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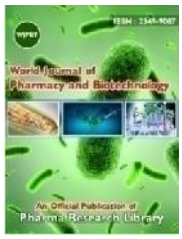

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# A Review on Nanotechnology in Cancer Diagnosis and Treatment

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**A B S T R A C T**

Cancer, a disease characterized by the uncontrolled growth and spread of abnormal cells, is still the second most common cause of death in the U.S. According to the American Cancer Society, about 571,950 Americans are expected to die in 2011 due to cancer, and that means more than 1,500 deaths per day. Current treatments for various cancers include surgery, radiation, hormone therapy, and chemotherapy. Although these conventional therapies have improved patients' survival, they also have several limitations. For example, conventional cancer chemotherapy has the cancer therapeutic agents distributing non-specifically in the human body, thus these drugs affect both cancerous and normal cells. This non-specific distribution of drugs limits the therapeutic dose within cancer cells while providing excessive toxicities to normal cells, tissues, and organs; and thereby causing several adverse side effects including hair loss, weakness, and organ dysfunction, leading to a low quality of life for cancer patients. Nanoparticles (NPs) have been of significant interest over the last decade as they offer great benefits for drug delivery to overcome limitations in conventional chemotherapy. They can not only be formed in a range of sizes (1-1000nm) but also be made using a variety of materials including polymers (e.g. biodegradable polymeric nanoparticles, dendrimers), lipids (e.g. solid-lipid nanoparticles, liposomes), inorganic materials (e.g. metal nanoparticles, quantum dots), and biological materials (e.g. viral nanoparticles, albumin nanoparticles). Nanoparticles for anti-cancer drug delivery had reached the first clinical trial in the mid-1980s, and the first nanoparticles (e.g. liposomal with encapsulated doxorubicin) had entered the pharmaceutical market in 1995.

**Keywords:** Cancer, Nanoparticles, Nanotechnology, Chemotherapy.

**A R T I C L E I N F O**

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## 1. Introduction

**Cancer Disease:** Cancer is a complex disease occurring as a result of a progressive accumulation of genetic and epigenetic changes that enable escape from normal cellular and environmental control. Cancer is a generic term for a group of more than 100 diseases that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells which grow beyond their usual boundaries, and which can invade adjoining parts of the body and spreads to other organs, a process referred to as metastasis. Metastases are the major cause of death from cancer. Cancer is a leading cause of death worldwide. From a total of 58 million deaths worldwide in 2005, cancer accounts for 7.6 million (or 13%) of all deaths. More than 70% of all cancer deaths in 2005 occurred in low and middle-income countries. Deaths from cancer in the world are projected to continue rising, with an estimated 9 million people dying from cancer in 2015 and 11.4 million dying in 2030.The most frequent cancer types worldwide are (a) among men: lung, stomach, liver, colorectal, oesophagus and prostate; and (b) among women: breast, lung stomach, colorectal and cervical. [1-3]

## 2. Nanotechnology

The field of nanotechnology was first predicated by Professor Richard P. Feynman in 1959 (Nobel laureate in physics, 1965) with his famous Cal Tech Lecturer entitled, “There’s plenty of Room at the Bottom”. Nanotechnology has achieved the status as one of the critical research endeavors of the early 21st century, as scientists harness the unique properties of atomic and molecular assemblages built at the nanometer scale. Ability to manipulate the physical, chemical, and biological properties of these particles affords researchers the capability to rationally design and use nanoparticles for drug delivery, as image contrast agents, and for diagnostic purposes. New technologies using metal and semiconductor nanoparticles are also under intense development for molecular profiling studies and multiplexed biological assays. Recently functional nanoparticles have developed that are covalently linked to biological molecules such as peptides, proteins, nucleic acids, small-molecule ligands. Medical applications have also appeared, such as the use of super paramagnetic iron oxide nanoparticles as a contrast agent for lymph node prostate cancer detection and the use of polymeric nanoparticles for targeted gene delivery to tumor vasculatures.[4-9]

**Nanoparticles:** In this review we are trying to focus on the role nanoscience in cancer diagnosis and therapy. It is expected that nanotechnology will be developed at several levels: materials, devices and systems. At present, the nanomaterials level is the most advanced in scientific knowledge as well as in commercial applications. A decade ago, nanoparticles were studied because of their size-dependent, physical & chemical properties. Nanomaterials, which measure 1–1000 nm, allow unique interaction with biological systems at the molecular level. They can also facilitate important advances in detection, diagnosis, and treatment of human cancers and have led to a new discipline of nano-oncology**,** for nanoparticle-drug complexes to be effective in delivering their payloads directly to cancer cells in living subjects, they must fulfill certain criteria (Fig. 1):

- The nanoparticle must be able to bind or contain the desired drug(s).
- The nanoparticle-drug complex must remain stable in the serum to allow systemic delivery of the drug.
- The nanoparticle-drug complex has to be delivered to tumor cells (either by receptor-mediated interactions or via the EPR effect), thereby reducing any unwanted complications from nontargeted delivery.
- The nanoparticle must be able to release the drug once at the site of the tumor.
- The residual nanoparticle carrier should ideally be made of a biological or biologically inert material with a limited lifespan to allow safe degradation.

