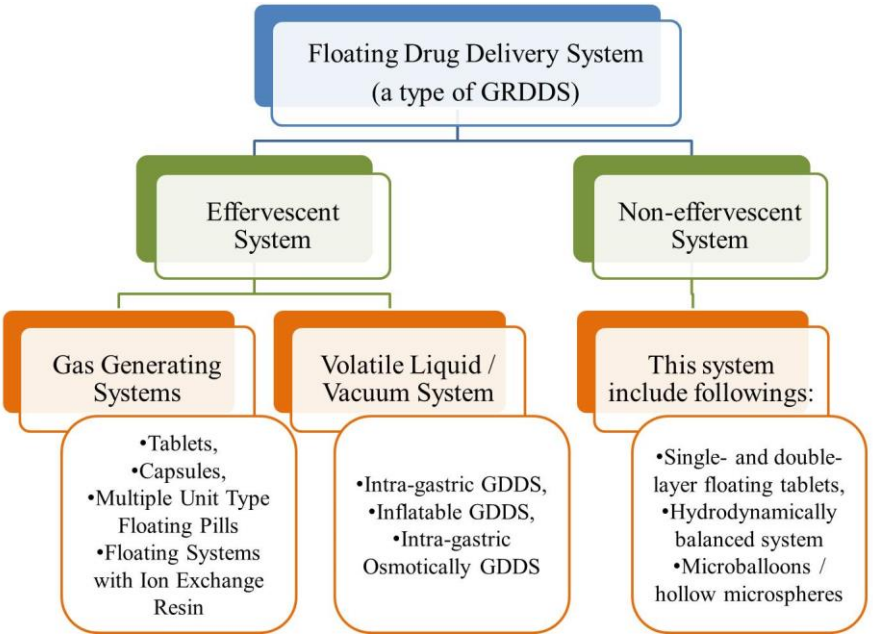


**Figure 4.4: Classification of Floating Drug Delivery Systems**

**Effervescent Systems**

A gas-generating material and volatile liquids are used in effervescent floating devices. Both single-unit systems and systems with many units have used this strategy.

**Gas-Generating Systems**

In the gas-generating floating system, effervescent substances like sodium bicarbonate, calcium carbonate, tartaric acid, and citric acid are combined with swellable

polymers like methocel and polysaccharides like chitosan. According to studies, 0.76:1 is the ideal stoichiometric ratio for the production of gas from citric acid and sodium bicarbonate. Due to the effervescent agent's interaction with the stomach fluid when this system comes into touch with it, $CO_2$ is released. The hydrocolloid matrix, which gives the tablet buoyancy and affects the drug release characteristics, traps the freed $CO_2$ gas.

The typical method for creating these systems uses resin beads that have been bicarbonate-loaded and ethylcellulose-coated. Water may pass through the covering, which is impermeable but porous. Because of the release of carbon dioxide, the beads float in the stomach.

**Matrix tablets:** Bicarbonates are added to hydrocolloid matrix-forming gelling agents such HPMC, chitosan, alginate, or other polymers, together with the medication, to create single layer matrix tablets. Bilayer tablets may also be made by placing a gas-generating matrix in the first layer and placing the medicine in the second layer for the SR effect. These mixes are also used to make floating capsules.

**Matrix tablets with carbopol:** Due to its pH-dependent gelling feature, carbopol only forms a gel at alkaline pH levels, hence acidic gastric juice normally does not cause gelling. However, because carbonate creates an alkaline milieu, Carbopol causes swelling and gelling when gas-producing bicarbonates are added to it. However, to sustain the integrity of the core, this system can be covered with a permeable elastic polymer like Eudragit.

**Coated effervescent core:** A medication and an effervescent substance are combined to make the tablet, which is then covered with a polymeric coating made of a material like Eudragit RS and a plasticizer. The coating is more permeable to $CO_2$ gas and water and has a higher elongation value. Therefore, the production of $CO_2$ gas causes the stomach juice to float.

**Floating pills:** A double layer coat surrounds the SR medication pill in the floating pill system. To prevent NaHCO3 and tartaric acid from coming into direct contact with one another, the inner layer is an effervescent layer with two sub-layers. PVA and shellac make up the swellable, porous layer that is the outer layer.

