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Short Commentary

Application of Different Types of Nanoparticles in Cancer Early Diagnosis and Therapy

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Abstract

Cancer is one of the highest leading causes of human death across the globe. This current scenario of increasing cancer deaths poses a need to explore more effective cancer diagnosis and treatment methods. The use of nanotechnology in medicine, one of the most advanced fields of scientific research, has become a boon for cancer patients. Nanomedicine has been proven to be one of the most revolutionary alternatives with its extraordinary characteristics such as high selectivity, high specificity, targeted anti-cancer drug delivery approach, drug-receptor binding, cell-receptor binding, low toxicity, renal purification, bio-compatibility, immune compatibility, and cancerous cells identification. This review article aims to present a clear understanding of the various types of nanoparticles such as carbon nanotubes, nano quantum dots, nanoshells, and metallic nanoparticles used for the early diagnosis and treatment of cancer. Specially designed nanoparticles offer superior merits compared to conventional cancer detection and treatment methods. Nanomedicine has applied its innovative ideas and unique characteristics in the vast field of cancer biology. In addition, an in-depth study of the main types of nanoparticles currently available for higher and more effective cancer diagnosis and treatment, as well as their future scope, is also examined.

Keywords: drug delivery system, functionalized carbon nanotubes, nano quantum dots, superparamagnetic iron oxide nanoparticles, nanoshell

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1 INTRODUCTION

Cancer is one of the most complex illnesses and one of the leading causes of human death across the globe. The main causative mechanism behind cancer remains elusive. Tumors, cancer invasion pathways and malignant tumor progression have signaling mechanisms that contribute to tumor spread and metastasis. Identification of tumor growth and progression along with the real-time analysis of the malignancy transformation is one of the highly researched topics in cancer biology and a matter of critical concern in cancer detection. Early diagnosis of cancer is of great significance to reduce patients' pain. The accelerated growth and spread of cancer cells in the body lead to a high risk of treatment failure due to delayed diagnosis[1].

With the recent advancements in medical diagnosis, there are various in-vivo molecular imaging techniques

available for cancer detection such as computed tomography (CT), which is the first choice of diagnosis as it displays abnormalities in cell or tumor formation. Another diagnostic tool is magnetic resonance imaging (MRI), which can show metastasis and the spread of cancer. Positron emission tomography (PET) is another method that detects any hyperactive cells and high cellular growth and quickly analyzes the biochemical activity. Single photon emission CT (SPECT) uses specific antibodies to detect cancer in the principles of antibody interactions. Optical imaging is another noninvasive technique that provides optical analysis of tumor formation. Ultrasound can locate the tumor formation and spread in the body. These diagnostic tools are extensively adopted based on the type of cancer suspected[2].

However, a major drawback of conven-tional imaging methods is that it fails to provide a comprehensive review and assessment of the disease state and a comprehensive understanding of the existing microenvironment within the cell[3].

The current treatment methodology for cancer depends majorly on the type and stage of cancerous cell growth[4]. Treatment methodologies used include surgical removal of cancerous tissues, chemotherapy, and radiation therapy[5]. Targeted immune therapies[6] also gained great attention in modern cancer treatments. Various treatment therapies have also been researched and introduced, such as hormonal therapy, hyperthermia, stem cell transplant, and targeted gene therapy.

The drawbacks of all cancer therapies are side effects such as drug instability, the development of multiple drug resistance, and multiple drug interactions during treatment. A major challenge to current cancer treatment includes the drug delivery system and the damage caused to normal tissues. Multi-drug resistance poses a big threat and a rising fear among patients and is a great challenge for scientists and oncologists. Cancer patients who receive chemotherapy also acquire chemoresistancey[7]. An excessive dose may cause substantial toxicity. The main contributors to repeated failures of treatment for various types of cancer are underlying persistent genetic mutations and delayed diagnosis. The intensive occurring cell growth can be inhibited at an early stage with the aid of early cancer detection and management. Hence, there exists an urgent need to implement efficient early diagnosis strategies as well as more efficient treatments to reduce cancer deaths.

