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Development of Targeted Drug Delivery Systems

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ABSTRACT

From the era when the therapeutic response of drug depends mainly upon the interaction of drug molecules with the cell on the cell membrane- related Biological receptors. To achieve this goal the correct amount of drug has to be delivered to the site of action along with simultaneous control of the drug input rate. Generally after administration of drug located carrier's through only rate undesired biodistribution of drug molecule systemic administration of drug molecules limitations viz, rapid clearance from the systemic circulation either by metabolism inhibited penetrate target tissues or undesired non- specific uptake by sensitive normal tissue or cell cells

INTRODUCTION:

The limitation can be circumvented by "targeting" the drug to the site of action in the required amount by employing various purpose-specific drug delivery systems. This delivery system if appropriately engineered can be provided the desired therapeutic response without or with side effects associated with conventional drug dosage form.In 1902, Paul Ehrlich proposed the concept of magic bullet.He postulated that therapeutic molecules like drugs; vaccines or macromolecules such as DNA, etc could be successfully delivered to desired therapeutic site in the optimal quantity.

The drug molecules could exert their effects with the significant and prompt in vivo response.

The general concept of targeted drug delivery:

Minor access- drug carrier-circulation – it is divided into 2 parts 1.target tissue 2. Non-targeting tissue – Major Pathway

Major access – target drug/carrier- circulation it is divided into 2 parts 1. Target tissue 2. Non-target tissue- minor pathway

IMPORTANCE OF DRUG TARGETING

Targeting can be achieved if the target compartments are distinguishable from the other body compartments, convincingly, on the basis of its biochemistry surface characteristics or etiological variations and also if the active drug could be placed predominantly in the proximity of target site.

The restricted distribution of patients drug to non – target sites could apparently maximize the benefits of targeted drug delivery.

CLASSIFICATION OF VARIOUS TYPE OF TARGETING STRATEGIES

DRUG TARGETING- is basically divided into 2 parts Passive & active

Passive- •EPR effect •localized delivery

Active- • Ligand receptors • Antigen- anybody •Aptamer

TARGETING DRUG DELIVERY TO ORGANS

Brain Targeting

The advances in our understandings enable us aware of mechanisms involved in the pharmacodynamic activity of neuroactive agents, physiopathology, and etiology of neurogenerative disorders as well as impediments and limitations to effective therapeutics.The drug accessibility to the central nervous system (CNS) is mainly limited by the blood-brain'-barrier (BBB).In the treatment of diseases or conditions that result from the lack of simple hormone and peptides, the administration of these compounds in controlled fashion could provide effective management of diseases & therapy conditions such as diabetic neuropathy, amyotrophic lateral sclerosis (ALS) & Huntington's diseases, and parkinsonism diseases may be treated with better pharmacodynamic effects using targeted drug strategies. Brain related diseases of diverse etiology are the major causes of debilitation, agony, and death. The management of brain-related diseases with the present available therapeutic system is very difficult, as an insufficient amount of drug reaches to the brain due to highly lipophilic nature of blood-brain -barrier.

Drug delivery to the brain requires advances in both, drug delivery technology and drug discovery.

Due to the presence of the blood -brain barrier only small lipid-soluble drugs in circulation are ultimately delivered to the brain cells.

Therefore, practical strategies are required for mediating drugs transports across blood brain barrier .the emerging strategies for selective delivery to the brain arise from the investigation that critically reveals the physiological mechanisms involved with the solute transport across the blood -brain- barrier.

LIMITATIONS IN BRAIN UPTAKE OF DRUGS

Numbers of drugs peptide biological response modifiers and monoclonal antibodies and Fc fragments are presently available which have been proven valuable in inhibiting a variety of malignant infections diseases and rectification of Neurotransmitter and enzyme in balance in tissue culture systems however, their in vivo therapeutic efficacy is frequently compromised due to their inhibitory to reach and maintain active concentration at the diseased site located

in brain. They are few more cases where inadequate pharmacokinetics can limit drug therapy when a disease is located within the central nervous system.

This problem is commonly encountered in patients with acute cerebral bacterial or viral infections, as well as with Neurodegenerative diseases, such as Parkinson's Huntington's

Or the Tay-such disease. However, the most extreme cases are encountered by neurooncologist in treating patients with brain tumors. Transport mechanism operating at BBB for peptides and protein can be classified into the following categories:

•Transport via carrier-mediated systems

•Receptors mediated transcytosis (RMT)

•Absorptive mediated transcytosis (AMT)

The brain following its systemic administration has been examined by a number of investigators. The factors identified include the following.

•The time-dependent plasma concentration profile of the compound, this id related to its distribution and elimination process.

• The binding of the agent's to plasma constituents and tissue, and binding off-rates from them (plasma clearance).

•The permeability of the BBB to the agent.

•local cerebral blood flow

The cerebral availability of peptide/ drugs, therefore, depends on the route of administration or intracarotid arterial administration provides the high concentration in CSF and diffusion of the peptide drug from CSF through an interstitial fluid (ISF) is significantly limited.

CONCLUSION:

Future prospects

Targeted drug delivery is the major focus of current research. After the concept of the magic bullet, only a few targeted formulations could reach the market. The discovery in the area of

molecular biology, biotechnology and pharmacogenomics regulatory demand the practical key issues of targeting of biomolecules to the therapeutic site and hence remain to be the center of attention. Tumour-targeted drug/gene delivery is the most demand therapeutic requirement of the coming future.

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