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Role of Nanomedicine in Cancer Treatment: Emerging Trend and Prospects

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ABSTRACT:

Cancer is a Complex disease that affects many cellular physiological systems. For cancer treatment, nanomedicines can be used to reach specific targets due to their small size, thus increasing their bioavailability and reducing side effects. Because of its great promise and effectiveness in treating many cancers, nanotechnology has emerged as a novel approach to treating a wide range of various Cancer .Cancer treatment is usually limited to chemotherapy, radiation therapy, and surgery. However, a type of nanotherapy has emerged as an advanced cancer treatment that reverses the side effect of chemotherapy. Over time, nanotherapeutics have evolved with design strategies such as geometry, size, composition, or chemistry to overcome biological barriers. It has been shown to have many advantages, including the ability to carry different treatments, longer duration of action, increased therapeutic index, and reduced toxicity. This review highlights recent advances in cancer treatment using nanoparticles as drug delivery vehicles, cancer targeting cancer ,diagnosis.

Key words : Nanomedicine ,targeted drug delivery, nanoparticles ,Active targeting, passive targeting, combination therapy.

Introduction:

One extremely innovative biotechnology method that has several uses, particularly in the environmental and medicinal domains, is nanotechnology . The primary objective of therapeutic intervention is the complete removal of the tumor, which can often be accomplished through surgery in the early stages of the disease. More than 15 cancer nanomedicines have received regulatory approval, which is comparable to the number of approved antibody drug conjugates. In this context, it is noteworthy that the translation of cancer nanomedicines has been criticized far more than antibody-drug conjugates[1] .

Over the past twenty years, significant progress has been made in understanding cancer biology. The World Health Organization (WHO) reported that in 2012, cancer was responsible for 8.2 million deaths, accounting for 13% of total mortalities. Projections indicate that over the next two decades, the incidence of cancer may rise from 14 million to 22 million cases. In addition to the challenges posed by the development of resistance to anticancer agents, the effective delivery of these compounds to tumor tissues is crucial in minimizing toxicity associated with systemic exposure. Nanotechnology has emerged as a key player in improving the targeted delivery of anticancer drugs to affected tissues, thereby enhancing their efficacy and reducing adverse side effect [2]

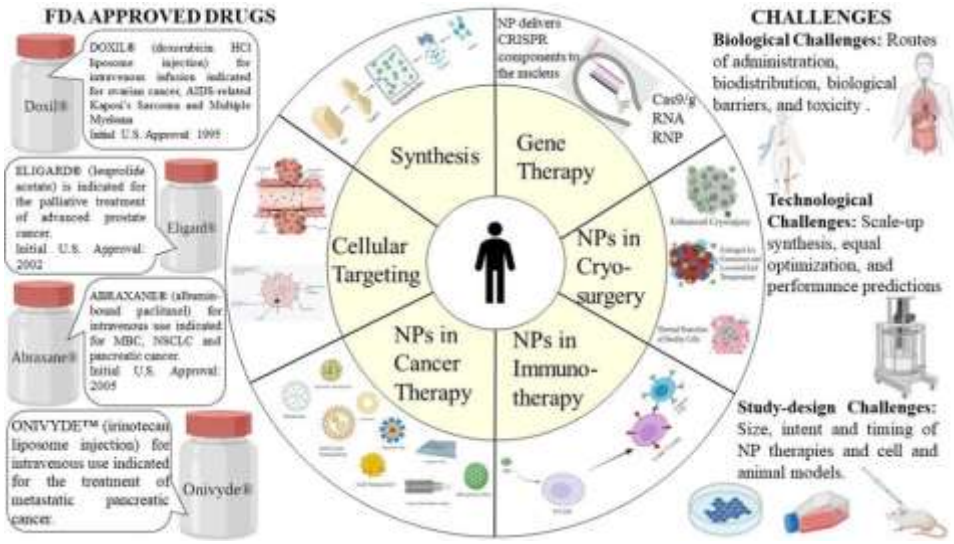

Fig 1.1 The fig describe Multifunctional cancer nanomedicines and drugs that treat tageted drug delivery and challenges

However ,nanomedicines are an emerging treatment by targe targeting ting the affected site and less side effects.Nanomedicine has attracted a lot of attention lately because it may be able to overcome some of the drawbacks of conventional treatment approaches, providing opportunities for increased effectiveness and reduced adverse effects. Usually ranging in size from 1 to 100 nanometers, nanomedicines has unique physicochemical characteristics that can be adjusted to maximize its interactions with biological systems. Since 1930 ,chemotherapeutics are used to treat cancer .But this conventional treatment has lots of side effects such as pain , hair fall , lack of action.

