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Review

Current and Emerging Roles of Nano pharmacology in Cancer Therapy

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Abstract

Nano pharmacology, a field that merges nanotechnology with pharmacological science, is significantly reshaping cancer treatment by introducing more precise, effective, and individualized therapeutic strategies. This review examines the current landscape and future directions of nano pharmacological methods in oncology, with particular focus on their contributions to drug delivery, diagnostic tools, and treatment modalities. Engineered nanoparticles including liposomes, dendrites, silica-based carriers, and gold-coated Nano shells have demonstrated the ability to enhance drug solubility, minimize adverse systemic effects, and improve localization of anticancer agents. Technological progress in this area has also impacted modalities such as radiation, immune-based treatments, and gene-targeting therapies, employing both passive and active targeting techniques, intelligent drug release systems, and improved navigation through biological barriers. Additionally, nanoscale technologies like quantum dots, carbon nanotubes, and autonomous nanodevices have shown promise in early tumor identification and real-time monitoring of therapeutic responses. As the biological understanding of cancer deepens, nano pharmacology offers a flexible and innovative framework to address challenges such as drug resistance, low therapeutic efficacy, and the demand for personalized treatment regimens. With ongoing scientific progress, this discipline is poised to become a foundational element in the evolution of precision cancer care.

Keywords: Cancer Therapy, Drug Delivery, Chemotherapeutics, Nanotechnology, Nanoparticles (NPs), Immunotherapy, Precision Oncology, Multi Drug Resistance (MDR), Quantam Dots (QD).

INTRODUCTION

Cancer therapy has witnessed transformative advancements over recent decades, yet challenges such as systemic toxicity, drug resistance, and non-specific targeting continue to limit the efficacy of conventional treatments. Nanopharmacology an interdisciplinary field integrating nanotechnology and pharmacology has emerged as a promising approach to overcome these limitations. By engineering nanoscale drug delivery systems, researchers can enhance the bioavailability, selectivity, and controlled release of anticancer agents, minimizing harm to healthy tissues. Current applications include liposomal formulations, polymeric nanoparticles and antibody-drug conjugates, many of which have already gained regulatory approval or entered clinical trials. Looking forward, the field is rapidly evolving with the advent of smart nanocarriers, stimuli-responsive systems, and personalized nanomedicine platforms, all of which are poised to redefine cancer treatment paradigms. This paper explores both the established contributions and future potential of nanopharmacology in revolutionizing oncology care.

Although new targets and therapies can advance cancer treatments, the dynamic nature of cancer finds a way to survive. The strategy against cancer needs to shift from finding new therapies to improving existing therapies and diagnostics in innovative, effective, and plausible ways. Pain is experienced by 55% of patients undergoing cancer treatment and 66% of patients with advanced stage cancer. [1]

Nanotechnology has ushered in transformative advancements in cancer diagnostics and treatment. NPs offer unique advantages such as enhanced biocompatibility, reduced toxicity, greater stability, improved permeability, precise targeting capabilities, making them highly effective in cancer therapies. These NPs, categorized by type, exploit tumor-specific features of drug delivery systems (DDS), address the limitations of traditional therapies and overcome Multi Drug Resistance (MDR).

Combination therapy combines two distinct treatment techniques, nanoparticles (NPs) and photosensitive therapy, and is thought to be more successful than standalone therapies in the treatment of breast cancer. Advanced and metastatic tumors pose challenges to these standard methods, with the aim of utilizing cytotoxic chemotherapeutic drugs, either after or without surgery, to disrupt tumor cell division and inhibit growth. Additionally, the overexpression of specific proteins in tumor cells poses a challenge for MDR. Radiation therapy, a localized treatment, affects only the area of the tumor, yet side effects may arise from damage to neighbouring healthy tissues. Given the adverse effects associated with traditional cancer treatment approaches, exploring well-considered novel alternatives becomes crucial. This work looks at the detection of trace quantities of tamoxifen (TAM) using nickel oxide NPs modified with a carbon paste electrode (NiO-CPE) in a NaOH (Potential of Hydrogen: pH 13) electrolyte. Cyclic voltammetry (CV) demonstrated an irreversible behavior with a 315-mV peak separation. The addition of TAM lowered the peak current, indicating that it interacted with NiO prior to the electrode response. The surface coverage (Γ) was 2.7 × 10−5 mol/cm2, and charge transfer coefficients (αa and αc) shifted with TAM presence. The rate constants (ks and KO) also varied, indicating that TAM influenced both the anodic and cathodic peak currents, with potential pathways depicted for clarity.