When the system comes into touch with water or stomach juice, these substances pass through the swellable membrane and cause the reaction that produces $CO_2$ gas inside the system. As CO2 gas does not escape from the outer membrane, a system resembling a balloon is created that can float. Regardless of the pH or viscosity of the medium, this system floats completely in about 10 minutes and stays buoyant for up to 5 hours.

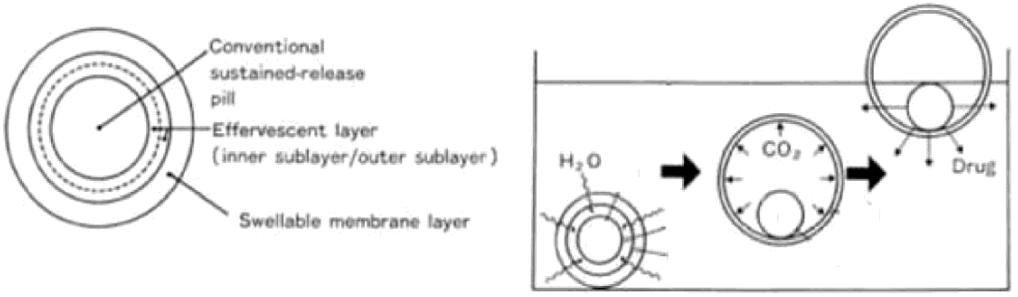


**Figure 4.5: a) Pill's Structural Properties; b) Pill's Floating Mechanism**

**Floating based on ion-exchange resin:** This system included negatively charged medication attached to resin and bicarbonate-loaded ion exchange resin beads. A semi-permeable membrane was used to further enclose the beads.

The chloride ion of HCl acid reacts with bicarbonate when it comes into contact with stomach juice, creating $CO_2$ gas that is trapped by the semipermeable barrier. $CO_2$ production hence causes floating systems. Due to the leakage of CO2, uncoated beads don't appear to be floating.

**Programmable drug delivery:** Programmable drug delivery systems include a bicarbonate-containing balloon, rubber disc, spring, valve, and non-digestible HGC body.

**Volatile Liquid Systems**

In volatile liquid systems, liquids that volatilize at body temperature, such as ether and cyclopentane, are delivered into an inflatable chamber, permitting inflation of the chamber in the stomach. In this method, hydrophilic polymers are frequently utilised to regulate the medication release rate.

Single- and double-layer effervescent floating tablets and multiple-unit effervescent floating systems are three different types of effervescent floating systems.

In order to create **single-layer effervescent tablets**, the effervescent agent, polymer, medicine, and excipients are thoroughly combined.

**Bilayer effervescent floating tablets** have two layers: one layer contains the medication, polymer, and $CO_2$ gas-generating agent; the second layer has a drug for quick release together with excipients without $CO_2$ and polymer.

Sustained-release tablets are used as seeds in **multiple-unit effervescent floating systems** that are encased in two layers. While tartaric acid, calcium carbonate, and sodium bicarbonate are among the effervescent substances found in the inner layer, swelling-inducing polymers are found in the outer layer.

**Non-Effervescent systems**

Excipients of the gel-forming or highly swellable cellulose type, polysaccharides, and matrix-forming polymers including polycarbonate, polyacrylate, polymethacrylate, and polystyrene are most frequently utilised in this type of FDDS.

The method entails combining the medication closely with hydrocolloids that form gel after oral administration and expand when in contact with stomach fluid while maintaining relative integrity, shape, and bulk density of less than unity. The air retained by the swelling polymers inside the outer gelatinous barrier contributes to the buoyancy of these dosage forms.

Single Unit Non-Effervescent System

**Floating tablet**

It is a matrix tablet with a single or double layer of layers. Incorporating gel-forming hydrocolloids like HPMC, the most used polymer for floating, helped create matrix tablets. Low viscosity HPMC grades are used for floating among the various grades. For floating tablets, a mixture of alginate and HPMC is also created. Bilayer matrix tablets are created by placing drug-loaded polymers in one layer and floating polymers in another, causing the entire unit to float and stay in the stomach.

