EURASIAN EXPERIMENT JOURNAL OF MEDICINE AND MEDICAL SCIENCES
(EEJMMS) ISSN: 2992-4103
©EEJMMS Publications Volume 6 Issue 2 2025

Nanomedicine: Applications in Cancer Treatment

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ABSTRACT

The integration of nanotechnology into medicine has ushered in a new era of cancer therapy, characterized by precision, efficiency, and minimized toxicity. Nanomedicine, which involves the application of nanoscale materials and techniques for diagnosis and treatment, has shown transformative potential in oncology. This paper explores the development and implementation of nanoparticles for drug delivery, diagnostic imaging, and therapeutic interventions in cancer treatment. It reviews various types of nanoparticles, such as liposomes, polymeric carriers, metal-based particles, and quantum dots, and their synthesis, targeting mechanisms, and clinical applications. Particular emphasis is placed on how nanoparticles exploit tumor microenvironment characteristics to achieve enhanced permeability and retention (EPR) for targeted delivery. Despite the promise, the paper also highlights existing challenges, including issues of scalability, heterogeneity of tumor response, safety uncertainties, and regulatory barriers. Ultimately, nanomedicine is poised to revolutionize cancer management, but its full potential hinges on overcoming clinical and translational hurdles.

Keywords: Nanomedicine, Cancer Treatment, Nanoparticles, Targeted Drug Delivery, Tumor Microenvironment, EPR Effect, Clinical Applications, Polymer-Based Carriers, Biomedical Nanotechnology, Oncology.

INTRODUCTION

The advent of nanomedicine offers a significant opportunity to enhance treatment for various diseases, particularly cancer. Defined as the development of therapeutics and diagnostics at the nanoscale, nanomedicine is increasingly recognized for its potential in anticancer therapy with greater safety and efficiency. This article discusses recent advancements in cancer treatment using nanoparticles as drug-delivery vehicles, particularly in targeted and combination therapies. Despite progress since the US National Cancer Program's early focus on defeating cancer, the disease remains a leading cause of death. Experts suggest re-evaluating the cancer research framework, noting that treatment has shifted towards organ-based therapy rather than targeting diseases directly. Advances in genomics, proteomics, and systems biology have improved understanding of cancer's cellular and molecular drivers, elucidating how cancer cells proliferate abnormally. This insight encourages drug discovery to exploit cancer's vulnerabilities, potentially leading to highly effective "magic bullets" with improved potency and safety. However, the challenge remains to target cancer cells effectively without adversely affecting the surrounding healthy cells, given the statistical probability of off-target effects in treatment approaches affecting both cancerous and normal cells [1, 2].

Fundamentals of Nanotechnology

Clinical cancer nanomedicine is synonymous with the application of nanotechnology to create new or better therapeutics and/or diagnostic tools that are used for the detection, monitoring, prevention, intervention, and/or treatment of cancer. This includes a very broad range of endeavors, which boost collaborative efforts between chemists, engineers, biologists, physicians, and regulatory personnel with a goal of harvesting the unique physical and chemical properties of nanomaterials to yield products that will change the way that cancer is treated and monitored. Nanoparticles (NPs), which are typically nanoscopic structures that have at least one dimension between 1 and 100 nm, are a type of nanotechnology. It is important to note, though, that not all nanomedicine is based on the direct use of

NPs as the functional unit. For example, NP-based reagents for magnetic resonance imaging and photothermal therapy may not fit into this definition. Rather, the surrounding global issues must also be considered. In addition to their extraordinary promise as new therapeutics, nanoscale technologies in drug delivery systems and diagnostic devices are also considered here. Generally, innovation maturing from academic research, non-academic lab research, or industrial research will eventually have to undergo some regulatory scrutiny to ensure that the product is safe and effective before it is applied to mankind and/or enters the market. The level of scrutiny depends on the type of product: drug, device, or therapeutic agent. NPs may be used alone or assembled into larger structures that homogeneously immobilize specific targeting ligands, imaging moieties, therapeutic effector molecules, or cytolytic radioisotopes. The broad range of diseases that NPs are capable of treating, the considerable amount of important research yet to be carried out, and the potential to commercialize novel formulations are undoubtedly important draws for the brightest minds in research [3, 4].

