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Review Article

REVIEW ON APPLICATION OF NANOTECHNOLOGY IN MANAGEMENT OF CANCER

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ABSTRACT

Cancer remains a major global health challenge, with diverse types and complex etiologies contributing to its high prevalence and mortality. Nanotechnology has emerged as a transformative tool in cancer management, offering advancements in diagnosis, targeted therapy, and treatment modalities. By leveraging the unique properties of nanoparticles, such as their ability to target specific cancer cells and deliver therapeutic agents with high precision, nanotechnology promises to enhance the effectiveness of cancer treatments while minimizing side effects. This review highlights the importance of nanotechnology in cancer management, detailing its mechanisms, applications, and the types of nanoparticles involved, including quantum dots, metallic nanoparticles, and lipid-based nanoparticles.

Keywords: Nanotechnology, Cancer management, Targeted therapy, Nanoparticles, Quantum dots, Metal nanoparticles, Gene therapy, Imaging, Photothermal therapy

INTRODUCTION

Cancer is a disease that can develop in any of the body tissue and from that each of the cancer type consists of its unique features, cancer begins when a cell breaks free from the normal restraints on cell division and begins to follow its own proliferation. The name cancer derives from an observation by “Hippocrates” more than 2,300 years ago. The term “Korkinoma”, in Greek came then later, Cancer in Latin. The Hooke in 1600s, and Virchow in 1800s, came to an observation that the living tissues are composed of cells and all the cells arise as direct descendants of other cells (Jayesh, 2022).

Cancer is a disease characterized by uncontrolled cell proliferation that spreads from an initial focal point to other parts of the body to cause death. For these reasons, it is key to ensure earlier detection and treatment of cancers to reduce disease spread and mortalities (Hu *et al*., 2016).

Prevalence of Cancer All over the World

Cancer is one of the leading causes of death in the world, as shown by the 2022 cancer statistics, predicting 1,918,030 new cases of cancer and 609,360 related deaths per year. The classic therapeutic options when approaching a cancer patient are chemotherapy, radiotherapy, and surgery. The choice of approach depends on several characteristics, such as the cancer stage and location or patient’s fitness, which is compromised by the disease itself, worsening with each treatment intervention in the long term. These treatments can reduce cancer recurrence and mortality but have important side effects that can lead to severe

complications and to the risk of death from other diseases (Sell *et al*., 2023).

Factors that enhance the emergence of cancer include rising pollution, radiation, sedentary life, unbalanced diet, infection with oncogenic microorganisms, and other variables (eg, heredity) which are also becoming common in developing countries. Any of these variables can cause a damage in host cells' deoxyribose nucleic acid (DNA) genes known as oncogenes that lead to cancer. Individual cells that have achieved immortality and are capable of replicating at incredible rates surpass all healthy functional cells resulting in death (Dessale *et al*., 2022).

Types of cancers

These are given as follows:

Carcinoma

Cancer that begins in the skin or in tissues that line or cover internal organs. There are a number of subtypes of carcinoma, including adenocarcinoma, basal cell carcinoma,squamous cell carcinoma, and transitional cell carcinoma.

Sarcoma

Cancer that begins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue (Harika *et al.*, 2015).

Leukemia

Cancer that starts in blood-forming tissue such as the bone marrow and causes large numbers of abnormal blood cells to be produced and enter the blood.

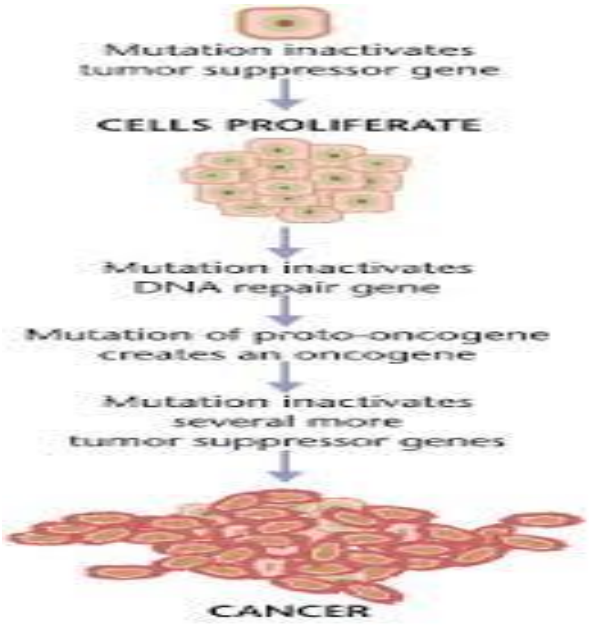
Lymphoma and myeloma

Cancers that begin in the cells of the immune system.