**Floating capsule**

**HBS™ CAPSULES**

It is an equilibrium hydrodynamic system. It is a medication in a hard gelatine capsule with a high concentration of one or more highly swellable hydrocolloids (20–75%), such as HPMC, HPC, HEC, Na-CMC, etc.

As the capsule shell dissolves in the stomach, hydrocolloids hydrate to create a colloidal gel barrier that protects the surface and preserves the shape of the capsule. As a result, an increase in volume results in a reduction in the overall bulk density and adds buoyancy. "Receding boundary" is created when the gel structure regulates the rate of fluid-in and drug-out diffusion. The immediate adjacent hydrocolloid layer is hydrated when the external surface dissolves or erodes, and the process keeps the floating for a long time.

## BILAYER CAPSULE

Non-compressed bilayer formulation fills the capsule. One layer releases drugs, and the other is a floating layer. Both layers are made up of hydrocolloid gelling substances such gelatine, gums, polysaccharides, and HPMC. When the capsule comes into touch with stomach fluid, the capsule dissolves, and the bilayer mixture creates a gelatinous mass that sufficiently binds the two layers together.

**Tablets with hollow cylinder**

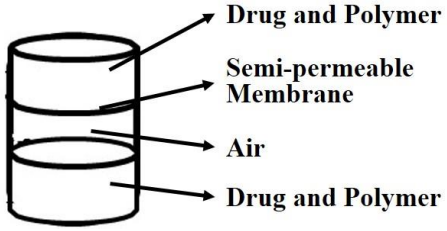


**Figure 4.6: Tablets with Hollow Cylinder**

Two HPMC matrix tablets with drugs inside are inserted inside an impermeable, hollow polypropylene cylinder to create the device (open at both ends). The total system density was low due to the fact that each matrix tablet sealed one of the cylinder's ends, leaving a void filled with air in the middle. Up until at least one of the pills was dissolved, the device remained afloat.

**Micro-porous Reservoir**

This device included a drug reservoir enclosed in a surface-pored, microporous chamber. The entire contraption has buoyancy thanks to a floating chamber that was affixed to one surface. Drug gently disintegrates out through microscopic pores.

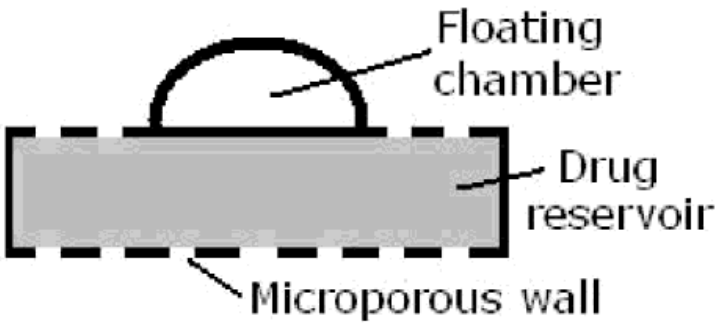


**Figure 4.7: Micro-Porous Reservoir**

**Multi-layer flexible film**

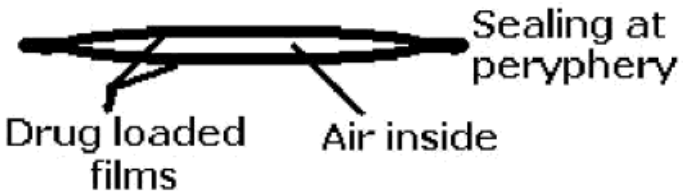


**Figure 4.7: Multi-layer Flexible Film**

The apparatus consists of two films that are joined at their peripheries and sealed in a way that traps some air between the films, creating an air pocket that lends buoyancy. Out of two films, one is a water-insoluble polymer matrix-based carrier film with a drug dispersed or dissolved therein, and the other is a barrier film that sits on top of the carrier film. A copolymer of water-insoluble and drug- and water-permeable polymers makes up barrier film.