CURRENT EMERGING ROLES OF NANOPHARMACOLOGY IN CANCER THEARPY

Nano pharmacology is a branch of pharmacology it deals with the nanotechnology with living systems focusing on improving drug efficacy and reducing side effects through target drug delivery system and controlled release. The interactions between traditional drugs and physiological systems at nanoscale level. Drug design and drug delivery to selected targets to improve pharmacodynamics and kinetic profiles toward safer and effective treatment is known as Nano pharmacology.

Categorized Nano pharmacology

- ❖ Defining targets
- ❖ Development of drugs and carrier systems
- ❖ Studying target-drug interactions
- ✓ **Pharmacokinetic interactions**
  - Absorption
  - Distribution
  - Bio transformation
  - Excretion
- ✓ **pharmacodynamics interactions**
  - Receptor interaction
  - Receptor sensitivity
  - Neurotransmitter release/Drug transportation
  - Electrolyte balance
  -

✓ **Pharmaceutical interactions**

Usually, the binding sites of macromolecules are more hydrophobic in nature than the surface, and so this enhances the effect of a mic interaction. The drop off in ionic bonding strength with separation is less than in other intermolecular interactions, so if and interaction is possible, it is likely to be the most important in itial interaction as the drug enters the binding site monitoring the target-drug interaction outcomes.

1) Loss of therapeutic effect
2) Toxicity
3) Unexpected increase in pharmacological activity
4) Beneficial effects e.g additive & potentiating (intended) or antagonism (unintended).
5) Chemical or physical interaction. e.g I. V incompatibility in fluid or syringes mixture.

Nano pharmacology Target

1. Slow-release nano pharmacology

The slow-release nano pharmacology studies the question on how to realize the slow release and the influences of slow release on the drug metabolisms and the therapeutic effects.

2. Controlled release nano pharmacology

The controlled-release nano pharmacology studies how to realize the smart release of the drugs according to the therapeutic needs in the cellular and tissue micro environments

3. Bio barrier penetration nano pharmacology

Bio-barrier-penetration nano pharmacology studies the capabilities of nano drugs to passing through bio-barriers, Blood-brain barrier

4. Air-blood barrier

To realize the treatment of some focal diseases where the traditional drugs can't arrive because their incapability of penetrate bio barrier. [2]

Cancer

Cancer, also known as a malignant tumor or malignant neoplasm, is group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body.

- It may be either benign or malignant in nature.
- Each type of cancer is unique with its own causes, symptoms, and methods of treatment. Like with all groups of disease, some types of cancer are more common than others.
- Not all tumors are cancerous; benign tumors do not spread to other parts of the body.

Stage I cancers are localized to one part of the body; usually curable.
Stage II cancers are locally advanced.
Stage III cancers are also locally advanced.
Stage IV means the cancer has spread to other parts of your body. If also called advanced or metastatic. [3]

Treatment for cancer

Surgery: Surgery can be used to diagnose, treat; or even help prevent cancer in some cases. Most people with cancer will have some type of surgery.
Chemotherapy: Chemotherapy (chemo) is the use 01 medicines or drugs to treat cancer.
Radiation therapy: Radiation therapy uses high-energy particles or waves to destroy or damage cancer cells. It is one of the most common treatments for cancer, either by itself or along with other forms of treatment.
Immunotherapy: Immunotherapy is treatment that own immune system to help fight cancer.
Targeted therapy: Targeted therapy a newer type of can treatment that uses drugs or to substances to more precisely identify and attack cancer cells, usually while doing little damage to normal cells.
Stern cell transplant: (peripheral blood, bone marrow, and cord blood transplant) use to treat cancer.
Hyperthermia: The idea of using heat to treat cancer has been around for some time, but early attempts had mixed results. Today, newer tools allow more precise delivery of heat; and hyperthermia being studied for use against many types of cancer. [4]

