Controlled Release Oral Drug Delivery System

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- **Controlled drug delivery is one which delivers the drug at a predetermined rate, locally or systemically, for a specified period of time.**

- **Continuous oral delivery of drugs at predictable & reproducible kinetics for predetermined period throughout the course of GIT.**

- **To modify the drug release pattern by either increasing or decreasing its rate.**

- **Delivery of a drug at predetermined rate and/or location according to the body need and of disease state, for a definite time period.**

Potential Problems Of Conventional Dosage Forms;

1. Lack of temporal delivery

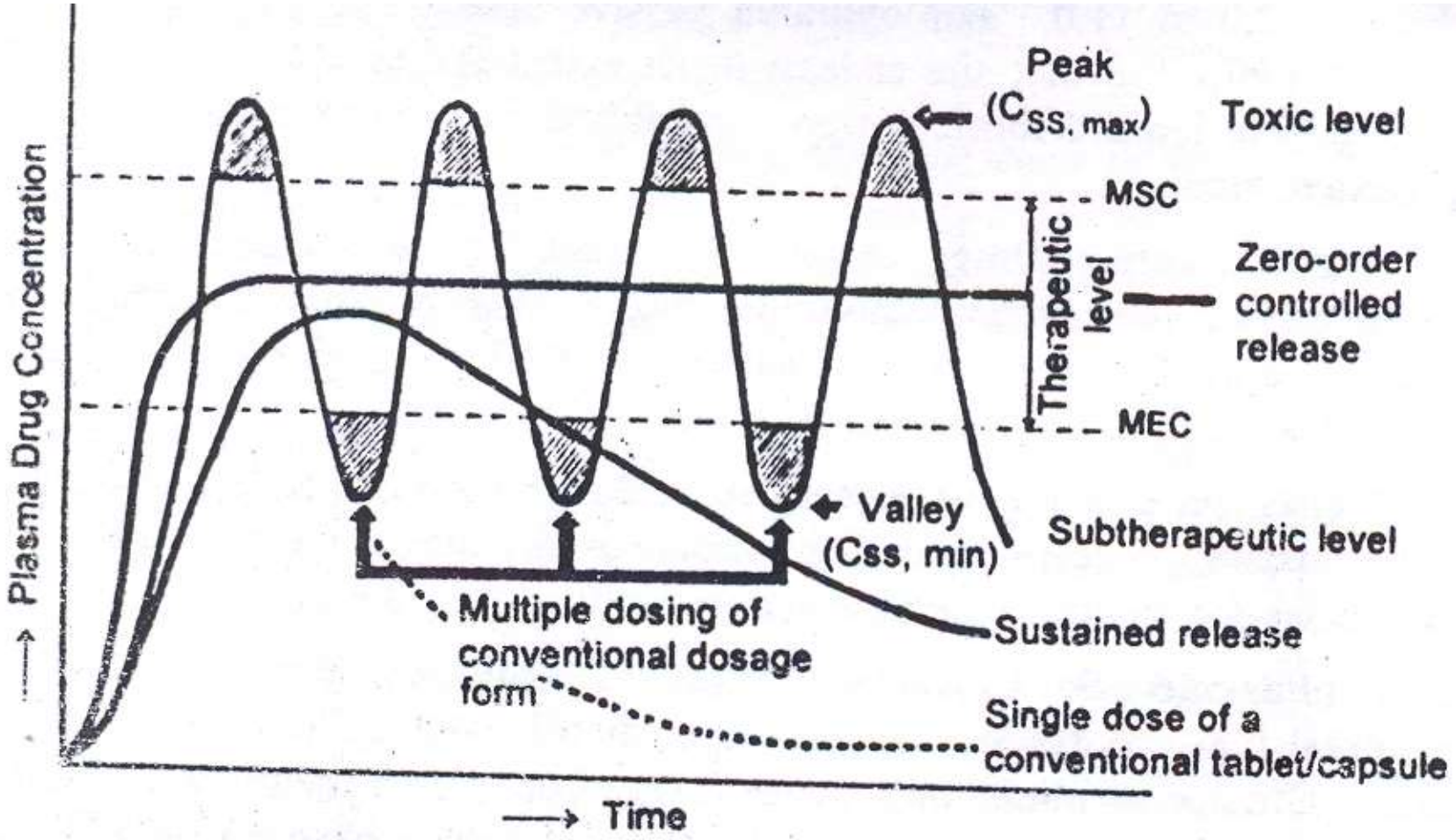
2. Repeated dosage after specific interval. If the interval is not proper there will be large peaks and valleys

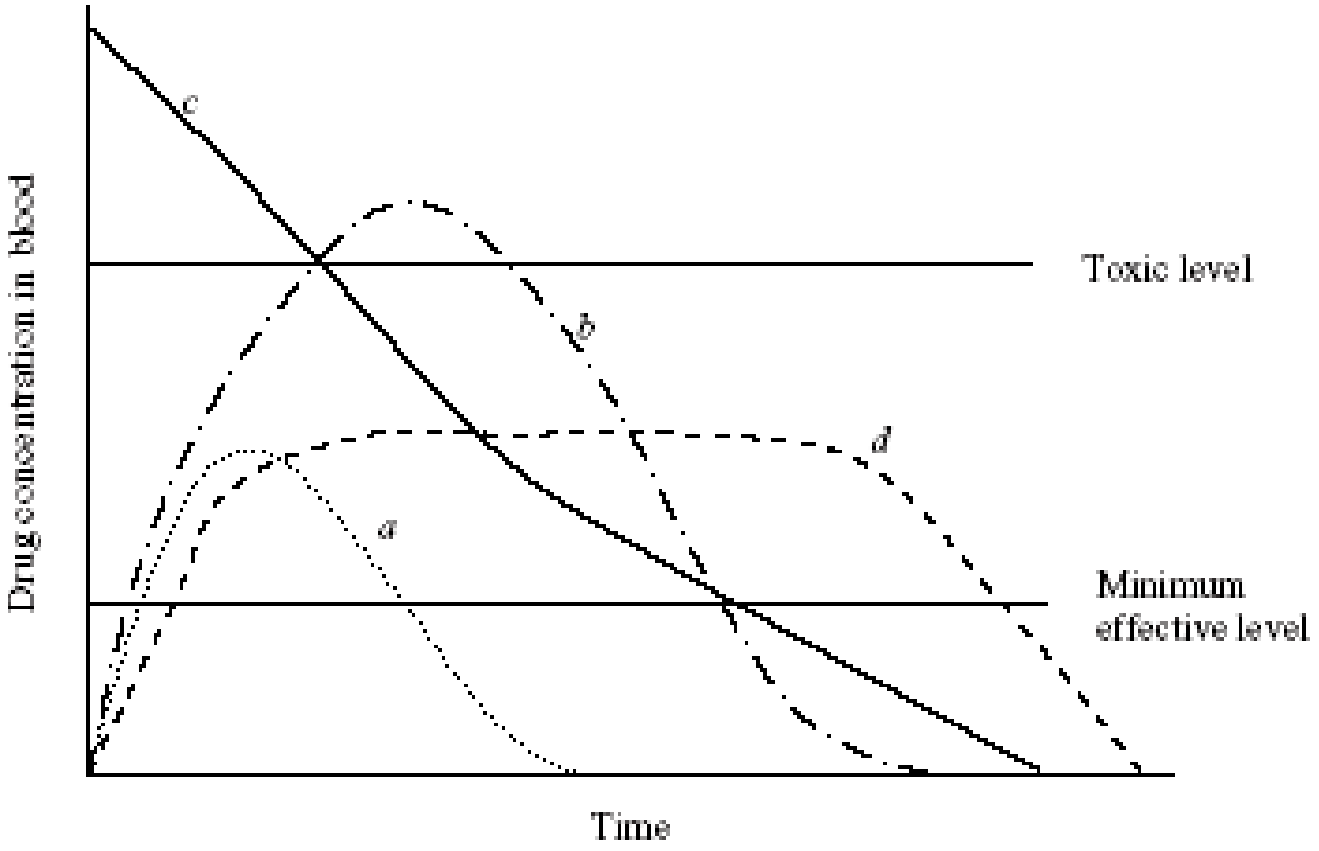
3. Patient non compliance

4. Increased untoward effects

Such like problems of conventional dosage form stimulates the researchers to develop modified release dosage form.

Plasma concentration time profile





Theoretical plasma concentration after administration of various dosage forms: (*a*) standard oral dose; (*b*) oral overdose; (*c*) IV injection; (*d*) controlled - release system.

Challenges in Oral Drug Delivery

- **Development of drug delivery system**
  Delivering a drug at therapeutically effective rate to desirable site.
- **Modulation of GI transit time**
  Transportation of drug to target site.
- **Minimization of first pass elimination**

Advantages

- Total dose is low.
- Reduced GI side effects.
- Reduced dosing frequency.
- Better patient acceptance and compliance.
- Less fluctuation at plasma drug levels.
- More uniform drug effect
- Improved efficacy/safety ratio.

Disadvantages

- Dose dumping.
- Reduced potential for accurate dose adjustment.
- Need of additional patient education.
- Stability problem.

Classification:

1. Delayed Release
2. Extended Release
3. **Site Specific Targeting**
4. Receptor Targeting
5. Fast Dissolve Drug Delivery System (Flash)

Delayed Release:

Example include enteric coated tablets , where a timed release is achieved by barrier coating epeated action tablets or spansules.

Extended Release:

These include any dosage form that maintains therapeutic blood or tissue level of drug for prolong time.

Site Specific Targeting:

In such system the drug delivery is targeted adjacent to or in the diseased organ or tissue.

Receptor Targeting

In such system the target is a particular receptor with in an organ or tissue.

Fast Dissolve Drug Delivery System (Flash)

It is type of solid dosage form that dissolves or disintegrate in the oral cavity without the help of water or chewing. Fast dissolution is achieved by forming loose network (Zydis, Eli Lilly), or by effervescent agent (Oraslav, Cima) or with mixture of disintegrating agent and swelling (Flash Tab, Prographarm)

Mechanism aspects of Oral drug delivery formulation.

1. Dissolution : a. Matrix b. Encapsulation
2. Diffusion : a. Matrix b. Reservoir
3. Combination of both dissolution & diffusion.
4. Osmotic Pressure Controlled System.
5. Chemically Controlled Release Systems
   a. Erodible Systems
   b. Drugs Covalently linked with polymers
6. Ion-exchange resin controlled released systems
7. Hydrogels

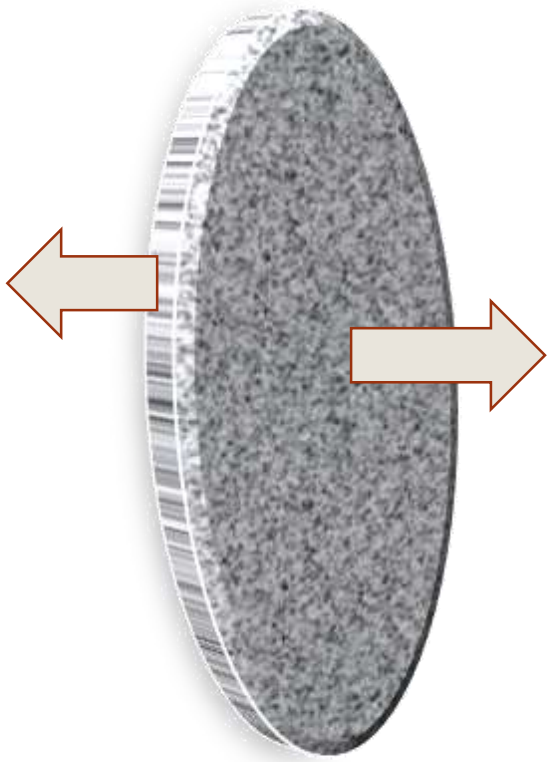
Matrix Type

- Also called as Monolith dissolution controlled system since the drug is homogenously dispersed throughout a rate controlling medium waxes (beeswax, carnuba wax, hydrogenated caster oil etc) which control drug dissolution by controlling the rate of dissolution;

  1. Altering porosity of tablet.
  2. Decreasing its wettebility.
  3. Dissolving at slower rate.

- Exhibit First order drug release.
- Drug release determined by dissolution rate of polymer.

