BASIS OF TARGETED DRUG DELIVERY

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- Target drug delivery system is a special form of drug delivery system where the pharmacologically active agent or 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.
- Targeted drug delivery implies for selective and effective localization of pharmacologically active moiety at pre identified (preselected) target in therapeutic concentration, while restricting its access to non-target normal cellular linings, thus minimizing toxic effects and maximizing therapeutic index.

- Advantages of drug targeting:
  - 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.

- Disadvantages of drug targeting:
  - Rapid clearance of targeted systems.
  - Immune reactions against intravenous administered carrier systems.
  - Insufficient localization of targeted systems into tumour cells.
  - Diffusion and redistribution of released drugs.

Controlled Release

- A system that:
  - Delivers an agent at a controlled rate for an extended time
  - Might localize drug action by spatial placement near where it is needed

Sustained Release

- Release of drug is extended in time
- Rate and duration are not designed to achieve a particular profile.

- To obtain a desirable therapeutic response, correct amount of drug should be transported and delivered to site of action with subsequent control of drug input rate.
- TDD improves the benefit/risk ratio associated with drugs.
- Approaches are being adopted either to control the distribution of drug by incorporating in carrier system or by altering the structure of the drug at molecular level or by controlling the input of drug into bio environment to ensure a programmed and desirable bio distribution.

- The site specific targeted drug delivery is an exclusive delivery to specific pre – identified compartment with maximum intrinsic activity of drugs and reduced access of drugs to non target cells.
- The controlled rate and mode of drug delivery to pharmacological receptor and specific binding with target cells, as well as bio environmental protection of drug are some of specific features of TDDS.

The drug may be delivered

- To the specific type of cell (or) even an intracellular region. Ex- tumour cells but not to normal cells,
- To a specific organ (or) tissues by complexing with the carrier that recognizes the target

REASON FOR DRUG TARGETING:

- In the treatment or prevention or diseases.
- Pharmaceutical drug instability in conventional dosage form solubility ,biopharmaceutical low absorption, high-membrane bounding, biological instability, pharmacokinetic / pharmacodynamic short halflife, large volume of distribution, low specificity, clinical, low therapeutic index.

Targeted drug delivery system should be-

- Biochemically inert (non-toxic), non-immunogenic.
- both physically and chemically stable *in vivo* and *in vitro.*
- 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.
- 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.

CARRIERS

- These are drug vectors which transport and retain the bio environmental protection of drug.
- These can do so either through an inherent characteristics or by acquired through structural modification .

IDEAL CHARACTERS

- It must able to cross anatomical barriers.
- It must be recognized specifically & selectively by target cells.
- The linkage of drug and directing unit (ligand) should be stable in plasma.
- It should be non toxic, non immunogenic and bio degradable.