Delivering chemotherapy

Nanotechnology's role in cancer therapeutics has been to improve the pharmacokinetics and reduce the systemic toxicities of chemotherapies by selectively targeting and delivering anticancer drugs to tumor tissues, Nanosized carriers can increase the overall therapeutic index of delivered drugs through nano formulations, where chemotherapeutic is either encapsulated or conjugated to the surface of nanoparticles. The selective delivery of nanotherapeutic platforms primarily depends on the passive targeting of tumors through the enhanced permeability and retention (EPR) effect, although other mechanisms were also proposed. The EPR phenomenon relies on tumor microenvironment defects like lymphatic drainage and increased tumor vasculature permeability, which facilitate the accumulation of nanoparticles (<200 nm) in the tumor Additionally, the timing or site 01 drug

release can be controlled by the use of external or internal trigger mechanisms such as ultrasound, pH, heat, or material composition itself. Several researchers are working towards developing nanomaterial-based delivery platforms to enhance chemotherapy's effectiveness while reducing its toxicity. For example, they are developing a strategy for photodynamic therapy, specifically tailored for bone marrow application (Alexander Zheleznyak, Monica Shokeen, and Samuel Achilefu, WIRES Nanomedicine and Nanobiotechnology, 2018), an area usually inaccessible to external radiation sources. Others are investigating the fundamental interactions between nanomaterials and biological systems to advance cancer diagnostics and therapeutics. This involves a focus on nanoparticle-based delivery systems that can penetrate physiological barriers to achieve targeted access to specific tumors, utilizing methods like mechanical particle deformation or using a synergistic approach for the delivery 01 paclitaxel and gemcitabine chemotherapeutics in mesoporous silica nano-constructs (Huan Meng, et al. ACS Nano, 2015). [5]

Delive augumenting radiotherapy

Radiation therapy is a cornerstone of modern cancer therapy alongside surgery, chemotherapy, and immunotherapy, with over half of all cancer patients receiving radiation therapy as part of their treatment regimen. Development of novel radiation sensitizers that can improve the therapeutic window of radiation therapy are sought after, particularly for tumors at an elevated risk of local and regional recurrence such as locally-advanced lung, head and neck, and gastrointestinal tumors. This review discusses clinical strategies to enhance radiotherapy efficacy and decrease toxicity, hence, increasing the overall therapeutic window. A focus is given to the molecular targets that have been identified and their associated mechanisms of action in enhancing radiotherapy. Examples include cell survival and proliferation signaling such as the EGFR and PI3K/AKT/mTOR pathways, DNA repair genes including PARP and ATM/ATR, angiogenic growth factors, epigenetic regulators, and immune checkpoint proteins. By manipulating various mechanisms of tumor resistance to ionizing radiation (IR), targeted therapies hold significant value to increase the therapeutic window of radiotherapy. Further, the use of novel nanoparticles to enhance radiotherapy is also reviewed, including nanoparticle delivery of chemotherapies, metallic (high-Z) nanoparticles, and nanoparticle delivery of targeted therapies – all of which may improve the therapeutic window of radiotherapy by enhancing the tumor response to IR or reducing normal tissue toxicity. [6]

Nano-Immunotherapy

Aiming to activate an effective antitumor immune response has ushered in a new era of cancer treatment. However, the efficacy of cancer immunotherapy is limited by low response rates and high systemic toxicity. Nanotechnology is an encouraging platform for the development of next-generation cancer immunotherapy to effectively treat advanced cancer. Nanotechnology-enabled immunotherapy has remarkable advantages, ranging from the increased bioavailability and stability of immunotherapeutic agents to the enhanced activation of immune cells and favorable safety profiles. Nanotechnology-enabled immunotherapy can target solid tumors through reprogramming or stimulating immune cells (i.e., nanovaccines); modulating the immunosuppressive tumor microenvironment; or targeting tumor cells and altering their responses to immune cells to generate effective antitumor immunity. In this Oration, I introduce the advanced strategies currently being pursued by our laboratory and other groups to improve the therapeutic efficacy of cancer immunotherapy and discuss the potential challenges and future directions. [7]

Delivering Gene Therapy

The proposal of gene therapy to tackle cancer development has been instrumental for the development of novel approaches and strategies to fight this disease, but the efficacy of the proposed strategies has still fallen short of delivering the full potential of gene therapy in the clinic. Despite the plethora of gene modulation approaches, e.g., gene silencing, antisense therapy, RNA interference, gene and genome editing, finding a way to efficiently deliver these effectors to the desired cell and tissue has been a challenge. Nanomedicine has put forward several innovative platforms to overcome this obstacle. Most of these platforms rely on the application of nanoscale structures, with particular focus on nanoparticles. Herein, we review the current trends on the use of nanoparticles designed for cancer gene therapy, including inorganic, organic, or biological (e.g., exosomes) variants, in clinical development and their progress towards clinical applications. [8]