Central nervous system cancers

Cancers that begin in the tissues of the brain and spinal cord.

Etiology of cancer



Diagnostic test of cancer

Cancer screening and surveillance methods include ultrasound, mammography, digital mammography, magnetic resonance imaging, computed tomography, positron emission tomography and magnetic resonance spectroscopy. Other techniques such as immunohistochemistry, in situ hybridization (FISH, CSH), PCR, RT-PCR (real time-PCR), flow cytometry and microarray are used nowadays for diagnosis (Kumar and Pawaiya, 2010).

Nanotechnology

Nanotechnology has led to several promising results with its applications in the diagnosis and treatment of cancer, including drug delivery, gene therapy, detection and diagnosis, drug carriage, biomarker mapping,

targeted therapy, and molecular imaging (Jin *et al*., 2020).

Nanotechnology is defined as the study and use of structures between 1 nanometer and 100 nanometers in size. Nanotechnology is the synergy of mechanical, electrical, chemical engineering, material sciences, microelectronics, and biological screening (Haque *et al*., 2010).

The need for an advanced technology to play an important role for cancer treatment is clearly evident in the statistics indicating that cancer incidence, prevalence, and mortality remain at exceedingly high levels. The need for an advanced technology to play an important role for cancer treatment is clearly evident in the statistics indicating that cancer incidence, prevalence, and mortality remain at exceedingly high levels.

Importance of nanotechnology in cancer

There are many types of nanoparticles, including metallic, magnetic, polymeric, metal oxide, quantum dots, graphene, fullerene, liposomes, carbon nanotubes, and dendrimers, which are used in breast, colon, and cervical cancer diagnosis. Additionally, they are important for some imaging functions. It has been found that nanoparticles remain in the blood circulation for a long period of time before reaching the target cells, where they traverse many biological walls such as cell membranes and interact with biological systems. Moreover, cancer-specific antibodies can be conjugated with nanoparticles for better cancer binding and detection. Many recent studies have demonstrated that nanoparticles and sensors have significant potential for increasing the sensitivity of tumor detection and improving cancer diagnosis. It has been reported that the detection of methylation patterns and mutations has been used as a marker for cancer diagnosis (Alrushaid *et al*., 2023).

Nanotechnology in cancer management has yielded various promising outcomes, including drug administration, gene therapy, monitoring and diagnostics, medication carriage, biomarker tracing, medicines, and histopathological imaging. Quantum dots (QDs) and gold nanoparticles are employed at the molecular level to diagnose cancer. Molecular diagnostic techniques based on these nanoparticles, such as biomarker discovery, can properly and quickly diagnose tumors. Nanotechnology therapeutics, such as nanoscale drug delivery, will ensure that malignant tissues are specifically targeted while reducing complications. Because of their biological nature, nanomaterials can cross cell walls with ease. Because of their active and passive targeting, nanomaterials have been used in cancer treatment for many years (Kher and Kumar, 2022).

Mechanism of Nanotechnology in Cancer Treatment

Active Targeting By Nanoparticles

There are several ways to target actively a specific site of body by a drug carrier. In order to achieve the active targeting of cancer sites, a variety of ligands are utilized to exploit any specific antigens expressed by cancer cells. The prostate-specific membrane antigen has been successfully targeted by conjugation of RNA A10 onto PLA-block-PEG co-polymers, which exhibited increased drug delivery to prostate tumor tissue compared to non-targeting nanoparticles. In the case of the active targeting by

immunoliposomes, binding to target cells and uptake by the RES are two kinetically competing processes. PEG chains have shown a successful avoiding of the RES uptake of liposomes, thus leading to an elevated blood concentration and enhanced target binding of immunoliposomes. Also, the presence of free PEG did not interfere with the binding of the terminally linked antibody to the antigen in pendant-type immunoliposomes (Alavi and Hamidi, 2019).

