ISSN 2959-409X

# Nanomedicine in Cancer Treatment: Mechanisms, Applications, and Future Directions

**Ryan Bohan Chen**

Norman North High School, Norman, Oklahoma, USA
Corresponding author: ryan.b.chen-1@ou.edu

**Abstract:**

Nanomedicine, an emerging field at the intersection of nanotechnology and medicine, holds significant promise for revolutionizing cancer treatment. By utilizing materials at the nanoscale, ranging from 1 to 100 nanometers, nanomedicine offers a versatile platform for targeting tumors, improving drug delivery, and minimizing side effects. This paper explores the design and preparation of nanoparticles, including common materials like liposomes, polymers, metals, and quantum dots, as well as their mechanisms of targeted delivery through both passive and active methods. Key applications of nanomedicine are discussed, particularly in chemotherapy, immunotherapy, and imaging. Clinical progress is highlighted through examples such as FDA-approved drugs like Onivyde for pancreatic cancer and experimental treatments like BIND-014 for metastatic prostate cancer. Despite rapid advancements, significant challenges remain, particularly in scaling up production and ensuring batch consistency. Safety concerns, such as nanoparticle toxicity and unintended accumulation in organs, must be addressed through rigorous testing and design improvements. Ethical considerations and regulatory hurdles also pose obstacles to the widespread clinical adoption of nanomedicine. Looking forward, multifunctionalization and personalized nanomedicine represent key areas of future growth, offering the potential for highly individualized treatments that combine therapeutic and diagnostic capabilities. Continued research and collaboration across scientific disciplines will be crucial in overcoming current limitations and unlocking the full potential of nanomedicine for cancer treatment.

**Keywords:** Nanomedicine; cancer treatment; targeted drug delivery; multifunctional nanoparticles; clinical applications.

## 1. Introduction

As a leading cause of mortality worldwide, cancer not only affects millions each year but also poses vast challenges to healthcare systems across the globe. Characterized by over one hundred distinct types, each with unique treatment demands, the battle against cancer requires innovative and effective strategies.

The modern era of cancer treatment traces its origins back to the 18th and 19th centuries, notably through pioneers like William Halsted. Halsted's development of the mastectomy, a surgical procedure for removing all or part of the breast to treat breast cancer, laid the foundational principles for subsequent cancer therapies and opened pathways for the evolution of diverse treatment methodologies. Since these early days, the field has witnessed significant milestones. Traditional approaches like surgical removal and chemotherapy, which involves using drugs to target cancer cells, have undergone continuous refinement. However, despite advancements, these methods face inherent limitations. For instance, chemotherapy often results in severe long-term side effects and may lead to the development of drug-resistant cancer cells. These issues highlight the need for more effective and less harmful treatment modalities. In response to these challenges, newer therapies such as targeted therapy and immunotherapy have emerged. Targeted therapy disrupts specific molecular mechanisms critical for cancer cell survival and proliferation, while immunotherapy enhances the body's immune response against cancer cells. Although relatively novel, these approaches have demonstrated significant potential in both laboratory and clinical settings, offering improvements over traditional therapies in terms of efficacy and side effects [1].

Among the most promising of these innovative treatments is nanomedicine, a term first coined in the 1990s. Nanomedicine applies nanotechnology—the manipulation of matter on an atomic, molecular, and supramolecular scale—to medical problems. "Nano," implying one-bil-

lionth, refers here to structures ranging from 1 to 100 nanometers. Nanotechnology has not only revolutionized medicine but also fields like engineering and environmental science, through the development of materials and devices that operate at the nanoscale [2]. Nanoparticles and nanomaterials, essential components of nanotechnology, are categorized based on composition, shape, and function. For instance, nanoparticles made from gold, silver, or iron oxide are categorized as metallic nanoparticles. Similarly, nanomaterials are classified by shape, size, and synthesis method, ranging from zero-dimensional (0D) structures to three-dimensional (3D) constructs. The precision of nanotechnology at the molecular level makes it particularly effective in diagnosing, treating, and preventing medical conditions. The vast potential applications within healthcare mean that nanomedicine could profoundly impact how cancer is treated, offering solutions that are both highly effective and minimally invasive [3].

