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**Rocky Yadav, Bineeta Dwivedi**

*Department of pharmaceuticals, Shri Ram  
College of Pharmacy, Morena (M.P.)*

**Ritika Gandotra, Ragini Mathuria,  
Priya Bhadoriya**

*I.P.S. College of Pharmacy, Gwalior  
(M.P.)*

## Correspondence

**Beenita Dwedi**

*Shri Ram College of Pharmacy, Banmor  
(M.P.)*

**Email:** [bineetadwd89@gmail.com](mailto:bineetadwd89@gmail.com)

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## Nanotechnology of Cancer Therapy: An Overview

**Rocky Yadav, Ritika Gandotra, Ragini Mathuria, Priya Bhadoriya, Bineeta Dwivedi**

### ABSTRACT

Nanotechnology is the study and use of structures between 1 nanometer and 100 nanometers in size. Nanotechnology is definitely a medical boon for diagnosis, treatment and prevention of cancer diseases. Nanoparticulate technology is of particular use in developing a new generation of more effective cancer therapies capable of overcoming many biological, biophysical and biomedical barriers that the body stages against a standard intervention. Nanoparticles that deliver chemotherapy drugs directly to cancer cells are under development. Nanomedicine application areas include drugdelivery, therapy, diagnostic, imaging and antimicrobial techniques. The formed nano particles can be used in wide range of therapeutic treatment of cancer. To overcome problems of systemic toxicity associated with chemotherapy and enhance treatment resolution of cancer therapies, nanotechnology is increasingly providing many novel approaches, especially to energy-based cancer therapies. Nonmaterial and biomarkers of cancer, general principle of drug targeting to cancer, intracellular mechanisms, and nanoparticles based formulation in market, several recent applications in medicine as diagnostic and therapeutic are discussed. This article aim to overview on all the parts of nanotechnology in cancer therapy.

**Key words:** Nanotechnology, Nanomedicine, Application of nanomedicine, Nanomedicine For cancer, Risks of nanotechnology.

### 1. INTRODUCTION

The use of nanoparticles in the field of cancer therapy is attractive for several purpose: they show unique pharmacokinetics, including minimum renal filtration; they have high surface to volume ratio facilitating modification with numerous surface functional groups that home, internalize, or stabilize; and they may be constructed from a wide range of materials used to encapsulate or solubilize therapeutic agents for drug delivery. The topology of a nanoparticle—core, coating, and surface functional groups—makes it particularly acquiescent to modular design, where by features and functional moieties may be switched or combined. Although much functionality of nanoparticles have been demonstrated, including some clinically arrogated drug formulations and also imaging agents, the merging of these into multifunctional nanoparticles capable of targeting, imaging, and delivering therapeutics is an exciting area of research that holds great promise for cancer therapy in the future. To include many features such as the ability to target tumors, evade uptake by the reticuloendothelial system (RES), protect therapeutics that can be released on petition, act as sensors of tumor responsiveness, and provide image distinction to visualize sites of disease and monitor disease progression, so that is show many desirable features in cancer disease. Some of these useful features, such as targeting, influence biological mechanism. Others are derived synthetically and enable external curious or manipulation that is otherwise not realistic in biological systems. In this chapter, we review both bio-inspired and synthetic nanoparticle functionalities that have been used in cancer therapy and address current efforts and future opportunities to combine these into multifunctional devices for better resolution in cancer therapy<sup>1-9</sup>.

## 2. NEED OF THE STUDY

Cancer is very harmful diseases in which abnormal cells divide uncontrolled and are able to invade other tissues. Cancer is not only just one disease but many diseases. There are more than 100 different types of cancers. Cancer is a multi-step process classically occurring over a prolonged period which is beginning with initiation followed by promotion and progression. Cancer is responsible for about approx. 19% of all deaths in the worldwide and is a major public health problem in many parts of the world. Deaths from cancer worldwide are projected to continue rising, with an estimated 12 million cases in 2020.

