Rate Controlled Drug Delivery Systems

Introduction of Rate Controlled Drug Delivery Systems

Introduction

- Rate controlled drug delivery systems are advanced pharmaceutical systems designed to control the rate of drug release from a dosage form into the body.
- In conventional dosage forms such as immediate-release tablets, capsules, and injections, the drug is released immediately after administration.
- **This may cause:**
  - Rapid increase in drug concentration in blood
  - High peak concentration that may cause side effects
  - Rapid decline of drug level below the therapeutic level
  - Large fluctuations in drug levels
  - Need for frequent dosing
- Rate controlled systems overcome these problems by releasing the drug slowly and in a controlled manner for a longer time.
- **They are widely used in:**
  - Sustained release formulations
  - Controlled release formulations

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Main Goals

- The main goals of rate-controlled drug delivery systems are to:
  - Maintain constant drug concentration in the body
  - Keep the drug level within the therapeutic range
  - Maintain this level for a longer period of time

Definition

- A Rate Controlled Drug Delivery System (RCDDS) is a pharmaceutical dosage form designed to release a drug at a predetermined and controlled rate for a specific period of time.
- **In simple terms:**
  - It controls how fast or slow a drug is released from a dosage form.

Therapeutic Window

- The therapeutic window is the range of drug concentration in the body where the drug produces a therapeutic effect without causing toxicity.
- It lies between:

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- **Minimum Effective Concentration (MEC)**
  - The lowest drug concentration that produces therapeutic effect
- **Minimum Toxic Concentration (MTC)**
  - The lowest drug concentration that produces toxic effects
- **Drug concentration conditions:**
  - Below MEC → Drug becomes ineffective
  - Above MTC → Drug produces toxic effects

- Rate controlled systems maintain drug concentration between MEC and MTC for a longer time.

Key Characteristics of Rate Controlled Systems

- Controlled and predictable drug release
- Maintenance of constant plasma drug concentration
- Reduced dosing frequency
- Improved patient compliance
- Reduced side effects
- Improved therapeutic effectiveness

Principles of Rate Controlled Drug Delivery Systems

- The basic principle of Rate Controlled Drug Delivery Systems (RCDDS) is to control the rate at which the drug leaves the dosage form and enters the systemic circulation.
- **Drug release is controlled through several mechanisms:**
  - Diffusion control
  - Dissolution control
  - Osmotic pressure control
  - Polymer degradation control
  - Swelling or erosion control

Diffusion Controlled Release

- Diffusion is the movement of drug molecules from an area of high concentration to low concentration.
- **In diffusion-controlled systems:**
  - The drug is enclosed within a polymer membrane or matrix
  - The polymer acts as a barrier
  - The drug slowly diffuses through the polymer

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Fick's Law of Diffusion

- The rate of drug diffusion depends on:
  - Concentration gradient
  - Diffusion coefficient
  - Surface area of membrane
  - Thickness of membrane

Mathematical Relation

- **Fick's law equation formatting**

$$Rate = \frac{D \times A \times (C_1 - C_2)}{h}$$

- **Where:**
  - D = diffusion coefficient
  - A = surface area
  - h = membrane thickness

Implications

- Higher concentration gradient → faster drug release
- Larger surface area → faster drug release
- Thicker membrane → slower drug release

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Dissolution Controlled Release

- In dissolution controlled systems, drug release depends on how fast the drug or coating dissolves into body fluids.
- The drug may be surrounded by slowly dissolving coating material.

A. Encapsulated Dissolution System

- Drug particles are coated with slowly dissolving polymers
- The coating dissolves gradually
- Drug is released slowly as the coating dissolves

B. Matrix Dissolution System

- Drug is dispersed inside a slowly dissolving matrix
- The matrix dissolves gradually in body fluids
- Drug is released as the matrix dissolves

Osmotically Controlled Release

In this system, drug release is controlled by **osmotic pressure difference**.

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Mechanism

- The drug is enclosed inside a semipermeable membrane
- Water from body fluids enters the dosage form
- Osmotic pressure builds inside the system
- Drug solution is pushed out through a small delivery orifice

Characteristics

- Can provide near zero-order drug release
- Release rate is independent of gastrointestinal conditions
- Drug release is highly predictable

Example

- OROS (Osmotic Release Oral System)

Polymer Degradation Controlled Release

- In these systems, the drug is embedded inside biodegradable polymers.
- Drug release occurs when the polymer degrades or breaks down.

