

NEW DRUG DELIVERY SYSTEM (NDDS)

- Demerits of conventional dosage forms.
 1. Large amount of drug is delivered to the site.
 2. Therapeutic concentration is not maintained.
 3. Repeated dosage is necessary.
 4. Less patient compliance.Fluctuations in concentration of drug in blood

Definition of NDDS -

- Therapeutic systems that incorporate drugs in a dosage form that releases the medication at a predetermined site, at a predetermined rate, and over an extended period of time from a single application.

Advantages of NDDS.

1. Delivery of the drug.
 - a) controlled rate.
 - b) slow delivery
 - c) Targeted delivery.
2. Longer duration of action.
3. ↑ Bioavailability.
4. ↓ Adverse effects.
5. ↑ compliance.

- Disadvantages of NDDS.
 1. High cost.
 2. In case of toxicity, it is not easy to remove the drug.

Types of NDDS.

- Prolonged release.
 - oral preparations
 - parenteral preparations.
- Local controlled drug delivery systems.
- Targeted drug delivery systems.

Prolonged Release oral preparations

- ① PRODRUGS - inactive form of the drug which undergoes biotransformation inside the body to pharmacologically active drug.

Eg: Levodopa → Dopamine.
Dipriferone → epinephrine etc.

Advantages:

- More stable.
- better bioavailability
- less side effects
- Prolong duration of action.

- ② Enteric coated tablets and capsules.

a) Drug coated with acid

resistant substance.

- (i) Prevent gastric irritation
- (ii) Prevent alteration of drug in the stomach.
- (iii) To get desired concentration of drug in small intestine.
- (iv) Retards rate of absorption and prolongs duration of action.

b) Drug coated with copolymers for drug delivery to colon.

③ Controlled release / Extended release / Sustained release preparations

* Release medication in a predetermined manner over an extended period of time.

1. Medicines incorporated in different layers - release drug at different time interval
OR

2. Granules of the drug can have different coatings that dissolve at different time intervals.
OR.

3. Medication can be covered with a gel which can swell and act like a semi permeable membrane.

Advantages

1. Therapeutic effect for longer time.
2. Less fluctuation.

3. ↓ frequency of drug administration.
4. ↓ Intensity / incidence of adverse effects

Prolonged Release Parenteral Preparations

Pumps

They deliver drugs at a predetermined rate for a specific period following a single application.

- computerised miniature pump.
- implantable pump.
- portable pump.

① computerised Miniature Pump.
These are programmed to release drugs at a definite rate either continuously or intermittently in pulses.

- insulin pump.
- GnRH pump.

② Implantable pump.
→ To deliver drug directly into an organ.
eg: Intrathecal administration of morphine,
Hepatic infusions of 5FU

③ Portable pump.

→ Pump connected to a motor delivers drug to a catheter and needle.

(2) Eg: PCA (patient controlled Analgesia) pump.

Pens

- portable convenient devices.
- eg: Insulin pen.
- use insulin cartridges.
- Insulin is injected s/c through a needle.
- preset amount is propelled by pushing a plunger.

Dermajet

- Needle is not used.
- painless.
- high velocity jet of drug solution is projected from a microfine orifice using a gun-like implement.
- solution passes through the superficial layer and gets deposited in the subcutaneous tissue.
- It is suited for mass inoculation.

Pellet Implantation

- Drug in the form of a solid pellet (sterile spheres formed by compression of drug powder).
- Drug is introduced with a Trochar and cannula.
- This provides sustained release of drug over weeks and months.
- Eg: DOCA, Testosterone

Non biodegradable and biodegradable implants

- Crystalline drug is packed in tubes/capsules and implanted under the skin.
- Slow and uniform leaching of the drug occurs over months, providing constant blood levels.
- Non biodegradable implant (eg: NORPLANT releasing levonorgestrel) has to be removed later on but not the biodegradable one.

Transdermal Therapeutic system (TTS)

- There are adhesive patches of various shapes and sizes (5-20 cm²).
- They deliver the contained drug at a constant rate into systemic circulation via the stratum corneum.
- Drug (in solution or bound to a polymer) is held in a reservoir between an adhesive backing film and a rate controlling micropore membrane.
- Undersurface is smeared with an adhesive impregnated with priming dose of the drug.
- The adhesive layer is protected by another film that is to be peeled off just before application.
- Drug is delivered at the skin.

diffusion for percutaneous absorption into circulation.

→ The micropore membrane is such that rate of drug delivery to skin surface is less than the slowest rate of absorption from the skin.