Nanoparticles: Types and Properties

Due to their unique size and properties, which are distinct from their bulk scale counterparts, nanoparticles represent a new class of intentionally engineered materials. Apart from this dimension scale-related research, important findings regarding the physicochemical properties and biological interactions of nanoparticles have instigated great interest in the biomedical field. As early as 1950s, various kinds of nanoparticles, including iron-oxide nano/microparticles for imaging of physiological systems, gold nanoparticles with variable sizes for SERS imaging and photothermal therapy of cancer cells, silver nanoparticles with antibacterial activity and biosafety evaluation, liposome with dual modal imaging properties, and quantum dots for targeting and imaging of malignant tumors, were fabricated and characterized. The interest has rapidly grown in recent years, as new nanoparticles with distinct designs and structural variations have emerged. Typically 1–100 nm in diameter, nanoparticles can improve the solubility and bioavailability of poorly water-soluble therapeutics, improve intracellular uptake and therapeutic efficacy, provide controlled and gated release of payloads based on stimuli, substantially minimize systemic toxicity, and be diagnosed and tracked after administration. Nanoparticles include different types of drug carriers, such as micelles, liposomes, polymeric NPs, metal NPs, and inorganic NPs. Nanoparticles can either encapsulate the therapeutic agents in their interiors or conjugate with them on their surfaces. The structural/functional properties, such as size, morphology, surface charge, mechanical strength, hydrophilicity and hydrophobicity, as well as biopharmaceutical properties of the nanoformulations (i.e., circulatory half-life, biodistribution, tumor accumulation, permeability in deep tumor regions, cellular uptake, therapeutic release profile) can be tuned by changing the fabrication/design formulation parameters. Drug release rates can potentially be spatiotemporally controlled to match biological/metabolic profiles by orchestrating the physicochemical properties of carriers, drug types, and external stimuli. The biodistribution and tumor accumulation of NPs could also be modulated by changing the formulation parameters, resulting in nanomedicines with different therapeutic spectra. The functions of nanoparticles can also be combined, by either co-encapsulation of different therapeutic agents, or by fitting distinctly different therapeutic modules on the same NP surfaces [5, 6].

Synthesis Methods for Nanoparticles

Nanoparticle synthesis methods are based on various physical, chemical, and biological processes in such a way that they provide different properties such as size, shape, charge, and manner of surface functionalization. One approach, termed "top-down", involves breaking bulk or large materials through mechanical processes such as grinding, milling, lithography, and other chemical or physical processes. Although these approaches can produce NPs suitable for several applications, including cancer diagnostics and therapy, they are generally limited by high capital and processing costs, lack of sterility, difficulty with controlling size, shape, polydispensity, distribution, purity, and charge on the surface of the particles, as well as environmental and hazardous waste concerns. The "bottom-up" approaches involve assembling or combining fine atoms and molecules to make larger ones via different methods. The main categories in this regard include chemical methods, atomic and molecular precipitation, self-assembly, electrochemistry, ultrasonication, sol-gel processing, etc. One or a combination of these methods may also be employed to obtain NPs suited for various applications. The "chemical" method includes chemical reduction, co-precipitation, and sol-gel processes. Chemical reduction is a method of synthesizing metal NPs where a suspension of metal ions undergoes reduction to produce metal or hybrid structures. Co-precipitation involves combining a compound that precipitates in an aqueous solution with metal salts to

obtain NPs by a dehydration process, controlling the pH or using surfactants that adsorb on their surface to stabilize them. This process, relatively attractive in terms of obtaining large quantities of microsized particles rapidly and economically, provides particles suited for fuel cells, sensors, and bio-detectors, absorbing and targeting agents for radioimmunotherapy. The "sol-gel" process yields a colloidal suspension of silica NPs in which their size increases with the amount of added precursor alkoxide. Combined with a thermal treatment, this provides NPs for drug or anticancer agent loading, delaying drug burst release for several periods, and enhancing drug targeting [7, 8].