## 2. Design and Preparation of Nanomedicine

### 2.1 Nanomedicine Material Design

The design of nanomedicine is complex, leveraging various material properties to achieve specific functions. The choice of material at the nanoscale is critical, as the diverse range of available materials offers significant versatility in nanomedicine applications. Commonly used materials include liposomes, polymers, metals, and quantum dots, each contributing unique benefits to medical applications [4].

Liposomes are spherical or multilayered vesicles with excellent biocompatibility, consisting of a lipid bilayer membrane that surrounds an aqueous core. Due to their amphiphilic structure, liposomes can encapsulate and deliver both hydrophilic and hydrophobic drugs, protecting them from degradation and ensuring efficient delivery. They can be further modified for controlled release in response to environmental triggers like pH or temperature. Additionally, the presence of phospholipids in liposomes allows them to be biodegradable, as enzymatic systems in the body can break them down over time.

Polymeric nanoparticles, which are colloidal particles dispersed at the nanoscale, are typically made from copolymers or bio-friendly polymers. Initially, some polymeric nanoparticles, such as poly methyl methacrylate (PMMA), were not biodegradable, leading to side effects like inflammation. However, the integration of biodegradable polymers, such as poly-lactic-co-glycolic acid (PLGA), into these nanoparticles has significantly reduced systemic toxicity [4].

Metallic nanoparticles, composed of metals such as iron, silver, and gold, possess unique properties due to their high surface area to volume ratio, resulting in high surface energy. The most common method of producing metallic nanoparticles is through the reduction of noble metals. Their distinctive electrical, magnetic, and thermal properties make metallic nanoparticles highly useful in medical imaging and other applications.

Quantum dots are semiconductor nanoparticles known for their electrical and optical qualities, which arise from quantum confinement effects when the nanoparticles are smaller than the Bohr radius. This results in varying wavelengths that can be used to manipulate electromagnetic radiation [5, 6]. The optical properties of quantum dots, including intermittent fluorescence signals and high brightness, make them ideal for applications such as imaging, where their tunable fluorescence properties allow them to serve as fluorescent probes [4].

### 2.2 Mechanism of Nanomedicine Targeting

Nanomedicine is often employed for the targeted delivery of therapeutic agents or imaging probes to specific locations in the body, such as organs, cells, or tissues. The targeting process is crucial as it enables the selective accumulation of nanoparticles at the desired site. Targeting in nanomedicine can be categorized into two main types: passive and active targeting.

Passive targeting relies on the inherent physical and chemical properties of nanoparticles, along with their interactions within the body, to achieve bioaccumulation at target sites. External factors, such as pH and light, can also serve as stimuli for drug delivery. Nanoparticle properties, including size, shape, and surface characteristics, are often manipulated to enhance their efficacy in reaching the target location. For instance, smaller nanoparticles may penetrate tissues more effectively, while larger particles might remain in the bloodstream for longer periods (Fig. 1, part a).

Active targeting involves modifying nanoparticles to enable direct binding to receptors or other cellular features at the target location, thereby facilitating precise delivery. This typically involves chemical or biological modifications to the nanoparticle surface to enhance nano-bio interactions. For example, ligands can be attached to nanoparticles to match specific receptors or antigens at the target site (Fig. 1, part b). Passive targeting can significantly improve the effectiveness of active targeting, creating a two-step system for the delivery of nanomedicine.

