WWW.IJRPR.COM

**International Journal of Research Publication and Reviews**

Journal homepage: www.ijrpr.com ISSN 2582-7421

# NANO THERAPEUTICS IN CANCER: A REVIEW OF CANCER TREATMENT

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ABSTRACT :

Cancer is a complex group of diseases characterized by the uncontrolled growth of abnormal cells which have the potential to invade nearby tissues and organs, as well as it grow to other parts of the body through metastasis. Defeating cancer remains one of the most significant challenges in modern medicine. Oncologists and researchers around the world are continually striving to overcome obstacles in the fight against cancer. Nano medicine encompasses a broad range of medical applications that utilize the principles and tools of nanotechnology. This holds immense promise for revolutionizing various aspects of healthcare, including diagnostics, drug delivery, imaging, and therapy. The mechanism involved in the treatment of cancer by Nano medicines are active targeting and passive targeting. Currently employed Nano therapeutics in the treatment of cancer involves Liposomes, Dendrimers, Nano emulsions, Extracellular vesicles, from inorganic materials, Solid lipid Nano particles.Overall, while Nanomedicine offers promising advancements in cancer treatment, researchers must remain vigilant and proactive in addressing the potential challenges, including the development of drug resistance, to maximize its therapeutic potential and improve patient outcomes.

Keywords: Nano Medicine, Cancer, Liposome, Dendrimers, Nano Emulsion

## Introduction :

Cancer is one of the highly fatal disease in the world. According to the latest Global Cancer Statistics, an estimated 20 million new cancer cases and nearly 9.7 million cancer deaths occurred worldwide in 2022.The global cancer incidence is expected to grow rapidly over the next 20 years due to demographic changes, environmental pollution, as well as increased prevalence of lifestyle, and other risk factors. Cancer can indeed result from mutations in the DNA of cells, which can be caused by various factors including both genetic predisposition and environmental influences. Carcinogens, which are substances or agents that can lead to the development of cancer, come in various forms including physical (radiations, UV light), chemical (cigarette smoke, asbestos, contaminants in air, food and water), and biological agents (virus, bacteria, parasite that can cause inflammation).

Understanding the various causes of cancer is crucial for prevention efforts and developing strategies for early detection and treatment.

Endometrial Cancer, Kidney Cancer, Leukemia, Liver Cancer, Lung Cancer, Melanoma, Different type of cancer involves Bladder Cancer, Breast Cancer, Colon and Rectal Cancer,

Non-Hodgkin Lymphoma, Pancreatic Cancer, Prostate Cancer, Thyroid Cancer.

Nanomedicine involves the application of nanotechnology for medical purposes, encompassing various aspects such as diagnosis, monitoring, control, prevention, and treatment of diseases.The major application involves: The Nano particles , Nano capsules and other Nano structures can be used for drug delivery, Nanotechnology-based imaging, Nano electronic biosensors used for detection of disease, Nanomaterials can be used to engineer scaffolds for tissue regeneration and repair, as well as to deliver growth factors and therapeutic agents to promote tissue healing and regeneration, Nanotechnology enables the design of novel therapeutic strategies, such as targeted cancer therapy using nanoparticles functionalized with ligands that selectively bind to cancer cells, or hyperthermia therapy utilizing nanoparticles to generate heat and destroy cancer cells. Overall, Nano medicine holds great promise for advancing healthcare by providing innovative solutions for diagnosis, treatment, and prevention of diseases, ultimately leading to improved patient outcomes and quality of life.