Mechanisms of Action in Cancer Therapy

As the interface of nanotechnology and medicine, nanomedicine is the design and development of therapeutics and diagnostic tools, distinguished by the nanoscopic scale of its delivery vehicles and diagnostic agents. At 1–100 nm in size, nanoparticles exhibit unique physicochemical properties distinct from their bulk counterparts. The quest for a way to remove chemotherapeutic toxicity and to augment efficacy has led to the exploration of nanoparticles as drug-delivery vehicles. The design of these targeted vehicles is predicated on a wealth of knowledge exploring the differences between malignant and normal cells, tissues, and organs. These targeted vehicles hold the potential to vastly improve upon the current standards in drug delivery, as the uses of Avastin and other monoclonal antibodies in cancer therapy have already proven. Multivalent surface modification with targeting ligands should provide selectivity to these tracking moieties, thereby limiting biodistribution to the tumor. Also, exceptionally small size and deformability of the vehicles should enable efficient navigation of the complex in vivo environment and quantitative cell accumulation. With the adaptation of agents to promote normal tissue permeation by filtration, the size of nanomedicine should marginally limit efficacy to tumoral cells. Kinetics of desorption should enable endosomal escape, thereby enhancing bioavailability of the drug payload. Enhanced cellular uptake would maximize the delivery of therapeutics to the intracellular milieu of target cells. In conclusion, the advent of nanomedicine marks an unparalleled opportunity to advance the treatment of disease states, including cancer. Such a promising future awaits, as emphasis in nanomedicine gradually shifts from basic science to the development of therapies for pre-clinical validation and clinical translation, and subsequently to widespread clinical use. The current standard paradigms, however, do not enable valid biomarker or drug candidate selection [9, 10].

Types of Nanoparticles in Cancer Treatment

The advent of nanomedicine marks an unparalleled opportunity to advance the treatment of a variety of diseases, including cancer. Nanomedicine is the design and development of therapeutics and diagnostic tools, distinguished by the nanoscopic scale of its delivery vehicles and diagnostic agents. Nanomedicine encompasses a broad range of healthcare applications, including imaging, detection, diagnosis, targeted drug delivery, and combination therapy. Among these applications, the most widely pursued area is drug delivery to the diseased site. The nanomedical field is catalyzing new approaches to combat diseases that had not previously been thought possible. Researchers have improved upon the current standards in drug delivery relating to biodistribution, intracellular uptake, and dosing efficacy by adjusting the delivery vehicles and loading therapeutics. The successful application of processes to improve the delivery of biomedical entities through functional nanoparticles is a revolutionary approach to disease treatment. Nanomedicine offers improved management of chronic diseases via better surveillance, more sensitive detection, and improved targeted delivery. Nanomedicine has focused on advancing drug delivery, imaging, and diagnostics over the past few years. These biomedical applications hinge heavily on the rapid progress of nanomaterials and nanotechnology. The unique properties of nanoparticles, such as large surface-to-volume ratio, small size, the ability to encapsulate a variety of drugs, and tunable surface chemistry, give nanoparticles many advantages over their bulk counterparts. A better advantage that nanoparticles have over bulk materials is the ability to modify their surface on can nanoscale. Multivalent surface modification with targeting ligands increases the likelihood of successful molecular recognition in an environment crowded with macromolecules. The small physical size of nanoparticles allows for efficient navigation of the complex in vivo environment while still enabling effective cellular uptake. The rapid and simple synthesis of nanoparticles enables reproducible labeling chemistry, providing consistent and homogenous delivery vehicles [11, 12].

Nanocarriers for Drug Delivery

In controlled drug delivery settings, polymers have emerged as drug carriers for the cure of cancer. Numerous polymer-based drug carriers have been explored, including organic nanocarriers and inorganic nanocarriers. Organic nanocarriers include liposomes, polymeric micelles, and dendrimers; inorganic

