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Review Article

Review on Targated Drug Delivery System

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ABSTRACT

Innovative drug delivery systems target disease or tissue directly, transforming treatment methods. These systems employ different tactics to surpass biological obstacles, aiming for accurate targeting and enhancing therapeutic effectiveness while reducing systemic side effects. Currently, 95 percent of newly developed drugs exhibit inadequate pharmacokinetic and biopharmaceutical characteristics. Therefore, it is necessary to create an appropriate drug delivery system that targets the therapeutically active drug molecule specifically to the intended site of action, while avoiding harm to healthy tissue or organs. When considering drug carrier soluble polymers, one can think about microparticles composed of insoluble or biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, neutrophils, fibroblasts, artificial cells, lipoproteins, liposomes, micelles, immune micelle, and monoclonal antibodies. Targeted drug delivery is a sophisticated technique that efficiently delivers drugs to specific areas of the body, enhancing treatment effectiveness by concentrating the medication in the desired organs/tissues/cells and minimizing potential side effects. In essence, targeted drug delivery aims to help the drug molecule reach the intended site more effectively. Drug delivery using nanotechnology will lead to the drug remaining in the bloodstream for a longer period, resulting in decreased fluctuations in plasma levels and consequently, reduced side effects. Other methods also encompass polymer-drug conjugates and nanoscale systems like liposomes, quantum dots, dendrimers, and more. Various other strategies exist too.

INTRODUCTION

Traditional forms of medication such as injections, liquid and solid oral forms, tablets, capsules, and creams & ointments have certain drawbacks. Administering medication through injection is highly intrusive and results in short-lived impacts. Despite its widespread popularity and effectiveness, oral drug delivery is not suitable for certain drugs such as protein or peptide drugs because of their limited absorption through the oral route. These could also be broken down in the digestive tract. Topical creams and ointments are

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limited to local effects, not systemic ones. Important factors like bioavailability, drug absorption processes, pharmacokinetic processes, and timing for optimal drug delivery are considered. In drug targeting, drugs accumulate selectively and quantitatively within the organ or tissue. A thorough comprehension of the scope of targeting simplifies the selection process for the targeting moiety, ligand, or carrier system. Additionally, precise delivery ensures that only a small quantity of the drug ends up in non-target organs and tissues, creating an effective and secure drug delivery method. Broadly speaking, drug targeting levels typically include three main levels: first, second, and third; in addition, the molecular level may also be considered the fourth level. Another method of categorizing targeting is through active and passive targeting, as well as reverse and physical methods utilized in the targeting process. [2] Targeted drug delivery involves delivering medication to a patient in a way that boosts the medication's concentration in specific areas of the body compared to others. The goal of targeted drug delivery is to focus the drugs in specific tissues while decreasing the drug levels in other tissues. This enhances effectiveness while decreasing adverse reactions. This enhances effectiveness while minimizing side effects. Drug targeting involves sending drugs to receptors or organs or any specific area of the body where one wants to deliver the drugs directly. The drug's therapeutic index is determined by its pharmacological response and safety, which depend on the precise targeting of the drug to its intended receptor while minimizing contact with non-target tissues. The goal of delivering drugs specifically to targeted areas can reduce overall toxicity while maintaining therapeutic benefits, enhancing the drugs' therapeutic index. Targeted drug delivery is an appealing way to achieve this differential distribution. [3]Modern technologies make it possible to administer drugs with specific release rates for long durations, ranging from days to years. Oral and transdermal drug delivery systems commonly provide drugs continuously for 24 hours, significantly enhancing drug effectiveness and reducing side effects. Implantable devices have the ability to administer medications in a localized manner for long periods of time, possibly extending to multiple years. Even though there have been notable advancements, there are still certain areas that require significant enhancements in order to achieve the next level of clinical significance. A specific field is focused on delivering drugs to solid tumors. The important clinical benefit of targeted drug delivery is its ability to direct drugs or drug carriers to reduce the harmful effects of drugs on the body. The effective transfer of promising cancer and gene therapies, especially for delivering small interfering RNA (siRNA), from research to medical treatment will heavily rely on specific drug delivery methods. Conquering the numerous obstacles in finding an effective targeted drug delivery method necessitates comprehension of the processes related to moving the drug or drug carrier to the intended location after intravenous (i.v.) injection, as well as considerations regarding particular diseases and the body's reaction to a drug delivery system. Anticipated marginal advancement in targeted drug delivery technologies in the future due to the current lack of clear acknowledgment of issues in the drug delivery field. Professor Alexander T. Florence recently outlined the unaddressed needs and difficulties in this field, shedding light on the overstated benefits of nanoparticle drug targeting. The ultimate objective is to enhance treatment efficiency and minimize adverse effects. TDDSs are distinct from traditional DDSs because they achieve targeted drug release at a particular site, whereas the latter relies on drug absorption through biological membranes [5].