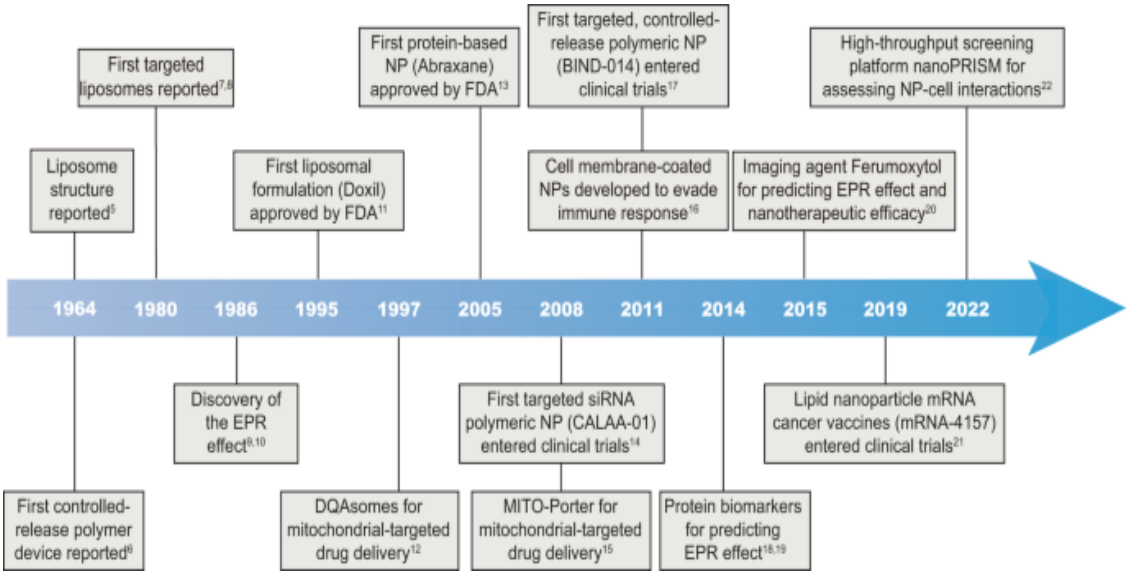
Nano drug delivery offers several advantages over conventional drug delivery methods, primarily due to the unique properties of Nanomaterials. Some of these advantages include:

Improved targeting, Enhanced drug solubility and bioavailability, Sustained and controlled release, Protection of drugs from enzyme degradation and harsh environmental conditions, Overcoming biological barriers .Ultimately, Nano drug delivery holds great promise for improving the efficacy, safety, and convenience of drug therapies by addressing the limitations of conventional drug delivery methods and enabling precise control over drug pharmacokinetics and biodistribution.

## 2. Nano medicines in cancer treatment

Nanomedicines have indeed emerged as a promising alternative in cancer treatment, primarily due to their ability to address key challenges associated with conventional therapies. Nanoparticles, the building blocks of Nanomedicines, offer unique advantages in targeting cancer cells through both active and passive mechanisms, enhancing drug bioavailability, and reducing toxicity.

- Targeting cancer cells: Nanoparticles can be engineered to specifically target cancer cells through active targeting mechanisms. This involves attaching ligands or antibodies to the surface of nanoparticles that recognize and bind to receptors or markers overexpressed on the surface of cancer cells. Additionally, nanoparticles can passively accumulate in tumor tissues through the enhanced permeability and retention (EPR) effect, which exploits the leaky vasculature and impaired lymphatic drainage commonly found in tumors.
- Improved bioavailability: Nanomedicines enhance the bioavailability of therapeutic agents by encapsulating them within nanoparticles. This encapsulation protects drugs from degradation and premature clearance in the bloodstream, allowing for prolonged circulation and increased accumulation at the tumor site.
- Reduced toxicity: Nanoparticles can help minimize the systemic toxicity associated with conventional chemotherapy drugs by selectively delivering them to tumor tissues. Targeted delivery reduces exposure of healthy tissues to cytotoxic agents, thereby reducing adverse side effects and improving patient tolerability.
- FDA-approved Nano-therapeutics: The FDA approval of Doxil® marked a significant milestone in the field of Nanomedicine for cancer treatment. Since then, several other Nano-therapeutics have been developed and approved for clinical use, including Abraxane® and Onivyde®.




In summary, Nanomedicines offer a promising approach for overcoming the limitations of conventional cancer therapies by leveraging the unique properties of nanoparticles for targeted drug delivery, enhanced bioavailability, and reduced toxicity.

**Fig 2.1 The origin and background of Nanomedicines in cancer therapy[9]**

## 3. Mechanism of targeting by Nano drug vehicles

The selection of a Nano medicine formulation for cancer therapy is crucial, with efficient targeting of cancer tissue and minimal side effects on normal tissue being key criteria. Nano-formulations for delivering anticancer drugs to tumor sites utilize various targeting mechanisms, including passive and active methods.