**Multiple Unit Non-Effervescent Systems**

The use of multiple unit dosage forms is preferable since they are said to lessen inter-subject variability in absorption and decrease the likelihood of dose dumping. Powders, granules, beads, microspheres, microcapsules, microballoons, and other dosage forms are available for these medications.

Bead Systems

## CALCIUM ALGINATE/PECTINATE BEADS

By adding sodium alginate solution to an aqueous solution of calcium chloride, freeze-dried calcium alginate beads are created. Ionotropic gelation, a chemical reaction that results in the formation of solid, spherical gel beads, occurs as a result. These beads are removed from the solution and freeze dried at 40°C for 24 hours. As a result, the beads' weight is reduced, providing buoyancy for up to 12 hours. Pectin can also be used to make gel beads, much like alginate.

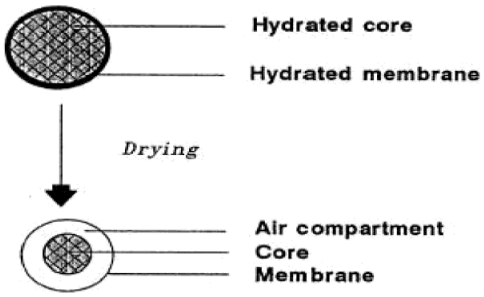


**Figure 4.8: Calcium Alginate/Pectinate Beads**

## ALGINATE BEADS WITH AIR COMPARTMENT

The difference between these and other calcium alginate beads is that the coating-membrane calcium alginate or calcium alginate and PVA mixture prepares the calcium alginate core via air compartment. When a bead dries, the internal core shrinks, creating an air pocket that gives the bead buoyancy. PVA, a water-soluble ingredient that causes membrane leaching and membrane pore formation, is added to coating mixtures to increase membrane permeability.

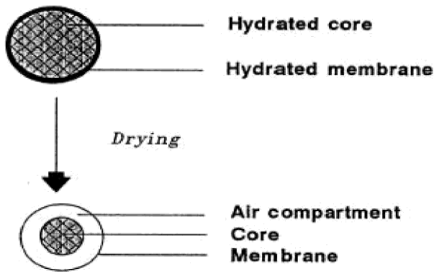


**Figure 4.9: Alginate Beads with Air Compartme**

## OIL ENTRAPPED GEL BEADS

Since they are lightweight and hydrophobic, vegetable oil is employed as a floating carrier by mixing it with a gel matrix of beads. Both calcium alginate beads and calcium pectinate beads are used to create oil-entrapped beads.

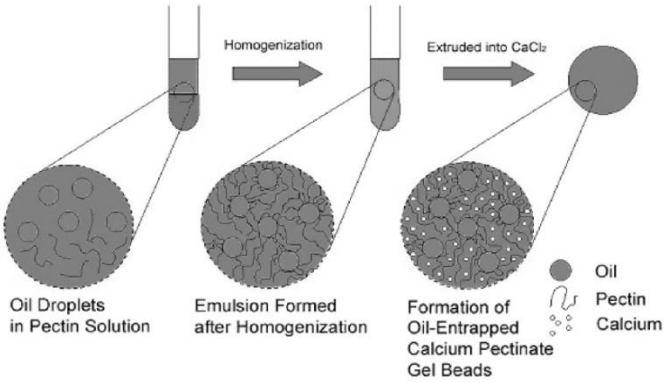


**Figure 4.10: Oil Entrapped Gel B Eads**

Due to pectin's ability to emulsify, an aqueous solution of pectin is combined with edible oil. Homogenization creates emulsion. In order to create beads, this emulsion is extruded into a calcium chloride solution, where they are separated, cleaned, and dried.

## CASEIN-GELATIN FLOATING BEADS

The emulsifying properties of casein lead to the inclusion of air bubbles, which serve as a reservoir of air for the floating system. Beads are made by heating mineral oil to a temperature of 60°C while adding a casein and gelatine solution dissolved in deionized water. The dispersion was swirled to create an emulsion, and the temperature was quickly dropped to 5°C before acetone that had already been cooled was added to create solid beads that dried under vacuum.