Fig no 1: Reason of targated drug delivery systems

Basic Principles and Applications of Targeted Drug-Delivery Systems

The main idea of drug targeting involves sending a large amount of drug to the desired location while reducing the amount reaching other areas. This principle helps enhance the effectiveness of the medication while reducing side effects caused by interactions with multiple targets, increased doses, and non-target concentrations.[6]Drug targeting involves the synchronized actions of a drug, its intended site of action, and the pharmaceutical vehicle. The goal is the particular organ, a singular cell, or a cluster of cells in a chronic or acute state that requires treatment and that the drug will act upon. The carrier is a specially designed molecule or system that is crucial for efficiently transporting the drug to specific locations.[7]

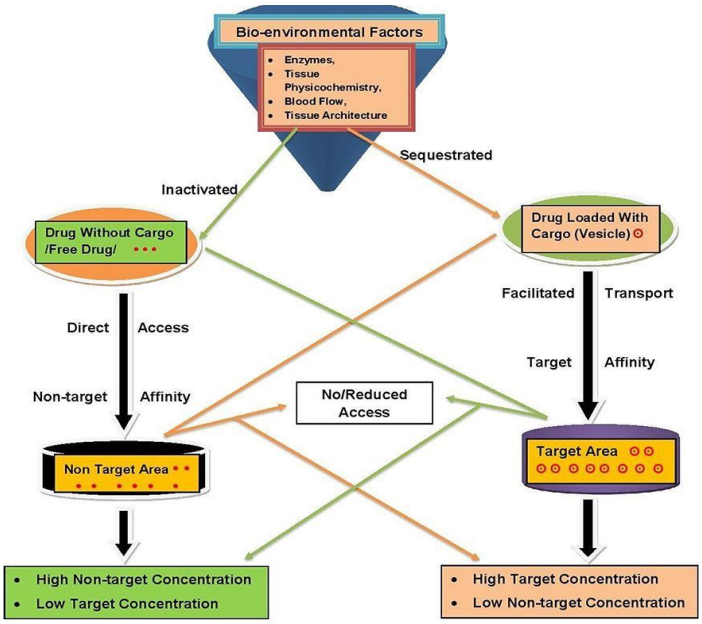

Fig no 2: Basic principle of targated drug delivery systems

To ensure the desired traits are met, designers of drug products must take into account the unique qualities of target cells and the transport vehicles that deliver drugs to specific receptors. Major

factors to consider are drug concentration, where the particles are located and how they are spread out, molecular weight, physical and chemical properties, enzymes, electric fields, physiological conditions, types and amounts of polymers and other substances, and the shape, charge, size, and density of the carrier system. [8]

Passive targeting and active targeting

Different drug delivery approaches are often categorized as either "passive" or "active" targeting strategies. However, these terms inaccurately depict what is actually happening in a living organism and can lead to confusion when defining a particular drug targeting approach. Passive targeting relies on the buildup of drugs near tumors with leaky blood vessels, known as the enhanced permeation and retention (EPR) effect. Further details on the EPR effect will be discussed below. Passive targeting occurs in most drug carriers, whether it is intentional or not. Even though the EPR effect may cause nanoparticles administered intravenously to accumulate in some organs, such as the liver, spleen, and lungs, the majority still end up in other organs. Does this indicate that unintentional organs are being targeted passively? If more than 95% of a given dose is found in unintended areas of the body, it can not be considered as selective targeting. The truth is that calling it "passive targeting" is incorrect. Instead, drugs or drug delivery systems are just distributed through the bloodstream. The phrase "passive targeting" should be substituted with "blood circulation and extravasation," for delivering drugs to areas beyond just tumors. Effective treatment utilizing "blood flow and leakage" can be accomplished by methods like targeted delivery, which restricts drug release and/or effects to specific locations in the body like a tumor but not the liver. Active targeting refers to the specific connections between a drug or drug carrier and the target cells, typically achieved through specific ligand-receptor interactions**.** [9] Ligand-receptor binding occurs only when both components are within a short distance (<0.5 nm). The concept of "active targeting" resembles directing a drug/drug carrier to a specific location, similar to how a cruise missile operates. Existing drug delivery systems lack the capability to autonomously navigate towards a specific target. They arrive at the specified location due to blood flow and leakage, then remain and spread within the tumor. The phrase "active targeting" refers to a particular interaction between a ligand and receptor for intracellular localization that happens post-blood circulation and extravasation. By using PEGylation to increase blood circulation time and enhancing the EPR effect, delivery to the tumor site is expected to be improved. Prior research has also indicated that having the tumor-specific ligand does not consistently lead to higher levels of nanoparticles gathering in tumors[10].

