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Review Article

Nanotechnology –Based Drug Delivery System

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ABSTRACT

Nanoparticles having a huge potential for use as an effective medicine delivery system. In this post, we discussed recent developments in nanotechnology-based drug delivery. Nanotechnology has gained interest recently as a potential remedy for medical and gene delivery problems. Nanosystems with different compositions and biological properties have been thoroughly studied for the transportation of genes and medicines. Achieving effective drug delivery requires an understanding of how nanomaterials interact with the biological environment, including how they target cell-surface receptors, release drugs, administer multiple drugs, stabilize therapeutic agents, and use molecular mechanisms of cell signaling that are involved in the pathobiology of the disease in question. Numerous anti-cancer drugs, including doxorubicin, 5-fluorouracil, dexamethasone, and paclitaxel, have been efficiently formulated using nanomaterials. Furthermore, chitosan, quantum dots, polylactic/glycolic acid (PLGA), and PLGA-based nanoparticles have all been employed for the delivery of RNAi in vitro. Brain cancer is one of the most difficult tumors to detect and treat since imaging and treatment tools cannot penetrate the blood-brain barrier and reach the brain. Nanomaterial-attached anti-cancer drugs, such as doxorubicin and loperamide, have been shown to be able to penetrate the unaltered blood-brain barrier and reach the brain at therapeutic dosages.

INTRODUCTION

Because cells absorb nanoparticles more effectively than larger macromolecules, these particles could serve as efficient systems for delivering and transporting drugs. Medications can be attached to the surface of the particles or embedded within their matrix for therapeutic use. The trajectory of a drug entering a biological system should be guided by a drug targeting mechanism. Various nanosystems with distinct compositions and biological properties have been extensively researched for drug and gene delivery purposes. It is essential to design nanosystems

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logically, taking into account their interactions with the biological environment, targeted cell populations, cell-surface receptors on the target cells, changes in these receptors associated with disease progression, the mechanism and site of drug action, and the retention of the drug. Administration Understanding the molecular mechanisms and pathobiology of the disease in question would be an effective approach to facilitate efficient drug delivery. The destiny of a drug entering the biological environment should be managed by a targeted drug delivery system. Nanosystems with diverse compositions and biological properties have been extensively researched for drug and gene delivery applications. The development of nanosystems should be methodically informed by their interactions with the biological environment, the specific cell populations they aim to target, the receptors on target cells, the alterations in cell receptors associated with disease progression, the mechanisms and sites of drug action, drug retention, the administration of multiple drugs, as well as the molecular mechanisms and pathobiology of the relevant diseaseUnderstanding the barriers to medication, such as the stability of therapeutic agents in living cells, is essential. Reduced drug effectiveness may occur due to the drug's inability to penetrate the cell, its lack of availability due to various delivery molecule characteristics, changes in the genetic makeup of cell-surface receptors, overexpression of efflux pumps, alterations in signaling pathways as the disease advances, or degradation of the drug. For instance, doxorubicin and cisplatin, which are two anti-cancer medications, are ineffective because of heightened DNA methylation that happens as cancer develops. This review encompasses the drug delivery aspects of nanomedicine, including how nanoparticles engage with cell-surface receptors, the biological responses and cellular signaling involved, as well as the research necessary for the widespread implementation of nanodelivery systems in healthcare. This review encompasses the drug delivery aspects of nanomedicine, including how nanoparticles engage with cell-surface receptors, the biological responses and cellular signaling involved, as well as the research necessary for the widespread implementation of nanodelivery systems in healthcare

Design Of Nanotechnology-Based Drug Delivery System

The utilization of nanoparticles in targeted drug delivery can improve drug bioavailability, assist in drug targeting, and facilitate the absorption of poorly soluble drugs at the disease site [8,9]. Figure 1 illustrates a schematic comparison between targeted and untargeted drug delivery systems. Numerous anti-cancer drugs, including doxorubicin [12], 5-fluorouracil [13], paclitaxel [10,11], and dexamethasone [14], have been effectively formulated using nanomaterials.

