Controlled and novel Drug delivery systems

Definition and Concept of Controlled Drug Delivery Systems (CDDS)

Definition

- Controlled Drug Delivery Systems are pharmaceutical technologies designed to deliver drugs at a predetermined rate, for a predefined duration, to achieve and maintain optimum therapeutic levels in the bloodstream or target site.

Concept

- In conventional drug delivery, medications are usually administered multiple times a day.
- This can lead to fluctuations in plasma drug levels, which might cause subtherapeutic effects or toxicity.
- Controlled drug delivery systems aim to overcome these limitations by:
    - **Maintaining drug concentration** within the therapeutic window.
    - **Reducing dosing frequency**, improving patient compliance.
    - **Minimizing side effects** by avoiding peaks and troughs in drug levels.
    - **Targeting the drug** to specific tissues or cells (in some advanced systems).

Types of Controlled Delivery Systems

1. **Sustained Release (SR)**: Maintains drug release over a prolonged period but may not be constant.
2. **Extended Release (ER)**: A general term for both sustained and controlled systems.
3. **Controlled Release (CR)**: Releases the drug at a constant (zero-order) rate.
4. **Targeted Delivery**: Directs the drug to a specific organ or cell type (e.g., cancer cells).
5. **Pulsatile Delivery**: Releases drugs at specific time intervals (useful in chronotherapy).

Mechanisms of Controlled Drug Release:

1. **Diffusion-controlled systems:**
    - ➢ Drug diffuses through a polymer membrane or matrix
    - ➢ Examples: Reservoir systems, matrix tablets
2. **Dissolution-controlled systems:**
    - ➢ Drug release is controlled by dissolution rate of the drug or its coating
3. **Osmotically controlled systems:**
    - ➢ Use osmotic pressure to push drug through a semi-permeable membrane

- Example: OROS (Osmotic Release Oral System)

4. **Bioerodible systems:**
   - Use biodegradable polymers that degrade over time, releasing the drug
5. **Ion-exchange systems:**
   - Drug is bound to a resin and released by ion exchange in GI fluids

Advantages

- Better bioavailability of drugs.
- Reduction in dose-related side effects.
- Enhanced patient compliance.
- Improved therapeutic efficacy.
- Suitable for chronic conditions like hypertension, diabetes.

Disadvantages:

- Higher cost
- Complex manufacturing and quality control
- Risk of dose dumping (if system fails)
- Limited flexibility in dose adjustment
- Not suitable for all drugs (e.g., those needing rapid onset)

Examples

- **Nifedipine SR tablets** for hypertension.
- **Depot injections** like Haloperidol decanoate for schizophrenia.
- **Ocusert** for glaucoma treatment (releases pilocarpine over 7 days).

Definition and Concept of Novel Drug Delivery Systems (NDDS)

Definition

- Novel Drug Delivery Systems refer to advanced drug delivery technologies that aim to optimize drug performance by controlling the rate, time, and place of release of drugs in the body, and sometimes modifying drug interaction with the body.

Concept

- NDDS represent an evolution beyond controlled delivery, incorporating biological, chemical, and engineering innovations.
- **They are often used for:**

- **Targeted delivery** (e.g., anti-cancer drugs to tumors).
- **Site-specific release** (e.g., colon-targeted tablets).
- **Environment-sensitive release** (e.g., pH-sensitive polymers).
- **Use of nanotechnology**, liposomes, micelles, etc.

Objectives of NDDS

- Improve drug solubility and stability.
- Increase bioavailability.
- Deliver drugs across biological barriers (e.g., blood-brain barrier).
- Decrease dosing frequency.
- Enable non-invasive delivery (like through skin or nose).
- Improve targeting and reduce toxicity.