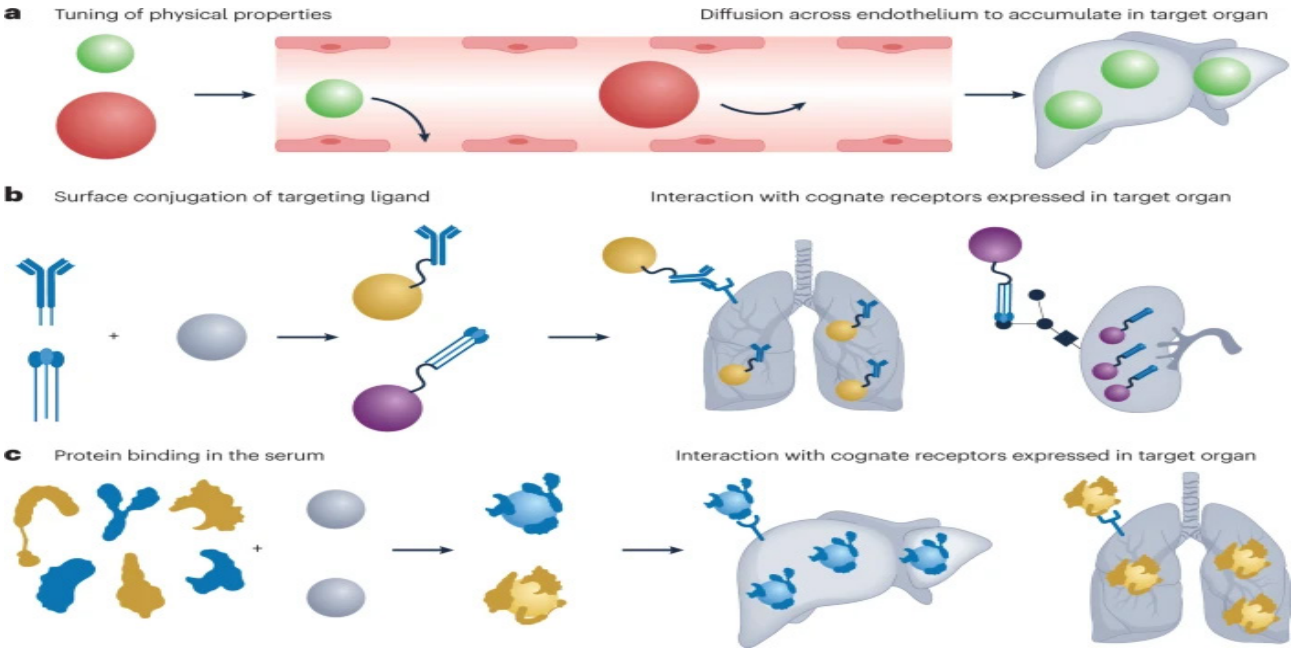


**Fig. 1 (a) Effects of particle size manipulation. (b) Interaction of engineered nanoparticles with target location [7].**

## 2.3 Nanomedicine Preparation

Before nanomedicines can be tested, they must first be synthesized under conditions that ensure safety and efficacy. Once the drug and material are selected, one of several methods is employed to synthesize nanoparticles. Synthesis methods are broadly categorized into top-down or bottom-up approaches [8].

Top-down synthesis involves reducing bulk materials to the nanoscale. One common top-down method is ball milling (Fig. 2), where bulk materials are placed in a container with small balls made of stainless steel, glass, or ceramics. The container is rotated, causing the balls to repeatedly impact the material, grinding it into smaller particles. The drug can be incorporated into the material either during the milling process or by exposing the ground material to a drug solution afterward, allowing it to absorb the drug through its surface.

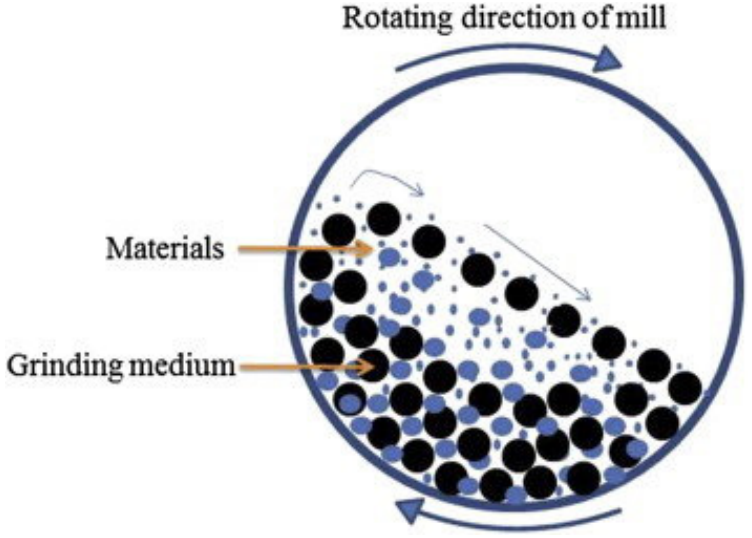


**Fig. 2 Schematic diagram of a ball mill [9].**

Bottom-up synthesis, in contrast, involves assembling fine particles to form larger nanostructures. The sol-gel method is a widely used bottom-up technique (Fig. 3). It begins by dissolving a precursor molecule, often a metal alkoxide, in a solvent to create a sol. The sol undergoes hydrolysis and condensation, increasing the viscosity of the solution until

it becomes a gel. The gel is then dried and aged to remove the solvent and form a solid material. If necessary, the dried gel is heat-treated to produce a crystalline material.