In cases of site-specific cancer proliferation, the most common reasons for the failure of the various therapies include the increase in drug intolerance, multidrug resistance, drug toxification, altered drug receptor sensitivity, and inappropriate cellular repair mechanism. Incomplete absorption of drugs is also a major drawback of traditional medication. Nanoparticles and nanotechnology have captured the attention of the new advanced sciences research and applications. Nanoparticles specialized in nanomedicine have reached the biggest breakthrough in advanced scientific research due to their innumerable unique properties in various fields[8]. Currently, a whole plethora of nanoparticles is undergoing vigorous research in the fields of advanced science and medicine. They have tremendous capabilities that promise to identify revolutionary implementations of nanoparticles in cancer early diagnosis and treatment[9].

The increasing number of deaths of cancer patients require advanced research and techniques such as nanotechnology in cancer detection and treatment. Due to the innumerable properties and characteristics of nanoparticles, they have recently been exploited and implemented in the fields of oncology[10]. Nanoparticles are considered the biggest boon for cancer patients[11]. This article focuses on deep insights and a detailed overview of the types of nanoparticles applied in the fields of cancer diagnosis, treatment, research, and their future scope.

Nanoparticles feature unique properties such as low molecular weight, high specificity, pharmacokinetic properties, rapid action, anti-microbial activity, and low toxicity. The use of specifically designed nanoparticles in cancer diagnosis helps visualize and understand the existing different pathophysiological conditions in cancer patients. Moreover, nanoparticles are considered effective biomarkers as they can distinguish between cancerous and noncancerous cells in molecular imaging techniques.

The nanoparticle detection system enables diagnosis at the lowest tissue level and with very high specificity compared to conventional histopathological diagnosis. Additionally, they have minimal or even zero side effects or damage to the patient's healthy tissues[12].

The nanoparticles used in cancer therapies provide efficient and improved treatment and less harm to the patient. It provides high specificity of the drug and minimum accumulation and regulates the release of pharmacologically active agents in vivo[13].

The therapeutically designed nanoparticles can reduce the occurrence and magnitude of the side effects caused by traditional therapies[14]. They also provide a highly localized drug delivery, which results in an enhanced specificity of the drug[15]. Among all the nanoparticles discovered, a size of 1-100nm is proven the most efficient size for diagnosis purposes.

Hence, nanoparticles with quality, efficiency, high specificity, and rapid action are the particles of choice. Nanoparticles enable the selective accumulation of drugs in tissues and can improve permeability and retention. The production of therapeutic nanoparticles is a novel therapeutic approach. Gold nanoparticles are widely used nanoparticles for cancer detection and treatment and have been highly demanded due to their extremely small size, high biocompatibility, high atomic number, high stability, high drug delivery specificity, and low toxicity and retention[16].

There are a variety of nanoparticles under clinical trials such as liposomes based nanoparticles, Doxorubicin marketed under the brand name Adriamycin, micelles, and polymers conjugated nanodrugs. Other Food and Drug Administration (FDA) -approved nanodrugs include doxorubicin, Paclitarel sold under the brand Taxol, DaunoXome also commonly known as Daunorubicin, Margibo commonly called Vincristine acts against lung cancer. Doxorubici/Caelyx is currently administered for various ovarian cancers and breast cancer therapy. Abraxane marketed as paclitaxel, one of the first nanodrug, is highly effective against various types of cancer such as ovarian cancer, breast cancer, lung, and pancreatic cancer. Feraheme is another FDA-approved nanodrug which is an iron-oxide nanoparticle that proved to be highly effective in form of Ferumoxytol injections highly effective in increasing the hematopoietic response rates in cancer patients[17].

The disadvantages posed by conventional methods such as high accumulation in the pathogenic root site, and reduced renal excretion of the drug are conquered by the nanodrugs due to their low molecular weight.

Nanoparticle drugs are considered a choice of treatment for cancer patients owing to their high drug absorbance due to their extremely small size and the ability to overcome the cell-cell, cell-tissue, and blood-cell barrier. Due to their micro size, they penetrate easily into the tissue at the target site and also have the ability to cross the epithelial cell layer. Nanoparticles exhibit a high degree of drug localization and cellular uptake at the molecular level. They can pass easily through the gastrointestinal tract mucosal layer and also the vascular tissues of the body. The main barrier to conventional drug delivery systems is the various biological barriers in the human body, which can be well addressed using nanoparticle drug delivery systems.