SDM

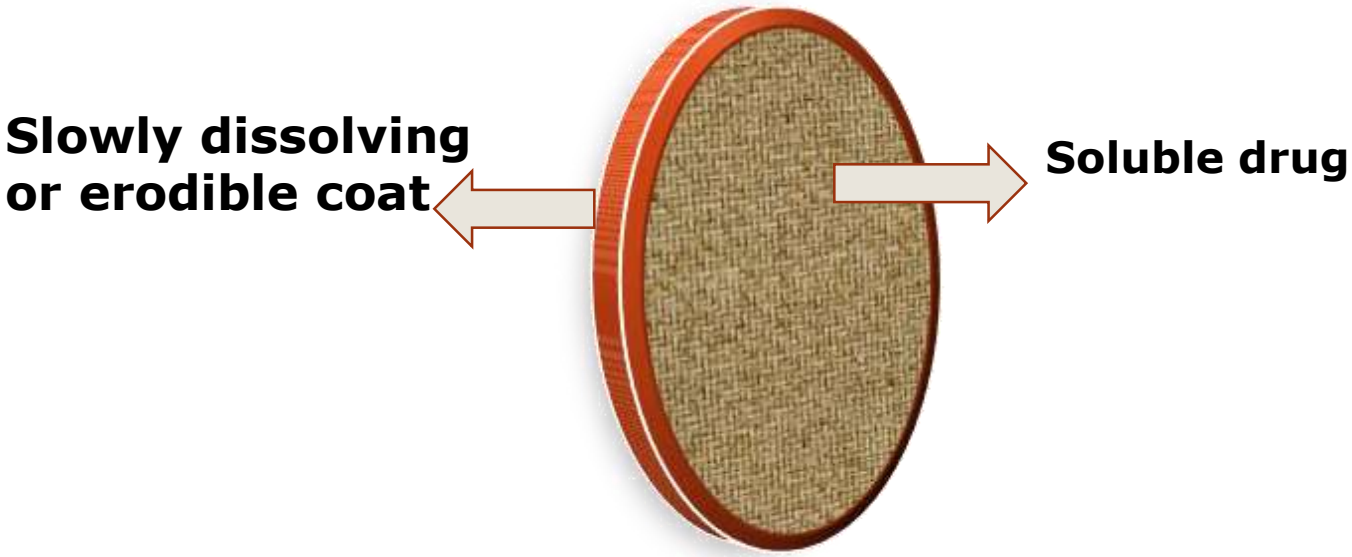


Soluble API mixed with SDM

IJD

Encapsulation

- Called as Coating dissolution controlled system since the drug encapsulated, with slowly dissolving material like cellulose, PEG, PMA (polymethylacrylates) & waxes.
- Dissolution rate of coat depends upon stability & thickness of coating.



Matrix Diffusion Types

- **Rigid Matrix Diffusion**

  Materials used are insoluble plastics such as PVP & fatty acids.

- **Swellable Matrix Diffusion**

1. Also called as Glassy hydrogels. Popular for sustaining the release of highly water soluble drugs.
2. Materials used are hydrophilic gums.

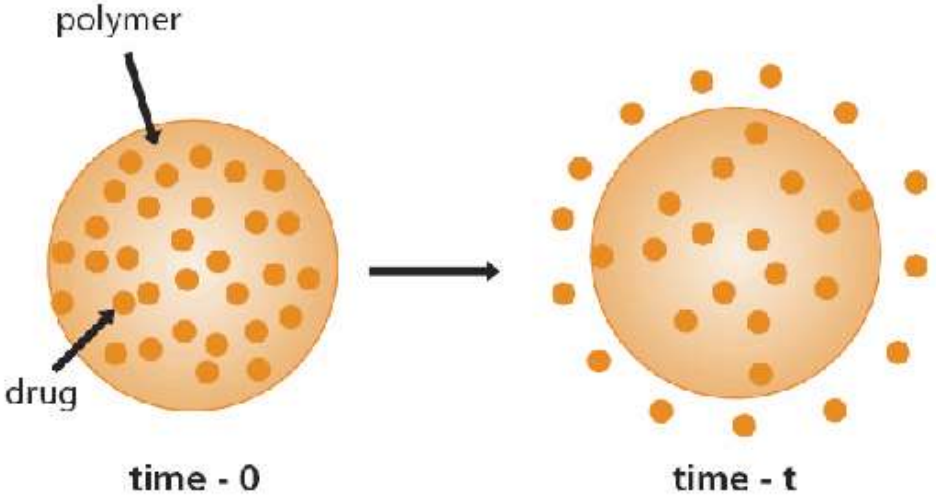
   Examples :

   Natural: **Guar gum, Tragacanth.**

   Semi-synthetic: **HPMC, CMC, Xanthum gum.**

   Synthetic : **Polyacrilamides.**

Matrix system



Rate controlling step:

Diffusion of dissolved drug in matrix.

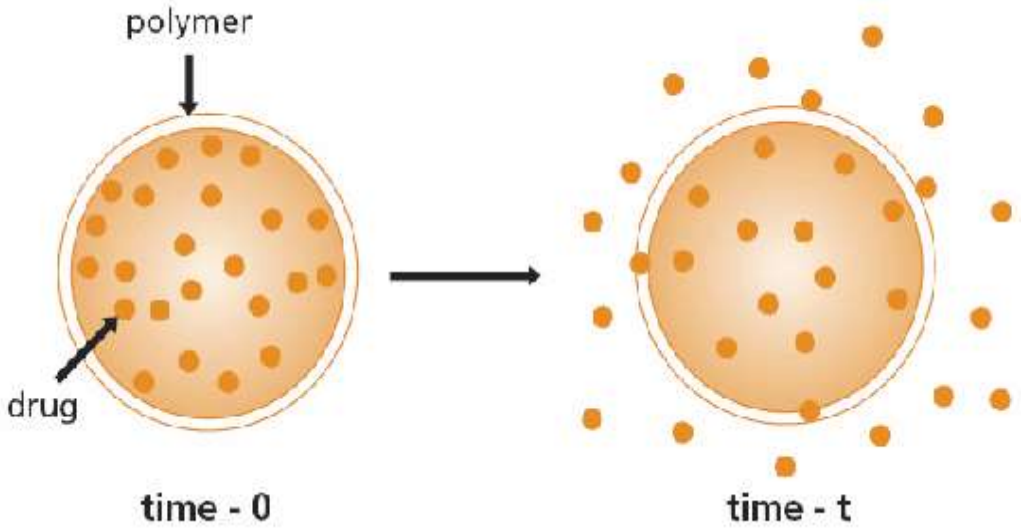
Matrix Diffusion Types

- Drug and excipients are mixed with polymers such as Hydroxypropyl methylcellulose (HPMC) and Hydroxypropyl cellulose (HPC).
- Tableted by conventional compression.
- Release from the tablet takes place by combination of :
  - water diffuses into the tablet, swells the polymer and dissolves the drug.
  - drug may diffuse out to be absorbed.

Reservoir System

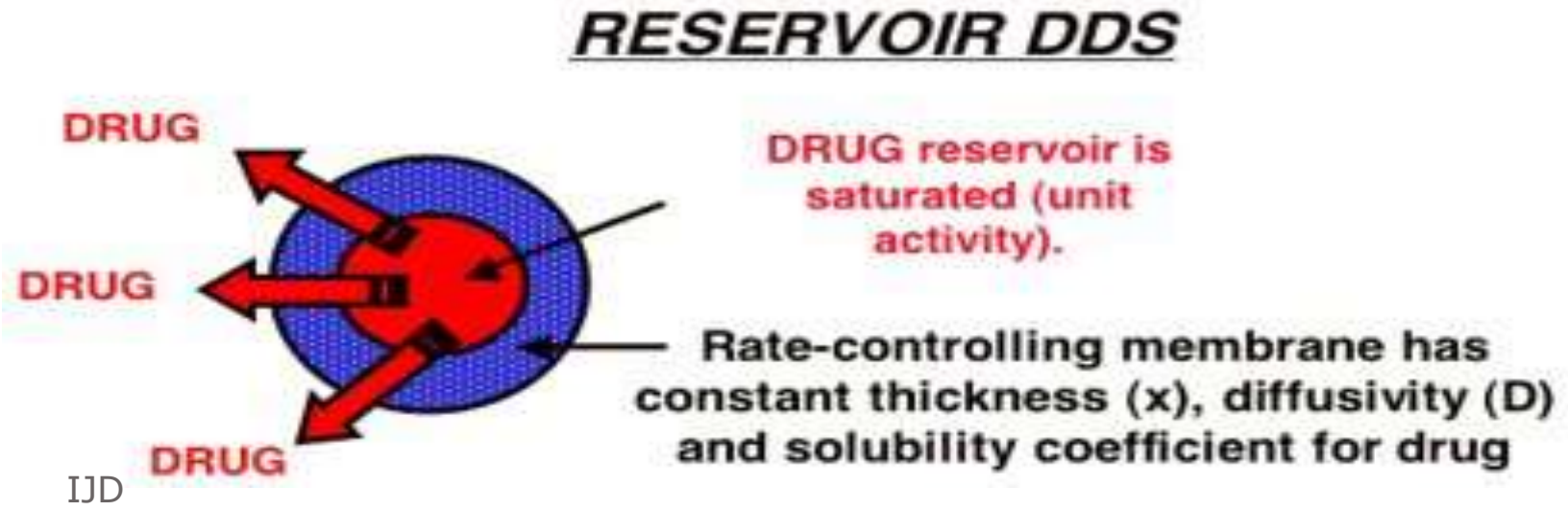
- Also called as Laminated matrix device.
- Hollow system containing an inner core surrounded in water insoluble membrane.
- Polymer can be applied by coating or micro encapsulation.
- Rate controlling mechanism - partitioning into membrane with subsequent release into surrounding fluid by diffusion.
- Commonly used polymers - HPC, ethyl cellulose & polyvinyl acetate.