Properties of ideal targeted drug delivery

1)It must be non-harmful, capable of breaking down naturally, compatible with living organisms, and have stable physical and chemical properties in both living organisms and laboratory conditions

2)Continueto paraphrase the textusing the same languageand word count. It must be able to transport the medication to specific cells, tissues, or organs while also ensuring even distribution through capillaries.

3)It must gradually and steadily free the substance for an appropriate duration in a manageable way.

4)The fourth section. It must effectively sustain the medication levels at the desired location within the appropriate range for an extended period.Ensure that drug losses are kept to a minimum by preventing leakage in the carrier system.

5) Carrier used must be biodegradable or easily eliminated from the body without displaying any toxic effects.

6) The process should be straightforward, easy to replicate, and affordable.[11]

Characteristics of targeted drug delivery

- Must have biochemical inertness.
- Must not provoke an immune response.
- Must remain stable both physically and chemically under in vivo and in vitro conditions.
- Must ensure adequate drug release for therapeutic purposes.
- Must ensure low drug leakage while in transport.
- Carriers utilized should either be able to biodegrade or be easily eliminated from the body. [12]

Applications of targeted drug delivery system

Liposomes have the potential to serve as a drug carrier for treating illnesses such as tuberculosis. The customaryThe way TB is treated is similar to chemotherapy and it is not very effective, possibly because chemotherapy does not reach a high enough concentration at the site of infection. The liposome delivery system enables improved penetration of microphages and enhances the buildup of concentration at the infection site. [13]

• Targeted drug delivery is commonly utilized for the treatment of various diseases such as vascular diseases and polygenic disorders. targeted drug delivery is primarily used to treat cancerous tumors, among other diseases. [14]

Parmaceutical application

- Cancer research
- Controlled-Release Vaccines
- DNA Encapsulation
- Ophthalmic Drug Delivery
- Gene delivery
- Intra tumoral and local drug delivery
- Oral drug delivery
- Nasal drug delivery
- Buccal drug delivery
- Gastrointestinal drug delivery
- Per oral drug delivery
- Transdermal drug delivery
- Colonic drug delivery
- Diagnostic uses of radioactive microspheres: Thrombus imaging in deep vein thrombosis, Blood flow measurements, Liver and spleen imaging. Bone marrow imaging. Tumour imaging.[14]

Strategies Of Drug Targeting

Passive Targeting: Drug delivery systems that target the systemic circulation are classified as passive delivery systems. Some colloids are an ideal substance for passive hepatic targeting of drugs, as they can be absorbed by the Reticulo Endothelial Systems (RES) in the liver and spleen.Inverse Targeting: In this targeting method, efforts are made to prevent the passive uptake of colloidal carriers by RES, causing it to be known as inverse targeting. In order to achieve reverse targeting, the regular function of RES is hindered by pre-injecting a substantial quantity of inert colloidal carriers or large molecules such as dextran sulphate. This method results in RES saturation and defense mechanism suppression. Targeting drugs to non-RES organs through this method is an efficient strategy. Active targeting: Instead of being naturally absorbed by the RES, the carrier system with the drug is directed to a specific site through modifications made on its surface. Surface modification techniques involve applying a bioadhesive, nonionic surfactant, or specific cell or tissue antibodies to the surface. Antibodies produced from a single clone or albumin protein can be utilized. Dual Targeting: A carrier molecule can target two sites and enhance the drug's therapeutic effect by having its own therapeutic activity. For instance, a carrier molecule with its own antiviral properties can be filled with antiviral medication, resulting in a combined synergistic impact of the drug conjugate. Double Targeting is when both temporal and spatial methods are used together to aim at a carrier system, resulting in what is known as double targeting. Spatial placement involves directing drugs to particular organs, tissues, cells, or even sub-cellular compartments, while temporal

delivery involves regulating the speed of drug delivery to the target site. 15]

