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Research Article

Therapeutics Diagnosis

A Short Review on Targeted Drug Delivery System: Focus on Advanced Therapeutics and Diagnosis

Devi R.[1*], Srinivasan R.[2], Jothi Lakshmi R.[3], Shiva Sakthi. A S.[4], Dhavamanikandan. A A.[5], Vel. K S.[6], David. E S.[7]

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[1*] R Devi, Assistant Professor, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

[2] R Srinivasan, Dean and Professor, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

[3] R Jothi Lakshmi, Assistant Professor, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

[4] Sree Shiva Sakthi. A, B. Pharm, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

[5] A Dhavamanikandan. A, B. Pharm, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

[6] Shakthi Vel. K, B. Pharm, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

[7] Sam David. E, B. Pharm, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

Delivering a drug to supply its therapeutic effect in the targeted site of diseased human tissue in a human body with low toxicity is known as targeted drug delivery system. It has numerous advantages like reducing the frequency of drug dosage of patients, also performing a uniform therapeutic effect of a drug with reduced side effects and toxicity. This system is also known as a "Smart drug delivery" Its ultimate goal is to achieve pharmaceutical and therapeutic effects in the system. Liposomes act as an important tool for targeted drug delivery systems which is a long-circulating macromolecular carrier with enhanced permeability and retention. This system mainly concentrates on delivering the nanoparticles of a drug only in the infected tissue without the interaction of healthy tissue. A Targeted drug delivery system is widely used in cancer therapy treatments such as chemotherapy to get the required therapeutic effect on the tumor.

Keywords: Therapeutic effect, nanoparticles, cancer therapy, Target, Liposomes

Corresponding Author

R Devi, Assistant Professor, Faculty of Pharmacy, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
Email: devivarshni@gmail.com

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Introduction

The method of delivering a drug to supply its therapeutic effect in the targeted site of diseased human tissue in the human body with low toxicity is known as targeted drug delivery system. This TDDS is otherwise known as smart drug delivery. [1] This system mainly concentrates on delivering the nanoparticles of a drug only in an infected tissue without the interaction of a healthy tissue.

Widely seen in the treatment of cancer [chemotherapy], to get the required therapeutic effect on the tumor. To target specific cells and deliver the drug to the cells, it must be designed by considering various properties of the drug and the cells.

They may be target cells, vehicles or carriers and specific receptors that bind to the ligand.

An ideal Targeted drug delivery system should have various characteristic properties

1. It must be non-toxic.

2. It must be stable in invivo and in vitro conditions.

3. It must be non-immunogenic.

4. It must have minimum drug leakage during transmission.

5. It must have uniform distribution to the specific cells, tissues, organs only

6. It must have a predictable and controlled drug release rate.

7. Drug release should not affect the action of the drug.

8. It must have assured therapeutic action.

9. The carriers should not stay in the body for a long period of time; it must be eliminated

10. It must be easy, cost efficient and reproductive to prepare the drug delivery system.

The targeted drug delivery system should have these characters to assure the desired therapeutic action with low adverse drug reactions.

Advantages:

- Better only on the transportation of the drug on a specific location
- Adverse drug reactions could be minimised by increasing the concentration of the drug at the targeted site and decreasing the concentration of the drug to the non-targeted areas.
- Wide range of drug carriers that are envisaged to deliver drugs that are nanoparticles, Polymers, liposomes, micelles
- It is preferred over conventional drug delivery methods.
- TDD increases the drug action and as well as bioavailability.
- delivering the drug to the whole body, this system is concentrated

Drug Targeting

Drug targeting is defined as the localization of the drug in its target which had been already determined. Thereby restricting the passage of the drug to the non-targeted areas to reduce drug toxicity and other harmful effects. This could be done with the help of carrier technology and specific sith targeting.

Classification

1. First order targeting

2. Second order targeting

3. Third order targeting

First Order Targetin

The first order targeting is used to explain the delivery of the drug to a specific organ or tissue. This includes using pharmaceutically active components that are selective to a particular site in the body. This approach is also known as the Magic bullet approach.

Example: Compartmental targeting in peritoneal and pleural cavity.