Passive targeting relies on the properties of tumor tissue to concentrate Nano-vehicles at the tumor site. Factors such as Enhanced Permeability and Retention (EPR) effect and Tumor Micro Environment (TME) properties play crucial roles. Tumor tissues exhibit neovascularization and poor lymphatic drainage, allowing nanoparticles to accumulate due to the EPR effect. However, the heterogeneity of the tumor microenvironment can lead to uneven distribution of nanoparticles. Nanocarriers can also utilize TME, barriers such as abnormal tumor vasculature and solid stress can hinder nanoparticle delivery. Properties like acidic pH and high redox potential for uniform drug delivery within tumors.

Strategies to improve passive targeting include using hydrophilic polymers (PEGylation) to reduce opsonization and prolong circulation time, and modulating tumor hypoxia to enhance drug delivery

Active targeting involves the use of molecules hybridized with carriers to specifically target cell surface receptors expressed by cancer cells. This approach enhances the specificity and efficacy of drug delivery to tumor cells.Immunotherapy, targeting immunosuppressive cells like tumor-associated macrophages (TAMs), is also promising for cancer treatment. Nanoparticles can modulate TAMs towards an anti-tumor phenotype and enhance therapeutic effects.

In summary, Nanomedicine formulations for cancer therapy should be carefully designed to maximize targeting efficiency while minimizing off-target effects. Passive and active targeting methods, along with strategies to overcome tumor barriers, offer promising approaches for improving the efficacy and safety of cancer treatments.

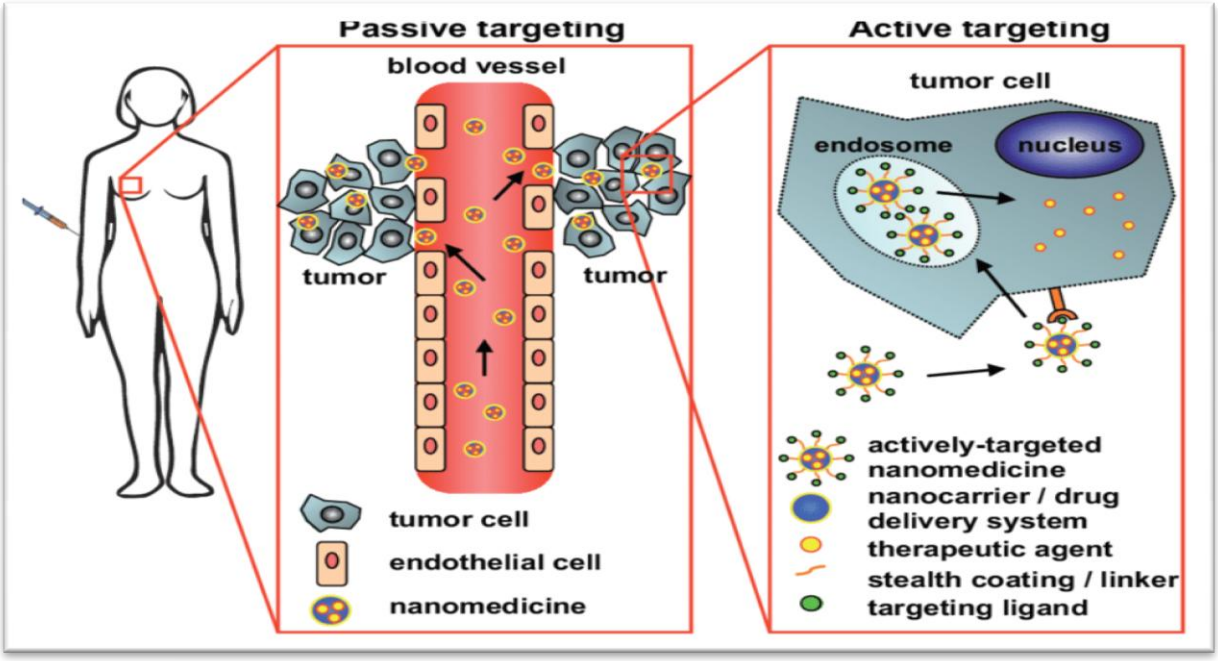
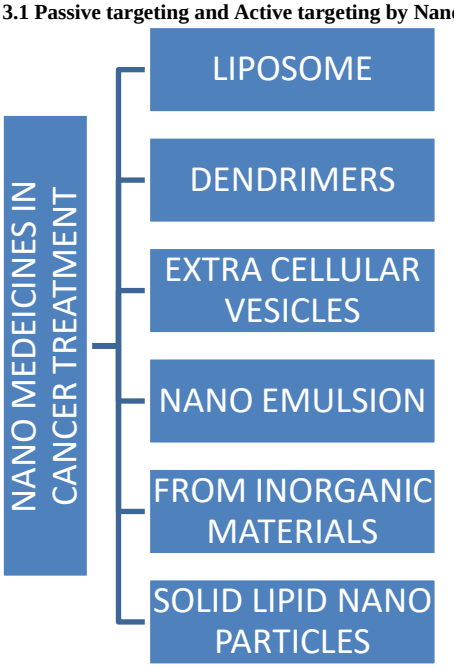