The main properties of nanoparticles are improved and effective delivery to the target site and high concentration on the target lesion[18]. Moreover, the available surface modifications are designed to be highly active and passive drug targeting. The nanoparticle drug delivery system provides high specific binding and internalization capabilities.

Nanoparticles are specifically designed to act in a specific manner based on pathophysiology, targeted delivery site, and interstitial space. Nanoparticles can target tumor cells through active and passive targeting techniques. The nanoparticle drug delivery system induces apoptosis in malignant tumor cells by activating an array of mechanisms while enhancing drug stability. The system depends on the nanocarrier molecules in cancer therapy, which target the tumor cells through the absorption and release of drugs to induce a highly specific targeting mechanism.

The most favorable advantages of nanoparticles supporting cancer therapy are their nanometer size and huge surface area, as well as their highly modifiable optical and magnetic properties, conquering drug resistance, lack of drug solubility, side effects of chemotherapy and radiotherapy, non-specific targeting of conventional drug delivery systems, and the possibility of impaired and significant treatment failure due to the inability of conventional drugs to reach the tumor.

In the current research, many types of nanoparticles play a role in cancer diagnosis, which can be broadly categorized as follows:

2 CARBON NANOTUBES

Carbon nanotubes (CNTs) are functionalized nanoparticles with chemically modifiable surfaces within a large surface area. This property is exploited for the diagnosis and treatment of cancer[19]. Due to their high mechanical thermal and electrical properties, they have proven to be more advantageous than conventional assays using imaging techniques. In many instances, biomarkers of cancer cells can only be detected in the later stages of cancer and the immunoassays performed are time-consuming, insufficiently specific, and also completely dependent on the biochemical properties of the tissue. To address this problem functionalized CNTs are of great help compared to the conventional diagnosis methods.

CNTs have unique characteristics to identify the surface protein of the target tissue, which diagnoses specific types of cancer with high efficiency. Their unique features include the presence of specific peptides and ligands that are specifically designed to recognize specific cancer receptors present on the outer surface of cells or tissues.

Currently, CNTs are applied widely in the diagnosis of tumors, along with traditional imaging techniques such as MRI scanning, PET, SPECT, and also various existing tumors biomarkers such as BRCA 1, 2

(biomarker for liver cancer), BCR-ABL (a marker of chronic myeloid leukemia), BRCA1/BRCA2 (biomarker for breast cancer), BRAFV600E (melanoma/colorectal cancer), CA-125 (ovarian cancer), CA19.9 (pancreatic cancer), CEA (colorectal cancer), EGFR (non-small-cell lung carcinoma), HER-2 (Breast Cancer), KIT (gastrointestinal stromal tumor), PSA (prostate specific antigen - Biomarker for prostate cancer)[20].

These biomarkers lack a high degree of specificity and also depend totally on the metabolic conditions and complete biochemistry of the underlying tissue.

However, CNTs are specifically designed to identify and differentiate between cancerous and non-cancerous cells, and can also be used to treat all major types of cancer, including predominantly proliferative lung cancer. It can be used as a potential mediator for drug carriers and therefore may serve as an alternative to current conventional screening methods[21].

CNTs have also been shown to be used in the diagnosis and treatment of almost all major types of cancer, such as lung cancer, and breast cancer. CNTs nanoparticles are composed of conjugated multi-walled carbon and show amazing visualization and visibility in ultrasound contrast, mainly for the detection of prostate cancer. They have a unique zeta potential of 38mV and a diameter of 30mm, which are used in chemotherapy for lymphoma cancer. The single-wall carbon nanotube-enabled drug delivery system is a novel approach, where the specialized CNTs can directly recognize the cancer-specific receptors on the targeted cells and then induce their drug through functionalized delivery. As this method provides zero exposure to healthy tissue or non-cancerous cells, patients experience almost zero side effects.

Multi-walled CNTs (MWCNTs) are another type of CNTs, which have been proven highly efficient in lymphatic tissue targeting.

Due to their efficient packaging and delivery abilities, carbon nanotubes have been applied for cancer treatment using gene therapy, which is of the most promising alternatives for advanced levels of treatment.