Reservoir System



Rate controlling steps :

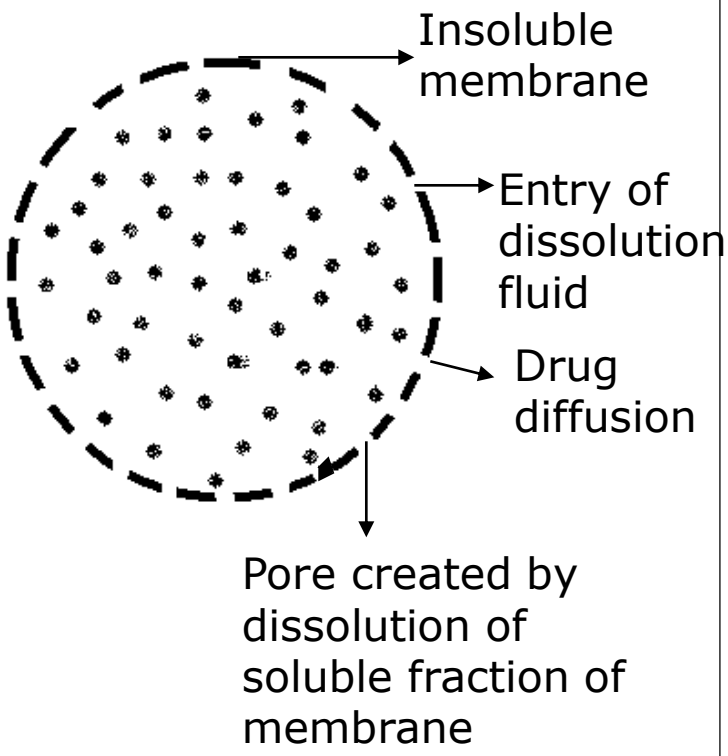
Polymeric content in coating, thickness of coating, hardness of microcapsule.



IJD

Dissolution & Diffusion Controlled Release system

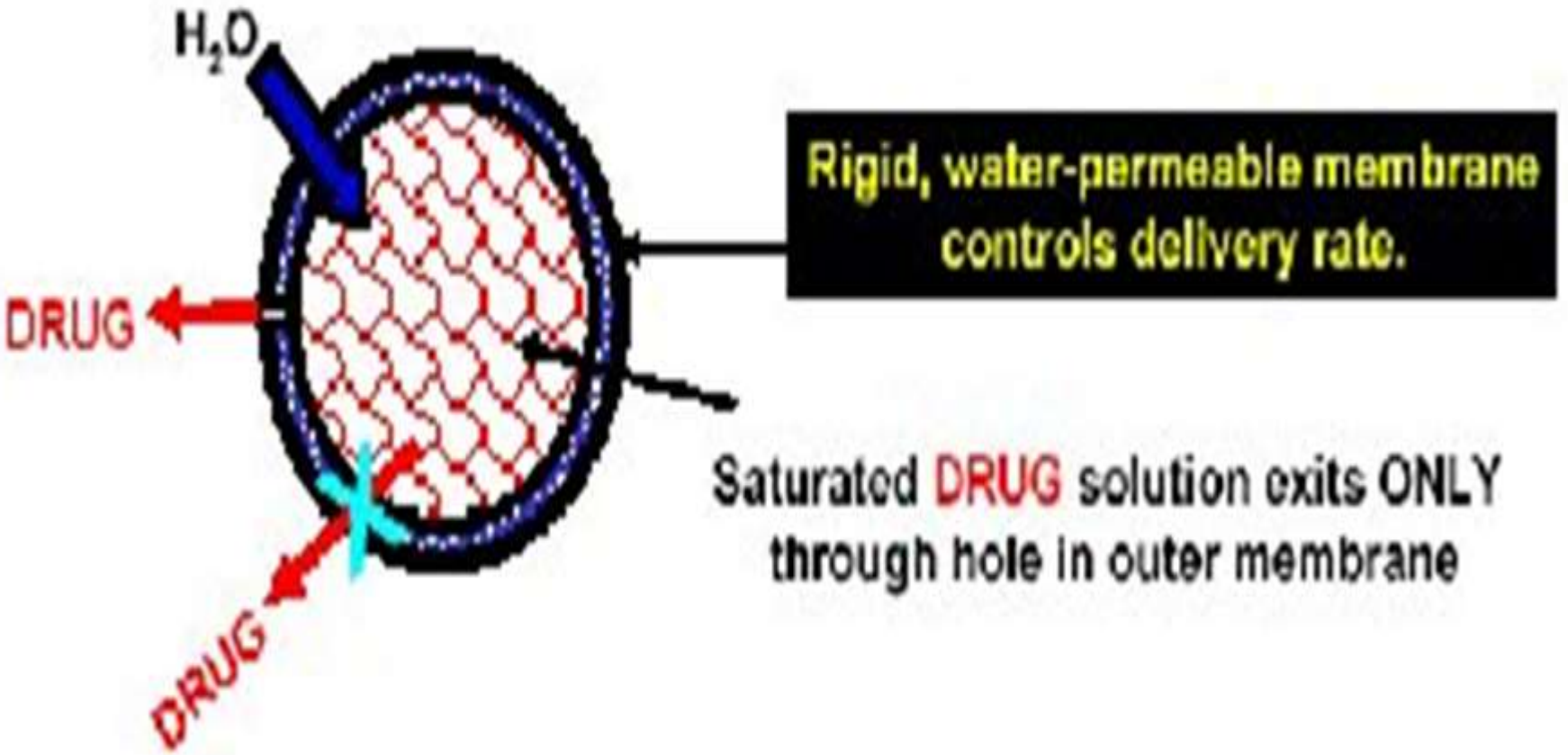
- Drug encased in a partially soluble membrane.
- Pores are created due to dissolution of parts of membrane.
- It permits entry of aqueous medium into core & drug dissolution.
- Diffusion of dissolved drug out of system.
- Ethyl cellulose & PVP mixture dissolves in water & create pores of insoluble ethyl cellulose membrane.



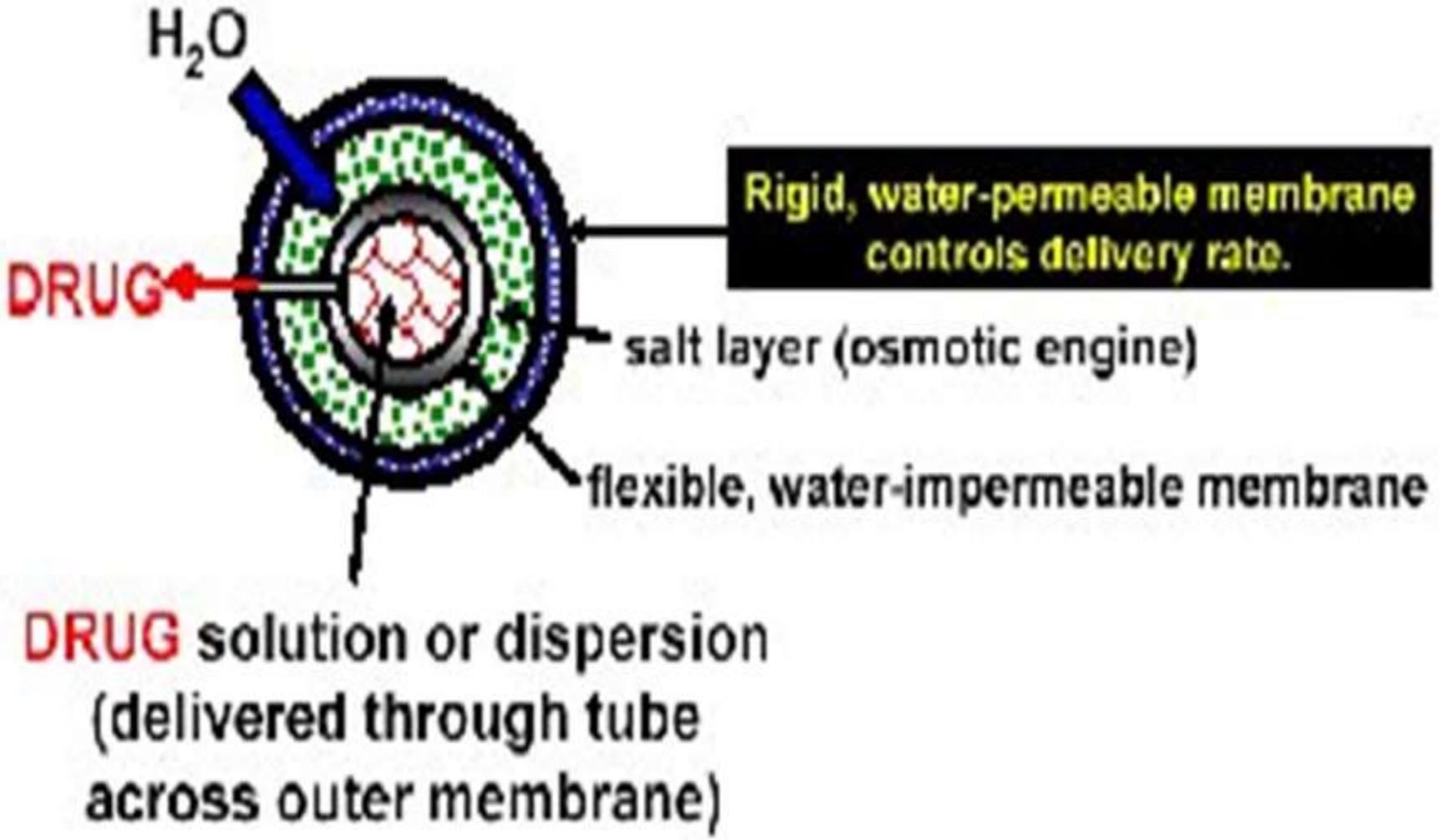
Osmotic Pressure Controlled System

- Drug may be osmotically active, or combined with an osmotically active salt (e.g., NaCl).
- Semi-permeable membrane usually made from Cellulose acetate.
- Drug is pumped out continuously because of osmotic pressure gradient.
- More suitable for hydrophilic drug.
- Provides zero order release

Osmotic Pressure Controlled System



Osmotic Pressure Controlled System



Chemically Controlled Released Systems

Systems that change their chemical structure, when exposed to biological fluids.

Mostly, biodegradable polymers, are designed to degrade as a result of hydrolysis of the polymer chains into biologically safe and progressively smaller moieties and thus releasing API.

It is of two types;

