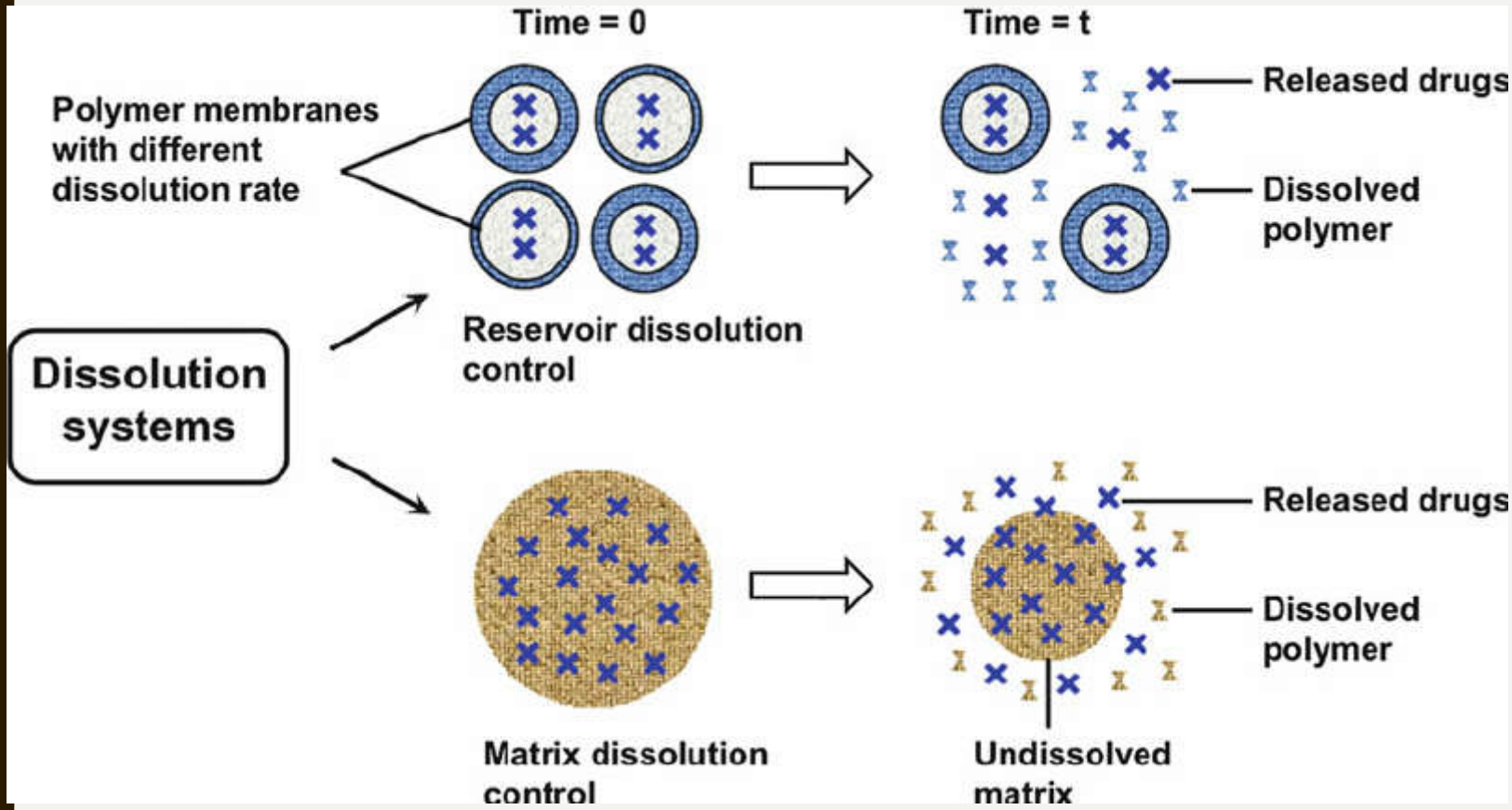
Oral Controlled Drug Delivery Systems

WEEK 12

- 1) Dissolution Controlled Systems
  - A) Via encapsulation
  - B) Via Matrix
- 2) Diffusion Control Systems
  - A) Reservoir Systems
  - B) Matrix Systems
- 3) Diffusion and Dissolution Controlled Systems
- 4) Systems using ion exchange resins
- 5) pH Independent Systems
- 6) Osmotic Controlled Release Systems
- 7) Density Adjusted Controlled Release Systems