Passive Targeting By Nanoparticles

In cancer, this process of passive targeting takes place in a non-specific way through gaps into the tumor interstitial space. These gaps between adjacent endothelial cells with a diameter up till 800nm exist in neoangiogenic blood vessels which serve to supply the tumor with nutrients. Tumor tissues use permeability factors as vascular endothelial growth factor (VEGF) to increase the permeability of tumor blood vessels. Nanoparticles, carrying encapsulated drugs, extravasate into the tumor interstitial space and passively target the tumor tissue. Once the drug is locally released the local concentration becomes many times larger than after conventional systemic intravenous administration. The altered lymphatic drainage of the tumor contributes to this effect. This type of passive targeting is known as "enhanced permeation and retention" (EPR) (Pauwels *et al*., 2008).

Tumor targeting through gene silencing

The regulation of gene expression in a cell to prohibit the expression of a specific gene is known as gene silencing. Due to its potential to suppress genes implicated in tumor formation, gene silencing grasps promising cancer therapy gene silencing is the process of altering gene expression on an epigenetic level. This is accomplished mostly through the use of antisense DNA and short interfering RNA. Gene silencing with small interfering RNA (siRNA) is another option. siRNAs can be delivered to cells by using a platelet cell membrane-coated metal (zinc)-organic framework (MOF). Using a simple one-pot method, synthetic siRNAs were loaded onto porous metal-organic framework (MOF) NPs. pH affects the structural integrity of MOF scaffolds. *In vitro* targeting and intracellular localization were performed on human SK-BR-3 breast cancer cells (HTB-30; American Type Culture Collection, Manassas, VA). To bind specifically to cancer cells, a platelet membrane coating was employed (Xu *et al*., 2022).

Examples of nanoparticles used

Quantum dots

Quantum dots (QDs) are nano-sized crystals capable of transporting electrons. Under UV light, QD can emit light of different colors with very high energy. QDs have an inactive site on their surface where specific antibodies can easily conjugate. Quantum dots are already used in drug delivery and treatment for lung cancer and can help clear up bacterial infections. In addition, conjugated QDs have been shown to inhibit P-glycoprotein gene expression in lung cancer cells by inducing miR-185 and miR-34b. miR-185 and miR-34b are potential targets for the treatment of lung cancer. Besides many benefits, QD also contains heavy metals such as cadmium, which are carcinogenic (Ren *et al*., 2010).

Polymeric Nanoparticles

The polymeric nanoparticle consists of two parts, a hydrophobic core which serves as

the container for anticancer agents and a hydrophilic shell which stabilizes the nanoparticle in aqueous environments. The drug can be loaded into polymeric nanoparticles through two methods: by physical entrapment or by chemical conjugation. A hydrophobic interaction between the core of the polymeric nanoparticle and the drug molecule allow the drug to be entrapped in the nanoparticle core. For instance, deoxychilic acid-modified heparin can self-assemble into 100~200 nm nanoparticles and its hydrophobic core can be used to entrap 4~12% of the total weight of doxorubicin. When the drug molecule is covalently conjugated onto the polymer, the chemical properties of the linker between the drug and polymer are critical. If the linker is too stable, drug release may be delayed, while if the linker is too unstable, drug may be released before the nanoparticle reaches the tumor. Therefore, a proper linker is very important to the drug-polymer conjugate (Wang *et al*., 2009).

Metal Nanoparticles (NPs)

Metal NPs have been explored in biomedical imaging, diagnostics, and treatment due to their versatile surface chemistry and tunable size and shape. AuNPs are safe and improve the delivery of immunotherapeutic agents. For example, the use of AuNPs in combination with modified CpG attenuates side effects and stimulates macrophages and DCs to significantly inhibit tumor growth. A scientist designed Fe_3O_4-ZnO core-shell NPs to deliver carcinoembryonic antigens into DCs. These complexes, which can also be used as imaging agents, can be rapidly and efficiently taken up by DCs, and enhance the tumor antigen-specific T cell responses in mice (Yan *et al*., 2019).