Carriers used in targeted drug delivery systems include:

- **Liposomes**: A type of colloidal carrier system that can transport and deliver drugs
- **Nanoparticles**: Can be modified with molecular markers to enhance active targeting
- **Dendrimers**: A type of drug delivery vehicle
- **Micelles**: A type of drug delivery vehicle
- **Biomimetic stem cells**: Have nanoparticle cores covered by stem cell membranes, which can evade the immune system
- **Alginate-based nanocomposites**: Can be used to develop curcumin carriers

Carriers Applied for drug targeting

Drug targeting can be attained by using carner systerrs h. The carriers are systems which required forTransportation of entrapped drug to target sites. The carriers entrap the drug moiety and deliver it into the target site without releasing it in the non-target site.[16]

Different types of carriers applied for drug targeting

There are lots of carriers applied in the targeted drug delivery system as following

• Nanotubes

Nanotubes are cylindrical carbon tubes used for drug delivery, easily filled and sealed with the necessary drug. They are commonly utilized to deliver drugs to cancer cells. Lau et al. utilized carbon nanotubes to target tumors in mice. Additionally, McDevitt and colleagues successfully targeted tumors using carbon nanotubes that were functionalized with antibodies and radiolabeled [17].

• Nanowires

It is a thin wire made of metal or other organic compounds with a very small diameter. Having a vast surface area enables the ability to modify the surface in order for the nanowire to attach to particular biological molecules when implanted in the body. It can be utilized to identify the reasons and therapy of brain illnesses, like parkinsonism and related disorders. This system is capable of managing Parkinson's and related illnesses. Furthermore, it can also be utilized for identifying and pinpointing tumors. Hong et al. utilized fluorescent zinc oxide nanowires for molecularly targeted cancer cell imaging [18].

•Nanoshells

Nanoshells consist of a hollow silica core covered by a gold shell and can be utilized for either diagnostic or therapeutic applications. Nanoshells equipped with antibodies on their exteriors can bind to specific regions, such as cancer cells. This method is highly efficient for specifically targeting the antineoplastic medication. Loo et al. researched how nanoshells can be used for both imaging and treating cancer.

• Nanopores

They possess minuscule openings that permit the entry of DNA molecules one by one. Therefore, enable precise and efficient DNA sequencing. This method holds promise in genetic modification and biotechnology. Schneider et al discovered DNA translocations through nanopores formed in graphene membranes.

• Niosomes

Niosomes are vesicles formed by non-ionic surfactants, capable of encapsulating hydrophilic and lipophilic drugs. Their greater stability compared to liposomes is attributed to the inherent characteristics of phospholipids. Research showed that niosomes are efficient in targeting antineoplastic drugs, anti-inflammatory, antibacterial, antifungal, and antiviral drugs. Liu and colleagues developed and assessed a new niosomal method for delivering daunorubicin (DNR) to target acute myeloid leukemia (AMI). Ahmed and team created piroxicam niosomes to focus on the pain site for analgesic and anti-inflammatory effects.

• Ufasomes

Ufasomes are vesicles containing unsaturated fatty acids that are formed by mixing fatty acids and ionic surfactant with cholesterol. Ufasomes make a suitable carrier for drugs meant to be applied topically. The stratum corneum, the outermost skin layer, is seen as the main obstacle to drug absorption. Using ufasomes as drug delivery systems can address this issue, as ufasomes are made up of a lipid membrane that can adhere to the skin. Kaur and colleagues conducted research to improve the antifungal effectiveness of oxiconazole loaded ufasome against Candida albicans [22].

CONCLUSION

Targeted drug delivery is now developing fast thanks to its potential to deliver drugs at specific sites. This causes injection of a lower amount of dose also as a big decrease in side-effects that were more pronounced earlier due to the inefficacy of any drug delivery system to deliver drugs at the precise site of action. The application of nano technology in drug delivery has particularly enhanced the delivery of medicine . There are numerous nanoparticles that have been approved for clinical use and, although they are still in their development stages, they hold the key2to the future of drug-targeting. Several other approaches have also been developed with similar results. They all outline the brilliant way forward for targeted drug delivery.

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