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Targeting Methods: A Short Review Including Rationale, Goal, Causes, Strategies for Targeting

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A BSTRACT

A type of intelligent drug delivery device known as targeted drug delivery is remarkable at getting the drug to the patient. While the targeted release system releases the medicine in a dose form, the conventional drug delivery method involves the drug being absorbed through a biological membrane. The enhancement of pharmaceutical action, the absence of negative side effects, and the reduction of the supplied dose are just a few of the advantages that targeted drug delivery systems have over conventional ones. The basic goal of a targeted drug delivery system is to ensure that the therapeutic agent only acts on sick organs while avoiding harming healthy ones, particularly when treating cancer with chemotherapeutic drugs.

Different carriers that keep and deliver the intact drug to a chosen organ or tissue might be used to target drugs. Various carriers, including nanotubes and nanowires, nanoshells, quantum dots, nanopores, gold nanoparticles, dendrimers, noisome, ufasomes, virosomes, cubosomes, nanobots, and transferosomes, can be utilized for drug targeting. Targeting drugs can be done through a variety of techniques, including passive, inverse, active, ligand-mediated, physical, dual, and double targeting. The medicinal substance can be delivered to a specific spot with the help of medication targeting, which prevents toxicity in other organs.

Targeted drug delivery is a cutting-edge technique for giving medications to patients in sequences that are specifically designed to increase the concentration of the drug delivered to the targeted body part of interest (organs, tissues, or cells), which enhances treatment effectiveness by lowering adverse drug reactions. Targeted drug delivery essentially helps the drug molecule arrive to the preferred place. The inherent benefit of this method allows for the delivery of the needed medication at a lower dose and with fewer side effects. Research and development in the clinical and pharmaceutical areas are heavily focusing on this inherent benefit of targeted drug delivery systems as the foundation of treatments and diagnostics as well.

Keywords: Targeted Drug Delivery System (TDDS), RES system, Carriers, Polymers, Micro-molecules, Macromolecules, Nanoparticles, Liposome etc.

1. INTRODUCTION

A specific type of drug delivery system called a targeted drug delivery system ensures that the drug is delivered exclusively to the site of action and not to unintended organs, tissues, or cells. It is a technique for giving medication to a patient so that more of it is concentrated in some areas of the body than in others. The goal of targeted drug delivery is to increase the concentration of the drug in the target tissues while decreasing the relative concentration of the drug in the non-target tissues.

In drug targeting, the drug may be delivered to (3, 4)

1. The target site's capillaries.
2. The particular kind of cell, such as cancer cells.
3. specific organs or tissues that can identify the drug carrier

2. SCHEME AND RATIONALE FOR DRUG TARGETING

Drug targeting is appropriate for medications with poor therapeutic indexes, poor absorption, short half-lives, or excessive distribution volumes. All of these situations call for the formulation of the medications into the specific delivery mechanism. By altering the drug's improper disposition and lowering

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its presence in untargeted locations, targeted drug delivery systems reduce the negative effects. Treatment targeting also increases the therapeutic effectiveness of the treatment by limiting inactivation of the drug while travelling to the target region. Additionally, because the medicine is not degraded before it reaches the target area and does not interact with unintended cells, the overall dose is also decreased. This is especially significant when treating cancer because lower doses are less harmful to healthy cells (1, 2).

3. GOAL:

To obtain the desired drug response at selected sites without adverse interactions at other sites, the drug has specific effects with minimal side effects and a better therapeutic index. Ex- For cancer chemotherapy and enzyme replacement therapy.

4. Causes For The Usage Of Targeted Drug Delivery Systems (TDDS) (5)

There are various reasons for using a targeted drug delivery system, which include:

1. Drug stability is poor.
2. Drug absorption is poor.
3. The drug's short half-life.
4. The drug's vast volume of distribution.
5. Drug specificity is low.
6. The drug's narrow therapeutic index

5. THE IDEAL CHARACTERISTICS OF A TARGETED DRUG DELIVERY SYSTEM (TDDS)

The targeted drug delivery system must have the following characteristics: (3)

1. It must be stable, non-toxic, compatible with body fluids, and biodegradable.
2. Only administer the medicine to the intended place.
3. Maintain a constant rate of medication release.
4. The medication release rate has no effect on the pharmacological action.
5. Minimal drug leakage during delivery to the target place.
6. Using a carrier that is inert, biodegradable, or easily removed.
7. The medication delivery system preparation method should be straightforward, easy, and inexpensive.

6. THE BENEFITS OF DRUG TARGETING (6)

1. The drug administration protocol gets simpler.
2. The drug's toxicity is reduced by targeting a specific location.
3. A tiny dose can achieve the desired pharmacological response.
4. Stay away from the first-pass effect.
5. Increased medication absorption from the target site.
6. There were no peak and valley plasma concentrations as a result of drug targeting.

7. The Drawbacks Of Drug Targeting (7)

1. High dose frequency is caused by rapid medication removal from the body.
2. The immune response may be triggered by the carrier of the targeted drug delivery mechanism.
3. The drug delivery mechanism is not sufficiently localized at the tumor tissue.
4. The spread and redistribution of medications that have been released.
5. The targeted drug delivery system's manufacturing, storage, and administration necessitate a high level of competence in this discipline.
6. Drug accumulation at the target location may cause toxicity.
7. The product's stability will be tough to achieve.