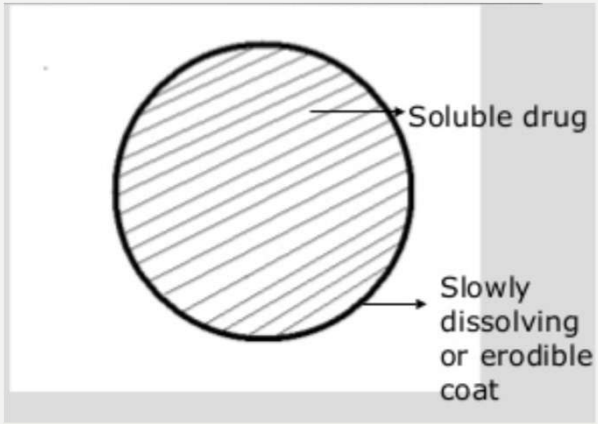
1. DISSOLUTION CONTROLLED SYSTEMS



Dissolution Controlled systems

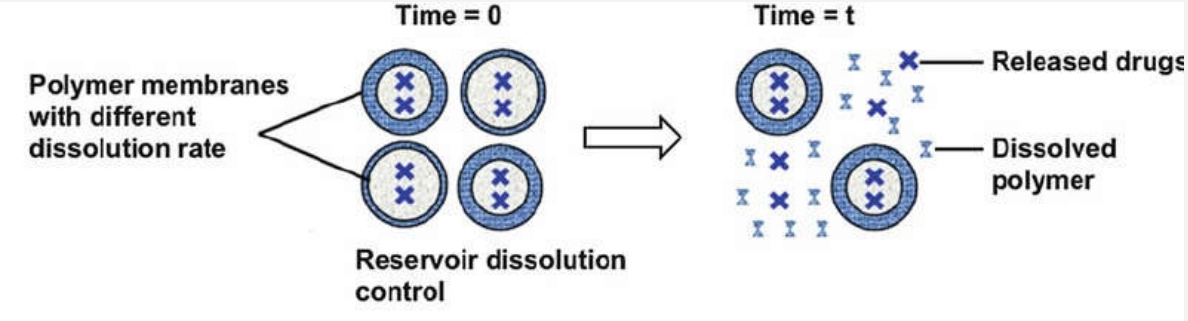
A) Dissolution control via encapsulation

In such systems, the active substance particles or granules are generally coated with a slowly dissolving material.



The time required for dissolution of the coating depends on ;

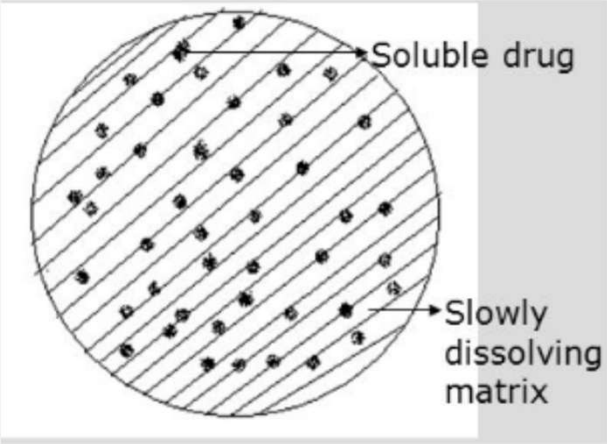
- Thickness of coating,
- Its solubility in water.



Dissolution Controlled systems

A) Dissolution control via matrix

The main approach in the design of these systems is compresion of active agent with slow dissolving carriers and thus controlling its release.