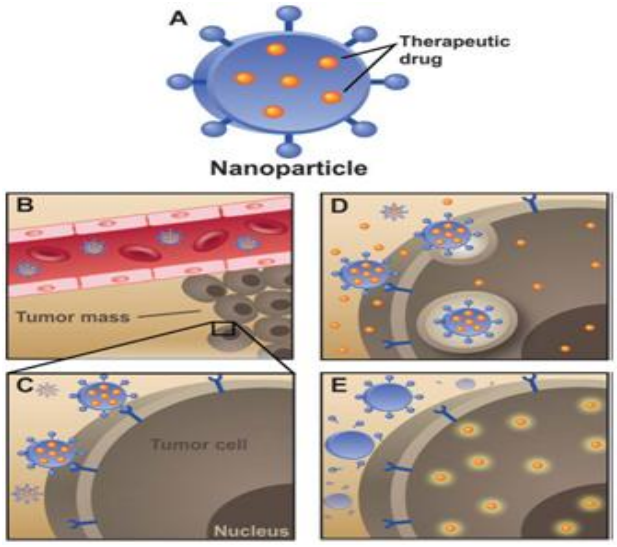


**Figure 1:** The Criteria Nanoparticles Need to Fulfill to Be Effective Carriers for Chemotherapeutic Drugs. (A) The nanoparticle carrier must bind or contain the desired chemotherapeutic drug(s). (B) The nanoparticle-drug complex must remain stable in the serum to allow for the systemic delivery of the drug. (C) The nanoparticle-drug complex must be delivered only to tumor cells. (D) The nanoparticle must be able to release the drug once at the site of the tumor. (E) After drug delivery, the residual nanoparticle carrier must be safely degraded.

**Biomarkers of Cancer**

Biomarkers or biomolecule markers include altered or mutant genes, RNAs, proteins, carbohydrates, lipids, and small metabolite molecules, and their altered expressions that are correlated with a biological behavior or a clinical outcome. Most cancer biomarkers are discovered by molecular profiling studies based on an association or correlation between a molecular signature and cancer behavior. In the cases of both breast and prostate cancer, a deadly step is the appearance of so-called lethal

phenotypes, such as bone-metastatic, hormone-independent, and radiation and chemotherapy-resistant phenotypes. It has been hypothesized that each of these aggressive behaviors or phenotypes could be understood and predicted by a defining set of biomarkers[10]. Biomarkers have tremendous therapeutic impact in clinical oncology, especially if the biomarker is detected before clinical symptoms or enable real-time monitoring of drug response. Protein signatures in cancer provide valuable information that may be an aid to more effective diagnosis, prognosis, and response to therapy. The recent progress of proteomics has opened new avenues for cancer-related biomarker discovery. Advances in proteomics are contributing to the understanding of patho-physiology of neoplasia, cancer diagnosis, and anticancer drug discovery. Continued refinement of techniques and methods to determine the abundance and status of proteins holds great promise for the future study of cancer and the development of cancer therapies.[11-12]

## 3. Nanotechnology in cancer therapy

**Quantum dots:** Quantum dots are novel semiconductor nanocrystals with broad potential for use in various applications in the research, management, and treatment of cancer. Quantum dots owe their fluorescence emission to electron excitation. To overcome the limitations of imaging in the visible spectra, such as autofluorescence from tissues like intestine and suboptimal tissue penetrance, some investigators have constructed quantum dots that fluoresce in the near infrared (NIR) spectra (700–1000 nm).[13] This property potentially makes NIR quantum dots attractive for in vivo imaging. NIR quantum dots have been used for in vivo lymphatic mapping in several animal models. Because of their composition of heavy metals and previous reports of cytotoxicity, the potential use of quantum dots in humans may be limited.[14-15]

**Gold Nanoparticles:** Colloidal gold nanoparticles are another attractive platform for cancer diagnosis and therapy. These are attractive because gold has been approved and used for treatment of human disease. Gold nanoparticles have been used as contrast agents in vitro based on their ability to scatter visible light Photoacoustic tomography has been used to image gold nanoparticles to a depth of 6 cm in experiments using gelatin phantoms[16]. Based on this property, photoacoustic tomography may be useful for in vivo imaging of gold nanoparticles. Gold nanoparticles also have been used as a platform for novel experimental cancer therapy. In a subcutaneous model of colon cancer, it was demonstrated that systemically delivered gold nanoparticles (size, approximately 33 nm) conjugated to tumor necrosis factor (TNF) accumulated in tumors[17,18].

