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A REVIEW ON TARGETED DRUG DELIVERY SYSTEM

Nidhi A. Bagmar, *Pooja R. Hatwar and Dr. R. L. Bakal

Department of Pharmaceutics, Shri Swami Samarth Institute of Pharmacy, At Parsodi Dhamangaon Rly- 444709 Maharashtra, India.

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***Corresponding Author**
Pooja R. Hatwar
Department of Pharmaceutics, Shri Swami Samarth Institute of Pharmacy, At Parsodi Dhamangaon Rly- 444709 Maharashtra, India.

ABSTRACT

Targeted drug delivery is an advanced drug delivery system that increases the concentration of a specific drug only to the desired body part (organ/tissue/cell), improving the therapeutic effect by reducing side effects. Targeted drug delivery systems offer several advantages over conventional systems, including increased pharmacological activity, reduced side effects, and reduced dosage. The main purpose of a targeted drug delivery system is to make therapeutic drugs only have pharmacological effects on diseased organs without affecting health, especially in the cancer treatment of chemotherapeutic drugs. Various types of carriers can be used for drug targeting, such as B. Nanotubes and nanowires, nanoshells, quantum dots, nanopores, gold nanoparticles, dendrimers, noise bodies, ufasomes, virosomes, cubes, nanorobots and transfer bodies. There are different drug targeting mechanisms such as passive targeting, reverse targeting, active targeting, ligand-mediated targeting, physical targeting, dual targeting, and dual targeting. Drug targeting is a useful delivery system for delivering therapeutic agents to specific sites without causing toxicity to other organs.

KEYWORDS: Targeted Drug Delivery System, Strategies, Carriers, liposome, Gold Nanoparticles.

INTRODUCTION

A target is a specific organ, cell, or group of cells that require treatment for a chronic or acute condition.[1] Targeted drug delivery is a method of delivering a drug to a patient in a manner that increases the concentration of the drug in certain parts of the patient's body relative to others.[2] Targeted drug delivery systems is preferable over conventional drug delivery systems because of some main reasons. The first one is pharmaceutical reason. Compared

with targeted drug delivery systems, conventional drugs have lower solubility and more drug instability. Second reason is its pharmacokinetic properties. Conventional drugs have poor absorption, short half-life, and large volume of distribution. The third reason is the pharmacodynamic properties of the drugs. Conventional drugs have low specificity and low therapeutic index compared to targeted drug delivery system. For these reasons, a targeted drug delivery system is better than conventional drug delivery systems.[3] The principle of TDDS is to deliver more drugs to the target of action and decrease the drug concentration near the target cell or tissue.[4] The system is based on a method that can deliver a certain amount of therapeutic agent to the target pain area in the body for a long time, increasing efficacy and reducing side effects. This helps regulate plasma and tissue drug levels in the body, thus preventing the drug from damaging healthy tissue.[5]

Ideal characteristics of a targeted drug delivery system are[3]

1. Should be biochemically inert.
2. Should not be immunogenic.
3. Drug release does not influence the drug action.
4. The therapeutic amount of drug released.
5. Minimal drug leakage during transfer.
6. The carrier used must be biodegradable and easily removed from body without any issue or modulation of the disease state.
7. The preparation of the delivery system should be simple or reasonably simple, reproducible and inexpensive
8. Drug leakage should be minimized during transport.