## 3. TOXICOLOGY OF NANOPARTICLES

People come into contact with many chemical substances in a various variety of ways, often resolutely, though unknowingly, through the products that they use every day for various purposes. It is implicit that anything readily available to the public has undergone laborious testing before it is cleared for use. For instance, toxicological studies for substances that may be used as food additives are overseen and congregated by the Federal Drug Administration, who keeps a list of those “generally recognized as Safe”. If a substance is considered GRAS, it has been shown through in vitro and in vivo experiments to be nontoxic, or has been used for a great number of years with no known negative effects that is harmful for human being. Once included in the GRAS list, a chemical is acceptable for use as a food additive as a safer and is thereafter NIT expected to prove nontoxic before use on human health. Products have appeared in recent years that contain NP assumed to be because the bulk forms of the chemicals are nontoxic. Given that materials can take on utterly different properties when reduced to the Nano scale, and their potential to penetrate more deeply into tissues and cells<sup>12</sup>.

## 4. NANOMEDICINE

With many products comprising NP on the rise consider the potential for novel biological uses. Nanomedicine mentions to the usage of nanotechnology in medical applications. While the study is very new, many promising utilizations have arisen in this field. Some of the important desirable unique properties of Nanomaterials gave already proven useful in biological applications. For instance, NP are on the same size scale as biological molecules, and so are better able to pierce tissues and cells. The surface reactivity of NP makes them easy to modify, either through the addition of drugs or targeting molecules to direct them to specific cell or tissue types. Current research in the field of Nanomedicine has mainly focused on the use of NP as imaging agents or drug carriers of prevailing therapeutics<sup>13</sup>. Other studies have found that adsorption or encapsulation of DNA-based vaccines onto/into NP enhances their important ability to induce

immunity through the protection of DNA to cell using nontoxic magnetic NP. The application uses DNA adsorbed onto magnetic NP that is then targeted to cells by smearing an external magnetic field. Magnetic NP has also shown ability in the area of drug delivery, as they can be targeted to desired areas in the body<sup>14</sup>. Liposomes are also another greatly researched nanomedicine, used as novel drug delivery agents. These are artificial Nano-sized Phospholipid bilayers engineered to contain a drug to be delivered to a target site including tumors. Nanomedicine has focused primarily on cancer treatment in an attempt to find more efficacious treatments that are simultaneously better tolerated by patients. Overall, NP has proved novel potential and wide-ranging utility in medical applications, and research is stable. The future of medicine looks to be tightly comprehensive matted that of nanotechnology<sup>14</sup>.

## 5. CANCER

### 5.1 Introduction of Cancer

Cancer is a critical disease characterized by uncontrolled multiplication of immature cells and spread of abnormal forms of the body's own cells. The branch of medicine apprehensive with the study, diagnosis, treatment and prevention of cancer is Oncology. Cancer may affect people at all ages, but the risk of most assortments increase with age<sup>15</sup>. All cancers begin in living cells that is body's basic unit of life. The genetic material of a cell can become damaged or changed, producing mutations that distress normal cell growth and division. When this happens, cells do not die when they should and new cells form when the body does not need them. The extra cells may form a mass of tissue called a tumor and known as cancerous cells or tissue<sup>16-17</sup>.

Targeted drug delivery is well-thought-out as a method in which drug-carrier complex, delivers drug to the pre-selected cell in a specific manner and then reduce the unwanted side effect of drugs. The drug should reach the target cell with the maximum concentration or with maximum effect. This can be achieved by protecting the drug from the bio-environment enroots to the specific cell<sup>18-19</sup>.

### 5.2 Epidemiology and Cast

Cancer is a term used to describe a varied group of diseases indicated by uncontrolled proliferation, tissue invasion, and often metastasis. According to the world Health Organization, it is one of the most conspicuous causes of death, killing 7.4 million people worldwide in the year 2004. This number is estimated to rise to approximately 12 million by 2030. In America alone, approximately 45% of men and 37% of women will develop some form of cancer in their lifetime, and about 24% of American

men and 21% of American will die from some of cancer. Health care in the United States in 2006 for treatment alone was \$103.1 billion according to the National Cancer institute's publication cast of cancer care. Significant amounts of money are also spent on cancer research; according to their numbers on research funding the National Cancer Institute alone currently budgets approximately \$4.7 billion annually, and contribution from private, for-profit companies equals that amount at last. This makes the research for inexpensive, safe, and effective treatments a high priority for biomedical researchers<sup>20-21</sup>.

