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A Review On Targeted drug delivery : Approach, concept And specific drug targeting.

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Abstract :

Targeted drug delivery system (TDDS) is the targeting the drug molecule at particular site of action. In the targeted organ or the tissue to reduce the amount of drug required for therapeutic efficacy. Basically the drug delivery is the system in which transport pharmaceutical in body to achieve desired therapeutic effect. In recent times there is specially focused on the smart drug delivery at appropriate time, dosage, and location with the maximum safety and efficacy.

Novel drug delivery system (NDDS) has enhance the therapeutic effectiveness of new drug and existing drug with targeted, managed and sustain delivery system. TDDS is where a drug is delivered to specific location than the whole body or organ. Combine diverse field of science TDD is aiming to managing and controlling the pharmacokinetic and pharmacodynamic properties. TDDS is different from other drug delivery system that they acquire on specific targeting on site and release of dosage form.

Keywords : Targeting, carriers, liposomes, organs, pharmacotherapeutic.

Introduction :

Development of new drug molecule is expensive and time consuming. Improving safety efficacy ratio of "old" drugs has been attempted using different methods such as individualizing drug therapy, dose titration, and therapeutic drug monitoring. Delivering drug at controlled rate, slow delivery, targeted delivery are other very attractive methods and have been pursued vigorously. It is interesting to note that considerable work and many publications from USA, Europe are authored by Indian researchers.

Need of Targeted drug delivery system (TDDS) :

The need of targeted drug delivery system over conventional delivery system is because it is not only enhance therapeutic effect but also the reducing the toxicity associate with small therapeutic effect at high dose. TDDS is much important than the conventional delivery system. TDDS is pharmacokinetic, pharmacodynamic, pharmaceutical, pharmacotherapeutic features with conventional delivery.

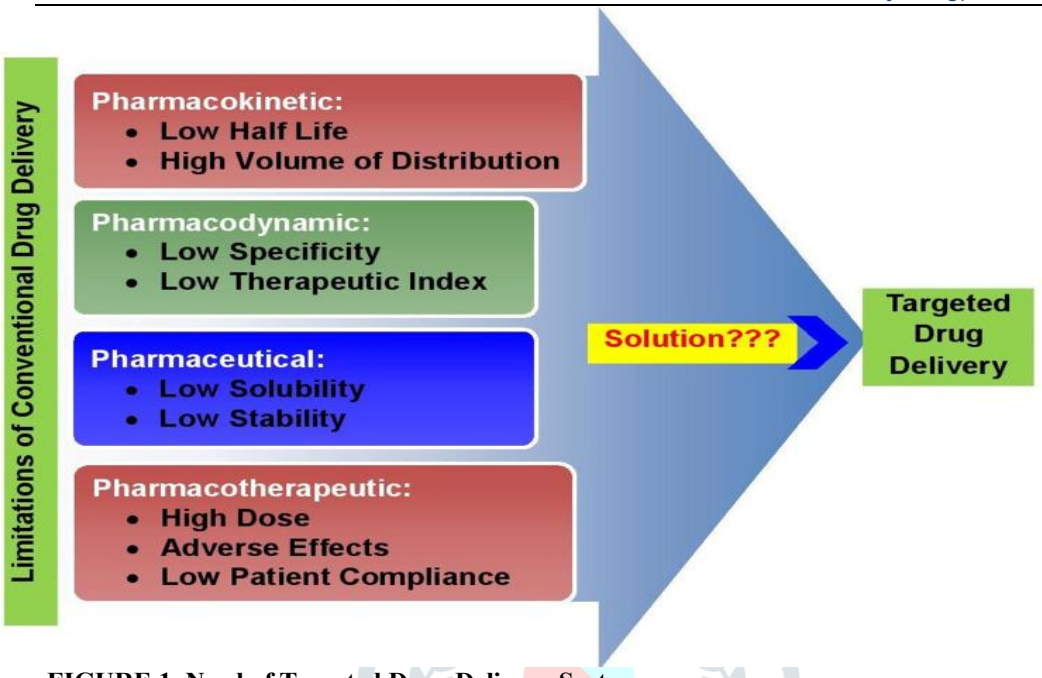


FIGURE 1. Need of Targeted Drug Delivery System.