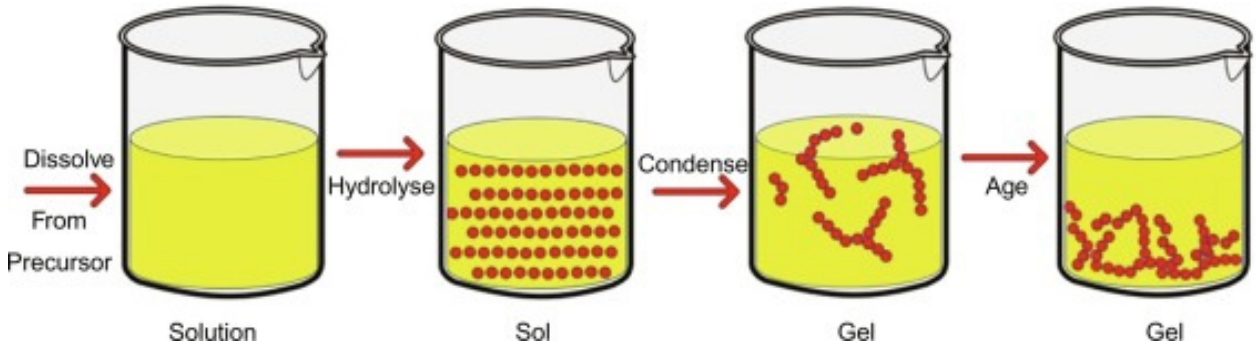


**Fig. 3 Sol-Gel Process [10].**

### 2.4 Characterization of Nanomedicine

Characterizing nanomedicine is crucial for understanding its interaction with biological systems and ensuring the safety and reliability of the nanomedicine [11]. Various methods are used to analyze the physical and chemical characteristics of nanoparticles. For example, dynamic light scattering (DLS) can measure particle size and size distribution by directing light at the nanoparticles and measuring fluctuations in the scattered light. The surface charge of nanoparticles, a key factor in stability and interaction potential, is often measured using zeta potential. A high absolute value of zeta potential indicates good stability, while a low absolute value suggests weaker stability. Surface modifications can alter the zeta potential, making it stronger or weaker as needed. The chemical composition of nanoparticles can be determined using energy-dispersive x-ray spectroscopy (EDX or EDS), which utilizes an electron beam to release characteristic x-rays from the particles, revealing their elemental composition.

## 3. Mechanisms and Applications of Nanomedicine in Cancer Treatment

### 3.1 Targeted Delivery and Tumor Penetration

In cancer treatment, the precise delivery of therapeutic agents to tumor cells is a critical aspect of nanomedicine. By concentrating drugs at the tumor site, treatment efficacy is increased, allowing for the inhibition of tumor growth and destruction of cancerous cells. Targeted delivery to tumors can be achieved through various mechanisms [12]. One approach is active targeting, where nanoparticles are modified with ligands to bind to overexpressed receptors on tumor cells, such as the human epidermal growth factor receptor 2 (HER2) in breast cancer [13]. After binding to the receptor, the nanoparticle enters the cell via clathrin-mediated endocytosis (CME). Clathrin-coated vesicles transport the nanoparticle into the cytoplasm, where it is released to exert its therapeutic effects.

Passive targeting is another approach that takes advantage of the enhanced permeability and retention (EPR) effect [12]. Tumors, due to their disorganized and rapid growth, often have abnormalities that create large gaps between endothelial cells, leading to increased vascular permeability. As shown in Fig. 4, this allows nanoparticles to enter tumor tissues more easily than normal tissues. Additionally, impaired lymphatic drainage within tumors leads to the retention of nanoparticles, resulting in higher concentrations of drug accumulation. Once inside the tumor tissue, the nanoparticle releases therapeutic agents that induce cancer cell death through mechanisms like apoptosis.