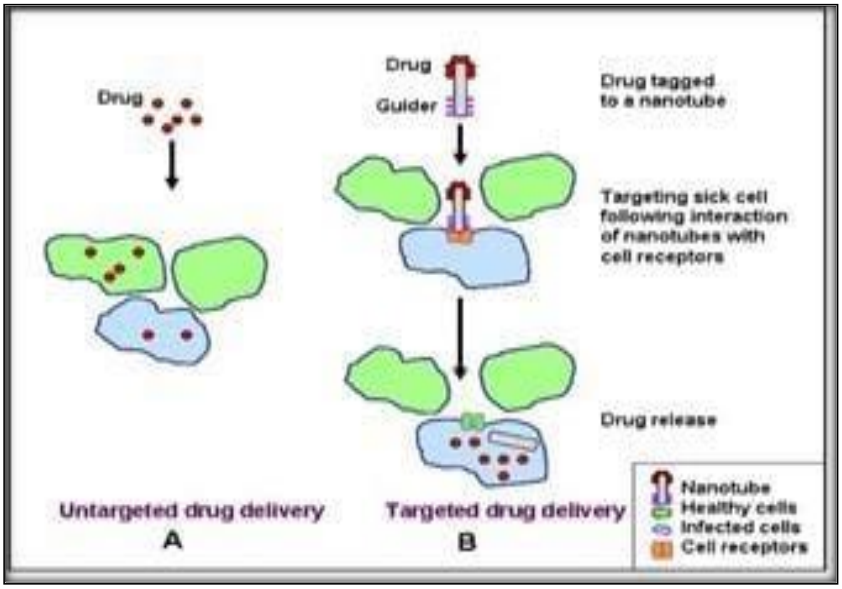

Figure No. 1

Dexamethasone, a glucocorticoid with an intracellular site of action, has been encapsulated in polylactic/glycolic acid (PLGA) and polylactic acid (PLA) based nanoparticles.One chemotherapy drug with anti-inflammatory and anti-proliferative properties is dexamethasone. Following the drug\'s binding to the cytoplasmic receptors, the drug-receptor complex is carried to the nucleus, where it causes the production of specific genes that regulate cell division .The application of colloidal drug delivery methods, such as liposomes, micelles, or nanoparticles, in cancer treatment has been thoroughly studied. Drug delivery systems are effective because of their compact size, decreased toxicity, regulated drug release time, and adjustments to the drug\'s pharmacokinetics and biological distribution. Chemotherapy fails to cure cancer far too frequently because certain tumour cells become resistant to several anticancer medications.

Nanoparticles Medicated Delivery of Sirna

Short interfering RNA (siRNA) has several applications and is emerging as a potent technique for controlling gene expression. Clinical studies of nucleic acid-based therapy will not be possible until significant advancements in the delivery mechanism have been made. Quantum dots (QD) have been demonstrated to deliver RNAi. [16] PLA and PLGA-based nanoparticles have also been used to deliver RNAi in vitro. [17] Even though siRNA delivery using various nanomaterials has shown some success, it is difficult to monitor their distribution and gauge the efficacy of transfection in the absence of a suitable monitoring agent or marker. Creating a transfection agent that is both efficient and self-tracking for RNA interference is a challenging task. Tan and others. [18]siRNA to the human epidermal growth factor receptor-2 (HER2/neu) using recently developed quantum dot-encapsulated chitosan nanoparticles. Because the chitosan nanoparticles contain fluorescent QDs, this novel nano carrier aids in siRNA monitoring. Chitosan/quantum dot nanoparticles surface-labeled with HER2 antibody, which targets the SKBR3 cells' HER2 receptors, have been used to deliver HER2 siRNA specifically to HER2-overexpressing SKBR3 breast cancer cells.