**Alkylating Agents**

Alkylating agents are able to target tumor cells in various and multiple phases of the cell cycle and are better suited for the treatment of slow growing cancers. Alkylating agents stunt tumor growth by cross-linking guanine nucleobases resulting in abnormal base pairing or DNA strand breaks. Tumor DNA is unable to uncoil and separate which prevents the cell from dividing. Typically, alkylating agents act nonspecifically requiring conversion into active substances *in vivo*[19]. Cisplatin is one of the most widely used antineoplastic alkylating agents for the treatment of certain cancers such as testicular, ovarian carcinomas, and carcinomas of the head and neck. The aqua cisplatin-DPPG micelles were converted into liposomes 100-160 nm in diameter by mixing with vesicle forming lipids followed by dialysis and extrusion through membranes, entrapping and encapsulating cisplatin with a very high yield.

**Lipid/Polymer**

Positively charged lipid-based nanoparticles are known to trigger strong immune responses when injected into the body. This can be problematic when attempting to use this type of nanoparticle as a drug delivery vehicle. Lipid-based cationic nanoparticles are a new promising option for tumor therapy, because they display enhanced binding and uptake at the neo-angiogenic endothelial cells, which a tumor needs for its nutrition and growth. By loading suitable cytotoxic compounds to the cationic carrier, the tumor endothelial and consequently also the tumor itself can be destroyed. For the development of such novel anti-tumor agents, the control of drug loading and drug release from the carrier matrix is essential. Screening of different matrices for a given drug may be useful for fast and efficient optimization of drug/lipid combinations in pharmaceutical development[21].

**Dendrimers**

Dendrimers are synthetic, nanometer-sized macromolecules that can be modified to suit a specific application. Several types of dendrimers are commercially available, among which Polyamidoamine (PAMAM) dendrimers are the most extensively studied for biological applications[22,23]. They have a unique architecture based on *â*-alanine subunits with primary amine groups on the surface that are available for the attachment of several types of biological material. Their aqueous solubility and biocompatibility are well suited to carry ligands, fluorochromes, and drugs for targeting, imaging, and drug delivery. Some of the issues associated with immunoconjugates, such as decreased solubility and reduced binding efficiency, can be addressed using dendrimers as carrier molecules attached to antibodies[24]. Several groups have studied the conjugation of dendrimers to antibodies for targeting applications. Antibody-dendrimer conjugates have been used for radiolabeling with minimal loss of immunoreactivity[25].

## 4. Conclusion

Cancer nanotechnology field has the potential to better monitor therapeutic efficacy, provide novel methods for detecting and profiling early stage cancers. Nanomaterials have unique features that are attractive, and can be applied to biosensing. The development of various nanomaterials and nanotechnology has enabled detection of cancer biomarkers with great precision and sensitivity that could not be achieved before. Many studies are being conducted on developing sensing mechanisms that will push down the detection limit as far down as possible. Nanotechnology shall help to detect cancer at an early stage and monitor the disease with much greater precision. Cancer will become a disease that will become amenable to complete cure via surgical resection.

FGT is advantageous over wet granulation technique considering some factors like less water required for granulation, uniform distribution of binder, no over wetting of granules and no spray nozzle is required and most importantly suitable for water sensitive drugs. But Analysis of the foam allows small particles to adhere to larger particles in the early stages of granulation, and then get more completely agglomerated through the entire operation.

**Table 1:** Current biomarkers use in cancer

| Cancer | Markers | Characteristics | Typical sample |
|---|---|---|---|
| Prostate | PSA (Prostate specific antigen), total and free. | High sensitivity in all stages, also elevated from some non-cancer causes | Blood |
| Breast | Estrogen receptors<br>Progesterone receptors | Over expressed in hormone-dependent cancer | Tissue |
| Lung (non smell) | CEA (Carcinoembryonic antigen) | Used in combination with NSA to increase specificity, used also for colon cancer detection. | Blood |
| Lung (smell) | NSE (Neuron-specific enolase) | Better sensitivity towards specific types of lung cancer. | Blood |
| Bladder | NMP22 (Matritech's nuclear matrix protein). BTA (Bladder tumor antigen) | NMP-22 assays tend to have greater sensitivity than BTA assays. | Urine |

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## 6. Reference

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