TYPES OF CARRIERS

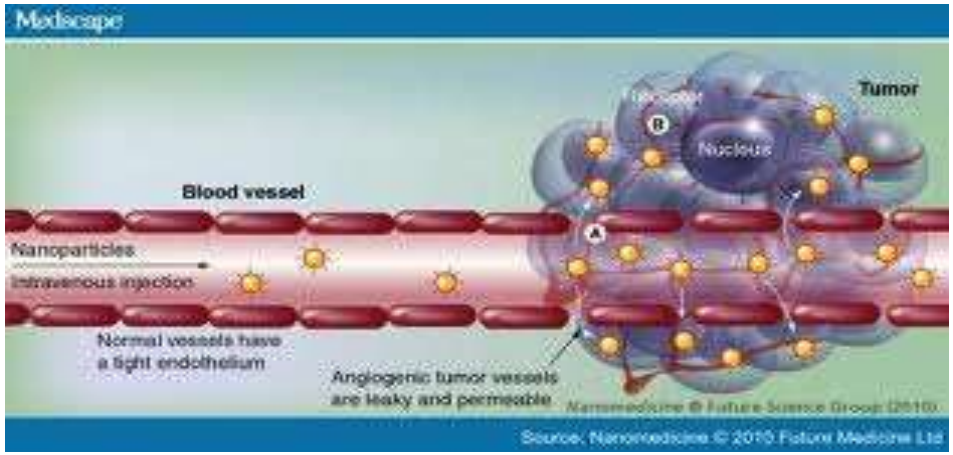
Based on nature of origin

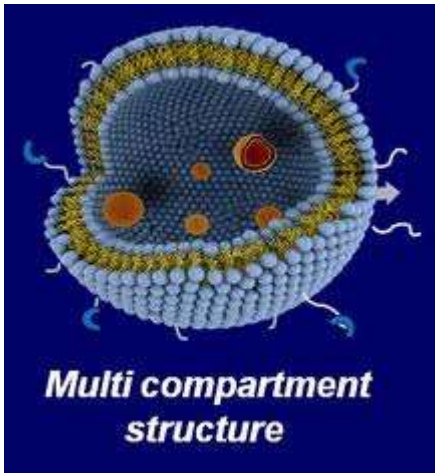
Endogeneous

- Low density lipoprotein, high density lipoprotein, chylomocrons, erythrocytes.

Exogeneous

- Microparticles, polymeric drug carriers.





General classification for drug carriers

1. **Colloidal carriers**

Liposomes, Niosomes, Pharmacosomes, Virosomes.

2. **Microparticulate systems**

Microparticles, Nanoparticles, Magnetic microspheres.

3. **Cellular carriers**

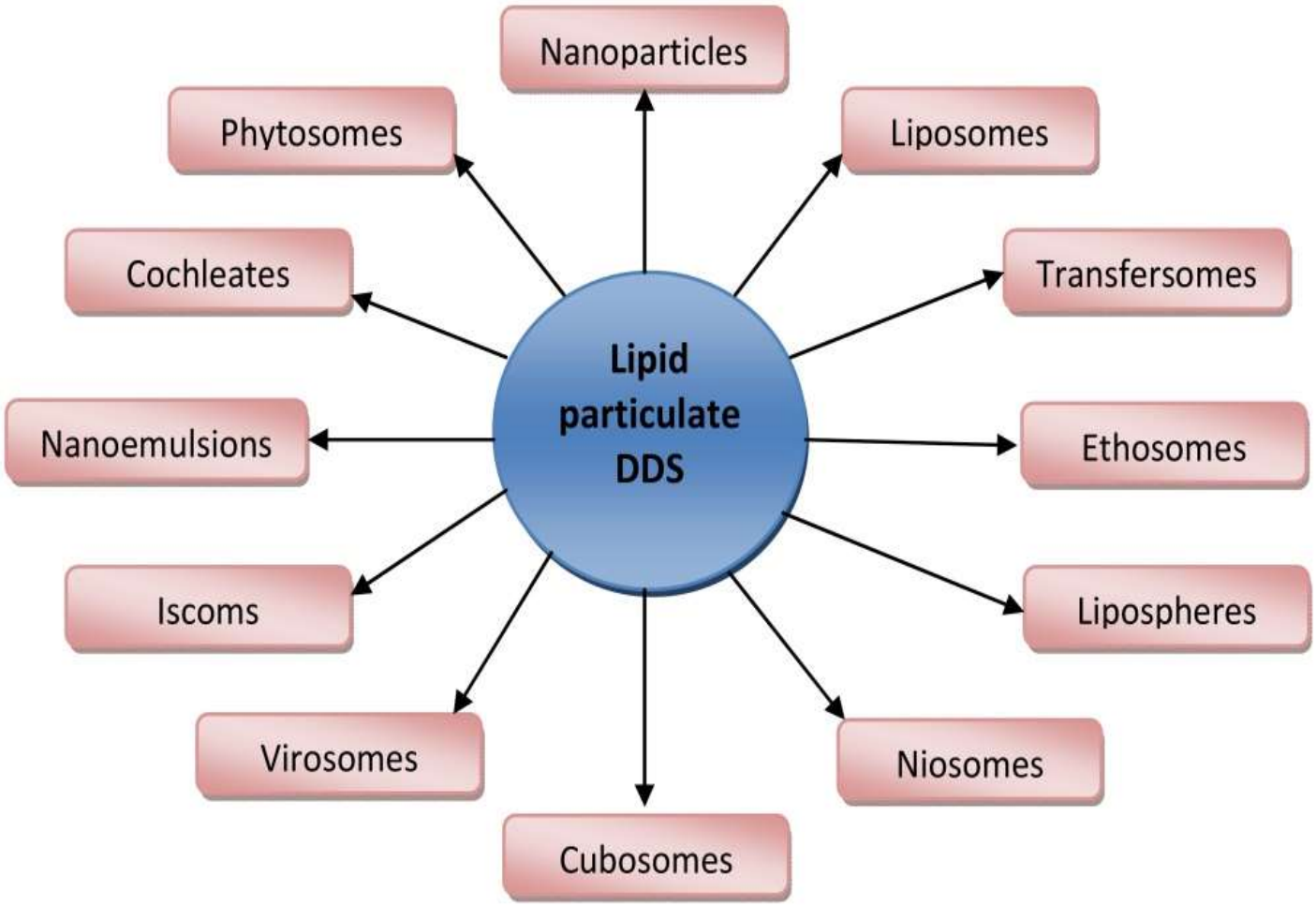
Resealed erythrocytes, Serum albumin.