**Micro-spheres**

Floating microspheres are non-effervescent drug delivery devices that are gastro-retentive. In a strict sense, hollow microspheres are spherical, empty particles without a core. These microspheres are often free-flowing powders made of proteins or synthetic polymers, and they should preferably be smaller than 200 micrometres in size. The potential for controlled drug release exists in solid biodegradable microspheres that contain a drug disseminated or dissolved throughout the particle matrix.

Low-density systems known as gastro-retentive floating microspheres have enough buoyancy to float over gastric contents and remain in the stomach for an extended period of time. The medicine is gently delivered at the correct pace as the system floats over the contents of the stomach, increasing gastric retention while minimising changes in plasma drug concentration.

## HOLLOW MICROSPHERES

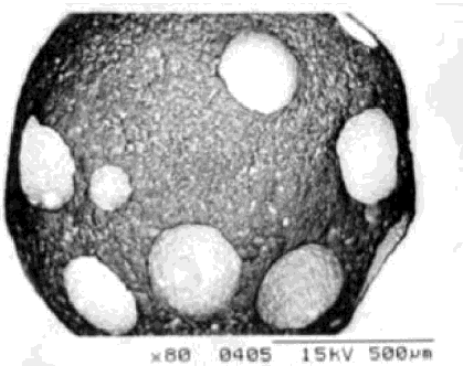


**Figure 4.11: Hollow Microspheres**

Using the solvent evaporation approach, hollow (porous) microspheres made of polymers like polycarbonates have been created. Following preparation, the organic solvent inside the microsphere evaporates, leaving holes inside. One can attain a high drug loading (50%) rate.

**The following are some benefits of hollow microspheres:**

- Reduces dosing frequency to increase patient compliance.
- Despite the first pass effect, bioavailability is increased because continuous drug release maintains a desired plasma drug concentration and prevents variations in plasma drug concentration.
- Drugs with short half-lives can produce better therapeutic results.
- Buoyancy lengthens the duration that food remains in the stomach.
- Controlled drug release over an extended length of time.
- It is possible to produce very palatable site-specific medication delivery.
- Increased absorption of medications that only dissolve in the stomach.
- Better than single-unit floating dosage forms because the medicine is released consistently and there is no chance of dose dumping with these microspheres.
- Avoiding gastrointestinal discomfort thanks to the drug's uniform release, sustained release effect, and ability to float thanks to the multi-particulate system.

## MICRO-BALLOONS

A process called emulsion solvent diffusion is used to create micro-balloons, which are hollow microspheres with drug-loaded outer shells and a chamber interior

that is completely hollow from the inside. The ethanol/dichloromethane organic phase of the drug and polymer is added to the PVA aqueous solution, which is kept at 40°C. As a result, the gas phase of the organic solvent is produced in the dispersed polymer droplet and escapes through an internal cavity that gives it its floating quality.

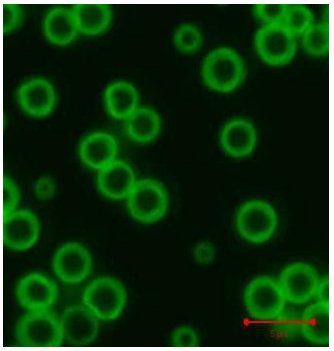

**Figure 4.12: Micro-Balloons**

**Floating powder**

A water-soluble salt of alginic acid (such as sodium or potassium alginate) with a pH independent hydrocolloid gelling agent (such as HPMC, HPC, or MC) and binder made up the floating powder, which could be put inside a capsule or compressed into a tablet. This formulation is special because it releases the medicine freely and at a controlled rate, irrespective of the pH of the environment.

## CARRIER SYSTEMS

**Calcium Silicate as Floating Carrier**

Drug, polymer (HPC), and calcium silicate as a floating carrier were used to create sustain release granules. Calcium silicate has a distinctively porous structure with multiple pores and a big individual pore volume. After being coated with polymer, the coated granules gained floatability from the air that was trapped in the pores of the calcium silicate.