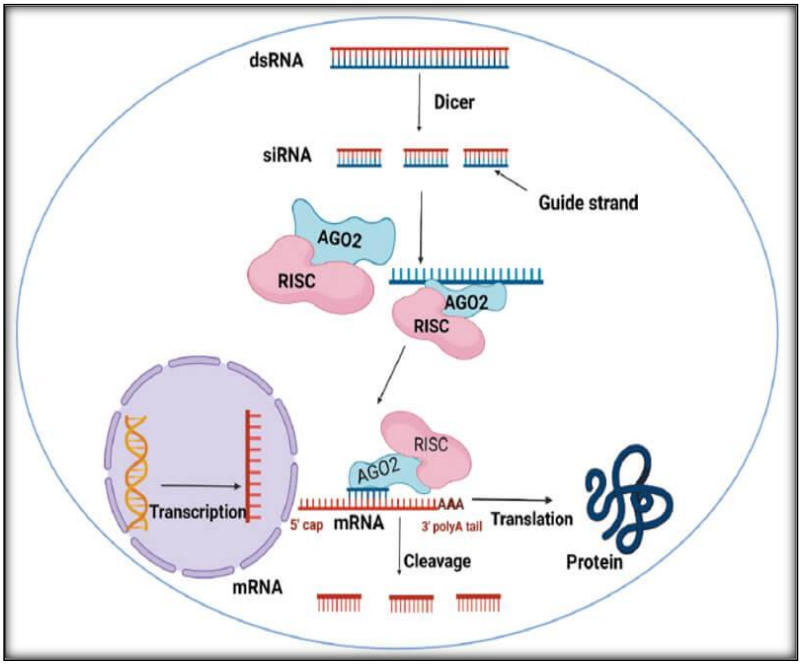

Figure No.2

Labelling nanoparticles with a fluorescent marker, like Cy-5, makes it easier to see the uptake and accumulation of nanotubes under a fluorescent microscope. Howard et al. recently found that K562 (Ph(+)) cells expressed 90% less BCR/ABL-1 leukaemia fusion protein when these nanoparticles were combined with siRNA specific to the BCR/ABL-1 junction sequence. The bronchiolar epithelial cells of transgenic EGFP mice also demonstrated efficient in vivo RNA interference after nasal administration of chitosan/siRNA formulations. These findings show the potential applications of this novel chitosan-based strategy in RNA-mediated therapy of systemic and mucosal disorders.

Cancer

Targeting cancer cells with nanoparticles

Cancer is now one of the most challenging diseases to diagnose and treat, and brain cancer is especially challenging since it is challenging to get imaging and therapy agents into the brain through the blood-brain barrier. Several researchers have found that these chemicals could be delivered into the brain by nanoparticles. [20–22] Apolipoprotein E has been suggested as the mediator of drug transport across the blood-brain barrier. [23] Loperamide, which does not cross the blood-brain barrier but has antinociceptive effects when injected directly into the brain, was loaded onto human serum albumin nanoparticles. After then, it was linked to apolipoproteinE.Mice administered this substance intravenously demonstrated antinociceptive effects in the tail-flick test.the efficiency of this drug delivery method. While one agent may help visualise the target through magnetic resonance imaging, a third agent attached to the PEBBLE may deliver a deadly dose of medication or toxin to nearby cancer cells. All three roles can be combined into a single, small polymer sphere to generate a potent cancer-fighting tool. Another anti-cancer drug, doxorubicin, can penetrate the intact blood-brain barrier and reach the brain at therapeutic concentrations when it is affixed to polysorbate-coated nanoparticles [24, 25]. Compared to current methods, smart superparamagnetic iron oxide particle conjugates can target and locate

brain tumours earlier and more precisely. Folic acid and polyethylene glycol are known to further enhance intracellular absorption.

