Nanotechnology Drug Delivery Systems: An Insight

Dr G.S.Virdi
GGS College of Modern Technology
Kharar Mohali

I. INTRODUCTION

One of the most important applications of nanotechnology in medicine involves use of nanoparticles to deliver drugs, and other therapeutic substances to specific types of cells (such as cancer cells). Nanosized structures and devices are smaller than human cells which are around 10,000 nm in diameter and similar in size to biomolecules such as enzymes, proteins (hemoglobin is 5 nm in diameter). Due to their small size, nanoparticles can also penetrate the blood-brain barrier which is impervious to most therapeutic and imaging agents.

To be suitable as a drug carrier, the size of nanoparticles should be small enough to avoid elimination from the body by Mononuclear phagocytic system (MPS) and big enough to avoid rapid renal filtration. The small size of nanoparticles allows them to interact readily with biomolecules on the cell surface (receptors) and within the cell, and thus allows better understanding of complex processes that govern the behavior of cells in their normal state and during the diseased state.

Nanoscale drug delivery systems have ability to cross cell membranes, thus drug can be delivered to specific organelles inside the cell. Nanoparticles have greater surface area to volume ratio, means more surface is exposed which results in faster dissolution of nanoparticles in solution. Fast dissolution results in greater bio-availability, small drug doses and less toxicity.

II. THE PROBLEM OF TRADITIONAL DRUG DELIVERY SYSTEMS:-

In traditional drug delivery systems such as oral or intravascular delivery, the drug or therapeutic molecules are distributed throughout the body through the systemic blood circulation. A majority of molecules do not reach their targets and subsequently, stay in the body causing side effects

The drug and therapeutic molecules have short plasma half-life, poor stability in serum and potential immunogenicity, and insolubility in water which results in their rapid clearance by MPS and limits their efficiency.

III. HOW NANOTECHNOLOGY CAN OVERCOME LIMITATIONS OF CURRENT DRUG DELIVERY SYSTEMS:-

Nanoparticles have the ability to encapsulate the water insoluble drugs within them and protect it from hydrolytic and enzymatic degradation in the gastrointestinal tract. The bioavailability of drugs is increased due to the specialized uptake of nanoparticles by absorptive endocytosis. Due to their small size nanoparticles are able to avoid opsonization by MPS and remain in the blood circulation for a longer duration of time as compared to microparticles and other traditional drug delivery systems.Through the chemical modifications the properties of nanoparticles can be manipulated and drug release can be controlled to achieve the desired therapeutic concentrationfor the desired duration of time. Drug targeting is important in chemotherapy, drug delivery system should target only the cancer cells while shielding the healthy cells from the drug.

IV. NANOPARTICULATE TARGETING:-

Nanoparticles may be delivered to specific sites by size dependent passive targeting or active targeting.

- *Passive targeting* occurs due to poorly differentiated vasculature of solid tumors by a process called angiogenesis. Angiogenesis is a process involving growth of formation of new blood vessels from old pre-existing ones. Poorly differentiated vasculature allows the extravasation of nanoparticles at tumor site. This process is also called Enhanced Permeation and Retention effect (EPR). For successful passive targeting, the nanoparticles should circulate in the blood for extended period of time, so that there will be multiple possibilities for the nanoparticles to pass by the target site. The circulation half lives of Nanoparticles can be further increased by coating with hydrophillic polymers such as polyethylene glycol and producing stealth nanoparticles (nanoparticles invisible to MPS).
- *Active targeting:* Active targeting involves use of targeting ligands such as antibodies, peptides (e.g cell penetrating peptides) which bind specifically to receptors, epitopes over-expressed on target site. Some examples of targeting ligands used in nanoscale drug delivery systems include folate, transferrin. By actively targeting nanoscale drug delivery systems it is possible to minimize the uptake of anticancer agent by normal cells thus minimizing the side effects of therapy.

V. NANO DRUG DELIVERY SYSTEMS:-

- *Liposomes:-*

  Liposomes are spherically shaped vesicles composed of natural phospholipids. The properties of liposomes can be varied with composition, size, and surface charge of lipids and also the method used for preparation.Liposomes can carry both hydrophobic and hydrophillic molecules inside them. The surface of liposomes can also be modified by attaching polyethylene glycol (PEG) chain to the lipid bilayer (stealth liposomes) to enhance their circulation time in the blood. Drugs can be actively targeted by conjugating liposomes with antibodies or ligands.

- *Dendrimers:-*
  Dendrimers are hyper branched structures that comprise of a inner core, a series of branches and outer surface with functional groups. Due to their nanometer size range, ease of preparation and functionalization they are attractive drug delivery systems.

  Due to the presence of internal cavities it is possible to encapsulate therapeutic agents in the inner core. The properties of dendrimers can be controlled by the functional groups on outer surface. Drug can either be encapsulated in the interior of the dendrimers or attached to surface functional groups.

- *Polymeric micelles:-*

  Polymeric micelles consist of amphiphillic block copolymers, which can self-assemble to form micelles in aqueous solution. They have a narrow size distribution in the nanometer range and core-shell structure, in which hydrophobic segments are separated from the hydrophillic exterior. Drugs can be partitioned in the hydrophobic core of micelles and the outer hydrophillic layer forms a stable dispersion in aqueous media. Like liposomes they can also be functionalized with PEG for stealth properties and with targeting ligands including antibodies to the micelle surface.

Finally, drug delivery from nanoscale drug delivery systems can also be modulated and triggered by external influence. Ultrasound and magnetism have been used to accumulate chemotherapeutic drugs selectively at tumor sites. The future of nanotechnology in drug delivery will depend on rational design of nanotechnology materials and tools based on detailed and thorough understanding of biological processes.

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