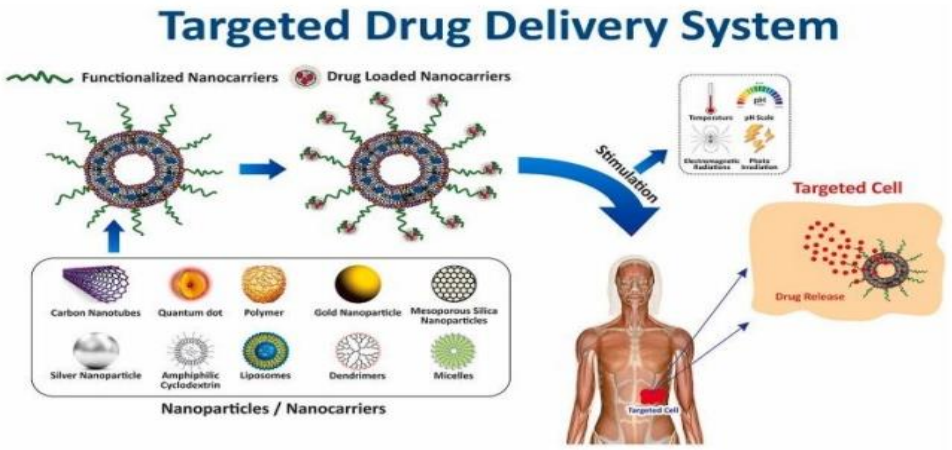

Fig 1: Targeted Drug Delivery System.[3]

ADVANTAGES[6,1,4,3]

1. Reduce drug toxicity by targeting specific sites.
2. A small dose can achieve the expected drug effect.
3. Drug consumption and treatment costs can be greatly reduced.
4. Target infectious cells to improve therapeutic effect compared to normal cells.
5. Drugs are released in a controlled manner over a longer period of time, reducing fluctuations in drug plasma levels.
6. It targets diseased tissue or a specific part of the body without affecting healthy tissue.
7. Intermittent administration can be avoided.
8. Improve patient compliance.
9. Avoid the first-pass effect.

DISADVANTAGES[6,4,3]

1. Rapid elimination of drug from the body resulting in high dose frequency.
2. Dissemination and redistribution of released drugs.
3. Professionals are required to handle and control the delivery to the place of use.
4. Degradation of digestive tract flora, first-pass metabolism, food interaction, etc.
5. Bioavailability is poor.
6. Complex manufacturing processes, management and storage must be further developed Skill.
7. Maintaining the stability of the dosage form is difficult.

COMPONENTS OF TARGETED DRUG DELIVERY[7]

Target: The term "target" refers to a specific organ, cell, or group of cells that require treatment for either a chronic or acute condition.

Carrier or marker: One of the special molecules or systems that is absolutely necessary for the efficient transportation of the loaded drug to the predetermined locations is the carrier. They are designed Carrier that transport or deliver drugs to the vicinity of the target cell by either encapsulating the drug or attaching a spacer moiety to it.

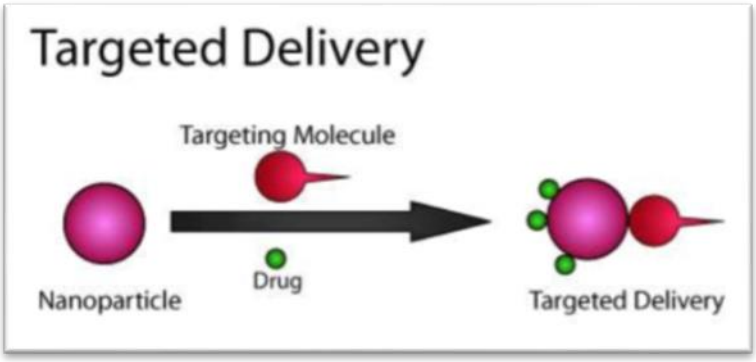

Fig 2: Nanoparticle Target Drug Delivery System.[5]

STRATEGIES OF DRUG TARGETING

1. Passive Targeting: Passive targeting often refers to drug delivery techniques that direct the medication into systemic circulation.[6] It refers to the accumulation of a drug or drug-carrier system at a specific place, such as an anti-cancer medication, the cause of which may be linked to disease-related physicochemical or pharmacological factors.[8] Conventional anticancer treatments rely on passive targeting because malignant cells collect a substantially larger concentration of the medication due to quicker and higher blood supply.[9] Drug activity or release is restricted to certain areas inside the body, such as a cancer, but not the liver. Other instances include the use of antimalarial medicines to treat leishmaniasis, brucellosis, and Candidiasis.[1]

2. Active Targeting: Active targeting is defined as a particular ligand-receptor interaction for intracellular localization that happens only after blood circulation and extravasation.[8] Active targeting is classified into three types: first-order (organ targeting), second-order (cell targeting), and third-order (intracellular targeting).[6] When coupled with nanoparticles, ligands such as antibodies, peptides, and nucleic acid aptamers can enable active targeting.[10]