### 5.3 Classification of cancer

Cancer can arise in all cell types and is classified by the heredity of the original transformed cell. Epithelial cells are found covering the body's surfaces on living body and lining the internal organs and cavities. Cells of this type that give rise to cancer are classified as 10 carcinomas. These are the most common types of cancer; they make up most prostate, breast, and lung cancers. Cells of the hematopoietic lineage are those that originate in the bone marrow and include erythrocytes and white blood cells of the immune system. Cancers that arise in this aristocratic are classified as leukemia and lymphomas. Leukemia arises in cells of the lymphatic system. Sarcomas typically are cancers that originate from connective tissues such as bone, cartilage, muscle, deep skin, or fat, although some cancers of solid masses of transformed celled tumors, though leukemia<sup>22</sup>. This work will mainly focus upon carcinomas, leukemia and lymphomas, though future work will comprise sarcomas.

### 5.4 Symptoms and causes

The ability of cancer to affect a large variety of cell types makes its symptom profile very diverse. Solid tumors can invade and compress surrounding tissues, leading to destruction of the functioning of body tissues and organs. Local symptoms can include swelling, pain and jaundice in body. Systemic symptoms are more invasive; weight loss, fatigue wasting and anemia are common to most cancer, and cancer type-specific symptoms can also occur. In addition, metastases can cause yet another set of symptoms, including enlarged liver, bone pain and neurological symptoms significantly. Alongside the symptoms of cancer, treatments often exhibit a multitude of negative side effects. Cancer is caused by an accretion of damage to the DNA of cells that leads to the deactivation of tumor suppressor genes and/or activation of oncogenes. Oncogenes are those that govern the ability of the cell to rapidly divide and multiply, while tumor suppressor genes are those that in normal cells prevent the too much growth and invasion of tissues.

### 5.5 Cancer Treatments in use today

Ionizing radiation is known for its capability to damage DNA, which can lead to cancer. It can also, however, be used to damage the DNA locally in tumors, causing cell death. Most forms of radiation therapy actually work via induction of free radicals, which is than damage the cancer cell's DNA. However, in hypoxic tumor environments there can be 2 to 3 time more resistance to radiation therapy. Side effects include damage to epithelium, swelling, fibrosis, or loss of elasticity in the area, hair loss, fatigue, and depression. Significantly, another side effect of radiation therapy is secondary malignancy 21-31 years after treatment, though this is not common. Existing chemotherapeutics attempt to inhibit the cellular functions that are most different between normal and cancerous cells such as cell division and DNA replication. While these metabolic processes occur more commonly in cancer cells, they also commonly occur in normally dividing cells, leading to the potentially dangerous side effects related with chemotherapy. Alkylating agents include commonly known drug such as Chlorambucil and work by adding alkyl groups to DNA, there by crosslinking the strand. This DNA damage leads to the initiation of apoptosis, likely through p53, so cancers with changes to this enzyme may have poor responses to these drugs. This group also contains the platinum complexes, such as Cisplatin and Carboplatin, which bind intra-or inter-strand guanine bases, also crosslinking DNA and triggering apoptosis. Cisplatin is also capable of forming protein-cisplatin complexes that inhibit glycolytic enzymes, there by attacking cancer cell metabolism. This makes cisplatin effective against cancers of multiple origins cervical and lung cancer and lymphoma<sup>23</sup>.

## 6. TYPES OF NANOPARTICLES APPLIED IN DRUG DELIVERY

### 6.1 Nanosuspension

A suspension of drug nanoparticles in a liquid is called as nanosuspension. A size of nanoparticle lies in between approx. 200 to 500 nm and outstanding desirable feature of nanosuspension is the increased saturation, solubility, increased dissolution rate of compound. The saturation and solubility increases below a particle size of 1 mm. An additional feature of nanosuspension is that they may induce changes in the crystalline structure increase the amorphous fraction in particle or even generating completely amorphous particles. Nanoparticles and Nanosuspensions show an increased adhesiveness to tissue. The oral administration of drug in the form of nanosuspension has been reported to enhance and improved absorption rate and bioavailability.

### 6.2 Solid lipid Nanoparticles (SLN)

The solid lipid nanoparticles are sub-micron colloidal carriers (50-1,000nm) which are consist of physiological lipid, dispersed in water or in aqueous surfactant solution. In order to

overcome the disadvantages associated with liquid state of oil droplets, liquid lipid replaced by a solid lipid, which ultimately transformed into solid lipid nanoparticles.