- Erodible Systems
- Pendent Chain System

Chemically controlled released Systems

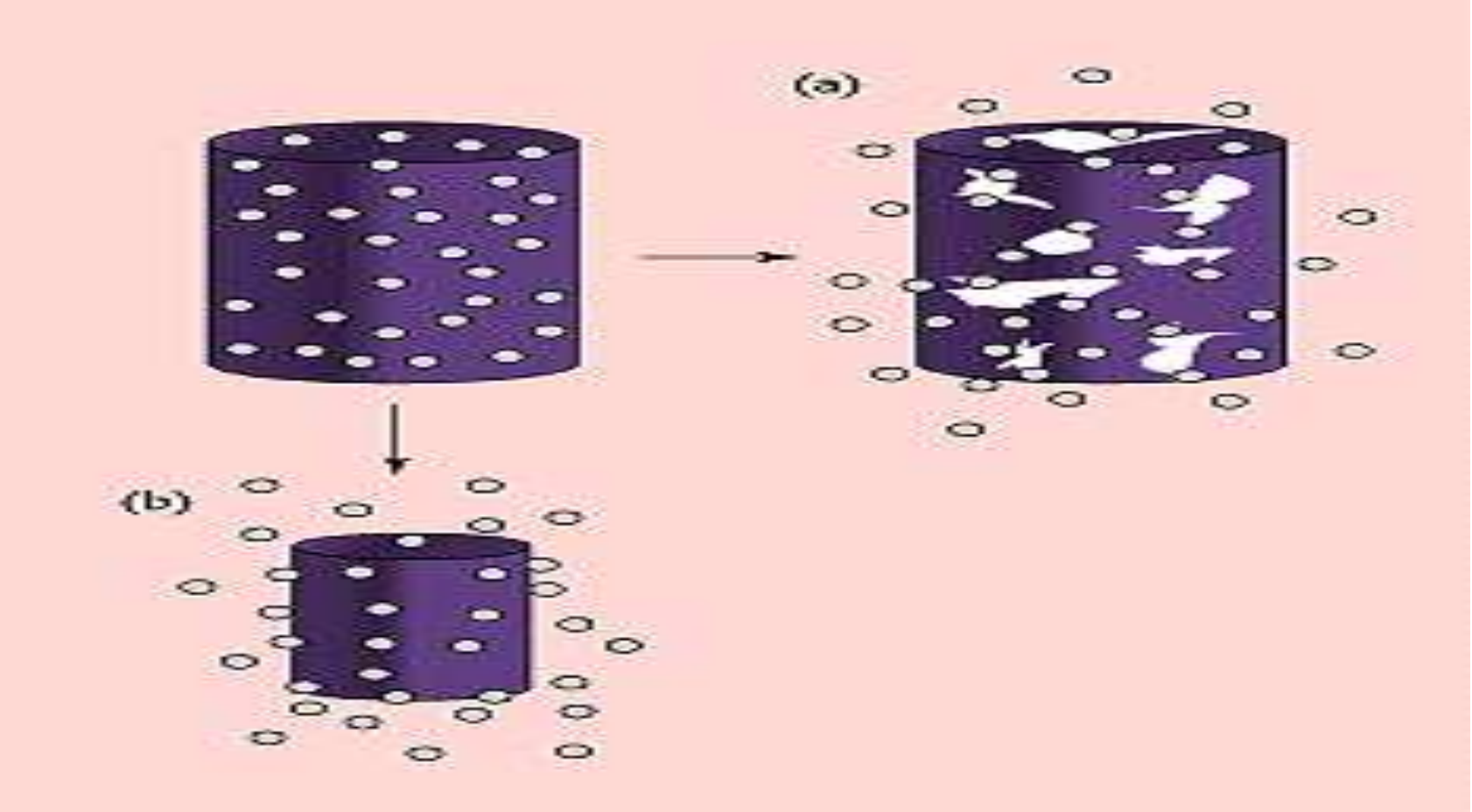
Erodible Systems

Two types;

Bulk Erosion: Polymer degradation may occur through bulk hydrolysis.

Surface Erosion: Degradation occur at the surface of the polymers e.g. Polyorthoesters & Polyanhydrides , resulting a release rate is proportional to the surface area of the delivery system.

Chemically controlled released Systems



Drug delivery from (a) bulk-eroding (b) surface-eroding biodegradable systems

Chemically Controlled Released Systems

Pendent Chain System

Consist of linear homo or copolymers with drug attached to its backbone chains. e.g. Hydroxy propyl methyacrylamide etc.

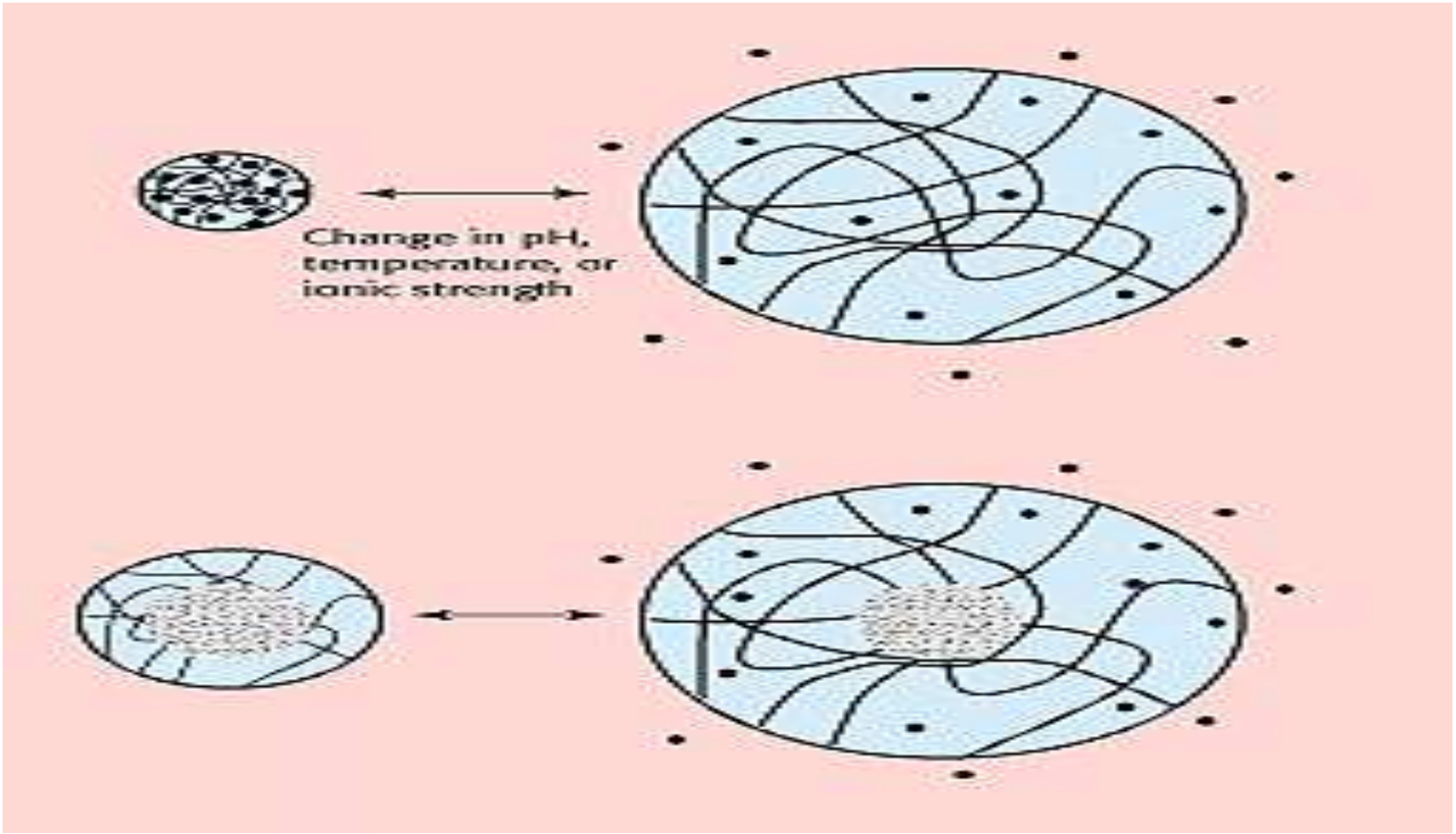
- ✓ Release drug by hydrolysis or enzymatic degradation of the linkages
- ✓ Follows zero order kinetics, cleavage of the drug is rate determining step.

Hydrogels

Three dimensional structures composed of primarily hydrophilic polymers having chemical or physical cross links which provides a network structure to hydrogels.

Insoluble because of network structure and provides desirable protection of liable drugs, peptides and proteins

Hydrogels



Drug delivery from matrix swelling-controlled release systems

Ion-Exchange Resins Controlled Release Systems

Such system provide control release of an ionic (ionisable) drug.

Ionisable drug is absorbed on ion-exchange resins granules and then granules are coated with water permeable polymers using spray drying technique.

H^+ Cl^- in the gastric fluid are exchange with cationic and anionic drugs from the ion-exchange resins.

Characteristics of Drugs Unsuitable for Peroral Sustained Release

Characteristics	Drugs
Not effectively absorbed in the lower intestine	Riboflavin, Ferrous Sulfate
Absorbed and extracted rapidly (short biologic half life i.e. < 1Hr)	Penicillin G, Furosemide
Long biologic half life i.e. > 12 Hr	Diazepam
Large doses required (> 1G)	Sulfonamides, Sucralfate
Drug with low therapeutic index	Digitoxin, Warferrin, Phenobarbital
Precise dosage to individual is required	Anticoagulants
No clear advantage for sustained release	Griseofulvin
If the pharmacological activity of the active compound is not related to its blood levels.	

Kinetics

Mathematical models are used to evaluate kinetics and mechanism of drug release from the tablets.

1. **Zero Order Release Model**
2. **First Oder Release Model**
3. **Hixson-Crowell Release Model**
4. **Higuchi Release Model**
5. **Korsmeyer-Peppas Release Model**

The model that give highest regration value "**r^2**" is considered as the best fit of the release data.

Zero Order Release Kinetics

Release kinetics independent of concentration of drugs in the dosage form is described as Zero Order Release Kinetics. Equation for Zero order release is;

$$Q_t = Q_o + K_o t$$

Where

Q_t= initial amount of drug

Q_o = cumulative amount of drug at time "t"

K_o = Zero order release constant

t = time in hours

First Order Release kinetics

Release kinetics dependent on the concentration of drugs in the dosage form is described as First Order Release Kinetics. Equation for First Order release is;

$$\log Q_t = \log Q_o + K_o t/2.303$$

Where

Q_t= initial amount of drug

Q_o = cumulative amount of drug at time "t"

K_o = First order release constant

t = time in hours

Hexson-Crowell Release Model

Describes drug release by dissolution and with changes in surface area and diameter of particles or tablets;

Its equation is;

$$\sqrt[3]{Qo} - \sqrt[3]{Qt} = K_{HC}.t$$

Where

Q_t= initial amount of drug

Q_o = cumulative amount of drug at time "t"

K_{HC} = Hexson-Crowell release constant

t = time in hours

Higuchi Release Model

Model suggests that the drug is release by diffusion.

Its equation;

$$Q = K_H t^{1/2}$$

Where

Q = cumulative amount of drug at time "t"

K_H = Higuchi release constant

t = time in hours

Korsmeyer-Pappas Release Model

Release kinetics dependent on the concentration of drugs in the dosage form is described as First Order Release Kinetics. Equation for First Order release is;

$$F = (M_t / M) = K_m t^n$$

Where

F = Fraction of drug release at time "t"

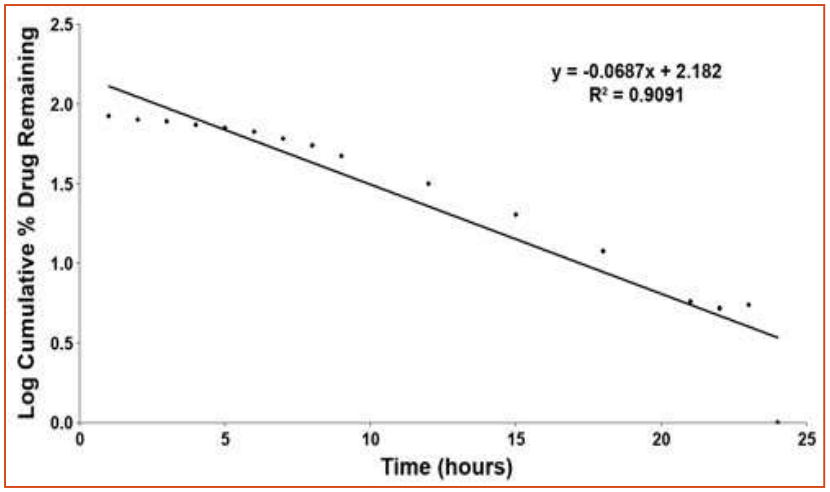
M_t = Amount of drug release at time "t"