3. Inverse Targeting: When the reticulo endothelial system (RES) prevents passive uptake of colloidal transporters, the process is called drug reverse target.[9] To restore the target, the normal activity of RES is inhibited by injecting large amounts of white colloidal or macromolecules such as dextran sulfate. This approach saturates the RES and inhibits its defense mechanisms. This type of targeting is a good way to target drugs to organs other than the RES.[7]

4. Dual Targeting: Dual targeting involves drug delivery where the carrier has a combination of trapped drugs, thereby increasing the therapeutic effect.[6] For example, ZnO

nanoparticles contain antibiotics, and when antibiotics are packaged into porous ZnO nanoparticles, both carrier and drug are effective for bacteria, so TDD corresponds to two purposes.[9]

5. Double Targeting: When temporal and spatial methodologies are combined to target a carrier system, also 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 (3).

6. Physical Targeting: To get the drug carrier to a predetermined location, physical targeting makes use of environmental conditional changes like pH, system temperature, light intensity, magnetic field, electric field, or ionic strength, as well as other small and even specific stimuli like glucose concentration or gaseous concentration.[9]

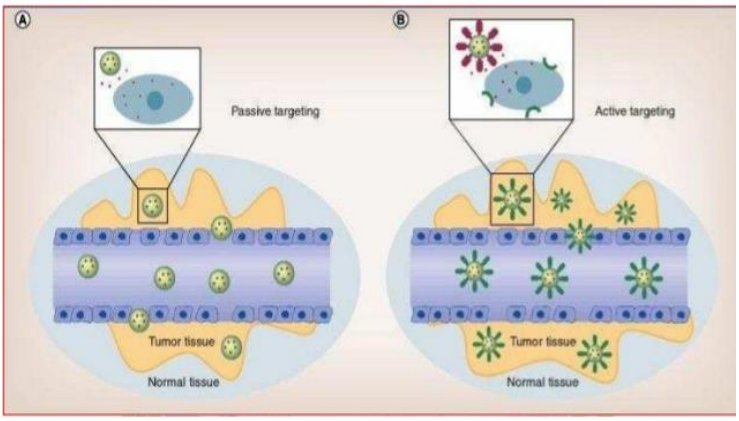

Fig 3: Types of Targeted Drug Delivery System.[1]

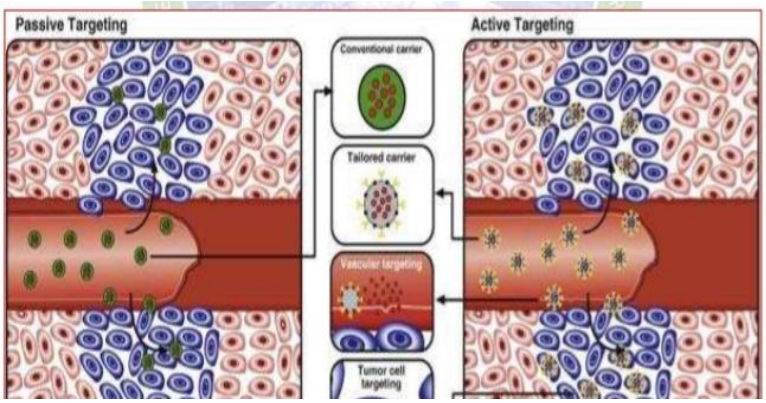

Fig 4: Types of Targeted Drug Delivery System (Active and passive targeting).[1]

Different types of carriers applied for drug targeting[11]

There are lots of carriers applied in the targeted drug delivery system which include:

1. Liposomes which are also known as vesicles of lipids.
2. Niosomes which are known by vesicles of surfactants.
3. Ufasomes which are also called vesicles of unsaturated fatty acids.
4 Pharmacosomes.
5. Virosomes.
6. Transferosomes.
7. Cubosomes.
8. Nanobots.
9. Nanocrystals.
10. Hydrogels.
11. Exosomes.
12. Quantum dots.
13. Gold nanoparticles.
14. Dendrimers.
15. Microsponges.
16. Nanoferrosponges.