**Fig 3.1 Passive targeting and Active targeting by Nano drug vehicles [8]**




### *3.1. LIPOSOMES*

Anti-cancer drugs usually are less selective which results into their toxicity to the normal cell. Liposomes have successfully been used to entrap the drug.

### *ADVANTAGES*

- Increase the circulation life time ( t1/2)
- Protects the metabolic degradation of the drug.
- Altered tissue distribution of the drug with enhanced uptake in kidney, myocardium.

***DISADVANTAGES***

- The capillary endothelium of RES tends to prevent selective delivery of liposomal drugs to solid neoplasm.

They can be administered orally or via injection, with intravenous injection being the primary route for various drugs, although other routes such as subcutaneous, intradermal, Intra peritoneal and intramuscular are also utilized. The mechanism of action of liposome drug delivery relies on the accumulation, uptake, and release of drugs, with interactions occurring via passive and active targeting. Passive targeting exploits the enhanced permeability and retention (EPR) effect in tumor microenvironments to enhance liposome retention at tumor sites. On the other hand, active targeting involves surface functionalization of liposomes to improve their drug-targeting ability.

Active targeting of liposomes for drug delivery to tumors often involves surface functionalization using various molecules like antibodies that can targetsurface antigen such as MCAM, Her 2 receptor, CD44, and growth factor receptors like VEGFR and EGFR.

Liposomes can also be targeted using stimuli-sensitive cleavage of coating polymers. Polymers like PEG, used for coating liposomes, enhance circulation but may reduce targeting.

**ANTI CANCER DRUGS USED IN LIPOSOMES**

| DRUG | ROUTE OF ADMINISTRATION | DISEASE |
|---|---|---|
| METHOTREXATE | TRANSDERMAL | BREAST CANCER |
| DOXORUBICIN | ORAL, I.V | OVARIAN CANCER |
| DAUNORUBICIN | I.V | ACUTE MYELOID LEUKEMIA |

***3.2.DENDRIMERS***

One of the key advantages of dendrimers lies in their high surface functionalization and targeting properties, which stem from their ability to be precisely engineered to suit specific targets.

Moreover, the ability to regulate the size of dendrimers enables passive targeting to tumor sites via the enhanced permeability and retention (EPR) effect. Additionally, they can be integrated into other types of Nanocarriers, such as encapsulating them in polymer shells. Furthermore, dendrimers have a high drug-carrying capacity and can be engineered for various drug release mechanisms. Common strategies include modifying the number of terminal groups and incorporating degradable spacers and pH-sensitive linkages. These mechanisms allow for controlled and targeted drug release, enhancing therapeutic efficacy while minimizing side effects. Despite their potential, dendrimer-mediated drug delivery has faced challenges such as rapid systemic elimination which can be overcome by adopting surface functionalization methods utilizing molecules like vitamins, antibodies. These strategies enhance the circulation time and bioavailability of dendrimer-based drug delivery systems, further improving their effectiveness in cancer therapy and other medical applications.

***3.3. EXTRA CELLULAR VESICLES***

EVs are derived from the endosomal compartment and contain a variety of biomolecules including lipids, proteins, and microRNA, which makes them attractive candidates for targeted therapy.One of the key advantages of EVs is their favorable cellular uptake properties owing to their biochemical composition. Additionally, they can be engineered for surface functionalization, enabling targeted delivery to tumor sites .Their ability to cross the blood-brain barrier makes them particularly promising for the treatment of brain tumors.Engineered EVs offer enhanced pharmacokinetic properties, drug load stability, and targeted therapy. For example, studies have demonstrated the effectiveness of EV-mediated delivery of drugs such as paclitaxel in models of cancer metastases, leading to improved therapeutic outcomes.