M = total amount of drug in dosage form

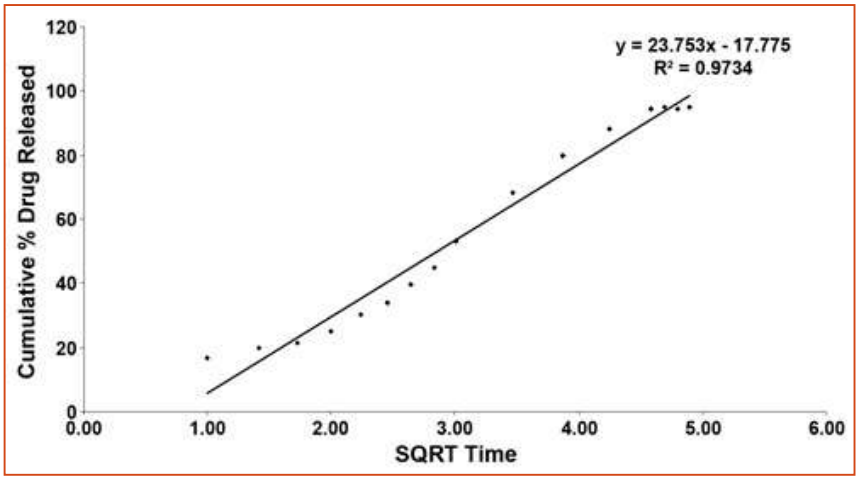
K_m = Kinetic constant

n = Diffusion or release exponent

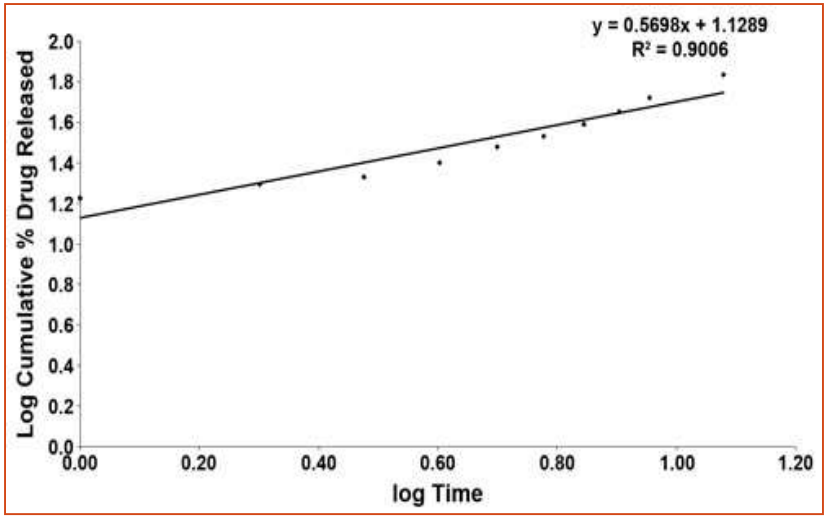
t = time in hours



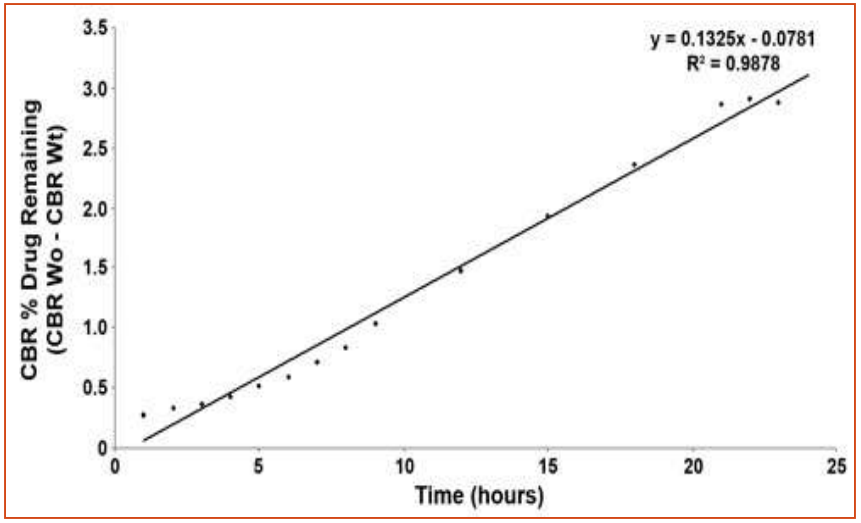
First Order Kinetics



Higuchi Model Kinetics

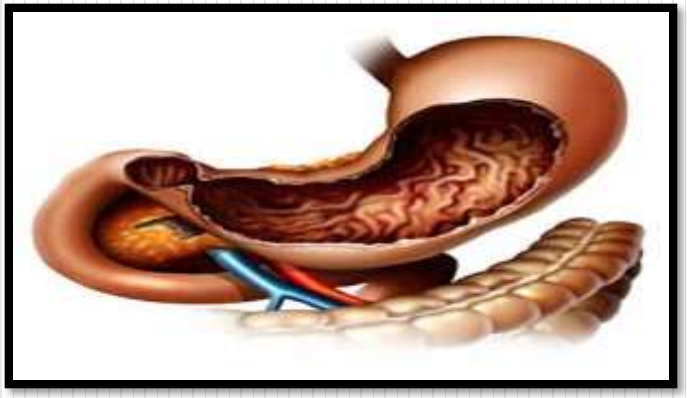


Korsmeyer –Peppas Kinetics



Hexson-Crowell Kinetics

GASTRORETENTIVE DRUG DELIVERY SYSTEM



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Introduction of Gastroretentive Drug Delivery System

Gastroretentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs. Thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. The buoyant dosage unit enhances gastric residence time(GRT) without affecting the intrinsic rate of emptying.

Need for Gastroretentive Drug Delivery System.

- Drugs acting locally in the stomach
  E.g. Antacids and drugs for H. Pylori viz., Misoprostol
- Drugs that are primarily absorbed in the stomach
  E.g. Amoxicillin
- Drugs that is poorly soluble at alkaline Ph
  E.g. Furosemide, Diazepam, Verapamil, etc.
- Drugs with a narrow window of absorption
  E.g. Cyclosporine, Methotrexate, Levodopa, etc.
- Drugs which are absorbed rapidly from the GI tract.
  E.g. Metonidazole, tetracycline.
- Drugs that degrade in the colon.
  E.g. Ranitidine, Metformin HCl.
- Drugs that disturb normal colonic microbes
  E.g. antibiotics against Helicobacter pylori

Advantages Of Gastroretentive Delivery Systems

- Improvement of bioavailability and therapeutic efficacy of the drugs and possible reduction of dose

  e.g. Furosemide

- Maintenance of constant therapeutic levels over a prolonged period and thus reduction in fluctuation in therapeutic levels minimizing the risk of resistance especially in case of antibiotics.

  e.g. b-lactam antibiotics (penicillins and cephalosporins)

- Retention of drug delivery systems in the stomach prolongs over all.

- Gastrointestinal transit time thereby increasing bioavailability of sustained release delivery systems intended for once-a-day administration.

  e.g. Ofloxacin

Limitations Of Gastroretentive Delivery Systems

- Require a higher level of fluids in the stomach.
- Not suitable for Drugs that…
  - Have solubility problems in gastric fluid.E.g. phenytoin
  - Cause G.I irritation. E.g. NSAIDS.
  - Are unstable in acidic environment.

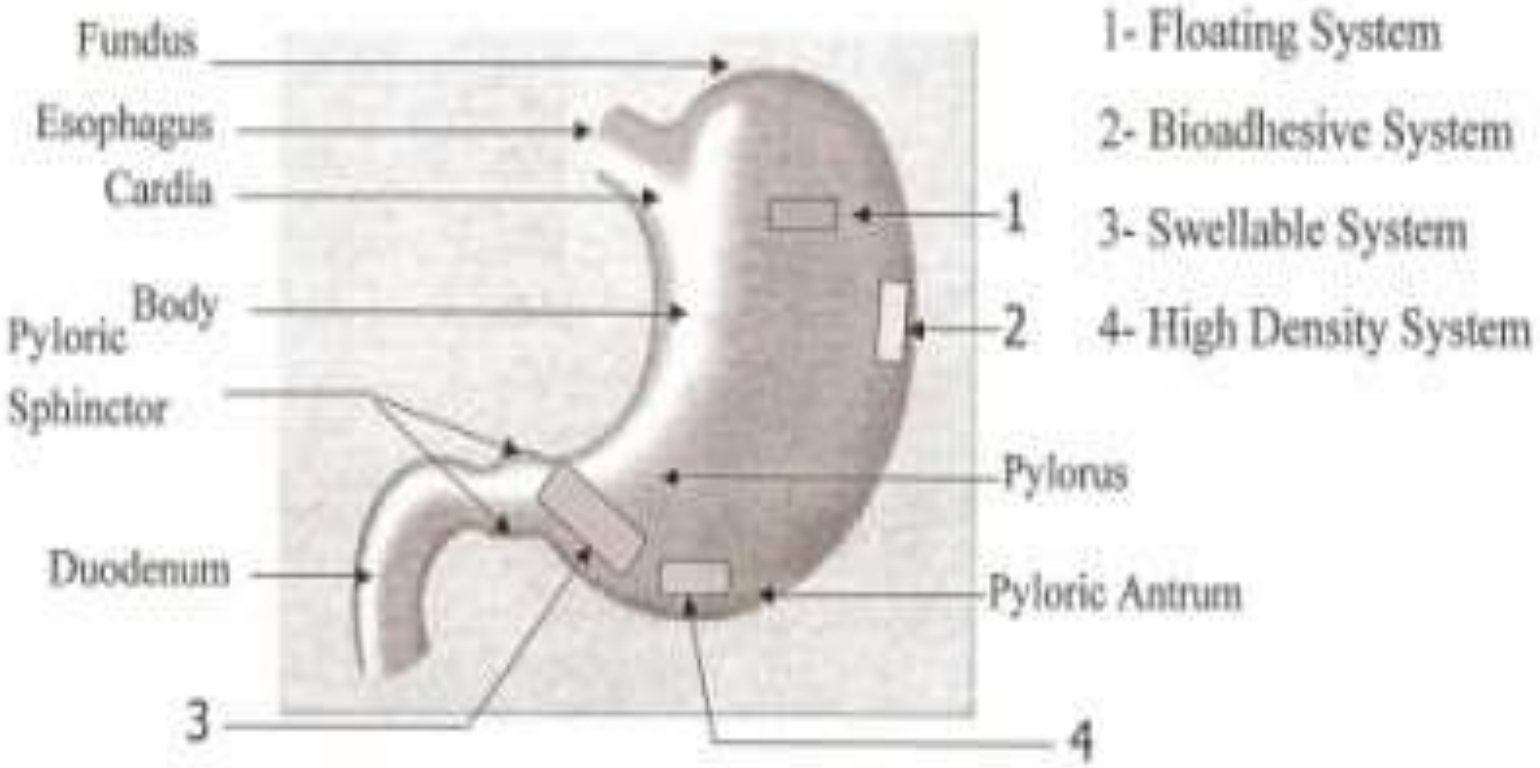
- Drugs intended for selective release in the colon
  E.g. 5- amino salicylic acid and corticosteroids etc.

- The mucus on the walls of the stomach is in a state of constant renewal, resulting in unpredictable adherence.

Physiology of Stomach

- The main function of stomach is to store food temporarily, grind it and then release it to duodenum.
- The end portion of stomach and starting of intestine means duodenum is joined by Pyloric sphincter, which a valve type unit and it can open maximum upto 12.8±7 mm. So dosage forms having higher size are retained more time in stomach.
- Gastric fluid volume in stomach is minimum of 25-50 ml at resting stage
- pH of gastric fluid is generally 1.5–2 in fasted state and may raised upto 2–6 in fed condition but it come back down soon by secretion of more gastric acid.
- Gastric Retention Time of any dosage form is generally 1-2.5 hours in fasted state but in fed condition GRT is increased, especially with fatty food.
- Food is passed out from stomach to intestine by gastric motility. There is specific motility pattern in fasted condition called as Migrating Myoelectric Complex (MMC) cycle. MMC is subdivided into four phases.