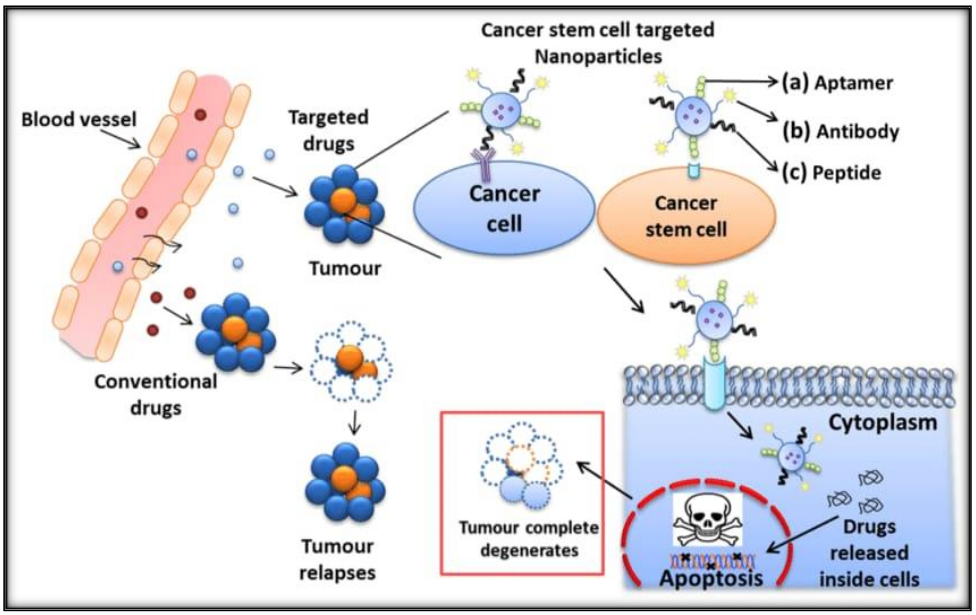

Figure No.3

Targeting angiogenesis with nanoparticles

Strong angiogenesis causes tumours to grow rapidly. Thus, one way to stop angiogenesis is to start tumor cells. A complex network of mediators controls angiogenesis, and new research indicates that integrin αvβ3 and vascular endothelial growth factors (VEGFs) are key regulators. Thus, a unique anti-angiogenesis approach for treating a broad range of solid tumours is the selective targeting of VEGFs and αvβ3 integrin. Coating nanoparticles with peptides that selectively bind to the αvβ3 integrin and the VEGF receptor is one method . [26] TheArg-Gly-Asp (RGD) sequence of the synthetic peptide is known to bind especially to the αvβ3 integrin expressed on endothelial cells in angiogenesis blood arteries, potentially limiting the growth and proliferationoftumours.The blood vessels and agiogenic tissue that surround the tumor tissue may be traced or removed with the aid of these FITC_GRGDS-[27]loaded nanotubes. Our research team has been investigating the biological effects of RGDSK self-assembling rosette nanotubes (RGDSK-RNT). These rosette nanotubes are a novel kind of nanotubes with biological inspiration and inherent water solubility during manufacturing [28, 29].These nanotubes are constructed from the guanine-cytosine motif. However, the ability of the RNT to adopt various functional groups at the G/C motif is one of its distinctive features, providing the nanotubes with functional versatility for certain biological or therapeutic uses. Therefore, in order to treat cancer, it might be conceivable to modify RNTs to target various therapeutic molecules in vivo.

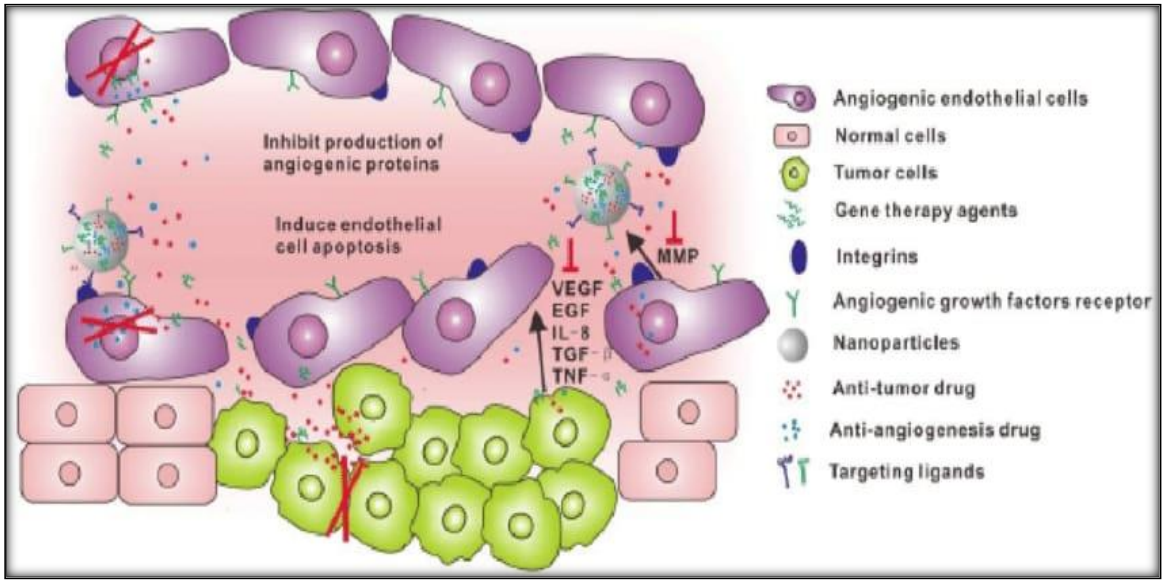

Figure No.4

Nanosystem In Inflammation

Targeting macrophages to control inflammation

It makes sense to use nanoparticles for macrophage-specific targeting because of the rapidity with which macrophages can recognise and destroy foreign particles. Because macrophages release a diverse array of inflammatory mediators, they can regulate inflammation in a number of illnesses. Consequently, macrophages could be therapeutic targets for a range of human and animal diseases. Although most infections can be eliminated by macrophages, several germs, such as Toxoplasma gondii, Leishmaniasp., Mycobacterium tuberculosis, and Listeria monocytogenes, have developed the potential ability to withstand the phagocytosis action of macrophages. These infections infiltrate altered lysosomes and interfere with the macrophage's ability to eliminate them by disrupting its molecular machinery.Therefore, it may be helpful to remove cellular reservoirs by delivering antimicrobial agent(s) via nanoparticles into pathogen-containing intracellular vacuoles in macrophages . [30,31]This technique can be utilised to reduce pro-inflammatory cytokine production, decrease adverse medication administration side effects, and increase therapeutic drug concentrations in the vacuoles of infected macrophages. Antileishmanial medications have been delivered to macrophages using polyalkylcyanoacrylates (PACA) nanoparticles. Macrophages did not secrete interleukin-1 in response to this nanomaterial. [32] Therefore, targeting macrophage infections in chronic disorders may benefit greatly from similarly constructed nanosystems. Amphotericin B, an antifungal and antilesishmanial medication, has been complexed with lipid-based nanotubes to produce a less toxic form of AmB. Gupta and Viyas developed AmB in trilaurin-based nanosize lipid particles (emulsomes) stabilised by soy phosphatidylcholine as a unique intravenous drug delivery technique for macrophage targeting. Nanocarrier-mediated delivery of macrophage toxins has been shown to be an effective way to eradicate unwanted macrophages in gene therapy and other clinically relevant conditions such as autoimmune blood disorders, T cell-mediated autoimmune diabetes, rheumatoid arthritis, spinal cord injury, sciatic nerve injury, and resten-osis