The FDA has approved Doxil, an anticancer medication, and a number of nanotherapeutics for the treatment of cancer. The first FDA-approved anticancer nanomedicines, which utilized the enhanced permeability and retention (EPR) effect, was liposomal doxorubicin in 1995.Various derivatives of doxorubicin have been developed and are now recognized for their effectiveness compared to free drugs in standard therapies.The creation of doxorubicin-loaded liposomes for the treatment of breast cancer marked the beginning of nanoparticle-based cancer therapy. Dendrimer and polymers were later used. Solid lipid nanoparticles and siRNA molecules with various nanoparticles were created for targeted therapy and treatment effectiveness, respectively, between 2000 and 2015.[3]

Principles:

Nanoparticles used to deliver dug in cancer treatments

In the development of cancer drugs, nanomaterials such as carbon nanotubes, polymeric micelles, and liposomes have demonstrated significant pharmacokinetic and pharmacodynamics advantages in the detection and management of cancer. A key component of smart nanoparticles are the drug carriers at the nanoscale. The following fundamental requirements must be met for a smart nanoparticle to be considered ideal: stimulus response material or structure, stable nanoscale size, adjustable surface charge, high encapsulation capacity, biocompatibility, degradability, low toxicity, etc.

Nanomaterials contain organic nanoparticles, inorganic nanoparticles , lipid based nanoparticles and polymeric nanoparticles .Organic nanoparticles contain dendrimer, liposomes ,polymerosome ,polymer micelle ,nanosphere ,etc. Particles that are nanoscale in size are called nanoparticles. Among the widely studied nanoparticles (NPs) are metallic nanoparticles, extracellular vesicles (EVs), polymeric nanoparticles (PNPs), and monoclonal antibodies (mAb). Colloidal macromolecules having submicron sizes between 10 and 1000 nm are known as PNPs. PNPs are drug carriers that deliver chemical medications to specific malignant areas with a sustained release . A nanocapsule or nanosphere is created when drugs are encapsulated or affixed to the surface of nanoparticles. Organic nanoparticles are the promising drug delivery system for cancer treatment because it improve the drug solubility and target drug delivery and reduced drug from degradation.

Dendrimer :A central core, a low-density interior made up of repeating branching units, and a high-density outside finished with surface functional groups are characteristics of the structurally defined macromolecule class known as dendrimers. Dendrimers, which can be synthesized on a massive scale with monodispersity, are symmetrically structured and nanosized, unlike their polymeric counterparts. Because of these special qualities, dendrimers are becoming more and more popular as nanoscaffold systems for drug delivery and other biomedical uses. [4]

Liposomes: The structure of liposome consist of lipid bilayer surrounding an aqueous core with the size ranging from 20 - 1000 nm. Natural phospholipids and cholesterol are the building blocks of these spherical vesicles. Because of their biocompatibility and amphiphilia, they are ideal for drug administration.

Inorganic nanoparticles include silica nanoparticles ,gold nanoparticles, carbon nanotubes ,quantum dots ,nanographene ,etc. carbon nanotubes :Based on the element carbon, carbon nanomaterials (CNMs) are a type of nanoscale material that fall into several categories. Because of their special mechanical,

electrical, thermal, and optical qualities, CNMs have found extensive application in a variety of industrial and medical domains . CNMs are thought to be safer and more biocompatible than metal-based nanoparticles in cancer therapeutic applications. Carbon nanotubes (CNTs) are cylindrical tubes made of sp2 hybridized carbon atoms. CNTs range in size from one nanometer to several micrometers. CNTs can be classified as single-walled carbon nanotubes (SWCNTs) or multiwalled carbon nanotubes (MWCNTs) based on the number of layers that form within them.