→ Any variation in the rate of absorption at different sites is offset by this.

• Usual sites of application

- chest
- Abdomen
- Upper arm
- Lower back
- Buttock
- Mastoid region

• Availability

In India

- GTN (glyceryl trinitrate)
- Fentanyl
- Nitroglycerine
- Estradiol

In other countries

- Isosorbide dinitrate
- Nifedipine
- Clonidine

For different drugs, TTS have been designed to last for 1-3 days

• Advantages

- Provides smooth plasma conc. of the drug without fluctuations

→ ↓ Interindividual variations (drug is subjected to little first pass metabolism)

- ↓ side effects
- More convenient

• Disadvantages

- local irritation and erythema usually mild.
- can be minimized by changing the site of application each time by rotation
- Discontinuation necessary in 2-7 % cases.

— Local controlled drug delivery systems

Ocusert

- Thin elliptical microcaps
- drug is in a reservoir form.
- slowly released through a membrane.
- By diffusion at a steady rate

eg: Pilocarpine ocusert used in treatment of glaucoma. placed under lower eyelid delivers pilocarpine for 7 days. Avoids the need for instilling eye drops repeatedly everyday.

Progestasert

- hormone releasing IOP inserted into the uterus. Delivers progestrone constantly at a specified rate (65µg/day)

for 1 year.

Drug Eluting Stents

- consists of a metallic stent backbone.
- covered with a polymer containing the drug.
- Drug is gradually released over 14-30 days.
- Targets drug locally.
- Minimises systemic exposure.
- eg: Antithrombotic drug coated stents to prevent restenosis.

Targeted drug delivery systems

Liposome

- Is a spherical shaped vesicle.
- composed of one or more phospholipid bilayers, which closely resembles the structure of cell membranes.
- Size → nm to several μ m.
- Water soluble drugs → trapped in central aqueous compartment.
- lipid soluble drugs → in lipid bilayer.
- Ability of liposomes to encapsulate hydrophilic or lipophilic drugs have allowed these vesicles to become useful drug delivery systems.

'structure of liposome' fig.

Liposome - classifications

① Multilamellar vesicles (MLV)

- several lipid layers.
- separated from one another by a layer of aqueous solution.

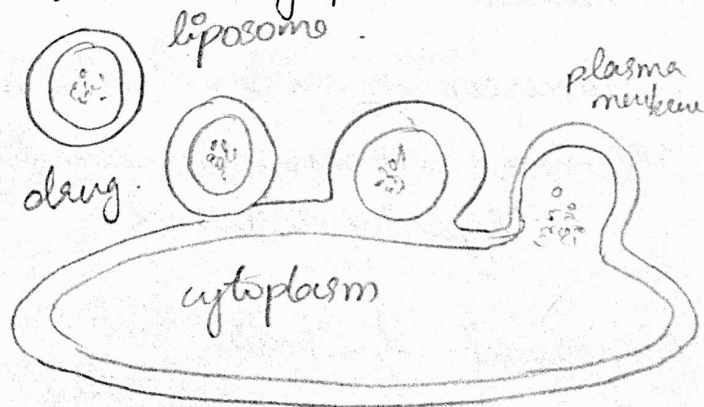
② Single unilamellar vesicles (SUV)

surrounded by single lipid layer. 25-50nm.

③ Large unilamellar vesicles (LUV)

→ surrounded by single lipid layer. 100nm

Mech: of drug delivery of liposome
lipid bilayer fuses with cell membrane, releases contents into the cytoplasm.



Liposome - uses

Delivery of genes, vaccines, drugs, etc.
eg: Amphotericin B (less nephrotoxic, better tolerated)

→ Scavels.

→ Anticancer drugs (Doxorubicin, Daunorubicin).

When administered, most vesicles accumulate at liver, spleen, lymph nodes, bone marrow and at sites of infection, inflammation and solid tumors.

Antisense Oligonucleotides

An antisense oligonucleotide (ASO) is a single-stranded deoxyribonucleotide, which is complementary to the mRNA target.

When administered → binds as complementary strand to mRNA → blocks translation.

e.g. Fomivirsen → CMV retinitis in AIDS patients.

Oblimersen → malignant melanoma.

Mipomersen → homozygous familial hypercholesterolemia.

Monoclonal antibodies

→ Derived from a single clone of cells.

Targets specific cells.

e.g. Abciximab → GP IIb/IIIa receptor antagonist (antiplatelet drug).