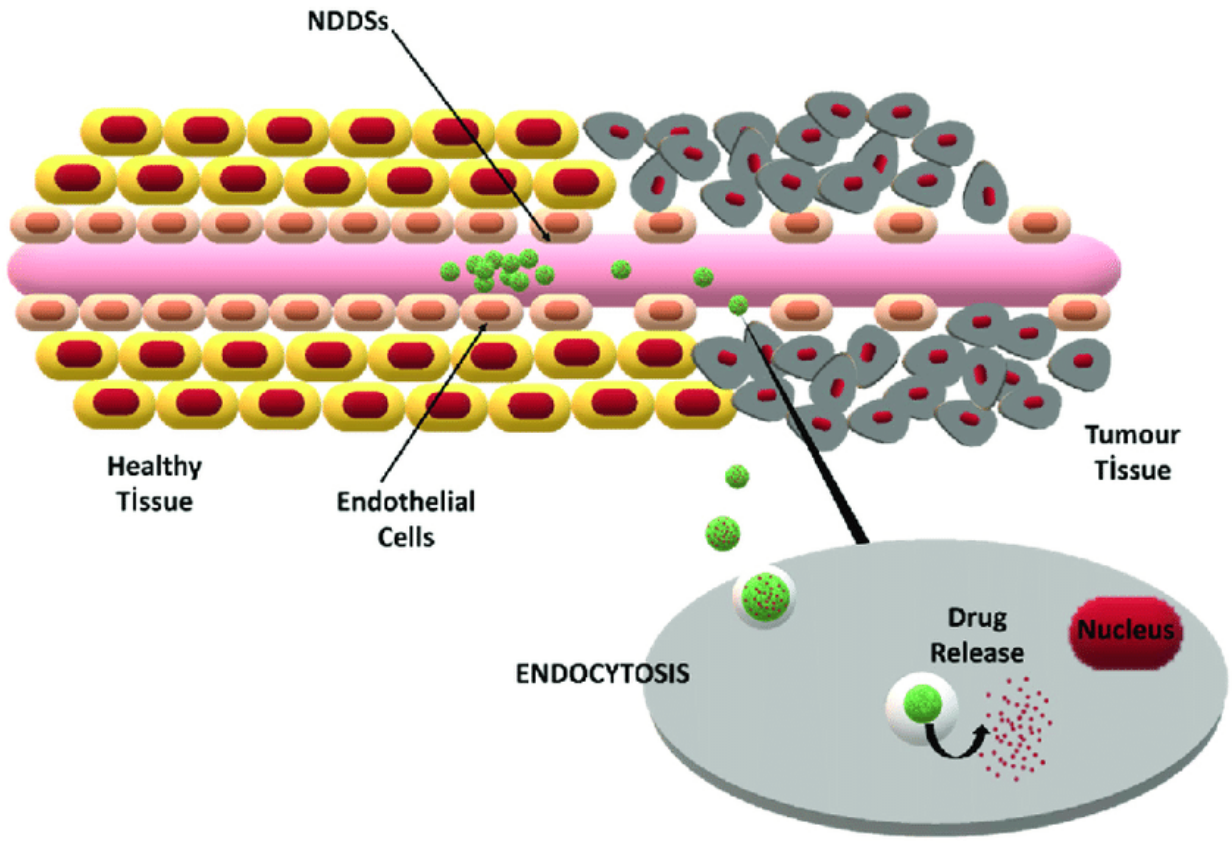


**Fig. 4 Role of EPR effect in tumor targeting [14].**

### 3.2 Application of Nanomedicine in Immunotherapy

Immunotherapy is a novel approach to cancer treatment that leverages the body's immune system to recognize and destroy cancer cells by amplifying or suppressing immune responses. One example is CAR-NK cell therapy, where natural killer (NK) cells are modified to express chimeric antigen receptors (CARs) that target specific antigens on cancer cells. Nanomedicine holds great promise for enhancing immunotherapy [15]. Nanoparticles can deliver cancer antigens directly to immune cells, stimulating an immune response more effectively than traditional antibodies and enhancing the immune system's ability to recognize and destroy tumors. Additionally, nanomedicine can deliver danger signals and immunostimulators to activate pathways that boost immunostimulation. In the tumor microenvironment, nanoparticles can also be used to deliver immune checkpoint inhibitors, improving the efficacy of immunotherapy.inhibitors directly to the tumor microenvironment.