A. Surface Erosion

- Polymer degrades layer by layer from the surface
- Drug release occurs gradually as outer layers erode

B. Bulk Degradation

- Polymer degrades throughout the entire matrix
- Drug diffuses out as the structure breaks down

C. Examples of biodegradable polymers

- Polylactic acid (PLA)
- Polyglycolic acid (PGA)
- PLGA (Poly lactic-co-glycolic acid)

These polymers are commonly used in **implantable drug delivery systems**.

Swelling Controlled Release

Some polymers absorb water and swell when they come in contact with biological fluids.

Mechanism

- Water penetrates the polymer matrix
- Polymer absorbs water and swells
- A gel layer forms on the surface

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- Drug diffuses through the swollen gel layer

Release Rate Depends On

- Rate of polymer swelling
- Polymer viscosity
- Drug diffusion rate

Examples of polymers

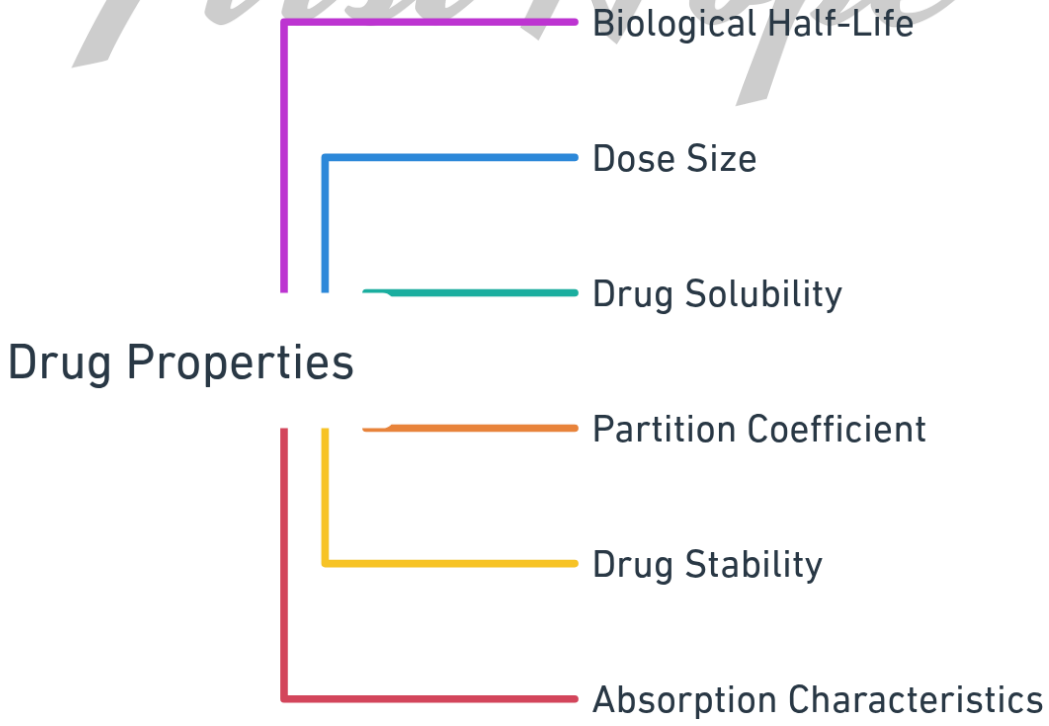
- Hydroxypropyl methylcellulose (HPMC)
- Carbopol
- Polyethylene oxide

Fundamentals of Rate Controlled Drug Delivery

- Several factors influence the design and performance of rate controlled drug delivery systems (RCDDS).
- These factors are mainly related to drug properties, biological factors, and polymer properties.

Drug Properties

Not all drugs are suitable for controlled release systems. Important drug properties include:



1. Biological Half-Life

- Ideal drugs should have a moderate half-life (2–8 hours).
- **Implications**
  - Very short half-life → large system required

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