UNIT VII

APPROACHES FOR PARENTERAL CONTROLLED DRUG ADMINISTRATION

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Approaches for parenteral controlled drug administration:

- Several pharmaceutical formulation approaches may be applied to the development of parental controlled release or sustained release formulations.
- The most commonly used techniques are as follows:
  - Use of viscous, water miscible vehicles such as an aqueous solution of gelatin or poly vinyl pyrrolidine.
  - Formation of thixotropic suspensions.
- **Use of water immiscible vehicles such as vegetable oil or water repelling agent such as aluminium mono stearate.**
- **Preparation of water insoluble drug derivatives such as salts, complexes and esters.**
- **Dispersion in polymeric micro spheres or microcapsules such as lactide glycolide homopolymer or copolymers.**
- **Co-administration of vaso constrictors.**
Depot formulation may be classified on the basis of the process used for controlled drug release as follows:

- **DISSOLUTION CONTROLLED DEPOT FORMULATION:**

  Rate of drug absorption is controlled by the slow dissolution of drug in the formulation or in the tissue fluid surrounding the formulation.

  \[
  \frac{dQ}{dt} = \frac{DAC_s}{h}
  \]
Two approaches to control dissolution

a) **Formation of salt or complexes with low aqueous solubility:**
   
   E.g. Aqueous suspensions of benzathine penicillin G from water soluble alkali salts of acidic pencillin G.

b) **Suspension of macrocrystals:**
   
   Large crystals are known to dissolve more slowly than small crystals. It is called ‘the macro crystal principle’ and can be applied to control the rate of drug dissolution.
   
   E.g: aqueous suspension of testosterone isobutyrate for I.M injection

Exception: Penicillin G procaine suspension in gelled peanut oil for I.M. injection.
The major drawback of these two types of injectables depot formulations is that the release of drug molecules is not of zero order kinetics as expected from the theoretical model defined in the equation.

Reasons:

- surface area of the drug solids diminishes with time because of increased drug release
- saturation solubility of the drug in the medium cannot be maintained easily because of rapid absorption.
2) **ADSORPTION TYPE DEPOT FORMULATION:**

- This type of depot preparation is formed by the binding of drug molecule to adsorbents.
- In this only the unbound, free species of the drug is available for adsorption.
- As soon as the unbound drug molecule are absorbed, a fraction of the bound drug molecule is released to maintain equilibrium.

\[
\frac{(C)_f}{(C)_b} = \frac{1}{a(C)_{b,m}} + \frac{(C)_f}{(C)_{b,m}}
\]

- E.g. vaccine preparations.
3) ENCAPSULATION TYPE DEPOT FORMULATIONS:

- This type of depot formulation is prepared by encapsulating drug solids within a permeation barrier or dispersing drug particles in a diffusion matrix.
- Both of these are made from either bio-degradable or bio-absorbable polymers.
- Release of drug is controlled by:
  - rate of penetration across the diffusion barrier
  - rate of biodegradation of the barrier macro molecules.

Eg: naltrexone pamoate releasing biodegradable micro capsules
4) ESTERIFICATION TYPE DEPOT FORMULATION:

- This depot preparation is produced by synthesizing the **bio-erodible esters** of a drug and then making up an injectable formulation.

- This formulation forms a drug reservoir at the site of injection.

- Rate of absorption is controlled by
  - interfacial partitioning of drug esters from reservoir to tissue fluid.
  - Rate of bioconversion of drug esters to regenerate active drug molecules.

- Eg: fluphenazine enanthate, testosterone 17 β cypionate in oleaginous solution.
References:

- Google search
Thank you!