Types of Novel Systems

NDDS Type	Mechanism / Feature	Example Drugs
Liposomes	Vesicles of phospholipids for targeting	Doxorubicin (Doxil)
Niosomes	Non-ionic surfactant vesicles	Diclofenac
Nanoparticles	1–1000 nm particles for intracellular delivery	Paclitaxel
Microspheres	Biodegradable particles for depot effect	Leuprolide
Osmotic pumps	Constant rate drug delivery via osmosis	Glucotrol XL (glipizide)
Transdermal Patches	Bypass GI tract and deliver drug via skin	Fentanyl patch

Differences between CDDS and NDDS

Parameter	Controlled DDS	Novel DDS
Focus	Rate and duration of drug release	Innovation in delivery route, targeting
Innovation Level	Moderate	High (uses biotechnology, nanotech)
Route Specificity	Less route-specific	Often designed for specific routes
Targeting Ability	Limited	High (e.g., site-specific delivery)
Examples	SR tablets, depot injections	Liposomes, nanoparticles, implants

Goals of NDDS:

- Reduce dose and dosing frequency
- Improve drug localization and targeting
- Overcome biological barriers (e.g., blood-brain barrier)

- Enhance patient convenience and compliance
- Facilitate delivery of new drugs, including peptides, proteins, nucleic acids

Parenteral Drug Delivery System

Definition

- Parenteral drug delivery refers to the administration of drugs by injection, bypassing the gastrointestinal tract, typically via intravenous (IV), intramuscular (IM), subcutaneous (SC), or intradermal (ID) routes.
- In the context of CDDS and NDDS, parenteral systems are engineered to release drugs in a sustained, controlled, or targeted fashion after injection.

Need for Parenteral CDDS/NDDS

- To reduce frequency of injections (improving compliance).
- To deliver poorly water-soluble or unstable drugs.
- For drugs with short half-lives.
- For targeted drug delivery (e.g., tumors, brain).

Why Use Parenteral NDDS?

- Rapid and complete drug absorption
- Can be used for poorly bioavailable or degraded oral drugs
- Suitable for proteins, peptides, vaccines, and targeted cancer therapies
- Achieve controlled, sustained, or targeted drug delivery
- Useful in emergency or long-term therapy

Controlled Parenteral Systems

A. Depot Injections (Sustained Release)

- Drug is formulated in oil-based or biodegradable carriers.
- Administered IM or SC.
- Releases drug over days to weeks.
- **Example**:
  - **Haloperidol decanoate** – antipsychotic, long-acting IM injection.

B. Microspheres and Microcapsules

- Biodegradable polymers like PLGA encapsulate the drug.
- Release via degradation or diffusion.
- **Example**:

- **Lupron Depot (Leuprolide acetate)** – controlled release for prostate cancer.

C. In Situ Forming Implants (ISFI)

- Liquid upon injection, solidifies in the body to form a depot.
- **Example**:
  - **Eligard** – Leuprolide acetate ISFI for 1–6 month release.

Novel Parenteral Systems

A. Nanoparticles and Nanosuspensions

- Particle size < 1000 nm.
- Enhances bioavailability and enables targeting (e.g., to cancer cells).
- **Example**:
  - **Abraxane** – albumin-bound paclitaxel nanoparticles for breast cancer.

B. Liposomes

- Phospholipid vesicles carrying hydrophilic/hydrophobic drugs.
- Can be PEGylated (stealth liposomes) to extend circulation time.
- **Example**:
  - **Doxil** – liposomal doxorubicin for ovarian cancer and Kaposi's sarcoma.

C. PEGylated Proteins

- PEG (polyethylene glycol) chains attached to therapeutic proteins.
- Increases **half-life**, reduces **immunogenicity**.
- **Example**:
  - **PEG-interferon alpha** for Hepatitis C.

Advantages

- Precise dose control.
- Useful for emergency and long-acting therapy.
- Bypasses first-pass metabolism.

Disadvantages

- Invasive; requires sterile techniques.
- Irretrievable once administered (cannot be removed easily).
- Higher cost and complexity of formulation.

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