after angioplasty. Another option is to use nanoparticles that have the capacity to destroy macrophages. Using a variety of macrophage cell receptors as therapeutic targets may be more successful.

Targeting Inflammatory Molecules

Over the past 20 years, a large number of cell adhesion molecules have been discovered. Cell adhesion molecules are glycoproteins found on the cell surface that act as receptors for attachment between cells and between cells and the extracellular matrix. [34–35] These cell adhesion molecules fall into four classes: integrins, cadherins, selectins, and the immunoglobulin superfamily. Both the effective migration of inflammatory cells, such as neutrophils and monocytes, into inflamed tissues and the generation of the host response to infections depend on these substances. However, there is compelling evidence that excessive neutrophil migration results in disproportionate tissue death and damage in inflammatory lungs. Consequently, there is a great deal of work being done to precisely regulate neutrophil migration into inflammatory tissues.Recent advances in our knowledge of cell adhesion molecules have influenced the design and development of drugs (such as peptides and proteins) for the potential treatment of autoimmune illnesses, cancer, and heart disease. [36–40] These compounds are important in thrombosis,cancer and autoimmune diseases such type-1 diabetes [41–45]. RGD peptides have been shown to target integrins αvβ3 and αvβ5, where as peptides generated from the intercellular adhesion molecule-1 (ICAM-1) have been shown to target the αvβ2 integrin.Peptides derived from αvβ2 can target cells that express ICAM-1Cyclic RGD peptides have been added to doxorubicin (Dox-RGD4C) and paclitaxel (PTX-RGD) to enhance their targeted distribution. Mice with human breast cancer cells (i.e., MDA-MB-435) survived the disease when treated with Dox-RGD4C, while all untreated control mice died [46].This substance targets the tumour vasculature's integrins αvβ3 and αvβ5 during angiogenesis. Extracellular regulated kinases (ERK) may govern apoptosis and cell survival through increased TNF-α[47] expression, decreased Akt activity, increased caspase-3 and caspase-8 activities, and -1 is upregulated during tissue inflammation and several different types of cancer, this combination may be useful for directing drugs to tumour and inflammatory cells. MTX has an anti-inflammatory effect because it inhibits the production of anti-inflammatory cytokines such as interleukin-6 (IL-6) and interleukin-8 (IL-8). Thus, the MTX-cLABL conjugate's capacity enhanced p53 and BAX activity.Our group is investigating the migration of neutrophils in cows and horses, the role of P38 kinases in cell signalling in human lung epithelial cells, and the connection between RGD-RNT and αvβ3 integrins. Cyclo(1,12)PenITDGEATDSGC peptide (cLABL peptide), found in the I-domain of the α subunit of Leukocyte Function-Associated Factor-1 (LFA-1), is known to bind ICAM-1. The cLABL peptide and methotrexate (MTX) have been joined to create the MTX-cLABLconjugate[48] Given that ICAMto suppress these cytokine production in TNF-α-activated human coronary artery endothelial cells was contrasted with that of MTX alone. More specifically than IL-8, MTX-cLABL inhibits the synthesis of IL-6.Further understanding of the process or mechanisms of internalisation and intracellular trafficking of cell adhesion molecules is required in order to use them to deliver medication molecules to a specific cell type or for the diagnosis of cancer and other disorders (such as cardiac and autoimmune diseases).

CONCLUSION

In cancer and inflammation, nanomedicine delivery technologies appear to have great potential for overcoming some of the barriers to efficient cell and molecular targeting. Furthermore, there is a significant opportunity to address drug resistance in target cells and assist drugs in overcoming obstacles such as those found in the brain. The chemicals are solely expressed in the targeted organs to prevent harm to healthy tissues. Second, it's important to understand how the drugs behave once they enter the nucleus and other sensitive cell organelles. Additionally, because nanosystems increase the effectiveness of drug delivery, doses might need to be adjusted.

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