8. CARRIES ARE USED TO TARGET DRUGS. (8)

1. Drug targeting can be accomplished through the use of carrier systems.
2. The carriers are the systems required for transporting the entrapped drug to the target areas.
3. The carriers entrap the drug moiety and transfer it to the target site while leaving the non-target site unaffected.

9. STRATEGIES OF DRUG TARGETING

Fig. No. 1: Representing Drug targeting strategies

1) Passive Targeting :

Drug delivery systems that affect systemic circulation are referred to as passive delivery systems.

With this approach, drug targeting develops as a result of the body's innate reaction to the physicochemical properties of the medication or drug delivery system.

It is a kind of passive process that takes advantage of the natural course of the biodistribution of the transport system, eventually accumulating in the organic compartments of the body.

2) Inverse Targeting :

This type of targeting attempts to avoid passive uptake of the colloidal vector by the RES (reticuloendothelial systems) and is therefore referred to as reverse targeting.

To achieve reverse targeting, normal RES function is suppressed by pre-injection of large amounts of native colloidal carriers or macromolecules such as dextran sulfate. This strategy causes the RES to become saturated and the defense systems to be suppressed

3) Active Targeting :

Conceptually, active targeting uses the modification or manipulation of a drug's carriers to redefine its biology.

In this approach, the delivery system carrying the drug reaches a specific site through modification on its surface, rather than through natural uptake by RES.

In the surface modification technique, the surface is treated with a nonionic bioadhesive surfactant or cell- or tissue-specific antibodies (e.g., monoclonal antibodies) or albumin proteins.

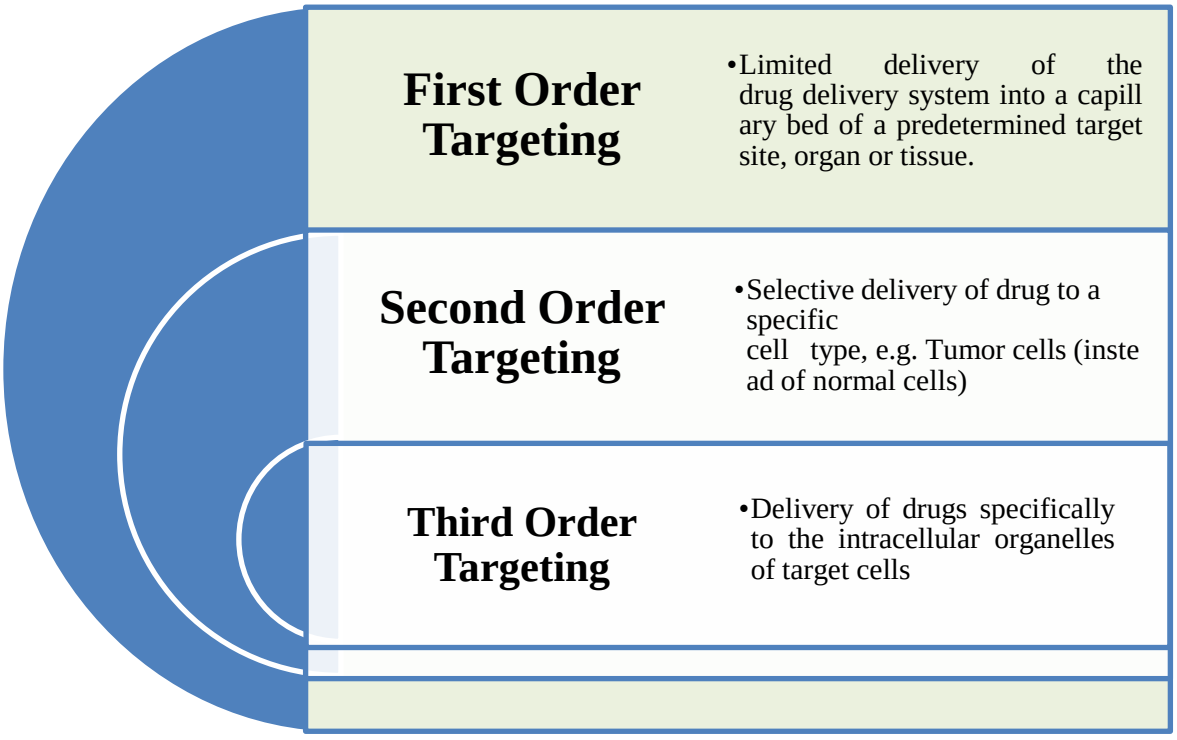

Fig. No. 2: Representing Active targeting

4) Ligand Mediated Targeting :

Achieved through specific mechanisms such as receptor-dependent uptake of natural LDL particles and synthetic lipid micro emulsions of partially reconstituted LDL particles coated with apoproteins.

5) Physical Targeting :

In this type of targeting, some properties of changes in the environment, such as pH, temperature, light intensity, electric field, ionic strength, use small and even specific stimuli such as glucose concentration to localize the drug transporter at a particular site.