nanocarriers include silica nanoparticles, clay nanocarriers, and metal nanocarriers. The infusion of drug carriers inside the cytoplasm of the cell is crucial for the potency of drugs in tumor treatment. There is a gap between epithelial cells in blood vessels in cancerous tissues, resulting in defective vascular architecture. Nanocarriers can extravasate across these gaps and can be assembled in tumor tissue, termed the enhanced permeability and retention (EPR) effect. Nowadays, numerous nanocarrier systems with complex compositions are synthesized to increase drug delivery efficiency. Broader applications of polymers stem from their tunable properties; for example, the molecular weight and structure of polymers can easily be controlled. Advantages of nanocarriers in cancer delivery include enhancing the therapeutic index of chemotherapeutic agents, improving drug efficacy, reducing drug toxicity, and increasing drug stability and solubility. Other advantages include their size appropriate for tumor targeting via the EPR effect, protective shielding of the drug, ease of surface modification, feasibility of multiple drug delivery, and providing a scope of combination therapy. A wide variety of usages of nanocarriers for drug delivery for cancer treatment, ranging from chemotherapeutic agents to bioactive miRNA for tumor suppression to small interfering RNA, have been described. Progress in the drug formulation and therapeutic efficacy of nanomedicine will be summarized. The assembly and disassembly of nanoscale drug delivery systems in cancer treatment will also be discussed with some specific examples. Additionally, challenges and perspectives for future development will be described. Induction of apoptosis and senescence in cancer cells has been known as a common approach for cancer treatment. For example, doxorubicin has been recently approved for cancer treatment in cardiovascular diseases and diabetes by inducing apoptosis. The discovery of bioactive compounds that target oncogenic mutations or overactivated signaling pathways in chemoresistant and aggressive tumor cells provides new coordinated strategies for cancer treatment. Exogenous cytotoxic agents with unacceptable toxicity and poor efficacy have limited clinical usage. Unfortunately, the underlying mechanisms involved in cell fate determination are still poorly understood [13, 14].

Clinical Applications of Nanomedicine

Nanomedicine is a promising field developing unique therapeutic and diagnostic tools using engineered nanoparticles. Currently, 24 nanomedicines are globally approved, with over 350 clinical trials exploring their potential in treating various diseases, notably cancer and neurodegenerative disorders. The prominence of nanomedicine is changing diagnostics and drug development, addressing applications from imaging to therapeutic options. The speed of progress has led to numerous approved nanoparticles for diagnosing and treating diseases, while many others are in development for additional uses. The focus of nanomedicine encompasses drug delivery, diagnosis, treatment, and monitoring, particularly for cancer. Understanding the biological distinctions between normal and malignant tissues is vital, along with the unique properties of nanoparticles. These nanoparticles serve as carriers for delivering drugs, biologics, and nucleic acids. Tumor vasculature differs significantly from normal vasculature in morphology, permeability, and blood flow. This difference leads to a notable accumulation of nanoparticles in tumor tissues unattainable by smaller agents. Cancer nanomedicine employs nanoparticles to deliver therapeutic agents effectively, with FDA-approved products including various liposomal, micellar, polymeric, gold, and silica nanoparticles for targeted delivery of drugs and contrast agents [15, 16].

Challenges in Nanomedicine

Over the past couple of decades, the understanding of various physicochemical properties of nanoparticles, construction strategies, and imaging techniques has significantly increased. However, the field of nanomedication is still at its initial developmental stage, and significant challenges are still encountered throughout the nanomedication developmental process, slowing down the introduction of new nanomedications for cancer into clinical usage. Major obstacles to nanomedication in cancer treatment. One of these challenges is the limitation encountered by the first generation of nanomedication. Most cancer nanomedicines rely on the EPR effect for passive tumor targeting. The EPR effect of most nanoparticles varies greatly according to the heterogeneity of the tumors, leading a given nanoparticle to show desired efficacy in some patients but not others. Moreover, there is evidence suggesting that the EPR effect is far more prominent in small animal models than in humans. To alleviate these challenges, the development of second-generation advanced nanocarriers designed to enhance targeting to tumors has been pursued. A more difficult challenge relates to the uncertainty regarding the safety of the utilized nanomaterials. Most clinical studies testing the safety and efficacy of nanomedicines have focused on bulk materials instead of their nanosized counterparts. Therefore, the true safety profile of the utilized nanomaterials may be far more serious than the currently thought safety profile. Since there is currently

no upper bar or company-sponsored post-marketing studies regarding cntn260, it is also vital to conduct prolonged safety and biodegradability studies. Furthermore, it is even more urgent to study the absorption, distribution, metabolism, and excretion of the employed nanomaterials in humans. There are certainly very significant concerns related to safety and quality assurance. For instance, in June 2018, the FDA requested the withdrawal of the Abraxane-containing drugs seen as being unsafe despite having received a clinical approval in the US [17, 18].