### 6.3 Polymeric nanoparticles

In polymeric nanoparticles drug is dissolved, entrapped, absorbed, attached or encapsulated into nanoparticle matrix. Depending on the method of preparation, nanoparticles, nanospheres or nanocapsules can be obtained with different properties and release features for encapsulated therapeutic agent.

### 6.4 Polymeric micelles

Polymeric micelles have been widely studied as drug carrier. Polymeric micelles have better thermodynamic stability in physiological solution, as indicated by their low critical micelle concentration, which makes polymeric micelles stable and inhibit their rapid dissociation *in vivo*.

Micelles systems are useful for the systemic delivery of water-insoluble drugs. Drugs can be segregated in the hydrophobic cores of micelles and the outer hydrophilic layer from stable dispersion in aqueous media which can then be administered intravenously.

### 6.5 Magnetic Nanoparticles

Magnetic nanoparticles are powerful and multipurpose diagnostic tool in field of medicine. Magnetic immunoassay techniques have been developed in which the main field generated by the magnetically labeled target perceived directly with sensitive magnetometer. Super paramagnetic nanoparticles are used as distinction agents in magnetic resonance imaging. The magnetic nanoparticle are coated with inorganic core of iron oxide with polymer such as dextran. Magnetic nanoparticles of indomethacin demonstrated selective targeting under magnetic field. Owing to its strength, following normal administration, the drug concentration was greater in the liver and spleen where endocytosis and phagocytosis could occur.

### 6.6 Carbon Nanotubes

Carbon nanotubes are a new form of carbon molecule around in a hexagonal network of carbon atoms, these hollow cylinders can have diameter as small as 0.7nm and reach several millimeters in length. Each end can be opened or closed by a fullerene half molecule. The small dimensions of nanotubes, combined with their notable physical, mechanical and electrical properties, make them unique materials. They also represent a very large specific surface area, are excellent heat conductors and display unique electronic properties, offering three dimensional

configurations. They have higher capacity for molecular absorption.

### 6.7 Liposomes

Liposome contains an internal aqueous core used for drug encapsulation, which is surrounded by a phospholipid bilayer. The use of phospholipid is covenant as it related to the biocompatibility of these Nano carriers. While the internal aqueous core is perfectly suited for the delivery of hydrophilic drugs, the phospholipid bilayer allows for the encapsulation of hydrophobic drug.

### 6.8 Nanoshells coated with gold

Gold nanoshells are new compound nanoparticles that combine infrared optical activity with the uniquely biocompatible properties of gold colloid. Metal nanoshells are concentric sphere nanoparticles consisting of a dielectric (typically gold sulfide or silica) core and a metal (gold) shell. By varying the relative thickness of core and shell layers, the Plasmon-derived optical resonance of gold can be affectedly shifted in wavelength from visible region of highest physiological transmissivity. By varying absolute size of the gold nanoshell, it can be made to either selectively absorb (for particle diameter < 75nm) or scatter incident light. Because the gold shell layer is deposited using the same chemical method used to grow gold colloid, the surface properties of gold nanoshells are virtually identical to those of gold colloid. Gold nanoshells can be used to treat breast cancer cells.

### 6.9 Ceramic nanoparticles

The newly emerging area of using inorganic (ceramic) particles with entrapped biomolecule has potential applications in many frontlines of modern materials science including drug delivery system. The advantages of ceramic nanoparticles include easy preparation with desired size, shape and porosity, and no effect on swelling or porosity with any alteration in pH.

### 6.10 Nanopores

Materials with defined pore-sizes in the nanometer range are of superior interest for a broad range of industrial application because of their desirable properties with respect to thermal insulation, controllable material separation and release and their applicability as templates or fillers for chemistry and catalysis. One of the examples of nanoporous material is aerogel, which is produced by sol-gel chemistry.

### 6.11 Nanowires

Nanowires are conductive or semi conductive particles with a crystalline structure of a few dozen nm and a high length