Approaches for the synthesis of nanomaterials

The two basic approaches for synthesis of nanomaterials:

1. In top-down approaches, bulk materials are divided to produce nanostructured materials. Top-down methods include mechanical milling, laser ablation, etching, sputtering, and electro-explosion.
2. The bottom-up approach involves to building nanostructures by assembling individual atoms and molecules into larger structures. [9]

Nano particles target tumor cells in two ways:

Passive targeting: Passive targeting is a strategy accomplished by integrating the therapeutic agent into a nanoparticle, allowing it to passively diffuse in the body in the aim to reach the target organ/tissues. In the context of gene therapy, passive targeting is based on nanoparticles (NPs) to precisely direct therapeutic agents to specific tissues or organs, without the need for specific targeting agents.

Active targeting: Active nanoparticle targeting involves incorporating targeting elements. It is mainly divided into antibody-based targeting, peptide-based targeting, aptamer-based targeting, and small-molecule-based targeting. This strategy aims to guide nanoparticles specifically to cells, tissues, or organs by exploiting unique physiological or pathological features of the target region.[10]

Different types of nano particles targeting tumor cells

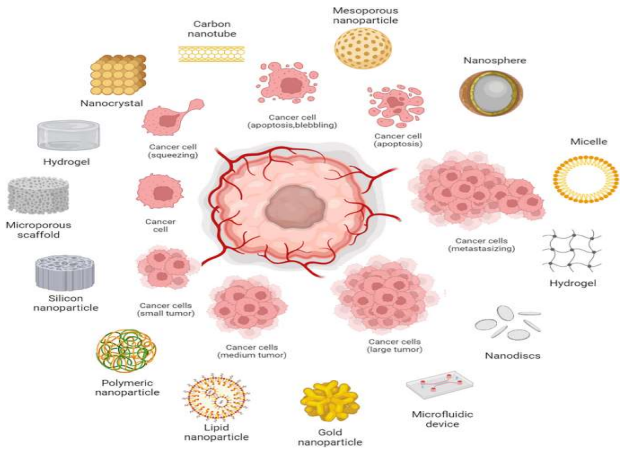

Fig 1: Types Of Nano Particles

Nanopore

Nano pores are the tiny holes that allow DNA to pass through one strand at a time, and will make DNA sequencing more efficient-As DNA passes through a Nano pore, scientists can monitor the shape and electrical properties of each base, or letter, on the strand. Because these properties are unique for each of the four bases that make up the genetic code, scientists can use the passage of DNA through a Nano pore to decipher the encoded information, including errors in the code known to be associated with cancer.

Carbon tubes/nanotube

Carbon nanotubes (CNTs), one of the most promising carbon-related nanomaterial's, have already achieved much success in biomedical field. Due to their excellent optical property, thermal and electronic conductivity, easy functionalization ability and high drug loading capacity, CNTs can be applied in a multifunctional way for cancer treatment and diagnosis. [11]

Quantum dots

The nanoparticle is a fast-growing sector of nanotechnology that offers new possibilities for disease detection and therapy. In the diagnosis of malignancy, fluorescent nanoparticles can be utilized to create diverse profiles of tumour biomarkers, and the availability of several genes and RNA segments by using fluorescent in situ hybridization. QD nanoparticles act as semiconductors and are useful for depicting cells and live creatures in fluorescent form. Depending on their composition and size, they can be a good source of light spanning from UV to IR. In the crystal core of a QD, there are around 100–100,000 atoms. The typical size of a QD is between 2 and −10 nm in diameter. The substance employed to manufacture Quantum dots, on the other hand, is responsible for the dimensions of the QD. [12]

Dendrimers

Physical encapsulation) as well as attached to the surface functional groups (covalent conjugations Dendrites represents a novel class of macromolecules, which are derived from branches upon branches type structural design. Dendrimers are emerging as promising drug-delivery molecule because of their extraordinary properties including membrane interaction, monodispersity, well-defined size, shape and molecular weight, etc. Drugs interact with dendrimers in three ways; (a) physical encapsulation, (b) electrostatic interactions, and (c)

covalent conjugations. Due to compact, globular structure and availability of interior cavity spaces and multiple surface functional groups, drug molecules can be encapsulated both in the interior of the dendrimers.[13]