### 3.3 Application of Nanomedicine in Chemotherapy

Chemotherapy involves the use of drugs to kill or inhibit the growth of cancer cells, but it often comes with significant side effects because it cannot distinguish between healthy and cancerous cells. This indiscriminate targeting can lead to severe side effects, such as hair loss due to the destruction of hair follicle cells. The incorporation of nanomedicine into chemotherapy offers solutions to these issues while also enhancing treatment efficacy [16].

One key advantage of nanoparticles is their ability to be modified with ligands for targeted drug delivery. Nanoparticles encapsulating chemotherapy drugs can deliver treatment directly to cancer cells, minimizing damage to healthy cells. In addition to their targeting abilities, nanoparticles can provide sustained and controlled drug release. This is often achieved by designing nanoparticles to degrade gradually in response to environmental factors such as pH or temperature, leading to a slow release of the encapsulated drug into the tumor microenvironment. This controlled release reduces the need for high doses of chemotherapy, thereby minimizing associated side effects.

An example of nanomedicine in chemotherapy is liposomal doxorubicin, in which the chemotherapy drug doxorubicin is encapsulated in a liposome. This formulation has been approved by the Food and Drug Administration (FDA) and is used to treat cancers such as breast and

ovarian cancer [17].

# 4. Current Clinical Applications and Challenges of Nanomedicine

## 4.1 Current Status of Clinical Research and Applications

While the potential for nanomedicine is vast, clinical approval is required before these treatments can be widely used in medicine. Clinical trials for nanomedicine are extensive, exploring a range of approaches for treating cancer. Fortunately, some nanomedicines have already passed the clinical trial phase and are in use. A notable example is Onivyde (irinotecan liposome injection), a chemotherapy drug used to treat pancreatic cancer [18]. In this formulation, irinotecan is encapsulated in a liposome, which allows the drug to be delivered directly to cancer cells. Once there, irinotecan is released and binds to the topoisomerase I–DNA complex, inhibiting DNA repair in cancer cells. This results in DNA damage and cell death. Other examples of clinically approved nanomedicines include Doxil and Abraxane.

In addition to approved treatments, many other nanomedicine therapies are currently undergoing clinical trials and show significant promise. One example is BIND-014, a nanoparticle containing docetaxel designed to target metastatic castration-resistant prostate cancer (mCRPC) [19]. BIND-014 is engineered to bind to prostate-specific membrane antigen (PSMA) in mCRPC cells. Once internalized, docetaxel is released, binding to microtubules and preventing their disassembly. This disrupts the cell cycle during mitosis, inducing apoptosis. Another promising example is Vaxol, a nanoparticle-based vaccine. When combined with cancer vaccines, nanoparticles carrying tumor-associated antigens can deliver these antigens more effectively to the immune system [20]. This enhances the immune system's ability to recognize and target cancer cells expressing these antigens. As research advances, more nanomedicine treatments targeting various types of cancer will enter and pass clinical trials, bringing us closer to the goal of curing cancer.

## 4.2 Safety and Toxicity Evaluation of Nanomedicine

For nanomedicine to become an effective treatment in clinical settings, it must first be proven safe [5]. A key aspect of this is understanding the biodistribution, metabolism, and excretion of nanoparticles in the body. While nanoparticles are designed to accumulate in tumors through the enhanced permeability and retention (EPR) effect, variations in size and surface charge can cause them to accumulate in other organs, such as the kidneys, lungs, and spleen. Additionally, once inside the body, nanoparticles may undergo chemical changes, interacting with biological systems. For instance, certain enzymes can break down specific nanoparticles. If not metabolized, nanoparticles can be excreted in various ways. Small nanoparticles may be filtered out of the body through the kidneys and excreted in urine, while larger nanoparticles may be processed by the liver and excreted in feces.

Despite their potential, nanomedicines can have toxic effects. The accumulation of nanoparticles in organs may lead to prolonged exposure, causing damage to the affected organs. Unintended interactions between nanoparticles and cells can also disrupt cellular processes, leading to cell damage. To address these concerns, efforts are being made to reduce the toxicity of nanoparticles while enhancing their efficacy. The flexibility of nanoparticle design—particularly the ability to manipulate shape, size, and surface properties—plays a key role in improving safety. Nanomedicines are rigorously tested in vitro and in clinical trials, and if they fail to meet safety standards, they can be modified and refined until they meet the necessary criteria for safe clinical use.