Quantum dots: An incredibly tiny metal particle, perhaps a thousand times smaller than a hair, is used to create quantum dots. These come in a range of shapes and are coated in different types of biomaterials. These dots glow when exposed to UV light, and their size determines the colour of the quantum dots. Quantum dots (QD)are nanoscale nanomaterial that are said to be zero dimensinal because charge carriers are confined so tightly in there directions They are verysmalli.e 2- 10 mm in diameter. Semiconducting nanoparticle contain metalloid crystalline core usually manufactured from Cdse or Cdte surrounded by zinc sulfide[5].

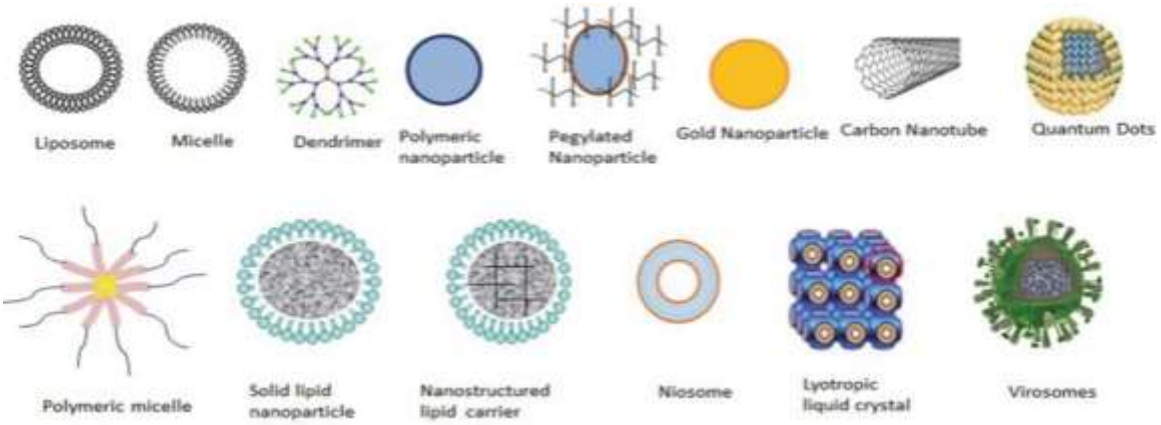

Fig1.2 : Carriers of nanomedicines

Passive targeting :

By incorporating the therapeutic agent into a nanoparticle, passive targeting is a technique that enables the drug to passively disperse throughout the body with the goal of reaching the target organ or tissues. Without the need for particular targeting agents, passive targeting in gene therapy uses nanoparticles (NPs) to precisely deliver therapeutic agents to particular tissues or organs. The size of the nanoparticles has a significant impact on passive targeting, which is primarily accomplished by diffusion transport. Longer circulation, greater accumulation in tumors or organs, and decreased renal clearance (NPs < 7 nm) are all favoured by an ideal size of 20 to 200 nm. Kidney filtration and hepatic clearance are decreased for sizes between 20 and 150 nm. However, compared to normal organs, the EPR effect offers a relatively moderate improvement in tumour specificity of 20–30% in delivery.The degree of perivascular tumour growth, the density of the stromal response, intratumor pressure, and the degree of angiogenesis and lymphangiogenesis are all factors that significantly influence the EPR impact [6].

According to the EPR effect, if the following requirements for nanoparticle design are satisfied, administered nanoparticles may accumulate in solid tumours with discontinuous endothelium: (1) nanoparticles with a size smaller than the tumour interendothelial gap cutoff size, and (2) nanoparticles with extended blood circulation periods. Long blood circulation durations for nanoparticles are justified by the need to enhance the likelihood of paracellular nanoparticle extravasation. The likelihood of paracellular nanoparticle transfer into the tumour increases with the amount of time the intravenous nanoparticles can stay in the bloodstream at high concentrations.

Coordination of drug behaviour, targeting location, and pharmaceutical carrier are all part of drug targeting.The enhanced permeability and retention (EPR) effect indicates that tumors tend to retain a greater quantity of polymeric NPs, proteins, liposomes, and micelles compared to other tissues . The target is the particular organ, cell, or collection of cells that the medication will interact with in a chronic or acute ailment that has to be treated. In passive targeting, the enhanced permeability and retention (EPR) phenomenon—which was initially reported by Maeda and Matsumura—causes macromolecules, including nanoparticles, to collect preferentially in the cancerous tissues[7].

