MOLECULAR PHARMACEUTICS

MPH:-201T

UNIT:- I

TOPIC:- TARGETTED DRUG DELIVERY

PRESENTED BY

(Dr.) Anupriya kapoor

ASSISTANT PROFESSOR

School of Pharmaceutical Sciences CSJMU, KANPUR

TOPICS COVERED

- Introduction
- Objective
- Method of drug delivery
- Rational
- Advantages
- Disadvantages
- Ideal properties
- Carrier or markers
- Properties of carriers
- Strategies of drug targeting
- Types of targeted drug delivery system

INTRODUCTION

- **Targeted drug delivery system is a special form of drug delivery system in which the medicament is selectively targeted or delivered only to its site of action or absorption and not to the non-target organs or tissues or cells.**
- It is a method of delivering medication to a patient in a manner that increases the concentration of the medication in some parts of the body relative to others.
- Targeted drug delivery seeks to concentrate the medication in the tissues of interest while reducing the relative concentration of the medication in the remaining tissues.
- This improves efficacy and reduce side effects.

OBJECTIVE

- To obtain desired pharmacological response at a selected sites without undesirable interaction at other sites, there by the drug have a specific action with minimum side effects & better therapeutic index.
- Eg: In cancer chemotherapy and enzyme replacement therapy.

METHOD OF DRUG DELIVERY

- To the capillary bed of the active sites.
- To the specific type of cell or an intracellular region. Ex: Tumour cells but not to normal cells.
- To a specific organ or tissues by complexion with the carrier that recognizes the target.

RATIONAL OF DRUG TARGETING

- In the treatment or prevention of diseases.
- Pharmaceutical drug instability in conventional dosage form
- Solubility problems are overcome
- biopharmaceutical low absorption
- high- membrane bounding
- biological instability
- pharmacokinetic
  - short half life
  - large volume of distribution
- pharmacodynamic parameters
  - low specificity
  - low therapeutic index.

ADVANTAGES

- Drug administration protocols may be simplified
- Drug quantity may be greatly reduced as well as the cost of therapy
- Drug concentration in the required sites can be sharply increased without negative effects on non-target compartments.
- No peak and valley plasma concentration.
- Selective targeting to infections cells as compared to normal cells.

DISADVANTAGES

- Rapid clearance of targeted systems.
- Immune reactions against intravenous administered carrier systems.
- Problems of Insufficient localization of targeted systems into tumour cells.
- Diffusion and redistribution of released drugs.
- Target tissue heterogeneity.
- Difficult to maintain stability of dosage form.

  E.g.: Resealed erythrocytes have to be stored at 4^0 C.
- Drug loading is usually low. E.g. As in micelles.

Therefore it is difficult to predict /fix the dosage regimen.

IDEAL PROPERTIES

- It should be nontoxic, biocompatible, biodegradable.
- Restrict drug distribution to target cells or tissues or organs and should have uniform capillary distribution.
- Controllable and predicate rate of drug release.
- Drug release does not effect the drug action.
- Therapeutic amount of drug release.
- Minimal drug leakage during transit.
- Carriers used must be bio-degradable or readily eliminated from the body without any problem and no carrier induced modulation of diseased state.
- The preparation of the delivery system should be easy or reasonably simple, reproductive and cost effective.

CARRIER

- Most important entity required for successful transportation of the loaded drug
- Drug vectors which, retain and transport drug; deliver it within or in the vicinity of target
- Do so through an inherent characteristic or acquired through structural modification.
- They are engineered vectors, which retain drug inside or onto them either via encapsulation and/ or via spacer moiety and transport or deliver it into vicinity of target cell.

PROPERTIES OF CARRIERS

I. It must be able to cross anatomical barriers and in case of tumour chemotherapy tumour vasculature
II. It must be recognized specifically and selectively by the target cells and must maintain the specificity of the surface ligands
III. The linkage of the drug and the directing unit (ligand) should be stable in plasma, interstitial and other bio-fluids
IV. Carrier should be non-toxic, non-immunogenic and biodegradable particulate or macromolecule
V. After recognition and internalization, the carrier system should release the drug moiety inside the target organs, tissues or cells

CARRIERS : ON THE BASIS OF ORIGIN

- Based on the nature of their origin

  Endogenous - LDL, HDL Chylomicrons, Serum albumin, Erythrocytes

  Exogenous - Microparticulates, Soluble polymeric and Biodegradable polymeric drug carriers.

Pharmaceutical carriers:

- Microcapsules
- Microparticles
- Lipoproteins
- Liposomes
- Micelles

LEVELS OF DRUG TARGETING

1) Passive Targeting :

Drug delivery systems which are targeted to systemic circulation are characterized as Passive delivery systems.

- In this technique drug targeting occurs because of the body's natural response to physicochemical characteristics of the drug or drug carrier system.

2) Inverse Targeting :

- In this type of targeting attempts are made to avoid passive uptake of colloidal carrier by RES (Reticulo Endothelial Systems) and hence the process is referred to as inverse targeting.
- To achieve inverse targeting, RES normal function is suppressed by pre injecting large amount of blank colloidal carriers or macromolecules like dextran sulphate
- This approach leads to saturation of RES and suppression of defense mechanism.
- This type of targeting is an effective approach to target drug(s) to non-RES organs.

3) Active Targeting :

- In this approach carrier system bearing drug reaches to specific site on the basis of modificationmade on its surface rather than natural uptake by RES.
- Surface modification technique include coating of surface with either a bioadhesive, nonionic surfactant or specific cell or tissue antibodies (i.e. monoclonal antibodies) or by albumin protein

- **Types**
  - First order targeting (organ compartmentalization).
  - Second order targeting (cellular targeting).
  - Third order targeting (intracellular targeting).

- **4) Ligand Mediated Targeting :** Achieved using specific mechanisms such as receptor dependent uptake of natural LDL particles and synthetic lipid microemulsions of partially reconstituted LDL particles coated with the apoproteins.
- **5) Physical Targeting :**
- In this type of targeting some characteristics of environment changes like pH, temperature, light intensity, electric field, ionic strength small and even specific stimuli like glucose concentration are used to localize the drug carrier to predetermined site.
- This approach was found exceptional for tumour targeting as well as cytosolic delivery of entrapped drug or genetic material.

6) Dual Targeting :

- In this targeting approach carrier molecule itself have their own therapeutic activity and thus increase the therapeutic effect of drug.
- For example, a carrier molecule having its own antiviral activity can be loaded with antiviral drug and the net synergistic effect of drug conjugate was observed.

7) Double Targeting :

- Temporal and spatial methodologies are combined to target a carrier system, then targeting may be called double targeting.
- Spatial placement relates to targeting drugs to specific organs, tissues, cells or even subcellular compartment. whereas temporal delivery refers to controlling the rate of drug delivery to target site.