4.Supra molecular delivery systems

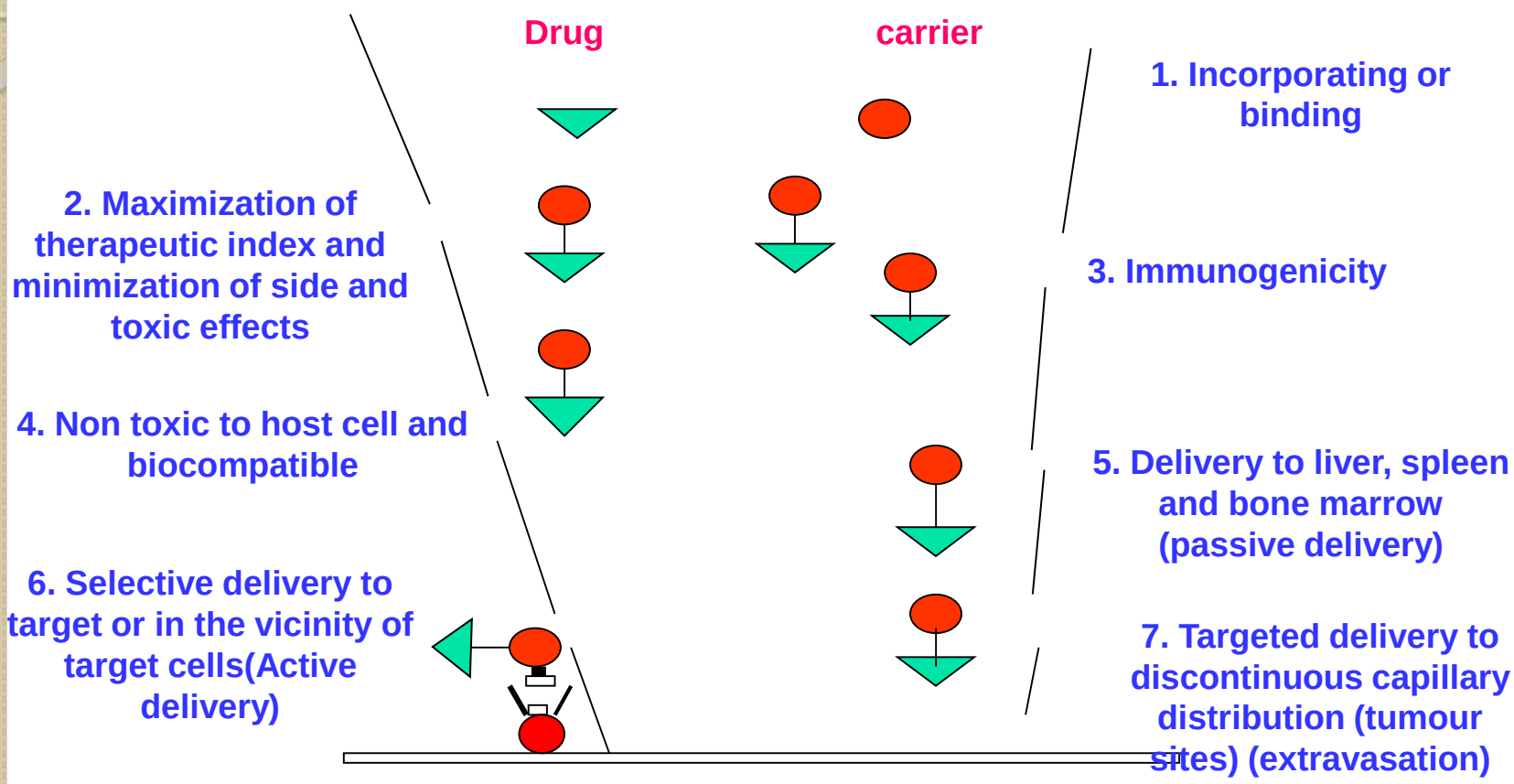
Micelles (Reverse micelles, mixed micelles), liqid crystals.