## 4.3 Application Prospects of Nanomedicine in Different Cancer Types

Given its broad applicability, nanomedicine has the potential to treat a wide variety of cancers [6]. As previously discussed, nanoparticles are being used in chemotherapy to target cancers such as breast, prostate, and pancreatic cancer. Nanomedicine can also be applied to treat other types of cancer, including lung, ovarian, and brain cancer. The versatility of nanomedicine stems from the ability to manipulate key properties such as size and surface charge to suit the needs of different cancers. Nanoparticles can also be modified in numerous ways, such as by adding ligands to the surface to target specific cancer cells. This adaptability makes nanomedicine a highly promising tool for cancer treatment, capable of targeting many different cancer types with the right modifications.

# 5. Future Directions and Research Challenges of Nanomedicine

## 5.1 Multifunctionalization and Personalized Treatment with Nanomedicine

Despite significant advancements in nanomedicine, there remains ample room for further growth. New applications are constantly emerging, and one promising area is the multifunctionalization of nanomedicine, which enables nanoparticles to perform multiple tasks simultaneously [21]. This includes combination therapy, where nanoparticles are modified to deliver multiple therapeu-

tic agents to specific cancer cells, enhancing therapeutic outcomes. Multifunctional nanoparticles can also be used for theranostics, which combines diagnostic imaging with therapeutic functions. Theranostic nanoparticles allow real-time monitoring of treatment while delivering therapy, providing valuable feedback for scientists to adjust and optimize the treatment.

In addition to multifunctionalization, nanomedicine can be personalized [22]. Personalized treatments tailor medical interventions to the specific characteristics of the disease and the patient, thereby improving efficacy. For example, in CAR-T therapy, a patient's T cells are extracted, modified with chimeric antigen receptors (CARs), and reintroduced to target cancer cells by binding to specific antigens. Similarly, nanoparticles can be engineered to target tumors by binding to specific cancer biomarkers, using ligands that recognize the tumor's unique molecular profile. Nanomedicine can also be adjusted based on the patient's individual characteristics, such as tumor type, stage, and drug metabolism profile. One example is the design of a therapeutic payload that responds to the patient's tumor microenvironment, releasing drugs in controlled doses to minimize toxicity.

### 5.2 Challenges in the Scale-up Production and Preparation of Nanomedicine

While nanomedicine holds great promise, significant challenges remain before its widespread application. One major hurdle is ensuring consistency in nanoparticle production. Small variations in nanoparticle size, shape, and surface properties can impact both safety and efficacy [23]. Achieving batch-to-batch consistency is critical, yet the complex synthesis and characterization processes make this difficult. Scaling up production from laboratory research to industrial levels introduces additional obstacles [24]. Many lab-scale production methods are not feasible for industrial use, requiring the development of new equipment that can function on a larger scale. This process demands considerable time and research. Moreover, large-scale production requires significant amounts of raw materials and equipment, contributing to higher costs and affecting the economic viability of nanomedicine production. Achieving effective industrial-scale production will require balancing cost with production quality.

### 5.3 Regulatory Approval and Ethical Considerations of Nanomedicine

Before nanomedicine can be used clinically, it must undergo a rigorous approval process [25]. This begins with preclinical evaluations, including in vitro studies, animal testing, and toxicological assessments to ensure safety. If these are successful, the nanomedicine enters clinical trials, where it is tested on patients in a series of phases to evaluate safety, side effects, and efficacy compared to existing treatments. Throughout this process, the nanomedicine must meet strict characterization and quality control standards to minimize the risk of toxicity or long-term adverse effects. In addition to patient safety, regulatory bodies also consider the environmental impact of nanomedicines. If all criteria are met, the Food and Drug Administration (FDA) can approve the drug for clinical use.

Ethical considerations are also critical in the development of nanomedicine [26]. For example, patients must give informed consent before receiving treatment, yet there is a risk that they may not be fully informed of potential risks. Evaluating the risk-benefit ratio is essential to ensure that the benefits of nanomedicine outweigh the risks involved. Researchers must also address the accessibility of nanomedicine, ensuring that it is available to all patients regardless of socioeconomic status or geographic location. Additionally, the potential environmental impact of nanomedicine highlights the need for sustainable disposal methods. Public education on nanomedicine is also crucial for fostering trust and addressing misconceptions, ensuring a positive perception of this emerging technology.