**Table 1:** The types of nanoparticles applied in the drug delivery system include<sup>24</sup>

| Sr. No. | Type of Nanoparticles            | Material used  | Application  |
|---------|----------------------------------|--|--|
| 1       | Nanosuspensions and Nanocrystals | Drug powder is dispersed in surfactant solution                          | Stable system preselected for controlled delivery of poorly soluble drug                   |
| 2       | Solid lipid Nanoparticles        | Melted lipid dispersed in Aqueous surfactant                             | Least toxic and more stable Colloidal carrier systems as alternative materials To polymers |
| 3       | Polymeric nanoparticles          | Biodegradable polymers   | Controlled and targeted drug delivery  |
| 4       | Polymeric micelles               | Amphiphilic block co-polymers  | Controlled and systemic Delivery of water insoluble Drugs                                  |
| 5       | Magnetic Nanoparticles           | Magnetite Fe <sub>2</sub> O <sub>3</sub> , Magnetite coated with dextran | Drug targeting diagnostics to in medicine and in various ways                              |
| 6       | Carbon Nanotubes                 | Metals, semiconductors or carbon   | Gene and DNA delivery<br>Controlled release of drug  |
| 7       | Liposomes                        | Phospholipid vesicles  | Controlled targeted drug delivery (Aqua and non-aqua drug)                                 |
| 8       | Nanoshells                       | Dielectric core and metal shell  | Tumor targeting drug delivery  |
| 9       | Ceramic Nanoparticles            | Silica, alumina, titanium  | Drug and biomolecule delivery system   |
| 10      | Nanopores                        | Aerogel, which is produced by cell gel chemistry                         | Controlled release drug carriers   |
| 11      | Nano wires                       | Silicon, cobalt, gold or Copper based nanowires                          | Transport electron in nano Electronics   |

/diameter ratio. Silicon, Cobalt, Gold or Copper-based nanowires have already been produced. They are used to transport electrons in nanoelectronics they could be composed of unlike metals, Oxides, sulphides and nitrites.

### 6.12 Dendrimers

Dendrimer-based drug delivery molecules have numerous potential advantages: dendrimers are analogous in size to proteins, being small enough (<5.0 nm in diameter) to escape the vasculature and target tumor cells, while also being below the inception of renal filtration to allow urinary excretion. For instance, acetylated dendrimers have been conjugated to folic acid, methotrexate, tritium, fluorescein and 6-

carboxytetramethylrhodamine, in order to allow synchronized treatment and drug uptake monitoring in tumors.

### 6.13 Quantum Dots

Quantum dots have the potential to melodramatically improve clinical diagnostic tests for the prompt detection of cancer. These engineered semiconductor particles combine cadmium with selenide in a tightly packed atomic structure that emits light in a spectrum of six colors, plus four near-infrared colors, as the dots decrease in size. By finely tuning the size of the dots, thousands of elusive color variations could be created. These tiny glowing particles, when conjugated with anti-bodies, peptides, proteins, or DNA, form bio conjugated dots that can act as markers on cells

and genes, giving scientists the ability to rapidly and differentially mark pathologic tissues<sup>25</sup>.

## 7. ADVANTAGES OF NANOPARTICLES

1. Fairly easy preparation of the system.
2. Targeted drug delivery.
3. Due to their small size Nanoparticles invade small capillary and are taken up by the cell which allows for efficient drug accumulation at the target sites in the body.
4. Good control over size and size distribution.
5. Good protection of the encapsulated drug.
6. Retention of drug at the active site and release drug at controlled manner.
7. Longer clearance time
8. Increased therapeutic efficacy significantly.
9. Increased bioavailability of drugs.
10. Dose proportionality.
11. Stable dosage forms of drug which are either unstable or have unacceptably low bioavailability in non-nanoparticulate dosages forms.
12. Increased surface area results in a faster dissolution of active agents in an aqueous environment for better result.
13. Faster dissolution generally associates with greater bioavailability.
14. Smaller drug doses which is reduces side effect.
15. Reduction in fed/fasted variability.
16. Less toxicity in human body.

## 8. DISADVANTAGES OF NANOPARTICLES

1. Extensive use of polyvinyl alcohol as a detergent –issues with toxicity.
2. Limited targeting abilities.
3. Discontinuation of therapy is not possible.
4. Cytotoxicity.
5. Pulmonary inflammation and pulmonary carcinogenicity.
6. Alveolar inflammation.
7. The disturbance of autonomic imbalance by nanoparticles having direct effect on heart and vascular function.

## 9. THERAPEUTIC APPLICATIONS OF NANOPARTICLES<sup>25</sup>

Nanoparticles with different compositions and characteristics and investigated for various therapeutic applications as follows:-

- Carriers of drugs and biological agents
- Carriers of gene and DNA

- Carriers of antigens & vaccines
- Controlled & targeted drug delivery
- Carriers of diagnostic agent
- Carriers of MRI contrast

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