By utilising the distinct physiological or pathological characteristics of the targeted area, this method promotes the preferential accumulation of NPs and permits targeted medication release. Determining the optimal size and load for nanoparticle penetration and accumulation in target organs or tissues requires consideration of organ physiology . Depending on the tissue or organ, these are some instances of the vascular wall's capillarity or permeability.

Passive targeting improve the bioavailability of drug and selective accumulation of EPR effect.This is predicated on the medicine or drugs building up in regions that target the place of interest, such tumour tissue. NPs are utilised as carriers in passive targeting, and they are guided to penetrate blood vessels more at the illness location, which provides the chance for considerable drug accumulation at the target.When combined with a medicinal substance, nanoparticles passively permeate the body. The EPR effect or slow lymphatic drainage causes the nanoparticles to aggregate near the illness site, where they are more likely to enter blood vessels[8].

Active targeting:

There are several ways to target actively specific site of a body by aa drug carrier .Many ligands are used to take advantage of any particular antigens that cancer cells express in order to actively target cancer areas.The. Targeted ligand include antibodies, polysaccharides and protiens . The effectiveness of chemotherapeutic drugs that are hampered by passive accumulation and the inability to precisely identify tumour cells is greatly increased by nanocarriers modified with targeting ligands, which enable fine spatial control in vivo.RNA A10 conjugation onto PLA-block-PEG co-polymers has effectively targeted the prostate-specific membrane antigen, resulting in enhanced medication delivery to prostate tumour tissue in comparison to non-targeting nanoparticles[9].

Actively targeting nanoparticles to receptor or other surfaces membrane proteins express on target cell Over 90% of a therapeutic agent is still mostly sequestered in reticuloendothelial organs, such as the liver and spleen, as a result of clearance by mononuclear phagocytes, despite improvements in biodistribution brought about by the EPR effect and PEGylation.A material with a high affinity binds to the surface of the nanocarrier during active targeting. The target cell receptor is where the ligand binds selectively .Small particles of substances as well as macromolecules like proteins, amides, oligonucleotides, and aptamers, as well as a broad spectrum of ligands like carbohydrates and folic acid, have been used for this purpose. While minimising binding to healthy cells, the desired ligand attaches itself to the targeted cell.[10]

For active tumour targeting, peptides and antibodies are typically used as carrier materials. As a result, several clinical products have been produced. A monoclonal antibody (mAb) that bi"ds precisely to tumour surface antigens can be used to create effective treatment systems .Trastuzumab (Herceptin), one of the humanised monoclonal antibodies, exhibits anticancer activity against HER2-positive human breast cancer (BC) cells and is useful in treating BC when HER2 overexpression is present. By inhibiting the progression of the cell cycle and speeding up the endocytosis and degradation of the receptor, trastuzumab reduces the expression of HER2 in cancer cells. In animal studies, trastuzumab also causes antibody-dependent cell-mediated cytotoxicity against tumour cells that express HER2. Trastuzumab's inhibition of angiogenesis and metastasis are further suggested mechanisms [11].