1. Liposome: The name liposome comes from two Greek words: 'Lipos' means fat and 'Soma' means body.[7] Liposomes are microscopic bilayer vesicles prepared using natural phospholipids. They can enter hydrophilic and lipophilic substances in aqueous media or in the phospholipid bilayer.[6] Bangham discovered liposomes while researching cell membranes in 1965. Liposomes are classified into several forms, including Multilamellar vesicle (MLV), Small unilamellar vesicle (SUV), Large unilamellar vesicle (LUV), and Cochleate vesicle.[3]

2. Niosome: Niosome is a vesicle-based nonionic surfactant. Niosomes are mainly composed of nonionic surfactants and cholesterol. They are similar to liposomes in that they both have a lipid bilayer. They are more stable than liposomes under production and storage conditions. They are used as hydrophilic and lipophilic drugs.[12] The niosomes are categorized as a function of the number of bilayer (MLV, SUV) or as a function of size (e.g. LUV, SUV) or as a result of the medication system (e.g., REV, DRV). The following is a description of the various colorful niosomes. The niosomes are categorized according to either their size or the number of bilayers (SUV, LUV) and (MLV, SUV) or as a result of the medication system (e.g. DRV, REV).[13]

3. Ufasomes: Ufasomes are dispersions of unsaturated fatty acid vesicles prepared by fatty acids and ionic surfactants (soap) in the presence of cholesterol. Ufasomes are good carriers for cosmetics.[6] They are considered good candidates for local drug release, as they cross the outer barrier originating from the lipid layer. They have advantages over liposomes in terms of stability and are cost-effective compared to liposomes.[11]

4. Pharmacosomes: The term pharmacosome is derived from the word Pharmakon, meaning drug and soma, meaning carrier.[6] These are called neutral molecules and have positive and negative charges. They are complexes of phospholipids and polyphenols.[11] These are amphiphilic lipid vesicle systems with phospholipid complexes that increase the bioavailability of low-water-soluble and fat-insoluble drugs.[2]

5. Virosomes: Virosomes are single lamellar vesicle drug delivery systems prepared from phospholipids.[6] This technology is a new carrier that can be added to vaccines or used as synthetic products. They are prepared with various reagents such as antigens, drugs and influenza proteins. They are only studied in the field of immunology.[11]

6. Transferosomes: A transferosomes is a device or a tool that can transfer drugs when applied on the targeted site through easy penetration of the skin. Transferosomes are mainly use for skin because of their self-optimized and ultra-flexible membrane properties.[14]

7. Cubosomes: Colloidal dispersion of bicontinuous cubic liquid-crystalline structure in water, producing surfactants to form nanostructured systems called "cubes" from 100 to 500 nm in size. Biocompatibility, bioadhesion, and the ability to promote drug release are important features that make CUBs potential drug delivery vehicles.[15]

8. Nanobots: Nanobots is the branch of nanomedicine that is also known as a micro-scale delivery system. They are very small in vision so they can easily traverse the human body. They have a broad range of applications in dentistry, nanoimpression, in the diagnosis of cancer and diabetes. Nowadays, they are also used in gene therapy with improved better therapy.[11]

9.Nanocrystals: Nanocrystals are the material having a dimension less than 100 nm and present in the form of one crystalline structure.[6] As a combination of chemical components and simple stabilizers, NCs can increase the solubility, dissolution rate, and bioavailability of

poorly soluble drugs or possibly new drug molecules that can be administered orally, intravenously, or other routes.[16]

10. Hydrogels: It is three dimensional, hydrophilic, polymeric networks capable of incorporating large amount of water or biological fluids. The network consists of homopolymers or copolymers and is insoluble in chemical or physical crosslinking. It exhibits thermodynamic compatibility with water and allows expansion in aqueous media.[17]

11. Exosomes: Their diameters vary between 40-100 nm. Exosomes are lipid bilayer vesicles. They are used in the diagnosis of diseases by revealing the characteristics of the drug release target.[9]