Second Order Targeting

The second order targeting involves the targeting of a specific cell, tissue or organ. This uses a pharmaceutically active component to deliver on an affected cell and not on a normal cell which also undergoes some enzymatic reactions. This is also known as prodrug approach.

Example: Selective drug delivery to the liver cells (kupffer cells).

Third Order Targeting

The third order targeting delivers the drug to the specific components of the intracellular region of the target cells. This uses a macromolecular carrier system to deliver the drug to the specific site and affects the response. This is also known as carrier targeting.

Example: Lysosomes.

Third order targeting is further classified into two types.

1.Passive Targeting: Passive targeting is based on the regular distribution activity of the carrier system. This involves in using a drug carrier complex which could not be eliminated by process such as metabolism, excretion, phagocytosis etc., thereby remaining in the blood circulation for a longer period of time exhibiting high bioavailability.

Examples: Some colloids are taken up by the RES particularly in the spleen and liver.

2.Active Targeting: Active targeting involves a specifically modified or functionalized drug carrier which is able to recognize and interact with the specific target.

Example: Antigen specific antibody.

Drug Carriers in Targeted Drug Delivery System

Liposomes, monoclonal antibodies, modified plasma proteins, lipoproteins, microspheres and nanospheres, micelles etc., are used as drug carriers in TDDS.

A. Liposomes

- Liposomes are artificial vesicles containing aqueous compartments surrounded by phospholipid bilayers. They are amphiphilic in nature so they could act as carriers for both hydrophilic and hydrophobic compounds. liposomes have a major advantage in the macrophage-specific drug delivery because they are fastly taken up by macrophages. Liposomes are also used for passive drug targeting, which also assures longer bioavailability and slow release of the drug molecules. As for therapeutic application liposomes are used in site avoidance drug delivery, specific site drug deliver, intracellular drug delivery and sustained release drug delivery.
- They also ensure the pharmacodynamic and pharmacokinetic properties of the drug. Liposomes are involved in adsorption, endocytosis, fusion, lipid exchange process to deliver the drug. There are different types of liposomes for drug delivery such as small unilamellar vesicle (SUV), large unilamellar vesicle (LUV), multilamellar vesicle (MUV).
- Even though the liposomes have advantages and application they too have some disadvantages such as short shelf life and stability, cost efficiency, complicated sterilization processes and some liposomes show toxicity too.
- There are some liposomes-based drug delivery systems available commercially and it is considered as a good drug carrier.

B. Monoclonal Antibodies

- Monoclonal antibodies are prepared by recombinant DNA technology, by using B cells and hybridoma technology which has a wide range of therapeutic uses for various diseases and plays a vital part in the antibody therapy. The development of monoclonal antibodies studies and research work are significantly developed over the years.
- These studies are mostly based on cancer and tumor therapy by recognition of antibodies to the antigens. The monoclonal antibodies are also generated against specific antigens.
- The usage of monoclonal antibodies is complex and still are in research till nowadays as it brings forth many complications.
- The second-generation monoclonal antibodies also provide a scope for the development of various drug-antibody delivering systems. The humanized monoclonal antibodies, the monoclonal antibodies obtained through animal resources play an important role in the growth of the monoclonal antibodies in the drug delivery systems.
- Monoclonal antibodies could also stimulate or alter the antigen and the immune system thereby causing an imbalance in the therapeutic in the drug-antibody delivering systems.
- Even Though there were many complications in using the monoclonal antibodies, it has high importance for all the carriers due its high specificity to its target.

C. Modified Plasma Proteins

- Modified plasma proteins are used as carriers in drug delivery systems because they are soluble even in small molecular weight, they are considered as a model carrier because modification of these plasma proteins is relatively easy compared to other carriers. These modifications are made specific for the drug and the site making them more effective in therapeutic action.
- Plasma protein-based nanoparticles are used in the treatment of AIDS, cancer, and other severe diseases.
- Other delivery systems based on modified plasma protein could also advance in the upcoming years.

