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Review Article

A Thorough Analysis of Targeted Drug Delivery Methods

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ABSTRACT

Technologies that transport medications to the body's location of action are known as drug delivery systems. Consider the pills or tablets we consume, or the injections we get for immunization. Over the past few decades, there has been a notable advancement in the field of medication delivery. One of the developments in drug delivery systems is the targeted drug delivery system. Even though Ehrlich first proposed the concept of medication targeting a particular location in the body more than a century ago, it has recently become a significant component of pharmaceutical drug delivery systems. When compared to conventional drug delivery methodologies, targeted drug delivery systems are more beneficial. The fundamental goal of the targeted medication delivery system is to confine the pharmacological effects of the therapeutic agent to the damaged organs only and exclude the rest of the organs. Carriers that maintain and bring the entire drug payload to the preselected organ or tissue can be employed for drug targeting.

INTRODUCTION

A sophisticated technique for administering medications to patients in a targeting sequence that raises the concentration of the drug delivered to the targeted organs, tissues, or cells enhances treatment efficacy by lowering adverse drug administration side effects. The pharmacologically active ingredient or medication is transported exclusively to its site of action or absorption, not

to the targeted organs, tissues, or cells, in this unique type of drug delivery system.

The rationale for site-specific drug delivery-

- (I) Irregular drug dosage form instability
- (II) solubility
- (III) low absorption
- (IV) high membrane binding
- (V) The instability of biology
- (VI) Limited half-life

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(VII) High distribution volume

Low Therapeutic Index

Objective - When there are few or no side effects and one wants an optimal therapeutic index, the idea is to target a specific area in the body in which a given pharmacologic response is desired without encountering activity where it is not required.

For example, people diagnosed with cancer receive chemotherapy and patients with certain enzyme deficiencies receive enzyme replacement therapy.

Ideal Characteristics

- (i) It must be physiochemically stable both in vitro and in vivo, nontoxic, biocompatible, and biodegradable.
- (ii) Limit medication delivery to specific cells, tissues, or organs; capillary distribution should be consistent.
- (iii) Regulated and consistent medication release rate.
- (iv) Drug release does not affect the drug action.
- (v) Drug release does not affect the drug action.
- (vi) The carriers must be biodegradable or easily removed from the body without causing any issues, and they must not cause the illness condition to change.
- (vii) The distribution system should be easy or somewhat simple to prepare, reproducible, and economically priced.



Advantages

(I) It may be possible to streamline drug administration procedures.

(II) By getting a medication to its intended location, toxicity is decreased and detrimental systemic effects are lessened.

(III) To get the desired effect, a lower dosage of the drug can be used.

(IV) Preventing hepatic first-pass metabolism.

(V) Improving target molecule absorption, including peptides and particulates.

(VI) The dosage is lower than with a traditional drug administration method.

(VII) No plasma concentration peaks or valleys.

(VIII) Targeting infected cells selectively in contrast to healthy cells.

Disadvantages

(I) Targeted systems are cleared quickly.

(II) Immune response to carrier systems given intravenously.

(III) Targeted systems are not sufficiently localized within tumor cells.

(IV) Drugs that have been released diffuse and redistribute.

(V) The formulation calls for extremely advanced technology.

(VI) Need administrative, storage, and production skills.

(VII) Toxicological symptoms may arise from drug accumulation at the target location.

(VIII) The inability to keep the dose form stable.

Carrier Or Markers In Targeted Drug Delivery

A carrier system can be used to distribute drugs in a targeted manner. A carrier is a unique molecule or system that is fundamentally necessary for the efficient delivery of a loaded medicine to the pre-selected locations. These are specially designed vectors that carry the medicine to the target area by encapsulating it or adhering to it with a spacer moiety.

Properties Of An Ideal Carrier

A medication delivery system must overcome a number of biological obstacles in order to provide

chemotherapy that works. In order to guarantee that the medication is administered precisely to the desired spot, it must be able to recognize and bind to target cells, penetrate anatomical barriers, and especially reach tumor vasculature. To avoid early drug release, the carrier must be stable in different bodily fluids and biocompatible, which means it must be non-toxic, non-immunogenic, and

biodegradable. The medicine should be released by the system into the sick cells or tissues in a controlled manner once it has reached the target. Microcapsules, liposomes, micelles, polymers, and microparticles are important carriers for attaining these characteristics.