Research efforts are underway to address scalability issues and optimize EV production methods for clinical applications. Once scalability challenges are addressed, EVs have the potential to revolutionize cancer therapy by providing efficient and targeted delivery of therapeutic agents.

***3.4. NANO EMULSION***

They can be formulated as water-in-oil or oil-in-water emulsions, using generally recognized as safe (GRAS) oils as vehicles, which offers the advantage of reduced side effects.Similar to liposomes, Nano emulsions can leverage the enhanced permeability and retention (EPR) effect for passive targeting of tumor sites. However, recent research has focused on surface functionalization of the outer oil portion of Nano emulsions to improve specific drug targeting to tumors. This involves the use of various molecules such as peptides (e.g., RGD peptide, transferrin), small molecules (e.g., biotin, folate), or specific antibodies targeting tumor surface antigens.Furthermore, active targeting methods for Nano emulsions are being explored, including the targeting of novel receptors such as the lysophosphatidic acid receptor, to enhance drug delivery specificity to particular tumor types.Their versatility allows for the loading of multiple drugs, promoting combinatorial drug use to enhance therapeutic efficacy. They also possess the inherent ability to overcome multidrug resistance mechanisms, a common challenge in cancer treatment. Moreover, they have the potential to utilize the drug itself as the emulsion without the need for additional carriers, simplifying drug delivery strategies.

***3.5. FROM INORGANIC MATERIALS***

Nanoparticles made from inorganic materials are another type of drug delivery system extensively employed in cancer treatment. Commonly utilized materials for these nanoparticles encompass gold and silver nanoparticles, carbon quantum dots, carbon nanotubes, metal oxide particles, and

mesoporous silica nanoparticles. These nanoparticles offer precise targeting, favorable pharmacokinetic profiles, the ability to encapsulate poorly soluble drugs, and diagnostic applications.The size and properties of nanoparticles play a critical role in the design of drug delivery systems. Nanoparticles typically function as carrier systems to incorporate active ingredients, facilitating the controlled release of the active compound at the targeted site to induce cell death.Overall, nanoparticles made from inorganic materials represent a versatile and effective approach for cancer treatment, offering precise targeting, enhanced pharmacokinetics, and the ability to encapsulate and deliver therapeutic agents to tumor sites.

### *3.6. GOLD/SILVER NANO PARTICLES*

Nanoparticles made of gold and silver possess the capability to deliver both small and large drug molecules to tumor sites. Their primary mode of drug targeting involves leveraging the enhanced permeability and retention (EPR) effect, along with exploiting tumor microenvironmental properties such as altered redox potential and pH.Additionally, due to their metallic nature, gold and silver nanoparticles can be utilized for hyperthermic treatment through techniques such as microwave irradiation following targeting to the tumor site. This hyperthermic treatment involves heating the nanoparticles to induce localized heating in the tumor, leading to cell death..The use of colloidal gold particles as drug delivery vectors of tumornecrosis factors has been tested in growing tumor in mice. The use of laser to destroy the tumor cells in human breast cancer tissue has been described by a technique using selective Nano thermolysis of self-assembling gold nanoparticles.This gold nanoparticles where coated with secondary Ab goat anti-mouse IgG. Colloidal gold nanoparticles can also function as safe and efficient gene delivery vehicles in gene therapy and immune therapy of cancer.Plasmid DNA encoding for murine interleukin-2 was complexed with gold nanoparticle. Gold nanoparticle showed significantly higher cellular delivery and transfection efficiency than other gene delivery vehicles. Gold nanoparticles conjugated with anti epithelial growth factor receptor antibody have been used to treat epithelial carcinoma by using selective laser Photothermal therapy.

## CONCLUSION

Indeed, Nano medicine holds great promise in revolutionizing cancer treatment by offering targeted drug delivery, reduced side effects, and improved efficacy. However, like any therapeutic approach, it comes with its own set of challenges and potential adverse effects. One significant concern is the possibility of developing drug resistance, a lesson learned from traditional cancer treatments. Understanding the fundamental processes of cell growth, division, and death is crucial for unraveling the mechanisms underlying cancer development and progression. This knowledge forms the basis for developing strategies for cancer prevention, diagnosis, and treatment.

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