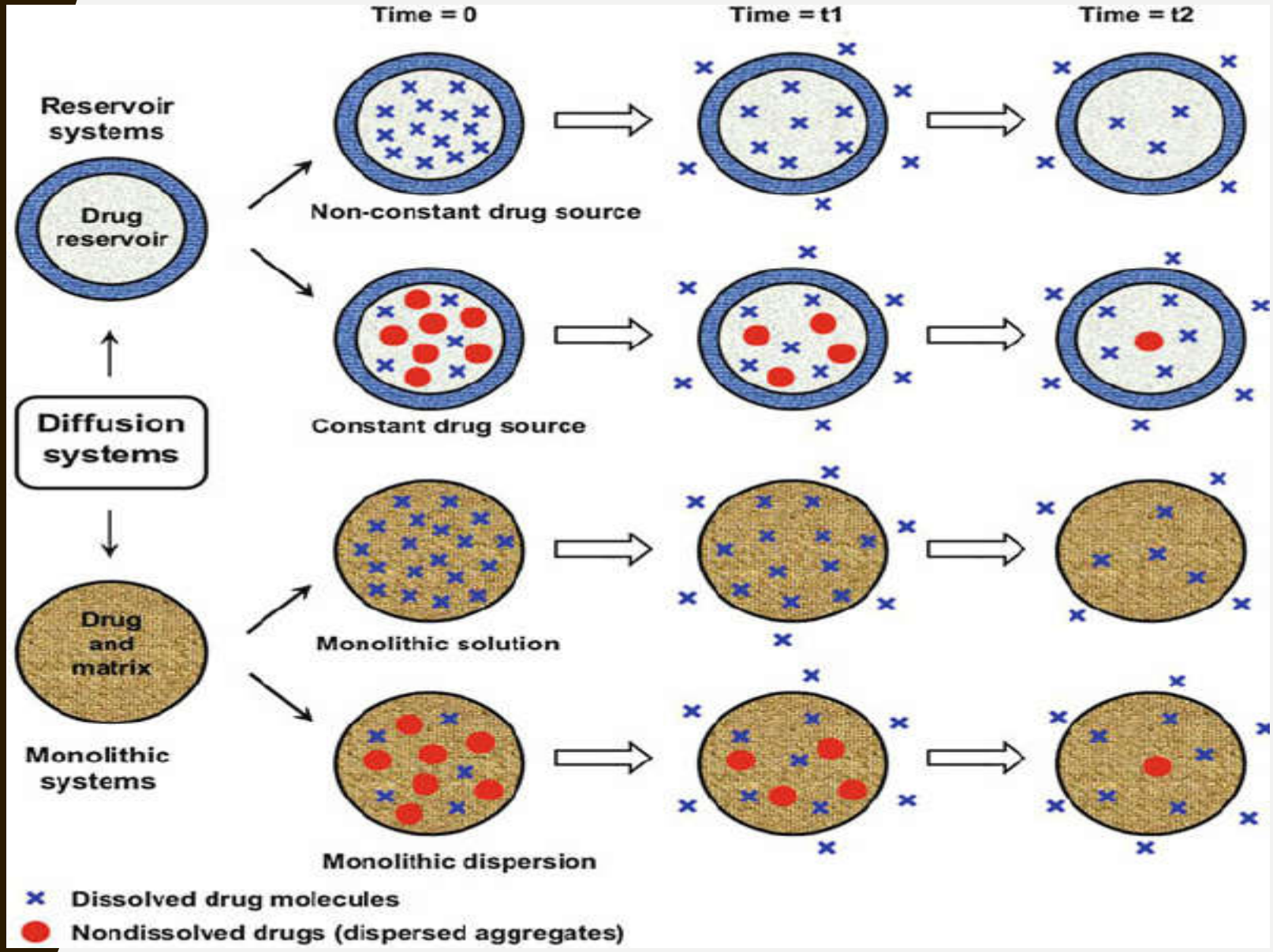
Release rate in these systems is controlled by;

- The rate of penetration of the ambient fluid into the matrix .

And this depends on;

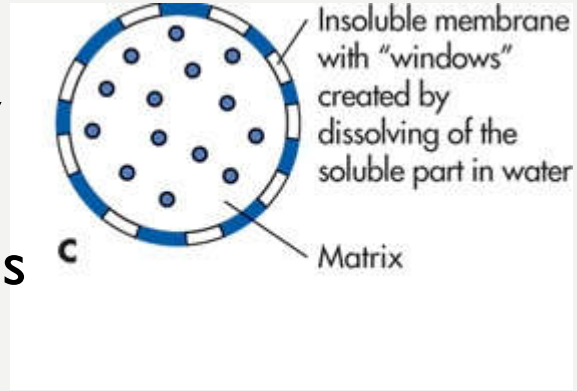
- Porosity of matrix tablet,
- Presence of hydrophilic substances,
- Wettability of the tablet and the particles.

