



Review Article

An Overview on Targeted Drug Delivery Systems

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ABSTRACT

Targeted drug delivery system is a novel method of delivering medication to specific targeted site of the body. It improves the efficiency of treatment and reduces the adverse effects of drug administration. This inherent advantage of targeted drug delivery system is under high consideration of research and development in clinical and pharmaceutical field as the backbone of therapeutics and diagnostics too. Active targeting and Passive targeting are the two strategies which are mainly used for drug targeting to the specified organ or tissue. Drug carriers which are used in this advanced drug delivery systems are lipoproteins, soluble polymers, artificial cells, liposomes, neutrophile, fibroblasts, immune micelle. The main objective of this system is to extend and target and a safe drug interaction with affected cells or tissues.

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INTRODUCTION:

Targeted drug delivery is a advanced method of delivery of drug to the patient in which the pharmacologically active ingredients are selectively targeted or delivered only to its site of action or absorption.^{1,2,3}As a theoretical concept it became most popular and found to be strong alternative for effective and site-specific treatment, but still the ‘magic bullet’ continues to be a challenge to implement it clinically.⁴While implementing a targeted release system the following design criteria for the system need to take into account. The drug properties, side effects of the drug, the route taken for the delivery of the drug, target site and the disease. The carriers transport the drug to the specific targeted site of action. Bio-degradable or readily eliminated carriers should be used in this system.^{5,6} Targeted drug delivery system has more advantages than conventional system as they have high solubility, less drug instability, high absorption, longer half-life and require less volume of distribution. These drugs have high specificity and high therapeutic index as compared to conventional drug delivery system.^{7,8,9}

HISTORY:

The concept of designing specified delivery system to achieve selective drug targeting has been originated from the perception of proposed drug delivery to be as a magic bullet. He explained targeted drug delivery as an event where a drug-carrier conjugate delivers drug exclusively to the preselected target cells in a specified manner. Bangham's (1965) observation on phospholipid hexagonal liquid crystals, that they are pre selective to the ions in a manner similar to bio membrane, led to the discovery of artificial vesicular system based on phospholipid amphiphiles. Gregoriadis. 1981 described drug targeting using novel drug delivery systems as old drug new cloths "MAGIC BULLET" Two components: The first one recognizes and binds the target The second one provides a therapeutic action in this target.^{10,12}

WHY TO TARGET A DRUG:

It is highly essential to target a drug to obtain a desired therapeutic response. The appropriate amount of drug should be delivered to the site of action with subsequent control of drug input rate. It is required to avoid distribution of drug to the tissue which seems to be unnecessary, wasteful and major cause of toxicity. It improves drug safety, drug efficacy and patient compliance.^{11,16}



Figure 1 : Reasons of Drug Targeting

Figure1: Reasons of Drug Targeting

IDEAL CHARACTERISTICS:^{13,19}

It should be inert and non-immunogenic. As well as physically and chemically stable in vivo and in vitro condition. Release of drug should be in a predicted and controllable manner. Whereas leakage of drug during transportation should be minimal.

In case carriers, biodegradable carriers must be used which can readily eliminated from the body without any problem and drug action should not get affected by release of drug whereas amount of drug get release should be therapeutic and uniform. capillary distribution should occur.

STRATEGIES OF DRUG TARGETING:

There are many strategies of drug targeting, few of them are:

1. Passive Targeting: Passive delivery systems are those systems in

which drug is targeted to systemic circulation. For passive hepatic targeting of drugs, some colloids to be taken up by the Reticulo Endothelial System (RES) especially in liver and spleen. Drug release are limited to selective sites within the body.^{17,24}

2. Active Targeting: Active targeting is a drug delivery strategy that uses nanocarriers modified with ligands to target specific cells or tissues. It can improve the efficacy of chemotherapeutic agents and provide more accurate drug delivery. Coating of surface is done by a bioadhesive, non-ionic surfactant or specific cell or monoclonal antibodies or by albumin protein.^{15,20}

3. Inverse Targeting: Inverse targeting refers to the avoidance made for passive

uptake of colloidal carrier by RES. This strategy leads to saturation of RES and retention of defense mechanism. Other strategies include modification and defined manipulation of the size, surface charge, composition, surface rigidity & hydrophilicity characteristics of carriers for desirable biofate.^{22,23}

