SYSTEMS FOR CONTROLLED DRUG DELIVERY AND DELIVERY MECHANISMS

5. WEEK

Drug Release Mechanisms from Controlled Release Systems

There are several mechanism types in the controlled release systems:

1. Diffusion Controlled Release Systems,
2. Dissolution Controlled Release Systems,
3. Dissolution and Diffusion Controlled Release Systems

5. Water Penetration Controlled Release Systems,
6. Ion Exchange Controlled Release Systems,
7. Magnetically Controlled Release Systems,
8. Mechanically Controlled Release Systems

1.Diffusion Controlled Release Systems

Diffusion is described as the migration of a substance from a region of higher concentration to a region of lower concentration.

In diffusion controlled release systems, drugs are trapped in and released via diffusion through inert water-insoluble polymeric membranes (reservoir systems) or polymeric matrices (monolithic systems or matrix systems).

- **Matrix Systems:**

The drug is dispersed in an insoluble matrix of rigid nonswellable hydrophobic materials or swellable hydrophilic substances.

- **Reservoir Systems:**

These system are hollow containing an inner core of drug surrounded in a water insoluble polymer membrane.

❖In matrix type diffusion controlled drug delivery systems, the system is prepared by homogenously dispersing drug particle in rate controlling polymer matrix from either a lipophilic or a hydrophilic polymer.

❖The drug dispersion in the polymer matrix is accomplished by either,

- ✓ blending therapeutic dose of drug with polymer or highly viscous base polymer, followed by cross linking of polymer chains,
- ✓ mixing drug solid with rubbery polymer at elevated temperatures.

The drug release form matrix diffusion controlled-release drug delivery systems with the drug homogenously dispersed in:

a) a lipophilic, nonswellable polymer matrix with a growing thickness of the drug depletion zone
b) a hydrophilic, swellable polymer matrix with a growing thickness of the drug-depleted gel layer, which resulted from drug release from the drug dispersing polymer matrix
c) an inert polymer matrix, excreted unchanged after release of the drug.

- The resultant drug-polymer dispersion is then molded or extruded to form a drug delivery device of various shapes and sizes designed for specific application.

- It can also be fabricated by dissolving the drug and the polymer in a common solvent, followed by solvent evaporation at an elevated temperature and/or under a vacuum.

The rate of the drug release from this system,

$$\frac{Q}{t^{1/2}} = (2AC_R Dp)^{1/2}$$

Where,

- $Q/t_{1/2}$: rate of release of drug
- A : initial drug loading dose in the polymer matrix
- C_R : drug solubility in polymer
- D_P : diffusivity of drug in polymer matrix

In matrix systems, the rate controlling steps are

- ❖ Diffusion of dissolved drug in matrix structure,
- ❖ Loading dose,
- ❖ Drug solubility in polymeric matrix structure.

- In the reservoir type diffusion controlled drug delivery systems, drug is totally or partially encapsulated within drug reservoir.
- Its drug release surface is covered by a rate-controlling polymeric membrane having a specific permeability.
- Drug reservoir may exist in solid, suspension or solution form.
- Polymeric membrane can be fabricated from a nonporous (homogenous or heterogeneous) polymeric material or a microporous (or semipermeable) membrane.
- The encapsulation of drug formulation inside the reservoir compartment is accomplished by injection molding, spray coating, capsulation, microencapsulation, or other techniques.
- For this concept, different shapes and sizes of drug delivery systems can be fabricated.

❖The rate of drug release defined by

$$\frac{Q}{t} = \frac{K_{m/r} K_{a/m} D_d D_m}{K_{m/r} D_m h_d + K_{a/m} D_d h_m} C_R$$

$K_{m/r}$ & $K_{a/m}$: Partition coefficient of the drug molecule from reservoir to rate controlling membrane & from membrane to aqueous layer, respectively.

D_d & D_m : Diffusion coefficient of rate controlling membrane and aqueous diffusion layer, respectively.

hm & hd : Thickness of rate controlling membrane and aqueous diffusion layer, respectively.

C_R : Drug concentration in the reservoir compartment.

In reservoir systems, the rate controlling steps are

- Polymeric content in the coating,
- Thickness of the polymer (membrane) coating,
- Partition coefficient of the drug,
- Diffusivity of the drug,
- Hardness of the system.

The diffusion controlled release systems possess many advantages such as

- the potential to obtain zero-order release kinetics with a constant drug source,
- the ease to control release rate by adjusting the physicochemical properties of polymeric carriers, and
- the low cost of the system.

However, this is not completely safe because of dose dumping from accidentally damaged systems, which may be toxic. In some cases, a surgical procedure may be necessary to remove the device. Obtaining perfect zero-order release kinetics and releasing high-molecular-weight drugs can also be challenging.

2.Dissolution Controlled Release Systems

In dissolution controlled release systems, drugs are coated with or encapsulated within slowly dissolving **polymeric membranes (reservoir systems)** or **matrices (monolithic systems),** respectively.

In monolithic systems, drug aggregates are distributed throughout the polymeric matrices. Dissolution of the drug aggregates and release of the dissolved drug result when the matrices dissolve. However, in reservoir systems, drugs are surrounded through a low soluble polymeric shell in which drugs are protected.

In dissolution controlled release systems, the solubility of the polymeric carriers is a key factor in controlling drug release. These systems are advantageous in that they have the potential to release high-molecular-weight drugs and do not need to be surgically removed.

However, they are also associated with drawbacks including potential toxicity resulting from dose dumping and/or dissolved polymeric materials and difficulty in obtaining perfect zero-order release profiles.

3.Dissolution and Diffusion Controlled Release Systems

In reality, controlled release systems will never be dependent on only dissolution or diffusion. In dissolution and diffusion combination systems, drugs are trapped in partly soluble polymeric membranes or matrices that will dissolve to create pores.

In this systems,

- 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 and drug dissolution.
- Diffusion of dissolved drug out of system.
- Ethylcellulose and PVP mixture dissolves in water, and create pores of insoluble ethylcellulose membrane.

The pores allow aqueous media to flow into the core of the system to drive the diffusion of encapsulated drugs. In general, either one mechanism (dissolution or diffusion) or a combination of both can occur during the release process. However, in some cases, one mechanism can be dominant over the other to allow easy mathematical description, such as dissolution rate-limited or diffusion controlled release.

In these systems, the rate controlling steps are

- ❖Diffusivity of drug,
- ❖Partition coefficient of drug,
- ❖Solubility of drug and polymers.