## 6. Conclusion

Nanomedicine, an innovative treatment leveraging nanotechnology, is poised to revolutionize cancer therapy. Comprising materials at the nanoscale (ranging from 1 to 100 nanometers), nanomedicine boasts a highly complex design. The use of diverse materials, such as liposomes, polymers, metals, and quantum dots—each offering distinct properties—provides remarkable versatility for treating various cancers. Key characteristics of nanoparticles include their size, shape, surface charge, and chemical composition. One significant advantage of nanoparticles is their targeting capability, which can be achieved through active and passive methods. Active targeting involves nanoparticle modifications, such as adding ligands to direct them to specific locations, while passive targeting relies on the inherent properties of nanoparticles to accumulate at certain sites. To utilize nanoparticles effectively, they must first be synthesized, typically through top-down or bottom-up approaches. Top-down methods involve breaking down larger materials into nanostructures, while bottom-up approaches assemble atoms or molecules into larger structures. Various techniques, including ball milling and the sol-gel method, are used to produce nanoparticles, which are then characterized through multiple methods.

In cancer treatment, nanoparticles can be employed in

several ways. A notable method is the use of both active and passive targeting to concentrate therapeutic agents within tumors. For instance, ligands can be added to nanoparticles to target overexpressed receptors on tumor cells, while the enhanced permeability and retention (EPR) effect facilitates the bioaccumulation and retention of nanoparticles within tumor tissues. Nanomedicine also plays a key role in immunotherapy by delivering signals that boost immune responses or inhibit tumor functions. Additionally, nanoparticles are used in chemotherapy, where they encapsulate drugs and, with the help of ligands, deliver them directly to tumors. This targeted delivery increases the efficacy of treatment while minimizing side effects by slowing or stopping cancer cell growth.

Nanomedicine has undergone significant development, with many forms now in clinical trials and some already approved by the FDA. A prominent example is Onivyde, which uses nanoparticles to encapsulate irinotecan for the treatment of pancreatic cancer, where the drug is released to induce cancer cell death. In addition to FDA-approved treatments, several promising nanomedicines are still in clinical studies, such as BIND-014 for metastatic castration-resistant prostate cancer and Vaxol for enhancing immune responses. However, despite rapid advancements, safety and toxicity protocols remain a priority to ensure the safe use of nanomedicine. Nanoparticles can accumulate in organs and interact unexpectedly with biological systems, leading to potential damage. Continuous efforts are being made to improve nanoparticle design through rigorous testing. These advancements have allowed nanomedicine to target a wide range of cancers, including lung, brain, and breast cancer, thanks to the versatility provided by nanoparticle properties that can be modified and adjusted in numerous ways.

As nanomedicine progresses, new developments are constantly emerging. Key areas of future growth include multifunctionalization and personalized treatments. The ability of nanoparticles to perform multiple tasks—such as imaging and delivering therapeutic agents—enhances treatment efficacy by providing real-time feedback for optimization. Personalized nanomedicine tailors' treatment based on the characteristics of the patient and tumor, improving outcomes by considering factors such as tumor type, stage, and drug metabolism. However, challenges remain in scaling up production. Achieving batch-to-batch consistency in nanoparticle synthesis is crucial, as slight variations in size, shape, and surface properties can significantly impact treatment. The transition from lab-scale production to industrial-scale manufacturing also presents economic and technical challenges, with the high cost of materials and equipment hindering widespread application. Even if these challenges are overcome, nanomedicines must still undergo rigorous preclinical and clinical testing before gaining approval from regulatory bodies like the FDA. Beyond regulatory concerns, ethical considerations arise, such as ensuring patients are fully informed about treatment risks and addressing potential environmental impacts. Public education is crucial to dispel misconceptions and foster trust in nanomedicine.

As nanomedicine moves forward, there is still much room for further research. Current treatment methods can be refined and optimized to enhance therapeutic efficacy, and continued efforts to overcome existing limitations will be vital for future progress. Collaboration among researchers, clinicians, and engineers will accelerate development by combining expertise across disciplines. The future of nanomedicine holds great promise, with advances expected across all areas. The ongoing development of nanomedicine is bringing us closer to achieving more precise, effective, and safe treatments—and ultimately, a potential cure for cancer.

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