4. **Ligand-Mediated Targeting:** Ligands are used as carrier surface groups in this type of targeting strategy. To serve as Homing Device to the drug, it can selectively direct the carrier to the pre-specified site of particular receptor units.¹⁴
5. **Physical Targeting:** Physical targeting is a strategy that uses nanoparticle fabrication techniques to influence tissue accumulation, adhesion and cell uptake. This strategy was found as an exception for targeting tumor as well as cytosolic delivery of genetic material.¹⁸
6. **Dual Targeting:** Here, the carrier molecules have their own therapeutic response. Hence, they increase the therapeutic effect of drug. It uses both biological and physiochemical strategies to increase the accumulation of nanoparticle within the TME (Toxic Metabolic Encephalopathy).^{26,28}
7. **Double Targeting:** It refers to the combined methodologies of temporal and spatial methods to target a carrier

system. It also increases drug's therapeutic activity.^{32,33}

8. **Combination Targeting:** This targeting system consists of carriers, polymers and homing devices of molecular specificity which provide a direct approach to targeting site.¹⁹

CARRIERS FOR TARGETING DRUGS:^{31,35,37}

There are many carriers available for targeting the drug. Few of them are

1. **Chitosan:** Chitosan is a good carrier for drugs because it is mucoadhesive, permeation enhancer, and forms a protective barrier for the drug.
2. **Nanoparticles:** These are considered one of the best carriers for targeted drug delivery. They are easily synthesized, functionalized, and have low toxicity, stability, and biocompatibility. Nanoparticles can target the active pharmaceutical ingredient to the target site by both passive and active mechanism.
3. **Liposomes:** These are the small spherical artificial vesicles made up of one or more phospholipid bilayers. These help to improve therapeutic index, rapid metabolism system and unfavorable pharmacokinetics, low solubility, lack of stability, irritation.

4. **Microspheres:** These are characteristically free flowing powders consisting of proteins or synthetic polymers which are biodegradable in nature and ideally having a particle size less than 200µm.
5. **Polymeric Micelles:** These are nano sized molecules used in drug delivery. They are made up of amphiphilic block co-polymers that self-assemble into a core shell structure. The core is hydrophobic and the shell is hydrophilic in nature.
6. **Resealed Erythrocytes:** These are potential drug delivery systems that can be used to target specific sites. They can also be used to obtain prolonged release of drugs. These are also known as drug loaded erythrocytes or carrier erythrocytes.

ADVANTAGES:^{27,38,29}

If we will start talking about advantages of targeted drug delivery system then at first we should say it may be simplified drug administration protocols. Now drug targeting can be achieved by the local administration of the therapeutic compound. However, technology is not yet advanced sufficiently for the design of magic bullet drug delivery systems, proposed by Paul Ehrlich at the turn of the 20th century (1902), in which the

drug is precisely targeted to its exact site of action.

But Systems are available to achieve site-specific delivery within the gastro intestinal tract for oral drug delivery. It contains enteric coatings prodrugs, osmotic pumps, colloidal carriers and hydrogels are appropriate for drug delivery system.

Technologies for targeted drug delivery advanced for parenteral administration are concerned with delivering drugs to specific targets in the body and also to protect drugs from elimination. To ensure more effective drug delivery, recent advances in biological and chemical sciences have led to the development of various smart technologies and targeting of drugs to specific sites within the body.

DISADVANTAGES:^{28,34}

If there are advantages means there must be some disadvantages as advantage and disadvantages are two side of single coin. No doubt targeted drug delivery is very safe but it requires a skill in manufacturing storage, administration and it may highly expensive. Like that diffusion, redistribution, rapid clearance and maintaining stability are few challenges associated with targeted drug delivery. At last we should not ignore yields, which are comparatively very less

in comparison to other drug delivery systems.

DECLARATION

There is no conflict of interest in publishing this review article.

CONCLUSIONS:

Research related to the development of targeted drug delivery system is now a days highly preferred and facilitating field of pharmaceutical world. It is now touching height of growths from the pharmacy point of view. It is quite hard for a drug molecule to reach its site of action in the complex cellular network of an organism. Targeted delivery of drugs, means to assist the drug molecule to reach preferably to the desired site. The inherent advantage of this method has been the reduction in dose & side effect of the drug. Overall, it may be concluded with the huge database of different studies, the science of site specific or targeted delivery of these drugs has become wiser. Manifestation of these strategies in clinical now appears to be possible in near future.

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