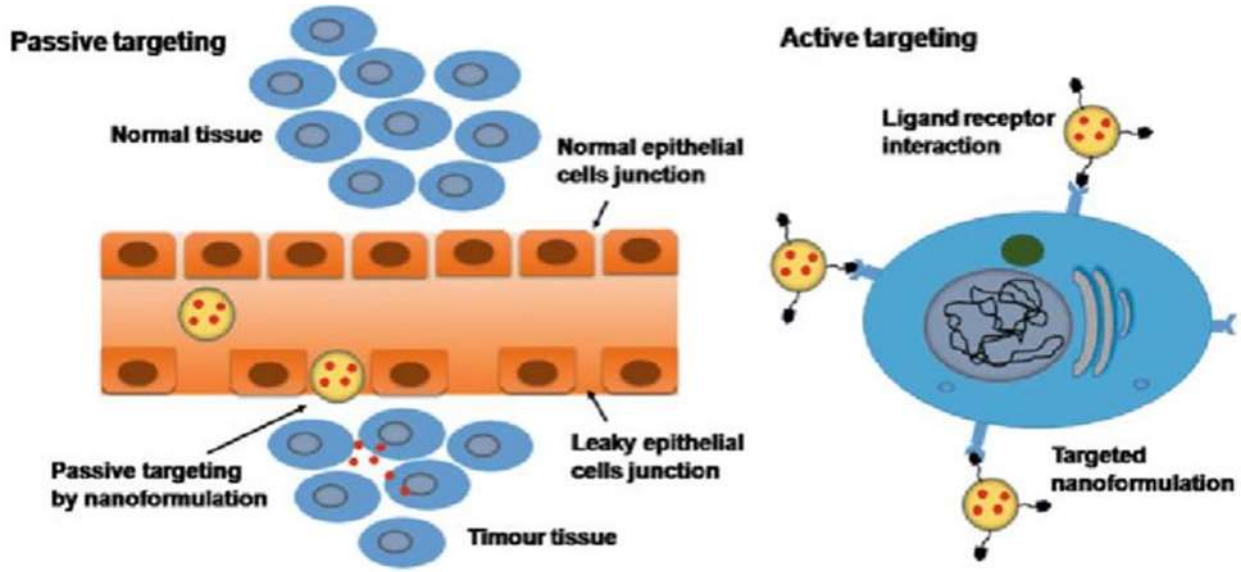

Fig1.3 Nanomedicines targeted drug delivery at affected cancer cell: by Passive targeting and active targeting .

Nanomedicine enhanced chemotherapy:

For instance, PTX can kill cells by preventing microtubule depolymerization in the cytoplasm 69, but DOX can cause cancer cells to undergo apoptosis by preventing topoisomerase II from functioning and causing DNA damage. Therefore, it is best to make sure that the right therapeutic agents with the suitable concentration can be found at the right location in order to achieve an acceptable therapeutic outcome.

Rapid clearance and non-specific distribution, however, always seriously impair the therapeutic efficacy of these chemical medications, leading to unavoidable systemic toxicity. Furthermore, one of the main causes of chemotherapy failure is the progressive development of a robust resistance mechanism (MDR) by tumour cells to chemotherapy medications over an extended period of time. Through a variety of techniques, nanomaterial-enabled chemotherapy now seeks to improve the effectiveness of traditional cancer chemotherapy regimens[12].

Combination therapy :

It has been demonstrated that combination therapy improves the effectiveness of cancer treatment. The optimal synergistic ratio minimises side effects while providing the appropriate combination therapeutic dose required for therapy. Cytarabine and daunorubicin, two chemotherapy medications, are intended to be used in an ideal 5:1 molar ratio for acute myeloid leukaemia.Small-molecule medications had previously been employed in clinical settings

with this combination; however, the effectiveness was restricted by inappropriate pharmacokinetics and poor solubility, necessitating co-administration with hazardous solvents. CPX-351 is presently undergoing phase III clinical studies after improving overall survival in patients who experienced their first relapse in phase I and II trials.

Theoretically, combination therapy may be more effective in addressing drug resistance and tumour heterogeneity. Multiple mechanisms are involved in cancers, which frequently progress through a series of consecutive mutations and develop intrinsic or acquired resistance[13].

Nanomedicine future applications:

Additionally, developments in nanomedicine might make it possible to do cellular-level surgeries, which would make it easier to remove certain diseased cells and fix damaged parts inside of individual cells. By treating biological issues that lead to ageing, this novel strategy has the potential to significantly increase human longevity [14].The application of nanotechnology in medicine has varpotential of applications ,contains :

- Personalized medicine
- More effective drug
- Regenrative medicines
- Nanorobots
- Multifunctional nanomedicine

Conclusion :

The benefits of nanotherapeutics in terms of pharmacokinetics, therapeutic efficacy, and safety have led to significant growth and development in the nanopharmaceutical sector during the last ten years.Nanomedicines hold significant promise for a variety of infectious diseases. Their small size and high bioavailability at the site of action enable them to deliver substantial medicinal benefits. Furthermore, nanomedicines can mitigate the toxic effects associated with traditional drugs and are considered cost-effective, especially when large doses of a particular medication are necessary, as they require only minimal quantities. Consequently, nanomedicine is regarded as a crucial therapeutic approach for numerous conditions, particularly cancer, and has the potential to lower treatment costs. This importance indicates that nanomedicines represent a burgeoning field that may serve as an alternative to conventional therapies in effectively targeting various diseases, especially cancer. The advancement of nanomedicine is poised to transform the healthcare landscape, addressing significant health challenges.

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