Platinum Nanoparticles

Platinum nanoparticles are widely used in medicine. Studies have shown that these platinum nanoparticles (PtNPs) possess intrinsic anticancer activity because of their antioxidant capabilities, which result in an inhibitory effect on the growth of tumors. In addition, targeting ligands linked to functionalized metal PtNPs have improved tumor targeting and PtNPs have facilitated better drug release and improved drug delivery efficiency. However, some recent studies have reported the toxic effects of nanoplatinum due to nanoparticle size, as nanoparticles were observed to accumulate in major organs and cells (Wang *et al*., 2018).

Gold Nanoparticles

Colloidal gold nanoparticles are the most commonly used nanoparticles for anti-carcinogenic drug delivery. Colloidal gold nanoparticles are more biocompatible than other nanoparticles. The physical and chemical properties of colloidal gold nanoparticles allow more than one protein molecule to bind to a single particle of colloidal gold. The use of colloidal gold nanoparticles as drug delivery vectors of tumour necrosis factor (TNF) has been tested in a growing tumour in mice. Although TNF has been evaluated in cancer treatment, it causes adverse effects like hypotension and in some cases causing organ failure resulting in death. But recent researches have shown that when coupled with colloid gold particles, therapeutic amounts TNF can be successfully delivered to destroy the tumour cells in animals (Subramani *et al*., 2009).

Dendrimers

Dendrimers are synthesized and branched macromolecules with a tree-like structure and specific shape and size. These structures are monodispersed. Their surface can be modified with chemical reactions and physical interventions. Drug molecules are attached to dendrimers in complex or capsule forms. In 70s, Fritz Vögtle and Donald Tomalia were the first ones who attempted dendrimers synthesis and invented tree-like structures by conjugating the monomers to each other. Vivagel® is the first dendrimer NP system that was introduced to the pharmaceutical market. Vivagel® products are used as local antiviral drugs for preventing the transmission of human immunodeficiency virus and herpes virus. According to the dendrimer structure, this product prevents the attachment of the virus to the host body (Aghebati-Maleki *et al*., 2020).

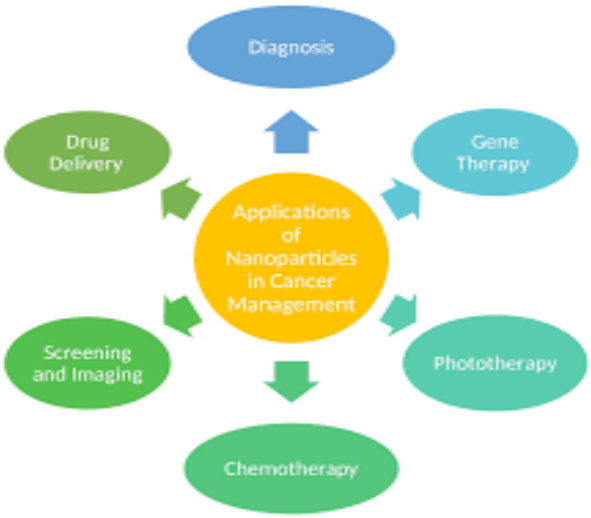
Magnetic nanoparticles

Magnetic nanoparticles like Fe3O4 (magnetite) and Fe2O3 (maghemite) are known to be biocompatible. They have been actively investigated for targeted cancer treatment (magnetic hyperthermia), stem cell sorting and manipulation, guided drug delivery, gene therapy, DNA analysis, and magnetic resonance imaging (MRI) (Fan *et al*., 2009).

Lipid-Based Nanoparticles

Liposomes are the most studied delivery systems due to the biocompatibility and biodegradability that they present. The main components of these nanoparticles are phospholipids, which are organized in a bilayer structure due to their amphipathic properties. In presence of water, they form vesicles, improving the solubility and stability of anticancer drugs once they are loaded into their structure. They are capable of encapsulating either hydrophobic or hydrophilic drugs. In addition to phospholipids, other compounds can be added to their formulations, such as cholesterol, which decreases the fluidity of the nanoparticle and increases the permeability of hydrophobic drugs through the bilayer membrane, improving the stability of these nanoparticles in blood (Garcia-Pinel *et al*., 2019).