Future Perspectives in Nanomedicine

The field of cancer nanomedicine is progressing in clinical applications, though it hasn't yet reached its full potential. Evidence suggests that encapsulating small-molecule drugs, nucleic acids, or other compounds could lead to effective cancer management or cures. The modularity in ligands, materials, and therapeutic nanoformulations positions nanoparticles (NPs) as a new class of therapeutics, not merely as drug delivery vehicles. Future clinic-ready platforms will likely facilitate the development of a diverse range of products. The extensive range of diseases that NPs can address, the significant research needed, and the potential for commercializing new formulations are promising. Companies are innovating therapeutics, diagnostics, and disruptive technologies. Nanoparticle-based systems present revolutionary opportunities for targeted therapies, enhancing circulation half-life, bioavailability, biodistribution, pharmacokinetics, and safety. Various systems, including liposomal formulations, micellar vehicles, and polymeric nanoparticles, have demonstrated efficacy in preclinical and clinical anti-cancer settings. Given the high cost of new treatments, immense efforts are focused on reformulating existing therapies into nano-scaled forms, creating new opportunities. This approach maintains synergistic drug ratios in combinational therapies and promotes consistent pharmacokinetics and biodistribution. Beyond reformulation, nano-scaled systems can deliver other therapeutic agents such as nucleic acids and unstable proteins, enhancing tumor-killing capabilities. NPs can also serve as carriers for physical agents to boost the effectiveness of traditional methods, particularly through modality combinations. The normalization of the tumor microenvironment improves anti-cancer drug penetration, while the co-delivery of adjuvants and antigens fosters strong immune responses. The realities of NP-based theranostics are emerging, as the industry aims to combine drug and imaging modalities, balancing anticipation with skepticism. Future perspectives on nanomedicine in cancer treatment have been discussed widely [19, 20].

Case Studies in Cancer Treatment

Nanotechnology has created tools that have been beneficial in biomedical sciences. The prominent approach for nanotechnology in chemotherapeutic drug delivery is to form nanoparticles (NPs). These NPs can assist in overcoming the barriers that thwart the use of some anticancer agents and lead to successful treatments for tumors that were previously untreatable. The design of NPs for drug delivery should overcome the challenges presented by the tumor microenvironment (TME) to achieve in vivo success. The appropriate capping of drug-loaded NPs in which the protection needs to be removed at the site of disease for drug activity. With the progression of nanomedicine from preclinical to clinical data for safe and effective use in cancer therapy, strategies that improve the disassembly of NPs in vivo are an emerging field. NPs, formed either by polymeric or lipidic materials, can allow for the transport of therapeutic and diagnostic agents, making it possible to improve early cancer detection. Any spherical object below 100 nm is considered a nanoparticle, while everything larger than 100 nm is a micro-particle. Their small size and large surface-to-volume ratio allow for the incorporation of agents or organic compounds within their core structure or favorably adsorbing them onto their surface. This essentially makes them a versatile and modular tool to encapsulate any biologically active entity. This attribute, together with their biocompatibility, flexibility of surface functionalization, biodegradability, and ability to cross biological barriers, greatly favors their therapeutic use. Overall, the material used for the formation, surface charge, and functionality, among several others, can totally modify the uptake, retention, and release of cargo for either a diagnostic or therapeutic role. Polymer or lipidic NPs have shown efficacy in active tumor-targeted delivery of therapeutics, leading to successful in vivo anticancer activity, while some inorganic NPs have proven diagnostic ability and provided a unique opportunity for tissue bioimaging [21, 22].

CONCLUSION

Nanomedicine has emerged as a powerful frontier in the battle against cancer, offering unprecedented opportunities for precision treatment and diagnosis. Through engineered nanoparticles, therapeutic agents can be delivered more effectively, improving bioavailability and reducing systemic toxicity.

Clinical successes, such as FDA-approved nanodrugs, affirm the viability of this technology in modern oncology. However, challenges persist, including the inconsistent effectiveness of the EPR effect in human tumors, gaps in our understanding of nanoparticle safety profiles, and regulatory complexities. Addressing these limitations through improved targeting strategies, comprehensive toxicological studies, and advanced nanocarrier designs will be essential for realizing the full promise of nanomedicine. As research transitions from preclinical innovation to widespread clinical implementation, nanomedicine stands to significantly improve outcomes in cancer therapy.

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CITE AS: Asiimawe Masika Agnovia (2025). Nanomedicine: Applications in Cancer Treatment. EURASIAN EXPERIMENT JOURNAL OF MEDICINE AND MEDICAL SCIENCES, 6(2):40-46