5. **Macromolecular carriers**

Protiens, glycoprotiens, lectins.


Lipid particulate DDS
Nanoparticles
Phytosomes
Liposomes
Cochleates
Transfersomes
Nanoemulsions
Ethosomes
Iscoms
Lipospheres
Virosomes
Niosomes
Cubosomes

REQUIREMENT OF DRUG



Schematic illustration of requirement of drug carriers

Microspheres

- There are various approaches in delivery of a therapeutic substance to the target site as its necessary for designing a controlled drug delivery system.
- One such approach is using polymeric microspheres as carriers for drugs.
- Microspheres are the free flowing powders containing of encapsulated (drugs) spherical particles of size ideally less than 125 microns that can be suspended in aqueous vehicle & injected by an 18 (or) 16 number needle.
- As we know that the capillaries of the human body are in the microns, so one can easily target the capillaries of lungs, blood, liver etc. by the use of microspheres.

Nanoparticles

- Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000nm.
- The drug is dissolved, entrapped, encapsulated or attached to a nano particle matrix.
- The major goals in designing nanoparticles as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action.

Levels of drug targeting

- Active targetting
- Passive targeting
- Inverse targeting
- Active targeting (Ligand mediated & Physical targeting)
- Dual targeting
- Combination targeting

Passive targeting

- Drug + carrier (modified by physical property)
- Target the drug to systemic circulation or to the reticuloendothelial system (RES).
- The physicochemical properties of the drug carrier are modified, so as to make it suitable to the target site.
- Molecular size and molecular weight, surface hydrophobicity, surface charge, and sensitivity to triggering are critical to bio distribution.
- Molecular weight -more than 30 KDa to escape elimination by the kidneys.
- Size of the drug-carrier complex in between 100nm-200nm.
- Surface nature must be hydrophilic to escape opsonisation in blood.
- Surface charge should be neutral to facilitate long circulation time.

Active Targeting

- Drug + carrier-(modified by physical property)+ ligand as homing device
- Make a drug- carrier complex more target specific, by attaching a homing device or a ligand to it.
- This attachment will help the TDDS in circulating in the bloodstream for a prolonged time and in accumulating at the target site.
- Exploits specific biological processes, such as, ligand-receptor recognition and interaction, to increase the concentration of the drug at a particular site. Examples of ligands are antibodies, peptides, sugars and vitamins.

Targeted Drug Delivery Systems

- Brain Targeted Drug Delivery
- Pulmonary Tageted Drug Delivery
- Opthalmic Drug Delivery
- Lymphatic Drug Delivery

LIGAND

- A ligand is some molecule which we attach to the drug delivery system, which acts as a homing device and takes the delivery system to the target.
- Ligands bind to the receptors. A ligand and its receptor form a complex because structurally they are complimentary to each other.
- Examples of ligands are

  Antibodies,

  Selectins (The selectins (cluster of differentiation) are a family of cell adhesion molecules (or CAMs)).

  Integrins (**Integrins are proteins that function mechanically, by attaching the cell cytoskeleton to the extracellular matrix (ECM), and biochemically, by sensing whether adhesion has occurred.**)

  Vitamins,

  Transferrin hormones and

  Low density lipoproteins.