Applications of nanotechnology in cancer



Nanoparticles in Cryosurgery

Cryosurgery is an advanced practice of freeze-destroying cancer tissue. Although this is less invasive and causes intraoperative bleeding and postoperative complications, certain drawbacks like inadequate freezing capacity and damage to adjacent cells need to be addressed (Bu *et al*., 2020).

Nanoparticles in gene therapy

Gene therapy involves introducing exogenous nucleic acids, such as genes, siRNAs, miRNAs, short hairpin RNA (shRNA), or

oligonucleotides, into target cells to correct overactive or defective genes and treat diseases. Exogenous nucleic acids can be administered in vivo or ex vivo to transfer genes into target cells. By the way of ex vivo administration, target genes are introduced (transferred or transduced) into target cells, such as autologous or allogeneic tumor cells, immune cells, or other cells, in vitro. These modified target cells are then transferred back into the body. Among these methods, ex vivo gene therapeutics using chimeric antigen receptor T-cells (CAR T cells) have been recognized as highly effective for treating tumors (Huang *et al*., 2024).

Nanoparticles in Multimodal Imaging

While various imaging techniques, such as MRI, CT, Positron Emission Tomography (PET), and infrared (IR) imaging, have been used for diagnosis and treatment monitoring, each one delivers different information on disease and its location. There is no perfect imaging method, as each technique has its advantages and disadvantages. Nanotechnology allowing production of multimodal contrast agents ("all in one") takes advantages of all these modalities. Of particular interest is the recent development of rare earth upconversion nanophosphors (RE-UCNPs) as potential contrast agents because of their optical and biochemical properties, such as sharp emission lines, long lifetimes, and nonphotoblinking. In particular, Yb^{3+} and Tm^{3+} codoped RE-UCNPs emitting at 800 nm have been used for a whole-body small-animal near-infrared imaging. This technique allowed detection of only 50 cells in a whole-body mouse imaging (Blasiak *et al*., 2013).

Nanoparticles in photothermal therapies

The use of laser light-induced hyperthermia/thermal ablation, i.e. photothermal therapy, has been traditionally considered as a non-reliable technique due tothe fact that human tissues show strong extinction coefficients in the visible range of the optical spectrum, this fact limiting photothermal treatments to supercial tumors. In addition, laser light energy is expected to be absorbed by both healthy and cancerous tissues, which leads to both a reduction in the efficacy of heat delivery within the tumor and an increment in thenon-specic damage of the adjacent tissues. However, photo-thermal therapy is nowadays attracting considerable attention because of the possibility of controlling the incorporation oflight-activated heating nanoparticles (L-HNPs) into tumors, allowing for high heat deposition in the tumor area at low laserlight intensities and thus minimizing the damage in the surrounding healthy tissue (Jaque *et al.*, 2014).

Nanoparticles in radio immunotherapy

RT is extensively utilized in the clinical management of several malignancies. Advanced nanotechnologies-mediated RT induces ICD, repolarizes or depletes TAMs, enhances NK cell function, promotes DCs antigen presentation, and reprograms peripheral neutrophils into APCs, thereby eliciting an immune response that causes tumors in unirradiated sites to recede and producing in some degree of abscopal effects. However, only a few clinical instances have been documented over time, indicating that RT-mediated abscopal effects fall far short of therapeutic requirements. Low induction

effectiveness of ICD, immunosuppressive TME, and low tumor-specific antigen presentation efficiency are some of the reasons why conventional RT is unable to encourage systemic antitumor immune. Recently, the integration of RT with immunotherapy, including ICB therapy and immunological adjuvants, has demonstrated efficacy in eliciting a potent systemic immune response against distant metastases (Huang *et al.,* 2024).

CONCLUSION

Nanotechnology offers transformative potential in cancer management by enhancing diagnostics, enabling targeted drug delivery, and improving treatment efficacy. Advanced nanoparticles, such as quantum dots, metallic nanoparticles, and lipid-based carriers, are at the forefront of these innovations. Their ability to specifically target cancer cells and deliver therapeutic agents with precision minimizes side effects and maximizes treatment effectiveness. As research progresses, the integration of nanotechnology into cancer care promises to further revolutionize how we detect, treat, and manage cancer, paving the way for more personalized and effective therapeutic strategies.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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