Characteristics of targeted drug delivery system:

1. Must biochemically inert.
2. Should be non immunogenic.
3. Should be physically and chemically stable in vivo and in vitro conditions.
4. Should have therapeutic amount of drug release.
5. Should have minimal drug leakage during transit.
6. Carriers used should be biodegradable or readily eliminated from the body

Approaches and levels of targeting :

Passive targeting :

When the biological and pharmacological factors play a task in the accumulation of the drug during a Specific site, it is called as passive targeting. The disease pathology or changed properties of the tissues In cancer allow gathering of drugs in these organs by passive targeting . Particularly cancer fenestrations Developed during angiogenesis are wider with pore sizes in the range of 100_600 nm whereas the normal Blood vessels would be only around 6 nm. If any foreign nanosized particle enters in the body by the intravenous route, immediately the body's defense Immune system is activated and releases opsonin's.

Active targeting :

Active targeting involves modification and the functionalization of the drug delivery system or carrier so as that the advanced reaches its acceptable website just like the architected carrier. Therein cases the molecular recognition is a lot of precise and there square measure hardly any possibilities for nonspecific interactions. active targeting means that a particular ligand– receptor sort interaction for animate thing localization that happens solely when blood circulation and extravasations.

Inverse targeting :

In inverse targeting, there is a degeneration of the biodistribution movement of the drug carrier system. There's activation of the RES system whenever a mixture drug delivery system is injected into the body because of opsonin then there is a laborious and quick biodistribution pattern followed. Inverse targeting could be a plausible commit to bypass the uptake of mixture particles by the RES .(18) There area unit some reportable approaches to avoid the RES-rich organs. a technique is to saturate the RES by pre injection of blank mixture carriers throughout a bigger quantity or use of macromolecules like dextran sulphate.

Commonly used carrier for Targeted drug delivery system :

There are different types of drug carriers, such as colloidal, polymers, monoclonal Abs, NPs, and cell. The nature of the drug, the target, and the disease state determine the selection of the carrier to be used. Abs, proteins, lipoproteins, hormones, charged molecules, and polysaccharides are used with carriers as targeting moieties.

Colloidal carrier :

Colloidal DDSs are nanoscale targeting vesicles of particulate or vesicular dosage form. They include liposomes, noisome, nanospheres, multiple emulsions, and ceramics. These type of drug vectors sequester, transport, and retain the active drug in route, while they elute or deliver it within or in the vicinity of the target, with the ability to modify the distribution profile.

Vesicular carrier :

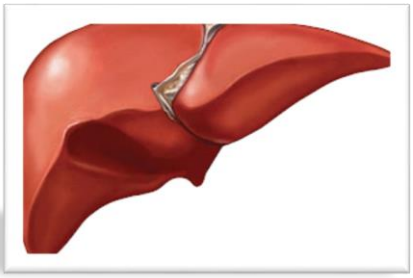
Novel vesicular DDSs have the objective of delivering the drug at a rate- and site-controlled manner as per treatment needs. Vesicular DDSs are used to improve the therapeutic index, solubility, stability, and rapid degradation of drug molecules.

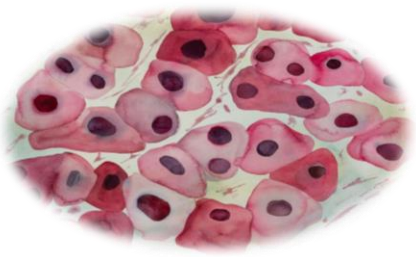
Microparticulate carrier :

Microparticles are DDS on the micrometer–millimeter scale. This microencapsulation technology allows protection of the drug from the environment, stabilization of sensitive drug substance and masking unpleasant taste. As such, they play an important role as DDSs, aiming at improved bioavailability of conventional drugs and minimizing side effects. Microparticulate systems includes microparticles, NPs, and magnetic microspheres.

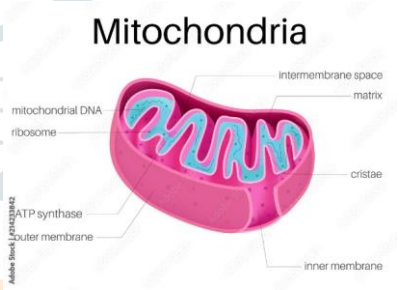
Levels of targeting -

First order targeting **Second order targeting**





Organ level targeting liver **Cell level targeting Hepatocytes**



Third level targeting intracellular targeting Mitochondria

FIGURE 2. Levels of drug targeting. Showing different levels of drug targeting in liver.