Strategies Of Drug Targeting



1. Passive Targeting

Passive targeted drug delivery systems are those that are intended to reach the systemic circulation. The body's natural reaction to the physiochemical properties of the medication or drug carrier system is what causes drug targeting in this technique.

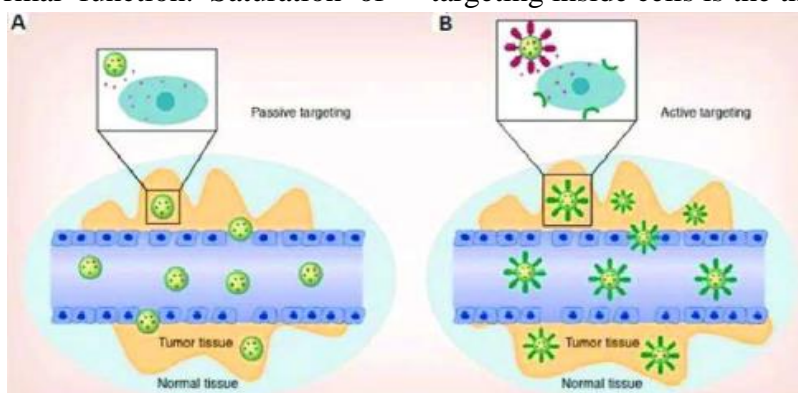
2. Inverse Targeting

This kind of targeting is known as inverse targeting because it aims to prevent the reticuloendothelial system [RES] from passively absorbing colloidal carriers. Inverse targeting is accomplished by pre-injecting a significant quantity of blank colloidal carriers or macromolecules such as dextran sulphate, which suppresses RES normal function. Saturation of

RES and inhibition of the defensive mechanism result from this strategy. Drugs can be effectively targeted to non-RES organs using this kind of targeting.

3. Active Targeting

Instead of using RES's natural absorption, this method uses surface modifications to deliver the medicine to a specified location. Techniques for surface modification include coating the surface with albumin protein, a bioadhesive, a nonionic surfactant, or particular cell or tissue antibodies (monoclonal antibodies). There are three forms of active targeting. Targeting organs is the first order of targeting; targeting cells is the second order; and targeting inside cells is the third order.



4. Ligand Mediated Targeting

Achieved through particular processes, including receptor-dependent absorption of LDL particles, or natural low-density lipoprotein, and synthetic lipid microemulsions comprising LDL particles that have been partially reconstituted and coated with apo proteins.

5. Physical Targeting

In this type of targeting some characteristics of environment changes like pH, temperature, light Intensity, electric field, ionic strength and even specific stimuli like glucose concentration are used to localize the drug carrier to predetermined site. This approach was found exceptional for tumor targeting as well as cytosolic delivery of entrapped drug or genetic material.

6. Dual Targeting

In this type of targeting approach carrier molecule itself have their own therapeutic activity and thus increase the therapeutic effect of drug. For example, a carrier molecule having its own antiviral activity can be loaded with antiviral drug and the net synergistic effect of drug conjugate was observed.

7. Double Targeting

Temporal and spatial methodologies are combined to a target carrier system, then 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.

8. Combination Targeting:

The combination targeting systems for site specific delivery of proteins and peptides are equipped with carriers, polymer and homing devices with molecular specificity. Modification of proteins and peptides with natural polymers, such as polysaccharides or synthetic polymers may alter their intrinsic physical characteristics, which play a crucial role on the targeting of a specific

compartment, organs or their tissues within the vasculature.

Biological Processes And Events Involved In Drug Targeting: Various biological processes and events that govern drug targeting are discussed below.

Cellular Uptake And Processing:

A drug frequently passes through various cells, membranes and organs to reach its target sites. Low molecular weight drugs can enter into or pass through various cells by simple diffusion processes. Targeted drug delivery systems often comprise macromolecular assemblies and are unable to enter into cells by such simple processes, instead they are captured by a process called endocytosis.

Endocytosis:

Endocytosis is the process where a cell absorbs extracellular material by engulfing it with their cell membrane to form a vesicle which is then pinched off Intracellularly. These particles do not pass through the membrane. It is simply engulfed and enclosed.

Exocytosis:

The reverse process where materials are expelled or secreted from a cell. This is used to clear wastes and secreted substances[hormones] produced by the cell. It may be excretion or secretion.