C. Lipoproteins

- Lipoproteins are amphiphilic in nature and used for effective cancer therapy in drug delivery systems. The lipoprotein-based drug delivery systems are developed significantly in recent years through intensive research and studies.
- High density lipoprotein (HDL) and Low-density lipoprotein (LDL) are termed as natural targeted liposomes. Especially HDL is used in various gene therapies. LDL is majorly used to deliver chemotherapeutic agents in the cancer treatment.
- For the production of major anticancer agents in the field of targeted drug delivery systems nanosized lipoproteins are majorly considered.
- The organization of the lipoprotein is a major factor in considering the lipoprotein for TDDS.
- The size and shape of the lipoprotein influences the activity of the lipoproteins in targeted drug delivery systems.

Microspheres and Nanoparticles

- Microspheres are small spheres having a size range of 0.1 to 200 micrometers are used in drug delivery systems for their size and their properties to act as a carrier. Microspheres vary in size, quality, uniformity and particle size distribution.
- The major objective of this delivery system is to deliver the drug into the target site and acquire its desired therapeutic effect. The most convenient route of administration
- of microparticles is the oral route. And also, microspheres increase the adsorption rate due its small size.
- As for nanoparticles which exhibit their sizes in nanometers and contain physical and chemical properties which are beneficial in drug delivery.
- In recent times nanoparticles are emerging as a promised hope for the invention of various drug delivery systems based on nanoparticles for complicated diseases. Because their main objective is to increase the drug efficiency and decrease its cytotoxicity.
- Microspheres and nanoparticles belong to the particle or soluble carrier type because they consist of biocompatible polymer structures.
- Depending upon the properties of the drug, they are formulated at the surface and inner core of the nanoparticles, the rate of release of the drug is influenced by the formulation of the drug in the nanoparticles. After they enter into the systemic circulation, these micro and nanoparticles cannot escape the phagocytic system and the Kupffer cells. so, this is exploited and the drug are delivered to these sites at ease for related diseases.
- The parenteral administration of the micro and nanoparticles has been in the preclinic

Micelles

- The micelles are basically the aggregates of surfactant molecules, which were used in the drug delivery system mostly as micelle microparticles. Micelles are used as drug carriers to enhance the transportation, safety, and other properties of the drug molecule.
- These micelle microparticles are mostly used in topical drug delivery systems which ensures sustained drug release and reduces degradation of the drug.
- The distribution of the micelle depends upon its micellar stabilization and its shell nature. They also contain functional groups to conjugate with the target moiety.
- Polymeric micelles are also used to entrap micro-sized drug molecules and by chemical conjugation act as a carrier for it. They are mostly small (10-100 nm) and greatly used for anticancer treatment.

- Micelle has a great scope in targeted drug delivery systems for the delivery of major hydrophobic drugs.

Soluble Polymers

- The chemistry of polymers allows them to be modified themselves in conjugates with the target by delivering the entrapped drug to the specific site. This shows increased bioavailability of the drug molecule due to the nature of the carrier system.
- Synthetic soluble polymers are in intensive research as they have good carrier properties in the drug delivering system. The entrapped drug in the polymers are also studied for their applications in the pharmaceutical field.
- These polymers are also used as drug carriers for anticancer agents for cancer treatments.

Example-(2-Hydroxypropyl) methacrylamide (HMPA).

- To study the release rate of drugs certain cellulose derivatives are also undergoing various studies.

Conclusion

A targeted drug delivery system involves the transportation of a pharmaceutical active component in the body to achieve the assured therapeutic effect. Better delivering the drug to the whole body, this system is concentrated only on the transportation of the drug to a specific location. The drug accumulation is high on the target site and low on non-targeted regions, thus reducing side effects, multitarget interaction, higher doses, non-targeted interaction. Targeting is much needed for drug delivery to avoid the disadvantage.

The role of this system involves the transportation of drugs, classified as active and passive drug delivery. TDDS needs carrier molecules, called a drug vehicle, which transports, retains, and delivers the drug to the specific target site. Depending upon the type of drug delivery system, they need carrier molecules like, liposomes, micelles, monoclonal antibodies, micelles, microspheres etc.,

The attention seeker of the targeted drug delivery system turned out to be the monoclonal antibodies, especially for cancer treatment. This system is an advanced version, similar to their advantage in this system, besides it faces a vast amount

Of challenges and overcomes problems like identifying the problem, analyzing it, and solving every problem that occurs during the target transportation of drugs. By technology development, we assert that the future of this system is with the vast growth of cancer treatment.

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