2) Diffusion Controlled Systems



3) Diffusion and Dissolution Controlled Systems

In such systems, the core of the active substance is surrounded by a partially soluble membrane. Diffusion of the active substance is provided from the pores formed by partial dissolution of the membrane .

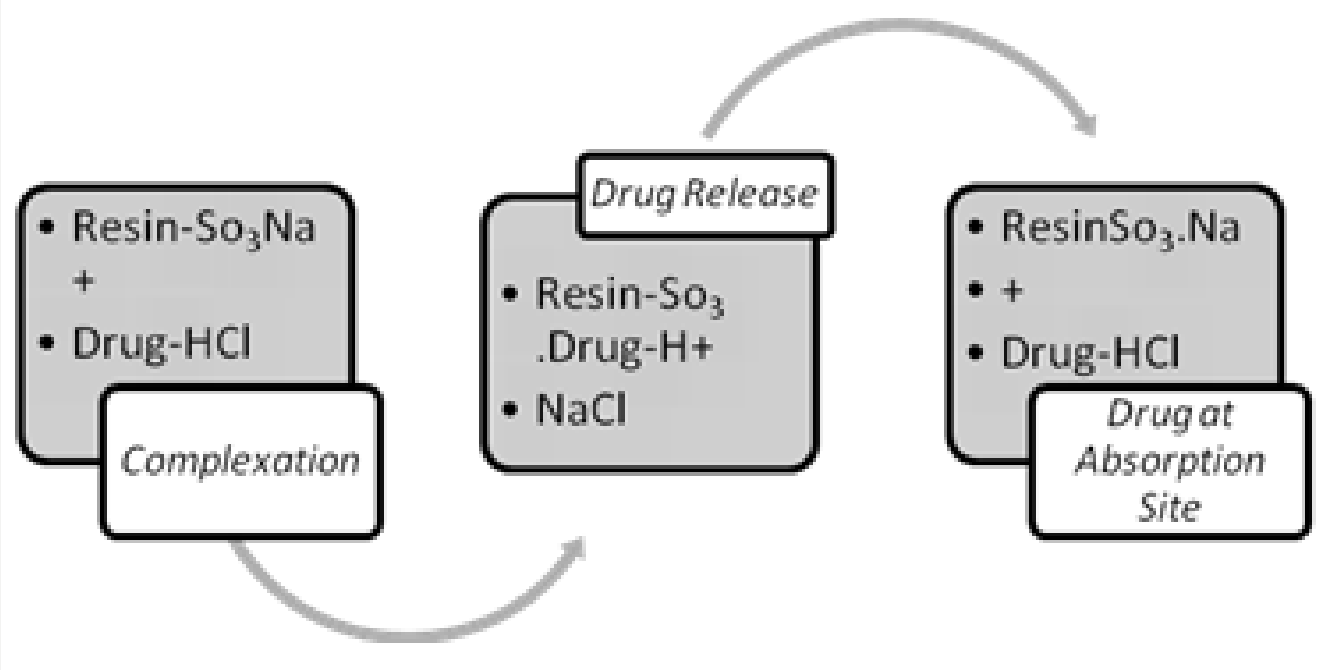


$$Q = AD\,(C_1 - C_2) / L$$

Q: Rate of release of active substance
A: Surface area
D: Diffusion of the active substance from pores
L: Diffusional path length
C1: Active substance concentration in the core
C2: Concentration of active substance in dissolution medium

4) Systems with Ion Exchange Resins

Resins are water-insoluble materials that carry anionic and cationic groups in repetitive regions on their structure. The complex is formed as a result of prolonged exposure of ionic resin with ionic solution of the active substance. When the complex contacts with gastric acid, the active substance is released slowly.



5) pH Independent Systems

Ideally, in controlled release systems, drug release from the dosage form is independent of gastrointestinal tract conditions, and is therefore independent of pH.

For active substances whose solubility is pH independent, water-insoluble polymers can easily be developed to provide pH independent release systems. However, most active substances have ionisation properties, these weakly acidic / weakly basic molecules or their salts show pH-dependent solubility.