Phagocytosis:

Phagocytosis is carried by specialized cells of mononuclear phagocyte system called phagocytes by absorption of specific blood component called "opsonin". Phagocytic vacuole fuses with one or more lysosomes to form phago lysosomes. Digestion of particles occurs by lysosomal acid hydrolysis, making drug available to exert its effect.

Pinocytosis:

Pinocytosis [a form of endocytosis] allows a cell to engulf large molecules and fluid that may be present in the extracellular region. The cell membrane folds inwards, encloses the fluid or



particle to be transported and then fuses to form a vesicle. The vesicle detaches from the membrane and moves to the interior of the cell. It is of 2 types [1] Fluid phase pinocytosis [2] Receptor mediated pinocytosis.

Fluid Phase Pinocytosis: Fluid phase pinocytosis is nonspecific and continuous process, where macromolecules adhere to general cell surface site.

Receptor Mediated Pinocytosis: Receptor mediated pinocytosis is a specific process where the macromolecules adhere to specific cell receptor site. Receptor mediated pinocytosis is a particularly efficient form of pinocytosis.

Transport Across The Epithelial Barrier

Here, the oral buccal nasal vaginal and rectal cavities are internally lined with one or more layers of epithelial cells. Depending on the position and function in the body epithelial cells can be varied forms. Three layers of physiology: [1] Epithelial [2] Lamia propria [3] Basal lamina. Low molar mass drugs cross the above by passive diffusion carrier mediated systems. The polar materials diffuse through tight junctions of epithelial cells. Passive transport is usually higher in damaged mucosa where as active transport depends on structural integrity of epithelial cells. Positively charged particles showed increased uptake than negatively charged counterparts. Absorption of drugs from buccal via transcellular and paracellular later being dominant.

Extravasation:

Many diseases result from the dysfunction of cells located outside the cardiovascular system thus for a drug to exert its therapeutic effects it must exit from the central circulation process of trans vascular exchange is called „Extravasation „, which is governed by blood capillary walls. There are various factors that control permeability of capillaries. These are-

- Pathological condition.

- Rate of blood and lymph supply.

- Physiochemical factors of drug.

The structure of the blood capillary varies in different organs tissues. It consists of a single layer of endothelial cells joined together by intracellular junctions. Depending on the morphology and continuity of the endothelial layer and the basement membrane blood capillaries are divided into [1] Continuous, [2] Fenestrated, [3] Sinusoidal. Continuous capillaries are common and widely distributed in the body exhibit tight inter endothelial junctions and an uninterrupted basement membrane. Fenestrated capillaries show inter endothelial gaps of 20-80nm. Sinusoidal capillaries show inter endothelial gaps of 150nm. Depending on the tissue or organ the basal membrane is either absent ex- liver or present in discontinuous ex- spleen and bone marrow. Macromolecules can transverse the normal endothelium by passive process such as nonspecific fluid phase trans capillary pinocytosis and passage through inter endothelial junction“s gaps or fenestrate or by receptor-mediated transport systems. Organs such as the lung with very large surface areas have a proportionately large total permeability and consequently a high extravasation, depending upon charge, shape, size, HLB & characteristics of macromolecules. The endothelium of brain is the strongest of all endothelia formed by continuous no fenestrated endothelial cells which show no pinocytic activity. Soluble macromolecules permeate the endothelial barrier more readily than particulate macromolecules the rate of movement of fluid across the endothelium appears to be directly related to the difference between the hydrostatic and osmotic forces.

Lymphatic Uptake:

Following extravasation drug molecules can either reabsorb into the blood stream directly or enter into the lymphatic system and return with the lymph to the blood circulation. Also, drugs



administered by subcutaneous intracellular transdermal peritoneal routes can reach the systemic circulation by lymphatic system. There various factors which influence the clearance of drugs from interstitial sites. These are – □ Route of administration □ Size and surface characteristics of particles □ Formulation medium □ The composition and PH of the interstitial fluid and disease within the interstitium The direct delivery of drugs into lymphatics has been proposed as a potential approach to kill malignant lymphoid cells located in lymph nodes.

CONCLUSION:

Targeted drug delivery system is a new approach intended for delivery of drug molecules to a specific site or organ within the body. The toxicity of the drug is decreased by targeting a specific site. It also results in reduction of dosing frequency. Though it has various minimal disadvantages but it will be more useful in the treatments of specific disease like cancer. Currently the scope of use and advancement of this specific targeting drug delivery is on another level of progress. Hopefully through advancement of this technique, the demerits or disadvantages will be reduced and it will be more useful in the upcoming years

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