**Gelucire® Granules**

Gelucire® is a brand name for a hydrophobic lipid that comes in different grades based on melting points and HLB values. As floating carriers, Gelucire® 39/01 and 43/01 grade have been employed. By using the melt granulation process, granules are created. Due of its hydrophobicity and low density, it provides buoyancy. It functions well as a carrier for medications with a high water solubility.

**High Density Systems**

The lower portion of the stomach is curled (called the Rugee) and lies horizontally below the location of the pyloric sphincter. By creating dosage forms with a density of greater than 1.004 g/cm$^3$ (the density of the usual stomach content) and the ability to endure the peristaltic movement of the stomach, one may take advantage of this geometry. These kinds of formulations, which have a high density of roughly 2-3, can be made by coating or combining the medicine with a heavy inert substance like iron powder, zinc oxide, titanium dioxide, or basal sulphate (Density = 4.9 g/cm$^3$).

**RAFT Forming Systems**

Antacid and medicine distribution systems for treating gastrointestinal infections and disorders have attracted a lot of interest. This system's method includes the development of viscous gel in contact with stomach fluids, which causes each component of the liquid to expand and create a continuous layer known as RAFT. Due to the low density produced by the production of $CO_2$, this raft floats on stomach juices. In order to make the system less thick and allow it to float on the stomach juices, this often comprises a gel-forming agent and alkaline bicarbonates or carbonates that are responsible for the creation of $CO_2$.

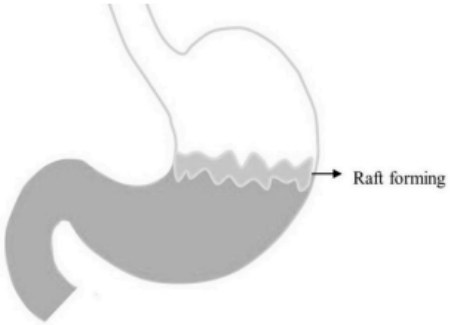


**Figure 4.13: RAFT Forming Systems**

**Expandable Systems = Plug Type Systems**

By expanding their capacity or changing their structure, expandable drug delivery devices are intended to have a longer GRT. For the system to work well, three main configurations must be taken into account: (1) small size for simple oral intake; (2) enlarged shape in the stomach to prevent passage through the pyloric sphincter; and (3) size decrease of the system after full drug release to facilitate evacuation. The two ways the system expands are through swelling and unfolding. Diffusion is the primary

mechanism from **swelling system** for medication release. Hydrophilic polymers, such as HPMC, polyethylene oxide, and carbopol, are used in these systems to add volume by absorbing water from the stomach juices. The polymer and drug are folded inside the gelatin capsule in **unfolding systems**. Gelatin dissolves when it comes into touch with stomach juice, releasing the enlarged shape that is mechanically desired.

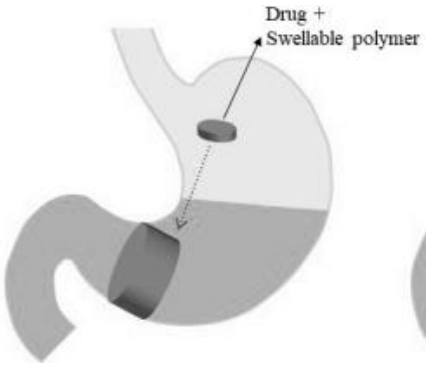


**Figure 4.14: Expandable Systems = Plug Type Systems**

**Superporous Hydrogel Systems**

This system has pore size larger than 100 μm, causing them to quickly enlarge to their equilibrium size as a result of capillary wetting and water absorption. The dose form can be readily evacuated from the stomach because the traditional hydrogel system is a lengthy process that takes many hours to attain equilibrium. Instead, the superporous hydrogel systems expand by at least 100 times and have sufficient mechanical strength to withstand pressure from stomach contraction, boosting the GRT. In these systems, highly extensible polymers such sodium alginate and croscarmellose sodium are used.