MWNT-NH3 SiRNA complexes and MWNT-Cl are approved and applied CNTs along with gene therapy.

PAA-g-MWCNTs (Polymerization of acrylic acid in poor solvent to specialize PAA-grafted-MWCNTs have been widely researched and show a high degree of specificity and targeting seen in the lymphatic system).

3 NANO QUANTUM DOTS

Nano quantum dots (NQDs) are novelly designed nanoprobes, which possess properties of high biocompatibility with human physiology and significantly high amount of quantum yields, photostability, and adjustable emission spectrum. Hence, they are applied as one of the most promising nanoparticles for cancer diagnosis and treatment and are considered one of the finest products of nanotechnology in cancer biology enabled with semiconductor properties[22]. NQDs also feature high efficiency in the targeted drug delivery approach due to the narrow emission spectra and a high degree of photochemical stability. NQDs-enabled probes are recorded to have a higher level of selectivity and specificity.

Cadmium and Selenium enabled NQDs, also referred to as CdSe NQDs, are another type of quantum dots coated nanoprobes, which are one of the most efficient nano-enabled drug to conjugate with cancer-specific ligands or antibodies to result in accurate and precise detection of the specific cancer signaling protein.

This advanced and novel approach is considerably faster than traditional imaging and identification techniques, saving detection time and providing higher accuracy.

NQDs conjugated with prostate-specific membrane antigen are another successful nanoparticle drug, which provides rapid identification for various cancer such as prostate cancer. Other biosensors and biochips based on NQDs have been developed, which contribute to the early detection of prostate cancer.

NQDs excel in the detection of breast cancer. By using NQDs conjugated to human epidermal growth receptor 2, multiplexed identification of cancer cells was performed in a simpler, cheaper, and less time-consuming way than traditional methods including in situ fish (Fluorescent in situ Hybridisation technique)[23]. In mouse lymphoma cells folate, NQDs conjugates are variously detected. Zinc along with antibody-coated NQDs are other researched NQDs, which have substantial strengths and capabilities to provide a high detection rate of cancer. NQDs are available in the size range of 600-900nm and offer significant advantages over conventional methods because of their ability to perform multiple screens in a single imaging session with a high degree of specificity.

The NQDs offer a complete analysis of the cancerous tissue and analyze the circulation, movement, directionality, inter-unclear interactions, and surface protein interactions, thereby producing a real-time analysis of the cells.

This complete real-time tracking of cancer cell activity facilitates enhanced diagnosis and treatment,

including more effective and sensitive methods of drug delivery.

4 MAGNETIC METAL NANOPARTICLES

These are basically superparamagnetic iron oxide nanoparticles (SPIONs), which have become highly promising nanoparticles for application in cancer diagnosis and treatment[24]. SPIONs offer a magnetically controlled and extremely sensitive targeted drug delivery system binding through the lianas and the bio receptors. They are characterized by superparamagnetism, high field diversity, biocompatibility, immune-compatibility, multifunctional, highly interactive and specific drug-binding ability, resolving the issues of inadequate drug distribution and tissue drug absorbance regulation.

SPIONs can acquire their activity against cancer cells with the help of other active external magnets. These specially designed nanoparticles have been used for the treatment of leukemia with the technique of hyperthermia, which potentiates the penetration effects into the cancerous cells. Such deep penetration is absent in conventional hyperthermia techniques for cancer therapy, which may result in adjacent damage to the normal tissues. SPIONs in hyperthermia are beneficial due to the ease and control of temperature analysis. These nanoparticles are also combined with immunotherapy and with different anti-cancer drug delivery systems for more advanced cancer treatments[25].

They are also applied in cancer diagnosis conjugated with conventional molecular imaging techniques such as MRI with help of other external magnetic systems, thereby providing highly specific analysis of the cancerous tissue[26].

SPIONs grafted with self-assembled polyethyleneglycol or dodecylamine grafts present numerous applications in cancer detection and treatment. Due to their sensitive cell-targeting properties, anticancer drugs are bound to these nanoparticles. Polyethyleneimine is conjugated with polymers of anions and cations for tissue targeting using electrochemical methods. They can bind to the drug and thus enhances the targeting of the cells in the drug delivery system[27].