PHYSIOLOGY OF GASTROINTESTINAL TRACT fig no. 2



STOMACH

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Factors Affecting Gastric Retention

- **Density-** GRT is a function of dosage form buoyancy that is dependent on the density.
- **Size-** Dosage form units with a diameter of more than 7.5mm are reported to have an increased GRT compared with those with a diameter of 9.9mm.
- **Shape-** Better GRT is possessed by tetrahedron and ring shaped devices.
- **Single or multiple unit formulation-** Multiple unit formulations show a more predictable release profile and insignificant impairing of performance due to failure of units
- **Fed or unfed state-** under fasting conditions, the GRT of the unit can be expected to be very short. However, in the fed state the 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.

Factors Affecting Gastric Retention

- **Caloric content-** GRT can be increased by 4 to 10 hours with a meal that is high in proteins and fats
- **Frequency of feed-** The GRT can increase, when successive meals are given.
- **Gender-**GRT in males (3.4±0.6 hours) is less compared with female (4.6±1.2 hours)
- **Age-** Elderly people, especially those over 70, have a significantly longer GRT.
- **Posture-** GRT is decreased while standing and lying on the right side where as lying on the left side GRT is increased
- **Drug-** Anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramide and cisapride
- **Disease state-** Gastric ulcer, diabetes, hypothyroidism increase GRT. Hyperthyroidism, duodenal ulcers decrease GRT.

APPROACHES FOR PROLONGING THE GASTRIC RESIDENCE TIME

- **Floating systems(FS)**

Non-effervescent systems

Effervescent systems

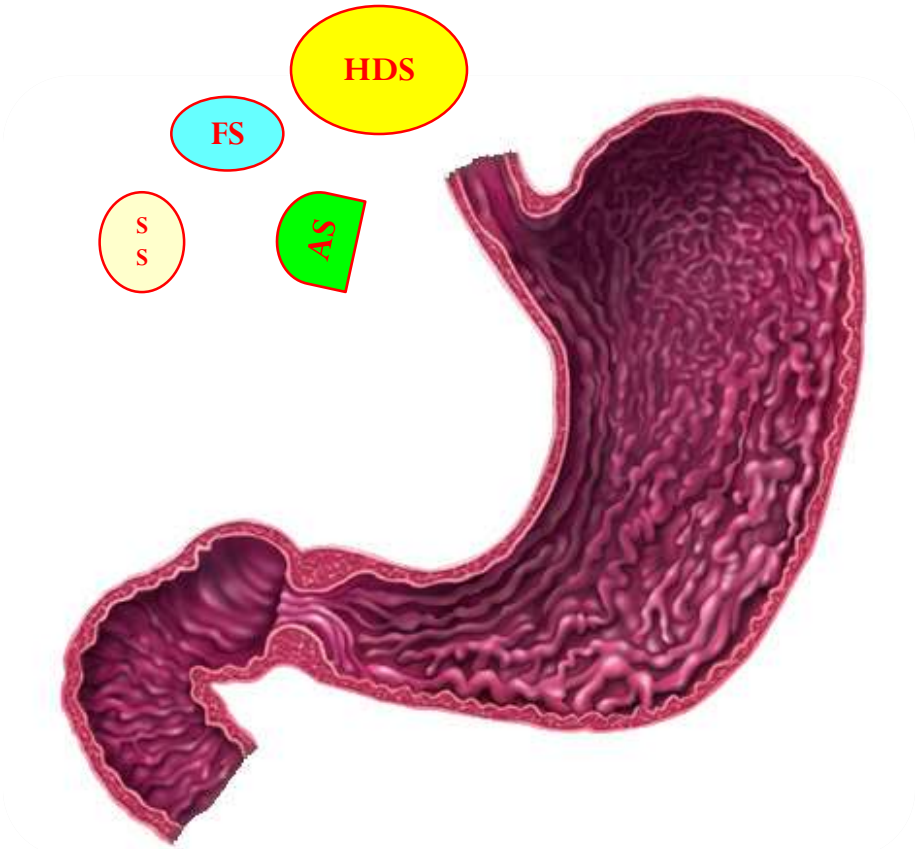
Raft forming system

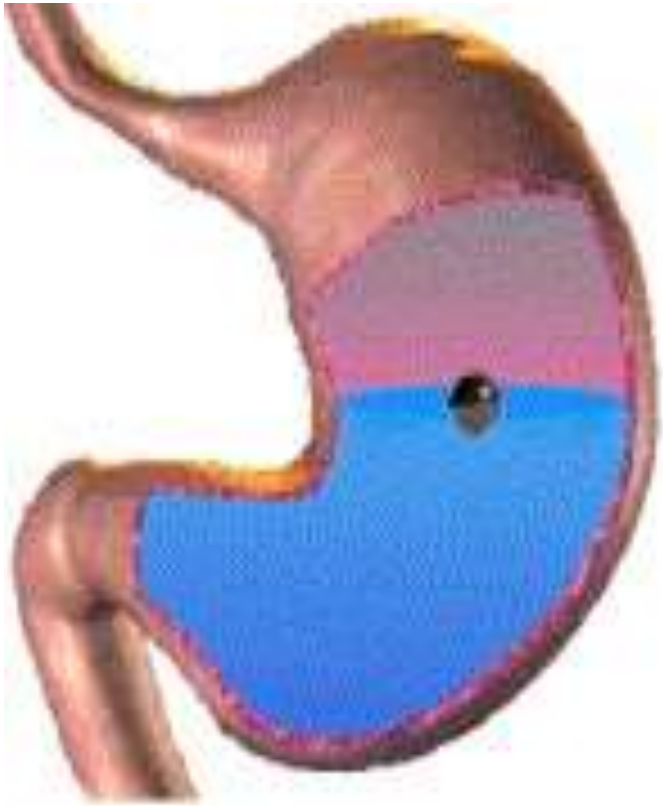
- **High-density systems(HDS)**
- **Swelling and expanding systems.(SS)**

Swelling systems

Unfolding systems

- **Mucoadhesive & Bioadhesive systems(AS)**





Intragastric floating system
(density > 1 g.cm^{-3})

High-density system
(density > 1 g.cm^{-3})

Floating drug delivery systems

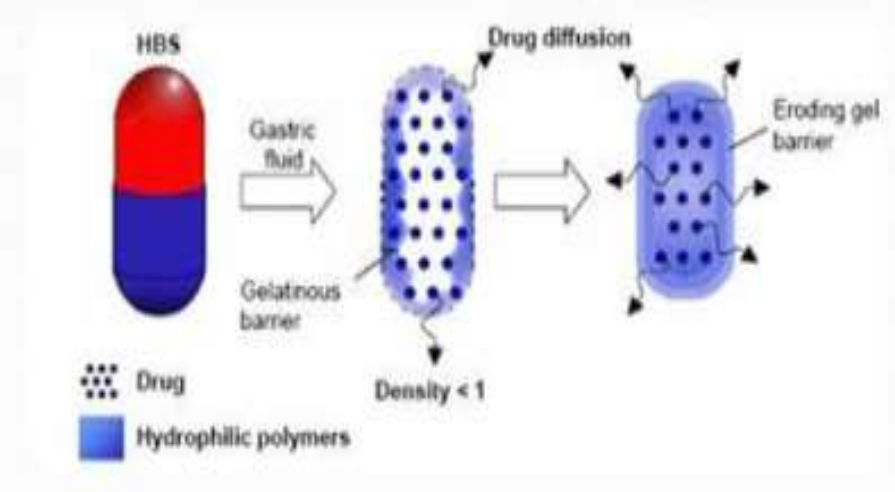
- Floating drug delivery systems is one of the important approaches to achieve gastric retention to obtain sufficient drug bioavailability.
- This delivery systems is desirable for drugs with an absorption window in the stomach.
- This have a bulk density less then gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period
- The drug is released slowly as a desired rate from the system.

The major requirements for floating drug delivery system

- It should release contents slowly to serve as a reservoir.
- It must maintain specific gravity lower than gastric contents (1.004 – 1.01 gm/cm3).
- The low density can be provided by the entrapment of air (e.g. hollow chambers) or by the incorporation of low density materials (e.g. fatty materials or oils)
- It must form a cohesive gel barrier.

Hydrodynamically BALANCED SYSTEMS

- These systems are single unit dosage forms containing one or more gel forming hydrophilic polymers such as HPMC, HEC etc



- Usually drug is mixed with a polymer and administered in gelatin capsules. These capsules readily dissolve in gastric fluid. The hydration and swelling of surface polymers produces a floating mass

Floating – a low density approach or Hydro-dynamically balanced systems

This system have a bulk density lower than gastric fluids and thus remain buoyant (3- 4 hours) in the stomach without affecting the gastric emptying rate for a prolonged period of time.

Mechanism

The system is floating on the gastric contents

↓

The drug is released slowly at a desired rate from the stomach

↓

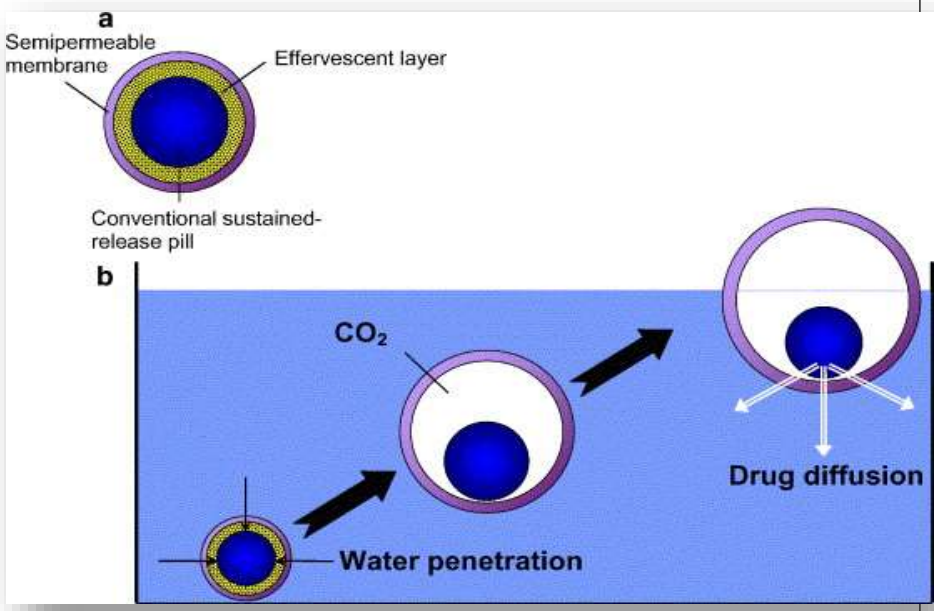
After the release of the drug, the residual system is emptied from the stomach.

↓

This results in an increase in the gastric retention time and a better control of fluctuations in the plasma drug concentration in some cases.

Effervescent systems

- These formulations contain carbonates or bicarbonates which generates CO_2 due to their reaction with acids either as natural gastric acid or coformulated as citric acid, tartaric acid



In case of single unit systems, effervescent substances are introduced in the hydrophilic polymers and CO_2 bubbles are trapped in the swollen matrix.

Types of Effervescent systems

- **Matrix tablets-** is prepared by incorporating bicarbonates in matrix forming hydrocolloid gelling agent like HPMC, chitosan, alginate or other polymers and drug.