Liposomes

Liposomes are self-assembling NPs with closed membrane structures. They are farmed by dispersion of phospholipids featured with hydrophobic anionic/cationic long chain tails and hydrophilic heads. Their specific structures enable water-soluble drugs to be entrapped in their aqueous core, while lipophilic drugs in the lipid bilayer. In addition, liposomes can effectively load various bioactive molecules, including enzymes and nucleic acids-They have been proven to be beneficial for therapeutic compound stabilization, cellular and tissue uptake of therapeutic compounds and bio-distribution of compounds to target sites in vivo. Liposomes can be prepared by disrupting biological membranes (such as by sonication and ethanol injection technique.[14]

Gold nanomaterials

Nano shells are miniscule beads coated with gold. By manipulating the thickness of the layers making up the nano shells, they have designed these beads to absorb specific wavelengths of light. The most useful nano shells are those that absorb near- infrared light, which can easily penetrate several centimetres of human tissue. The absorption 01 light by the nano shells creates an intense heat that is lethal to cells, these gold nano shells are shuttled into tumors by the use of phagocytosis, Phagocytes engulf the nano shells through the cell membrane to form an internal phagosome, or macrophage. Nanoparticle-based therapeutics have been successfully delivered taken up passively into tumors without the assistance of antibodies.[15]

Mesoporous silica nanoparticles

Mesoporous silica nanoparticle (MSN) coated with polydopamine (PDA) and loaded with umbelliprenin (UMB) was prepared and evaluated for its anti-cancer properties in this study. Then UMB-MSN-PDA was characterized by dynamic light scattering (DLS), Field emission scanning electron microscopy (FESEM), Transmission electron microscopy (TEM) and FTIR methods. UV-visible spectrometry was employed to study the percentage of encapsulation efficiency (EE%). UMB-MSN-PDA mediated cell cytotoxicity and their ability to induce programmed cell death were evaluated by MTT, real-time qPCR, flow cytometry, and AO/PI double staining methods. The size of UMB-MSN-PDA was 196.7 with a size distribution of 0.21 and a surface charge of −41.07 mV. The EE% was 91.92%. FESEM and TEM showed the spherical morphology of the UMB-MSN-PDA. FTIR also indicated the successful interaction of the UMB and MSN and PDA coating. The release study showed an initial 20% release during the first 24 h of the study and less than 40% during 168 h. The lower cytotoxicity of the UMB-MSN-PDA against HFF normal cells compared to MCF-7 carcinoma cells suggested the safety of formulation on normal cells and tissues. The induction of apoptosis in MCF-7 cells was indicated by the upregulation of P53, caspase 8, and caspase 9 genes, enhanced Sub-G1 phase cells, and the AO/PI fluorescent staining. As a result of these studies, it may be feasible to conduct preclinical studies shortly to evaluate the formulation for its potential use in cancer treatment.[16][17]

Nanorobot

They are tiny devices designed to work on a nanometre scale, or in the order of magnitude of nanometres (a nanometre is one billionth of a metre). Thanks to their very small size, nanorobots can interact directly with cells, performing multiple functions. Specifically, DNA nanorobots can transport specific molecules. Using these biological “tools”, Karolinska researchers managed to tansport a series of molecules, known as “ligands”, inside tumours; these molecules are able to bind to specific proteins on the surface of cancer cells, known as “Tumour Necrosis Factor (TNF) receptors”. Once activated by the ligands, the TNF receptors (which form part of the so-called “death receptors”) trigger the programmed death (or apoptosis) of the cells.[18]

CONCLUSION

Nanopharmacology stands at the forefront of a transformative shift in cancer therapy, offering a comprehensive toolkit to overcome the longstanding limitations of conventional treatments. Through innovative drug delivery systems such as liposomes, dendrimers, silica nanoparticles, and gold nano shells, nanotechnology enables precise targeting, controlled release, and reduced toxicity, thereby enhancing the efficacy and safety of chemotherapeutics and radiation therapies. Moreover, the integration of nanotechnology with immunotherapy and gene therapy expands the horizon of personalized and adaptive cancer treatments, improving therapeutic outcomes while minimizing systemic side effects. Emerging tools like quantum dots, nanotubes and nano robots further underscore the role of nanotechnology in advancing cancer diagnostics, imaging, and real-time treatment monitoring. As research continues to evolve, nanopharmacology promises to not only refine current oncology practices but also unlock novel, multi-functional strategies that are more responsive to the complexity and variability of cancer. The future of cancer therapy will likely be shaped by the convergence of nano-enabled

diagnostics, targeted delivery systems and patient-specific therapeutic platforms marking a new era in precision oncology.

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