SPIONs have also been produced in different polymers and dextran coatings. Other novel metal nanoparticles applied in the fields of cancer are Aurolase NU-0129, CNB-AU 8, and FERUMOXSIL, which is an FDA-approved iron oxide nanoparticle extensively used for cancer detection.

5 NANOSHELLS

Nanoshells (NSs) are spherically designed nanotools consisting of a metal outer shell that generally resembles a seashell. This special design contributes to enhanced biocompatibility and optical absorption. The shells are specifically designed to absorb specific wavelengths of light, and the absorption results in the radiation of large amounts of heat, which can be lethal to cancer cells. Raman scattering is an optical phenomenon seen in the NSs, which are highly improved as compared to conventional methods. NSs are used in drug delivery systems for various types of cancer, using a metal shell to bind specific anti-cancer drugs. NSs exhibit a specific ability to recognize cancer cells and engulf them in the tumor by performing phagocytosis, thus allowing their application in cancer therapy. They are highly efficient in providing tumor-specific imaging and are covered with the antibodies on their exterior for targeted therapy in breast and various ovarian cancer cases. These specially designed antibody-coated NSs can target human epidermal growth factor receptor-2, a major biomarker of breast cancer, and are passively absorbed.

6 CONCLUSION AND FUTURE PROSPECTS

Nanotechnology has been instrumental in applying nanomedicine to revolutionize the process of cancer detection and treatment. It has been a highly anticipated topic in cancer biology and has been greatly demonstrated in almost all types of cancer research.

Nanomedicine research enhances drug delivery methods for cancer patients significantly by improving pharmacokinetics, biocompatibility, and tumor targeting.

However, the nanoparticles cytotoxicity and cell toxicity must be analyzed prior to the clinical application.

Some nanomagnetic particles are found to build up and form reservoirs, contributing to systemic translocation and increasing cytotoxicity. Silver nanoparticles have been shown to increase cell toxicity and produce less renal purification. Nonetheless, other metals such as molybdenum, manganese oxide, and iron oxide synthesized nanoparticles show almost zero toxicity and complete elimination from the system.

The drug-polymer combination approach of nanomedicine is under vigorous research. Gold nanoparticles are strong alternative nanoparticles with zero oxidation incidence, zero toxicity, easy synthesis procedure, and easy upscaling. Hence, it has gained the highest demand from the industry[28].

Furthermore, design, synthesis, scale-up, marketing, and management all become an extremely costly tasks for the product[29]. Hence, cost-effectiveness is another matter of high concern. Therefore, there is a need to introduce more cost-effective, easy-to-synthesize, scale-up, and effective nanomedicines. SPIONs are thus

heavily utilized due to their minimal size, low deposition rate, and easy diffusion in the lymphatic and circulatory systems.

However, the bio-stability, bio-compatibility including its immune system interactions, and cell-cell interactions of the SPIONs in the lymphatic system of the body need to be analyzed[30]. The reported lack of some degree of quantification and optimization of NQDs, the safety of intact nanodrug delivery, and tolerance of nano drugs remains extremely important issue.

Challenges faced during the application of the nanodrug are the lack of homogeneity of the product synthesized[31], the different quantification of batch synthesis, and clinical application in cancerous cells. Scaling up is a difficult approach because nanomedicines seem to lose their potency due to insufficient quantification.

The ultimate goal is to achieve a completely rational approach and application of nanomedicine in cancer biology so as to ultimately meet the high demand of patients and medical science for higher and more effective diagnostic and therapeutic applications, such as the absence of side effects and pain as well as rapid recovery.

Overall, arguably the greatest innovation in nanomedicine is in cancer treatment and diagnosis. The tremendous initiative of researchers should be highly appreciated, and more extensive research in this area is highly encouraged.

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Conflicts of Interest
The author declared no conflict of interest.

Author Contribution
Choubey MH solely contributed to the manuscript and approved the final version.

Abbreviation List
CNTs, Carbon nanotubes
CT, Computed tomography
FDA, Food and Drug Administration
MRI, Magnetic resonance imaging
MWCNTs, Multi-walled CNTs
NQDs, Nano quantum dots
NSs, Nanoshells
PET, Positron emission tomography
SPECT, Single photon emission CT

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