12. Quantum dots: Quantum dots are nanocrystalline semiconductor particles with special optical properties that enable them to be used in tumor imaging.[6] Quantum dots are semiconductor nanostructures with a diameter of 25 billionths of a meter that can trap electrons in three dimensions and emit light when exposed to ultraviolet radiation.[7]

13. Gold Nanoparticles: Gold nanoparticles (AuNPs) have been widely exploited as nanomaterials for theranostic application because of their multifunctional characteristics in imaging, therapeutics and surface modification.[18] Gold nanoparticles are utilized for the detection of various types of cancerous cells, including breast cancer, lung cancer, and prostate cancer.[12]

14. Dendrimers: Derived from the Greek word 'dendron' meaning tree. Dendrimers are generally defined as monodisperse macromolecules with a highly three-dimensional structure that provides a high degree of surface activity and a wide range of functions. Dendrimers are a new class of polymer materials.[2]

15. Micro sponges: These are polymers with large pores and small spongy spherical particles. Microsponges are designed to efficiently deliver active drugs with minimal doses, reduce side effects, increase safety, and improve drug release. Microsponges are 5-300 µm in diameter and spheres can contain up to 250,000 pores. Microsponge delivery system (MDS) is also known as material phase porous microspheres as it is a patented microparticle system.[18]

16. Nanoferrosponges: These are nanocarriers made of metal ions that can be opened with magnets. Since these drugs directly target tissues, the metal nanosponges have enhanced penetration due to external magnetism. It is also known as one of the new best approaches to a targeted drug delivery system.[11]

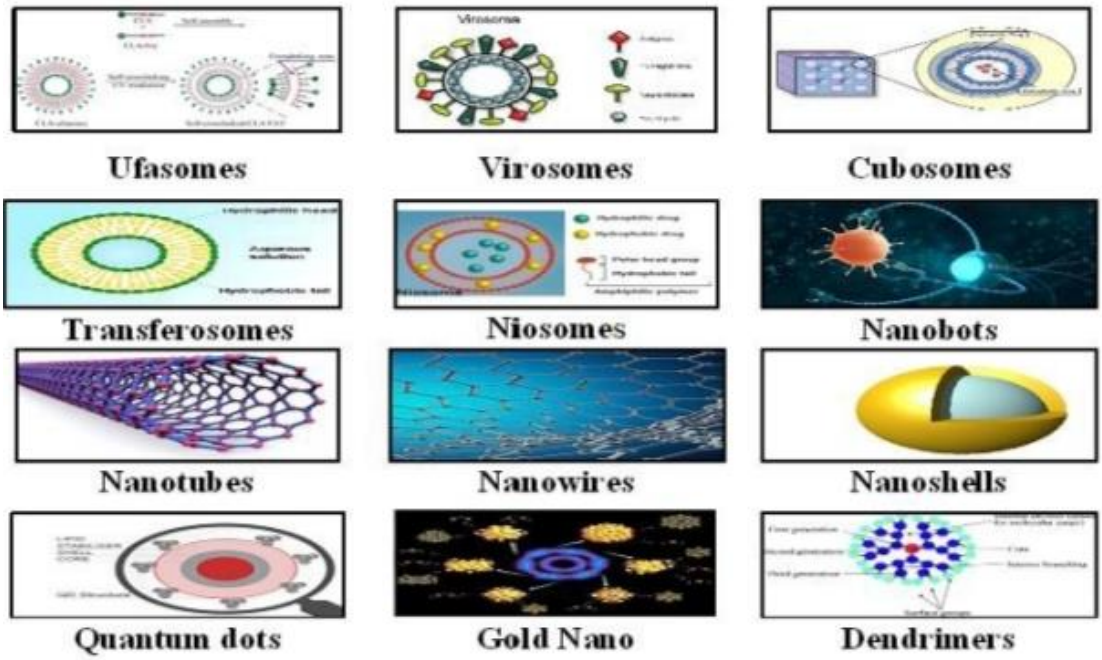

Fig 5: Different types of carriers for drug targeting.[6]

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