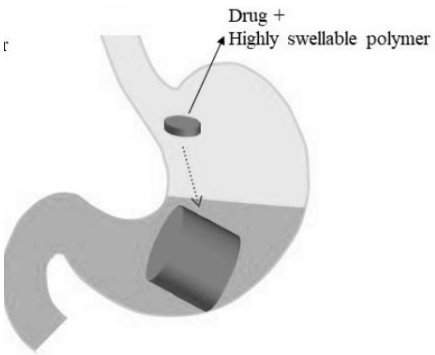


**Figure 4.15: Superporous Hydrogel Systems**

**Bioadhesive/Mucoadhesive Systems**

This method involves adding medications to a mucoadhesive agent, which can be a polymer made of natural or manmade materials. The mucoadhesion process, which typically consists of two stages: the contact stage and the consolidation stage, is made easier by the bonding that is produced between the polymer and mucosal surface. Although the process of mucoadhesion is extremely complicated and not entirely understood, several ideas have been proposed. There are several gastrointestinal mucoadhesive dosage forms that have been developed and published in the literature, including beads, microspheres, films, capsules, and tablets. Mucoadhesive polymers that are often utilised include carbopol, chitosan, sodium alginate, HPMC, polyethylene glycol, and poly (acrylic acid). Assisting in the binding of medication compounds to mucosal surfaces and extending the duration of drug residence at the application site are mucoadhesive polymers.

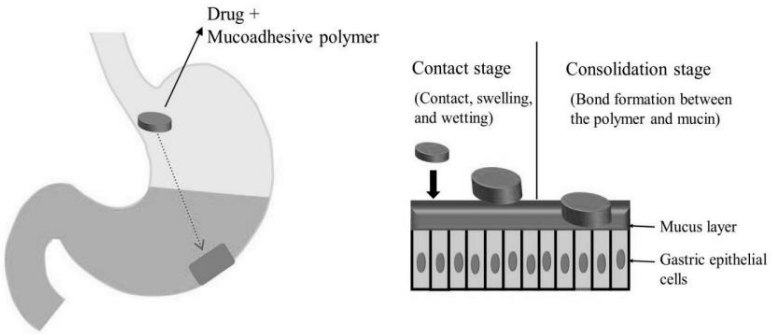


**Figure 4.16: Bioadhesive/Mucoadhesive Systems**

**Magnetic Systems**

A dosage form for magnetic systems comprises of an internal magnet, excipients, and the active medicinal component. To regulate the location of the dose form with an internal magnet, as shown in **Figure 4.17**, an extracorporeal magnet is put above the stomach. The extracorporeal magnet's location and magnetic field strength can have an impact on the GRT. However, precise placement of the magnet may be challenging, which reduces patient compliance. Magnetic systems have only been the subject of a small number of investigations, and their therapeutic relevance has not yet been determined.

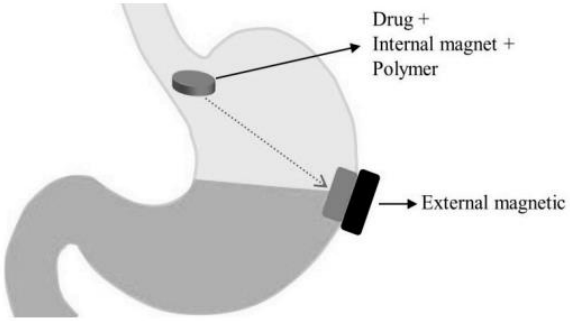


**Figure 4.17: Magnetic Systems**

**Ion-Exchange Resin Systems**

The water-insoluble cross-linked polymer (resin), which can be either cationic or anionic, makes up the ion-exchange resin system. The appropriate resins can be selected based on the drug's characteristics. Medicines should be released in the stomach in the case of GRDDS, hence cationic drugs can be used with this system. On top of a known drug concentration, a specified quantity of resin is added and blended uniformly for a certain amount of time. As they are adsorbed into the resin matrix, the drug ions from the solution replace the resin's cations. Resinates are such compounds of drug-loaded resin. The drug ions that are present in the resinates matrix are exchanged with the hydrogen ions when they come into touch with the resinates in the stomach's acidic environment. As a result, the resin particles are removed through the large intestine while the medication ions are discharged into the stomach juice. The particle size, cross-linking density, kind of ionogenic group, and nature of the pharmaceuticals all have a role in how quickly medications are released from resins.