Liposomes –

The name liposome is derived from two Greek words Lipos' meaning fat and 'Soma' meaning body. Liposomes are synthetic vesicles of small size and spherical shape. Liposome first described by the British hematologist Dr. Alec D Bangham in the year 1964.They can be prepared from cholesterol and natural non-toxic phospholipids. Being of hydrophobic and hydrophilic nature, small size, and biocompatible, liposomes are promising drug delivery system. Liposomes can trap hydrophobic as well as hydrophilic compounds, avoid decomposition of the entrapped combinations, and release the entrapped compounds at target site. The most advantageous features of liposomes, than other carriers, are the ability to incorporate and deliver relatively large amounts of drug, and the possibility to decorate their surface with different ligands. Moreover, liposomes have been used clinically as delivery systems because of their ability to increase both the safety and the efficacy of many drugs. For CNS drug delivery, pharmacokinetics and bio distribution, including binding to plasma proteins or degradation of the drug in blood, play an important role in the overall efficacy of the system. Limitations of liposomes include not only fast systemic elimination, but also metabolic degradation of the phospholipids, vesicle stability issue after large scale production and storage, and inability to provide sustained release of drugs. Indeed, some of these problems have been partially overcome and marketed liposomes of the newest generation are more stable with shelf-lives up to several months.

Commented [v1]: first step

However, it seems still difficult to ensure long-term administration into brain in the treatment of neurodegenerative diseases.

Classification

The Liposomes may be classified based on:

1) Structure.

2) Types

Liposomes, on the basis of their size and number of bilayers, are of the following three basic types:

1) Multilamellar Vesicles (MLVs): These liposomes have more than one lamella, and their size varies between 100-1000nm.

2) Small Unilamellar Vesicles (SUVs): These liposomes have a single lamella, and are smaller than 0.1uum in size. Composition of the membrane and the variation of SUVs is small when the liposomes approach the minimum size. aqueous medium influence the minimum size that can be attained.

3) Large Unilamellar Vesicles (LUVs): These liposomes have a single lamella and their size ranges from 0.1um to 1000nm (close to the size of living cells)

Vesicle size	Abbreviation	Diameters size	No of lipid bilayer
Unilamellar	UV	All size range	One
Small unilamellar	SUV	20-100	One
Mediumunilamellar	MUV	More than 100	One
Large lamellar	LUV	More than 100	One
Multi lamellar	MLV	0.5	5-25

2) Classification Based on Method of Preparation :

Different preparation and vesicle methods :

Single or oligolamellar vesicle made by reverse phase evaporation	REV
Multilamellar vesicle made by reverse phase evaporation method	MLV-REV
Stable plural lamellar vesicle	SPLV
Dehydration-Rehydration	DRV
Vesicle prepared by extrusion technique	VET

3) Classification Based on Composition :

Different Liposomes with their Compositions.

Conventional	Neutral or negativity charge phospholipids and cholesterol
Mucogenic	Reconstituted sendal virus envelope.
pH sensitive	Phospholipids such as PER or DOPE with either CHEMS or OA.
Cationic	Cationic lipid with DOPE

4) Classification Based upon Conventional Liposome:

Natural lecithin mixtures.

Synthetic identical, chain phospholipids

Liposome with glycolipids.

Advantages of targeted drug delivery system :

1. The toxicity of the drug is decreased by targeting a Specific site.
2. The desired drug response can be reached by a less Dose.
3. Avoid the first-pass effect.
4. Improvement in the drug absorption from the target Site.
5. Drug targeting resulted in no peak and valley plasma concentration.
6. The protocol of drug administration becomes simpler.

Disadvantages of target drug delivery system :

1. drug elimination from the body results in High dose frequency.

2. The carrier of the targeted drug delivery system

May result in the immune response.

3. The drug delivery system is not localized at the

Tumor tissue for sufficient time.

4. The diffusion and redistribution of released drugs.

5. The manufacturing, storage and administration

Of the targeted drug delivery system require high

Expertise in this field.

6.Toxicity may be raised from drug deposition at the Target site.

7.The stability of the product will be difficult to control.

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