- **Floating pills** system comes in contact with water or gastric fluid which penetrate inside through swellable membrane and CO2 gas is generated by reaction of inner effervescent mixture. As CO2 gas not goes out from outer membrane makes a balloon like system which can float.
- **Porous alginate beads-** are prepared by incorporating NaHCO3 and CaCO3.

Bicarbonates are added with stirring into aqueous solution of sodium alginate

↓

then mixture is added to solution of Calcium chloride with 10% acetic acid.

↓

due to acetic acid and bicarbonate, CO2 gas is generated and simultaneously gelling of beads by calcium ions are occurring

↓

producing the beads CO2 which goes out during stirring and creating porous structures in sodium alginate beads.

Non-Effervescent systems

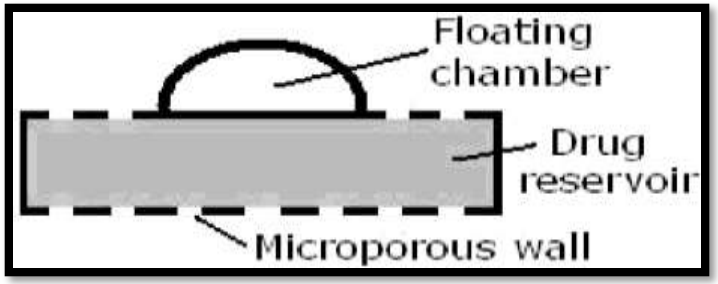
"Excipients are used gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers (polycarbonate, polyacrylate and polystyrene.)"

Single unit systems

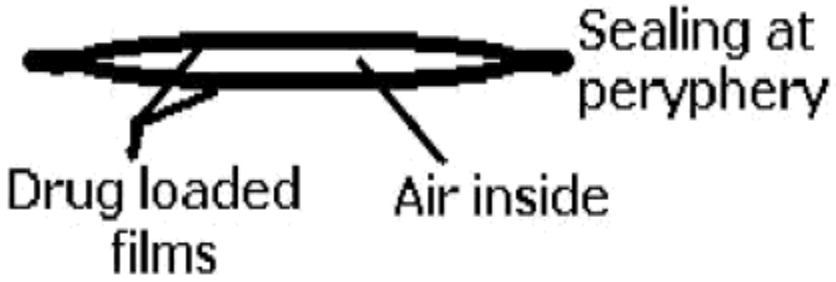
- **Floating tablet -** Matrix tablet were prepared by incorporating gel forming hydrocolloids like HPMC (low viscosity grade are use for floating purpose)

- **Floating capsule-**It is a hard gelatin capsule containing drug with high level of one or more highly swellable gel forming hydrocolloids (20-75%) like HPMC, HPC, HEC, Na-CMC etc.

Micro-porous reservoir-This device comprised of a drug reservoir encapsulated in microporous compartment having pores on its surface.

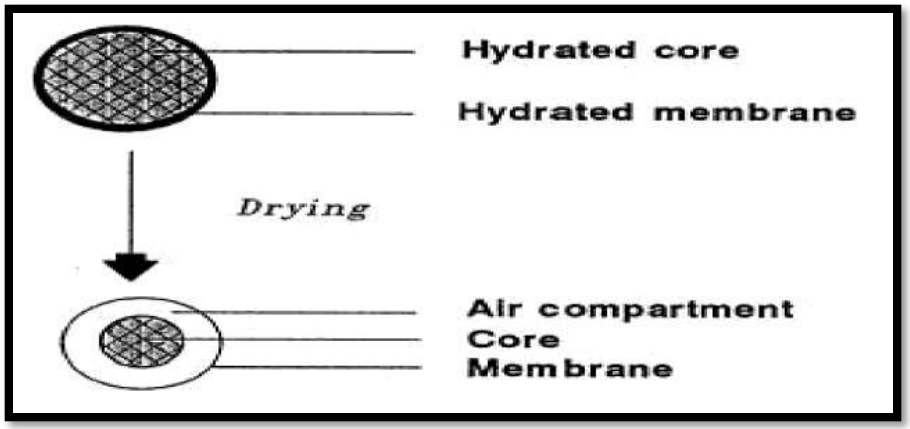


- **Multi-layer flexible film:** The device consist of two films which are sealed together along their periphery and in such a way as to entrap some air between two films and so make air pocket which imparts buoyancy.

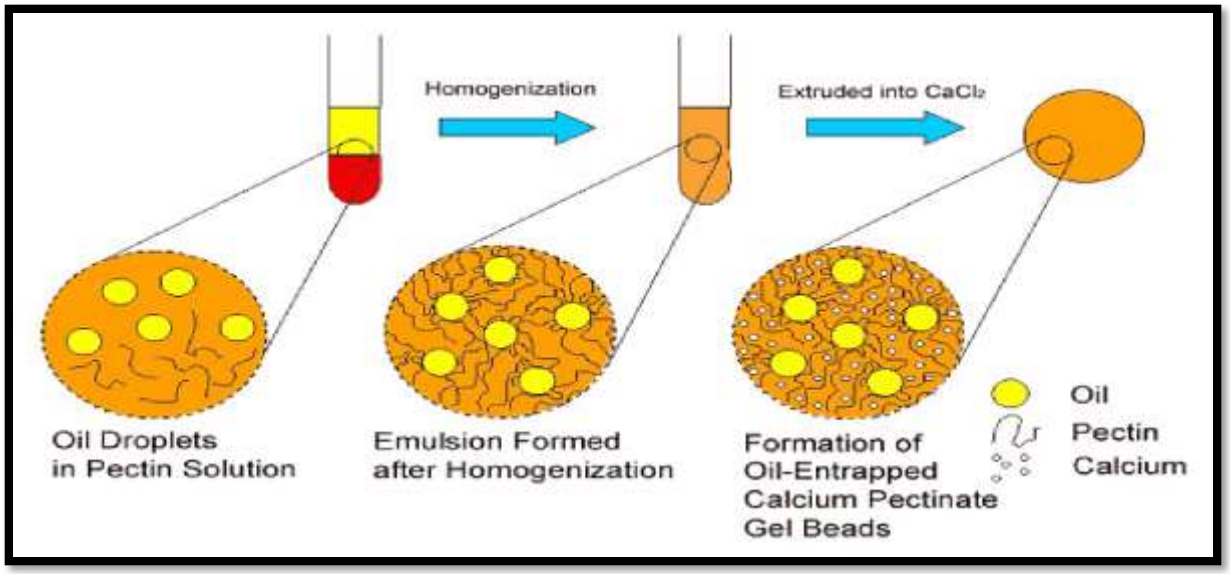


Multiple unit systems

- **Bead system**
- **Calcium alginate beads-** are produce by dropping sodium alginate solution into aqueous solution of calcium chloride. So due to chemical reaction named as Ionotropic gelation, gelation take place and forms solid spherical gel beads, which are separated from solution.
- **Alginate beads with air compartment**



Oil entrapped gel beads



- **Casein-gelatin floating beads-** Casein has emulsifying property and thus cause air bubble incorporation that act as air reservoir for floating system.

Microspheres -are characteristically free flowing powders consisting of proteins or synthetic polymers (size less than 200 micrometer). Solid biodegradable microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for controlled release of drugs.

Mechanism

Microspheres come in contact with gastric fluid

↓

The gel formers, polysaccharides, and polymers hydrate to form a colloidal gel barrier

↓

That controls the rate of fluid penetration into the device and consequent drug release.

↓

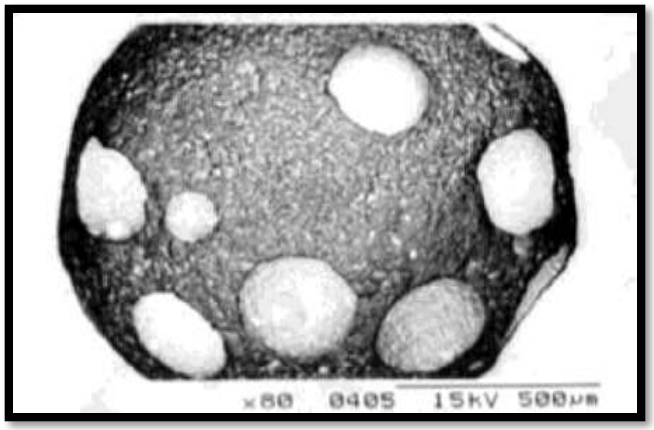
As the exterior surface of the dosage form dissolves, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer.

↓

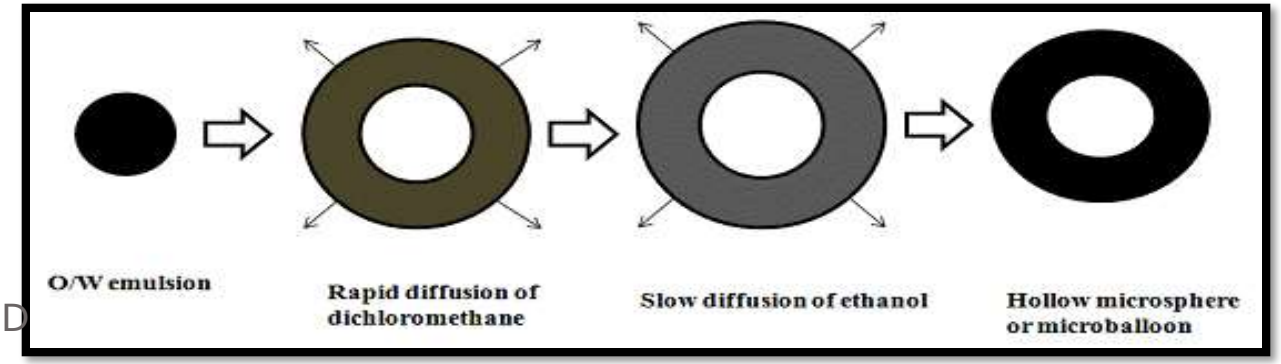
The air trapped by the swollen polymer lowers the density and confers buoyancy to the microspheres.

↓

Hollow microspheres -using polymers like polycarbonates have been prepared using solvent evaporation technique. After preparation of microsphere, organic solvent evaporates from it creating holes inside microsphere.



Microballoons -are the hollow microspheres which are completely hollow from inside forming cavity inside and drug loaded in their outer shells are prepared by an emulsion solvent diffusion method.



Raft forming systems

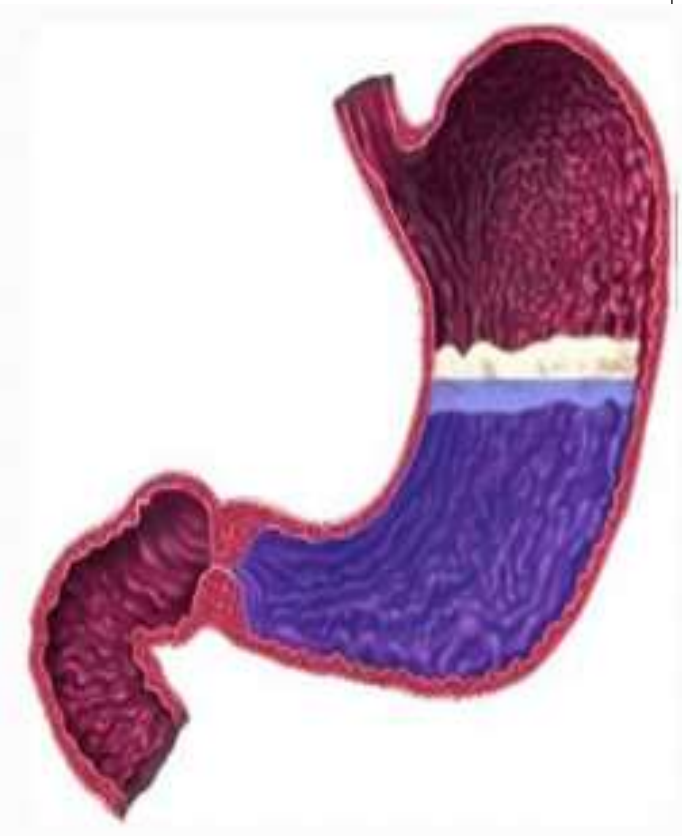
Usually this contains a gel-forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO2 to make the system less dense to float on the gastric fluids.