This approach has been recognized as unique for targeting tumors and delivering entrapped drugs or genetic material in the cytosol.

6) Dual Targeting :

In this targeted approach, the carrier molecule itself has therapeutic activity of its own, thereby enhancing the therapeutic effect of the drug.

For example, an antiviral drug can be loaded onto a carrier molecule with its own antiviral activity, and a clear synergistic effect of the drug conjugate was observed.

7) Double Targeting :

Double targeting is the term used to describe the targeting of the delivery system using both temporal and spatial methodologies.

Spatial distribution refers to the targeting of drugs to specific organs, tissues, cells, and even a sub cellular compartment, whereby scheduled delivery we mean controlling the speed at which the drug is delivered to its destination.

8) Combination targeting

These targeting systems include vectors, polymers, and specific molecular guidance devices that can allow direct approach to the target site.

Modification of proteins and peptides using artificial or natural polymers, such as polysaccharides. It may alter their physical characteristics and favor targeting the specific compartments. / Can change their physical properties and aid in aiming at certain distances.

10. COMPONENTS OF DRUG TARGETING

A target and the drug carriers or indicators needed to target the site are components of every medication (drug) delivery system.

1) **Target: -** The term "target" refers to an organ, tissue, or cell that needs to be treated.
2) **Drug Carrier or Marker Drug: -** Only a carrier system is capable of carrying out drug distribution. Molecules or other mechanisms are responsible for a drug's successful delivery to the target area. Carriers are vectors designed particularly to hold a medicine inside of them. Encapsulation makes it feasible for this to happen.
3) **Drug delivery Vehicles: -** These move the medicine either within the target or close by. The best medicine delivery method should be able to pass across barriers like the blood brain barrier. Target cells should be able to quickly recognize it, and as a result, the drug-ligand complex that is created should be stable. These must also be non-toxic and biodegradable. Drug carriers' biodegradable nature makes it possible for the body and physiological processes to quickly eliminate them, preventing any possibility of their buildup within cells where they can cause cytotoxicity. (13,14)

11. TYPE OF CARRIER

1) **Endogenous Particulate Carriers**
   Lipoproteins and serum albumin-resealed erythrocytes are two examples of endogenous carriers. Triglycerides and cholesteryl esters make up the lipoproteins, which are encased in a phospholipids monolayer. They are nonimmunogenic because they must have the benefit of being endogenous. High-density lipoproteins (HDL), low-density lipoproteins (LDL), very low-density lipoproteins (VLDL), and chylomicrons are the four types based on densities into which they are divided. (9)

2) **Pharmaceutical Carriers**
   Greater flexibility in structural and physiochemical features is possible when polymers are used as carriers. Microcapsules, microparticles, nanoparticles, and micelles are a few of the polymeric carriers utilized in drug delivery systems. Liposomes and solid lipid nanoparticles are two types of lipids used as carriers. (10)

3) **Carriers With Targeting Moieties**
   Targeting molecules bind to receptors that are specifically and purposefully present on target cells. In contrast to passive targeting, carriers with targeting moieties bind the moiety with the receptor to provide a more focused accumulation of medicines at the target region. Following are some examples of targeting molecules: antibodies, lectins, proteins, lipoproteins, hormones, charged polysaccharide molecules, and low molecular weight ligands. (11)

4) **Cellular Carriers**
   They are the carriers already present in the body of a living thing and have the innate ability to transfer and move medicines from one location to another. Some of the cellular carriers include erythrocytes, serum albumin, antibodies, platelets, and leukocytes. (12)

12. CONCLUSION

Targeted drug delivery can be achieved using a support system. The conveyor is one of the specialty molecules or systems typically required to efficiently deliver loaded drugs to preselected locations.

The complicated cellular network of an organism makes it challenging for drug delivery molecules to reach their target sites. Last but not least, targeted drug delivery is emerging as one of the most cutting edge methods in the medical sciences for the detection and treatment of a few fatal diseases. Research and development in the medical and pharmaceutical areas have grown significantly from their infancy and are currently at their peak. Overall, it can be said that the science of site-specific or targeted drug administration has gotten more mature and smart with time and the development of scientific technology thanks to the large database of many investigations.

The clinical use of all these techniques and cutting-edge technology ushers in a new era of therapy and diagnostics. Numerous issues that sprung up while developing drug targeting strategies for use in clinical settings with various therapies have been found, examined, and resolved, particularly with regard to the treatment of cancer. Many of these treatments are currently being sold and are in various stages of clinical testing. However, in light of improvements in our understanding of the various processes triggered by the injection of carriers or vehicles containing therapeutically relevant medicines with site specificity, such tactics should be continually evaluated. Utilizing the current 'bench to bed-side' expertise, new solutions under research should undergo frequent examination.

In addition, combining knowledge in the field of drug targeting with technical advancements in molecular biology and molecular medicine will make it easier to understand the cellular and molecular mechanisms behind disease in the next years.

Pharmaceutical carriers:

1. Polymers
2. Microcapsules
3. Microparticles
4. Lipoproteins
5. Liposomes
6. Micelles

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