Due to the gradual change in pH in the gastrointestinal tract, the weakly acidic and weak basic drug will exhibit different dissolution behavior in different regions of the gastrointestinal tract, resulting in intra- and interindividual variability in drug absorption and bioavailability.

The active substances dissolve in the ionized state and absorb in the non-ionized state.

Basic approaches used in the development of pH independent release systems of weak acidic drugs;

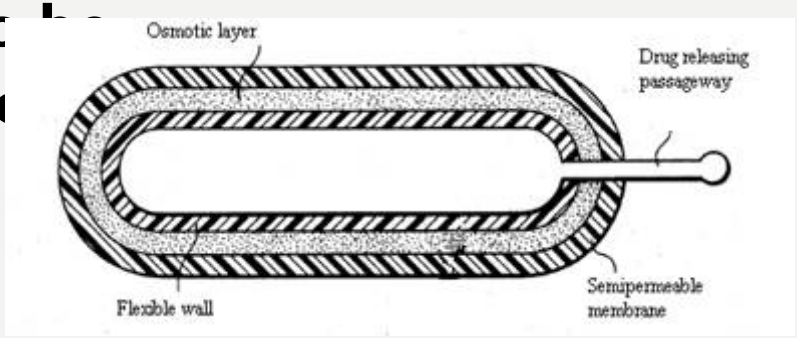
- Combination of neutral polymers with soluble polymers only in acidic pH environments
- The addition of pH modifying / buffering adjuvants to their formulations.

The methods used in the development of pH-independent release systems of weak basic drugs can be listed as follows;

- Combination of enteric and neutral polymers in formulations,
- Combination of neutral polymers with highly soluble substances at high pHs such as alginates,
- Adding pH modifying / buffering excipients to their formulations,
- Systems developed by combining water-insoluble and non-swelling polymers with water-soluble polymers.

6) OSMOTIC CONTROLLED RELEASE SYSTEMS

In these systems, osmotic pressure is the driving force that provides constant active substance release. Osmotic systems are systems that provide controlled release of the active substance in GIS. For the first time in 1955, Rose and Nelson introduced an implantable osmotic syringe that allowed the fluid to be released at constant spe several weeks.



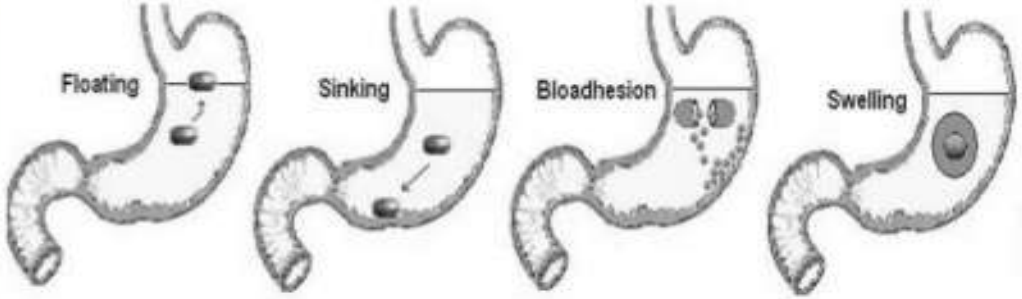
Currently marketed osmotically controlled tablets

Name	Marketer	Dosage form	Indication
Alpress®LP (Prazosin)	Novartis	ER Oral tablet	Hypertension
DynaCirc®CR (Isradipine)	Novartis	ER Oral Tablet	Hypertension
Glucotrol®XL (Glipizide)	Pfizer	Oros push pull tablet	Diabet
Procardia®XL (Nifedipine)	Pfizer	Oros push pull tablet	Angenia/Hypertension
Concerta™ (Methylphenidate HCl)	ALZA	Oros push pull capsule	Hyperactivity
Covera-HS® (Verapamil)	GD Searl-Pfizer	Oros push pull capsule	Angenia/Hypertension

7) Density Adjusted Controlled Release Systems

Approaches of Gastro retentive Drug Delivery Systems

- Altered density systems
- Floating systems
- Bioadhesive or mucoadhesive systems
- Expanded or Swelling systems
- Magnetic systems



ALTERED DENSITY SYSTEM

It mainly consist of 2 systems:

- High Density System
- Low Density System