Mechanism

The formation of viscous gel in contact with gastric fluids

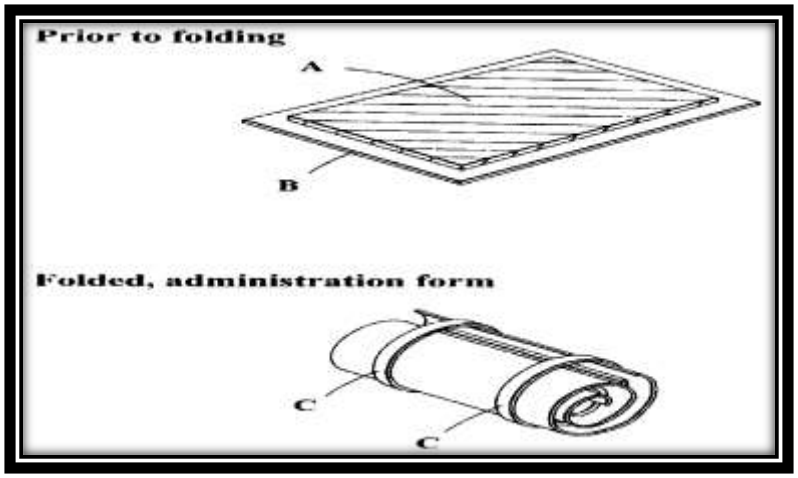
where in each portion of the liquid swells forming a continuous layer called RAFT.

This raft floats on gastric fluids because of a low density created by the formation of CO2.



- **Raft forming systems-** drug delivery for antacids and treatment of gastrointestinal infection and disorders.

Expandable approach or Plug type systems



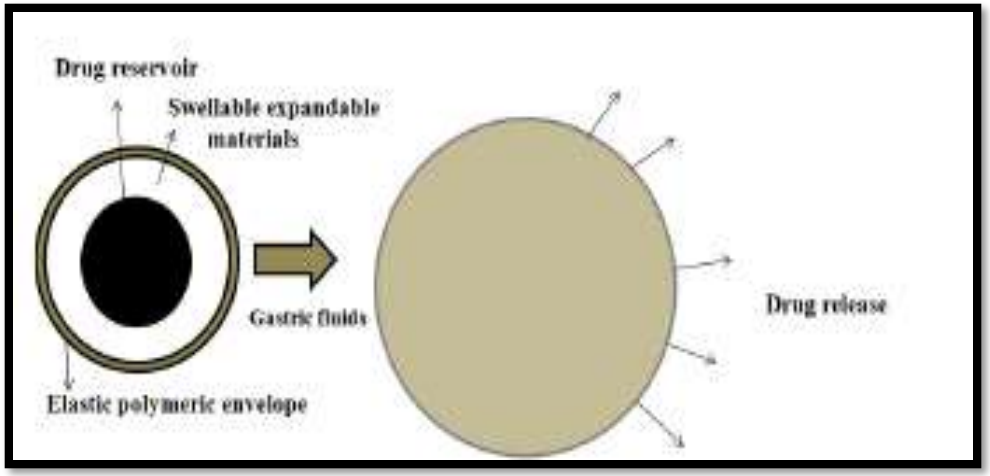
- They achieve larger size in stomach and size of whole system goes beyond the size of pyloric sphincter and thus the system retains in stomach.
- The expandable GRDFs are usually based on three configurations:

✓ A small collapsed configuration which enables sufficient oral intake

✓ Expanded form that is achieved in the stomach and thus prevents passage through the pyloric sphincter.

✓ A smaller form that is achieved in the stomach when the retention is no longer required i.e. after the GRDF has released its active ingredient, thereby enabling evacuation.

- **Swelling systems**- are generally matrix system containing hydrocolloids which by action of hydration and osmosis get swelled. **There are mainly 3 layers**: 1st swelling, 2nd diffusion and 3rd erosion layer.

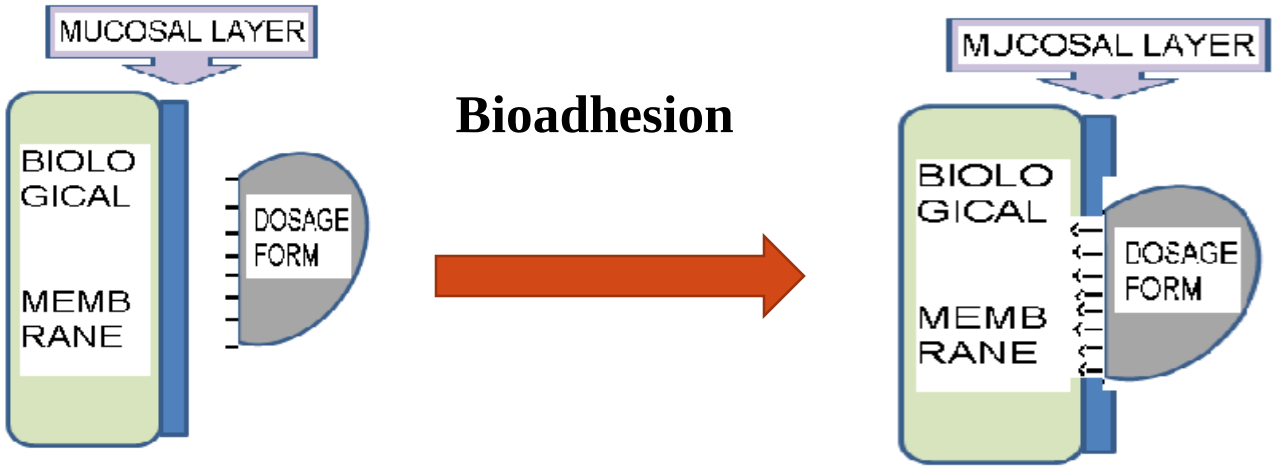


- **Unfolding systems**- Unfolding systems are systems which are actually of larger size but they are folded to decrease size and kept in capsules. In stomach these systems comes out of capsules and unfolds to larger size.

The important factor for unfolding system is shape memory. They should have sufficient shape memory such that they retain their unfolded (expanded) shape in stomach against gastric motility and not get folded again and escape out till the desired time interval.

BIO MUCO-ADHESIVE APPROACH

- Adhesive systems may adhere to mucin, which is cytoprotective gel layer on membrane of stomach wall or adhere to epithelial cells. And thus due to adhesiveness in stomach wall, retain in stomach.
- A bio/muco-adhesive substance is a natural or synthetic polymer (Carbopol, chitosan,Polymethyl vinyl ether, tragacanth, sodium alginate) capable of producing an adhesive interaction based on hydration–mediated, bonding mediated adhesion with a biological membrane or mucus lining of GI mucosa.



IJD

HIGH DENSITY APPROACH

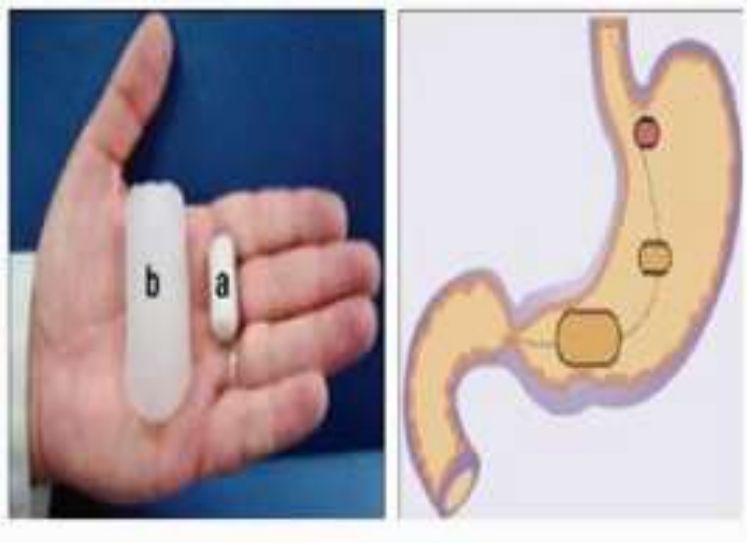
- The bottom part of stomach has curved shape (Rugae) and it is horizontally lower than the position of pyloric sphincter.

Advantage of such geometry can be taken by preparing dosage form having higher density around more than 1.004 g/cm3 (density of normal stomach content) and also capable to withstand peristaltic movement of stomach.

- These type of formulations having high density around 2-3 can be prepared by coating drug or mixing drug with heavy inert material like Iron powder, Zinc oxide, TiO_2 or $BaSO_4$ (Density = 4.9).

SUPER POROUS HYDROGELS

- These have a pore size ranging from 10 nm to 10 micrometre
- These super porous hydrogels swells to an equilibrium size because of their nature of rapid water intake by capillary wetting through their pores.
- They swell to larger size and can withstand a pressure with gastric contraction. And due to this larger size their passage through the pyloric sphincter is prevented.



MAGNETIC SYSTEM

In these systems the dosage forms contain a small internal magnet is placed externally over the abdomen. Because of this technique the dosage form with an internal magnet is retained in the stomach region until the external magnet remains.

EVALUATION OF GRDDS

IN-VITRO EVALUATION,

- **a) Buoyancy Lag Time-**It is determined in order to assess the time taken by the dosage form to float on the top of the dissolution medium, after it is placed in the medium. These parameters can be measured as a part of the dissolution test.
- **b) Floating Time-**Test for buoyancy is usually performed in SGF (Simulated Gastric Fluid) maintained at 370C. The time for which the dosage form continuously floats on the dissolution media is termed as floating time.
- **Water Uptake**

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

Where, Wt = weight of dosage form at time t

Wo = initial weight of dosage form

Marketed Products of GRDDS

Brand name	Delivery system	Drug (dose)	Company name
Valrelease®	Floating capsule	Diazepam (15mg)	Hoffmann-LaRoche, USA
Madopar® HBS (Prolopa® HBS)	Floating, CR capsule	Benserazide (25mg) and L-dopa (100mg)	Roche Products, USA
Liquid Gaviscon®	Effervescent Floating liquid alginate preparations	Al hydroxide (95 mg), Mg Carbonate (358 mg)	GlaxoSmithkline, India
Topalkan®	Floating liquid alginate Preparation	Al – Mg antacid	Pierre Fabre Drug, France
Conviron®	Colloidal gel forming FDDS	Ferrous sulphate	Ranbaxy, India
Cytotech®	Bilayer floating capsule	Misoprostol (100µg/200µg)	Pharmacia, USA
Cifran OD®	Gas-generating floating form	Ciprofloxacin (1gm)	Ranbaxy, India

CONCLUSION

It may be concluded that Gastroretentive drug delivery offers various potential advantages for drug with poor bioavailability due their absorption is restricted to the upper gastrointestinal tract (GIT) and they can be delivered efficiently thereby maximizing their absorption and enhancing absolute bioavailability.