Targeted Drug Delivery Systems

Targeted Drug Delivery Systems (TDDS)

What is a Targeted Drug Delivery System?

- A Targeted Drug Delivery System (TDDS) is a method of delivering medication so that the drug reaches a specific site in the body where it is needed, instead of spreading everywhere in the body.
- In traditional drug administration (tablets, injections, etc.), the drug travels through the bloodstream and affects both healthy and diseased tissues.
- This often causes side effects and reduces treatment efficiency.
- **A targeted drug delivery system is designed to:**
  - Deliver the drug specifically to diseased cells or tissues
  - Reduce side effects on healthy tissues
  - Increase therapeutic effectiveness
  - Lower the required dose of the drug
  - Improve patient compliance
- **For example:**
  - Chemotherapy drugs normally damage healthy cells and cancer cells.
  - If these drugs are delivered only to tumor cells, the treatment becomes more effective and less toxic.

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Objectives of Targeted Drug Delivery

The main objectives of TDDS are:



1. **Site-specific delivery**
   - ➢ The drug should reach the exact location of disease.

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2. Controlled release

- The drug should be released at a controlled rate.

3. Reduced toxicity

- Healthy tissues should not be affected.

4. Improved therapeutic index

- The ratio between effective dose and toxic dose improves.

5. Protection of the drug

- Some drugs degrade before reaching the target.
- TDDS protects them.

Components of a Targeted Drug Delivery System

A targeted delivery system generally has three main parts:

1. Drug (Active Pharmaceutical Ingredient)

- This is the therapeutic agent responsible for treating the disease.
- **Examples:**
  - Anticancer drugs
  - Antibiotics
  - Hormones
  - Proteins

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2. Carrier System

- The carrier transports the drug to the target site.
- **Examples of carriers:**
  - Liposomes
  - Nanoparticles
  - Micelles
  - Dendrimers
  - Polymer-based carriers
  - Antibody carriers
- **Functions of carrier:**
  - Protect drug from degradation
  - Increase circulation time in blood
  - Deliver drug to specific tissues

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3. Targeting Ligand

- A ligand is a molecule attached to the carrier that recognizes specific cells.
- **Examples:**
  - Antibodies
  - Peptides
  - Sugars
  - Vitamins
  - Receptors
  - Ligands bind to receptors present on target cells, which helps in drug targeting.

Concepts of Drug Targeting

- Drug targeting is based on directing the drug to a particular site in the body using biological or physicochemical mechanisms.
- The concept includes several important ideas.

Passive Targeting

- Passive targeting occurs when drug carriers accumulate at a particular site due to natural physiological conditions rather than specific binding.
- The most common example is tumor targeting through the Enhanced Permeability and Retention (EPR) effect.
- **In tumors:**
  - Blood vessels are abnormal and leaky
  - Large molecules and nanoparticles easily enter tumor tissue
  - Tumors have poor lymphatic drainage, so the particles remain trapped
- Because of this, nanoparticles accumulate more in tumors than in normal tissues.

Active Targeting

- Active targeting involves attaching a ligand to the drug carrier that specifically binds to receptors on target cells.
- **When the ligand binds to the receptor:**
  - The carrier attaches to the cell
  - The drug enters the cell through receptor-mediated endocytosis
- **Examples of targeting ligands include:**
  - Antibodies

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- Folate
- Transferring
- Peptides

- Active targeting improves the specificity of drug delivery.

Physical Targeting

- This type uses external physical factors to direct drugs to a specific area.
- **Examples include:**
  - Magnetic targeting using magnetic nanoparticles
  - Ultrasound targeting
  - Temperature-sensitive drug release
  - Light-triggered drug release

Chemical Targeting

- In this approach, chemical modifications of the drug allow it to accumulate in specific tissues.
- **Examples include:**
  - Prodrugs that activate only in certain tissues
  - pH-sensitive drug carriers that release drugs in acidic tumor environments

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Events Involved in Drug Targeting

- Drug targeting involves several sequential events.



Event 1: Administration of Drug Carrier

- **The drug-carrier system is introduced into the body through:**
  - Intravenous injection
  - Oral route
  - Implantation

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- Transdermal route

- Most targeted systems are given intravenously.

Event 2: Distribution in Blood Circulation

- After administration, the carrier enters systemic circulation.
- **During this stage:**
  - The carrier travels through blood vessels
  - It may interact with plasma proteins
  - It may be recognized by immune cells
  - A major challenge is removal by the Reticuloendothelial System (RES).
- **RES organs include:**
  - Liver
  - Spleen
  - Bone marrow
  - These organs remove foreign particles from blood.
- **To avoid this removal:**
  - Carriers are often coated with polyethylene glycol (PEG)
  - This process is called PEGylation, which increases circulation time

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Event 3: Accumulation at Target Site

- **The carrier accumulates in the diseased tissue through:**
  - Passive targeting
  - Active targeting
  - Physical targeting
- At this stage, the carrier localizes near the target cells.

Event 4: Recognition and Binding

- **If active targeting is used:**
  - Ligands on the carrier recognize specific receptors on target cells
  - Binding occurs through ligand–receptor interaction
- **Example:**
  - Antibody binding to antigen on cancer cells

Event 5: Cellular Uptake

- After binding, the carrier may enter the cell through endocytosis.

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