



## Nano Oncology - Applications of Nanotechnology in Cancer Diagnosis

Dr. B. Narasimha Rao\*, Dr. K. Ravindra Reddy, S. Rahath Fatima, S. Sadhiya Tabasum

Department of Pharmaceutics, P. Rami Reddy Memorial College of Pharmacy, Kadapa, Andhra Pradesh, India.

\*Corresponding author's E-mail: [simham1985@gmail.com](mailto:simham1985@gmail.com)

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### ABSTRACT

Nanotechnology plays a significant role in advances in oncology and nanooncology is perhaps the most important chapter of nanomedicine. Nanotechnology is the study and application of scale structures ranging from 1 to 100 nanometres. Cancer is the number one cause of death for people under the age of 85. Nanoparticles which provide directly with chemotherapy to the cancer cells being created. Nanomedicine device fields include prescription distribution, diagnosis, longitudinal, Imaging and techniques of the antimicrobials. Fears have started to increase over the possible dangers of certain nanotechnologies. This article aims to provide an overview of nanotechnologies present role in cancer therapy.

**Keywords:** Cancer, Nanoparticles, Chemotherapy, Nanocarriers, Nanomedicine.

### INTRODUCTION

Cancer is a disease characterized by uncontrolled growth and irregular cell distribution. This is an uncontrolled cell proliferation, where apoptosis has largely vanished and needs a very complicated treatment process. Cancer is one of the world's most serious deadly diseases today, more than 10 million people are diagnosed with this disease every year and it is the world's second most common cause of death. Many factors, such as age, gender, local environmental factors, diet and genetics influence the incidence of cancer and cancer types.

Cancer is a common illness which has been researched extensively. Traditional chemotherapy treatments cause many toxicity problems for patients because they are not selective for tumour cells. The goal is to find a way to avoid the problem, i.e. to develop a system that can use therapy to target cancer cells, avoiding healthy ones.

#### How Cancer Arises

Cancer is caused by gene damage which regulates the growth and division of cells. Genes carry the essential cell function instructions. Cancerous cells need a blood supply for development. To supply oxygen and essential nutrients a molecule causes the surrounding blood vessel to expand towards the cell<sup>4</sup>.

Cancer may be treated by changing the damaging gene process or preventing the flow of blood to the cells. Genetic changes which cause cancer can be inherited from parents to their children. These can also occur over the lifespan of a individual as a result of errors that occur when cells divide or as a result of damage to the DNA system caused by other chemical exposures. Cancers that cause environmental exposure include chemicals and radiation, such as ultraviolet sunlight, such as cigarette smoke. Cancer cells generally experience more genetic changes than normal cells, such as mutations in DNA.

#### Spread of Cancer

A cancer that spreads from the place it started to spread to a different location in the body is called metastatic cancer. The process which spreads cancer cells to other parts of the body is called metastases. Metastatic cancer has the same name and cell count as the original cancer. For example, Breast cancer which grows into and forms a metastatic tumor in the lung is metastatic breast cancer but not lung cancer.

Current treatment for cancer includes surgery, radiation, hormone therapy, and chemotherapy. Chemotherapy is an essential strategy to treat the disease. In treating cancer cells traditional chemotherapy is especially unspecific, leaving normal healthy cells susceptible to adverse drug reactions. Clinical variability and therapeutic resistance were demonstrated by the nature of the genetic and phenotypic stages. In recent years, major efforts have been made to develop nanotechnology to enhance the delivery of anticancer drugs to tumor tissue, thus reducing their dissemination and toxicity in healthy tissues.

#### NANOTECHNOLOGY

Nanotechnology is the creation of useful materials, devices and structures used between 1 and 100 nanometers to manipulate matter on an extremely small scale.

A nanometer is one billionth of a meter—80,000 the width of a human hair, or about ten times a hydrogen atom's diameter. As for in vivo imaging and therapeutics, nanotechnology is also making rapid progress.

Such technology would most likely have major consequences in the near future for the treatment of cancer patients. Recent advances in nanoscale engineering have resulted in the development of a broad variety of new technologies, including nanoscale devices (quantum dots,



nanoshells, gold nanoparticles, carbon nanotubes) under investigation<sup>4</sup>.

#### Advantages:

1. Improved therapy with reduced invasiveness.
2. The negative effects of medication and surgery have decreased.
3. Faster diagnostic instruments, smaller ones, and more versatile.
4. Cost-effectiveness of medications and therapies for the general treatment of diseases.
5. Nano's clinical approach benefits from untreated medical conditions, such as cancer.
6. Reduced mortality and morbidity, and increased in return for permanency.

#### WHY NANOTECHNOLOGY IN CANCER?

Because of its small size, nanoscale devices can effectively interact with biomolecules both on the cell surface and within cells. This offers plenty of new ideas for treating cancer. At the heart of this research are future uses of these new cancer imaging and therapeutic technologies. Two methods active and passive targeting, were used to steer nanoparticles to tumor sites. Effective targeting involves binding ligands to different nanoparticles of the tumour. Passive nanoparticles targeting benefits from the size of the nanoparticles and the unique features of the tumor vasculature<sup>3</sup>.

#### Polymer-based nanocarriers for targeted cancer therapy

For the targeted delivery of cancer therapeutic mobility, an array of polymeric nanocarriers, i.e. polymeric NP's, polymeric micelles, dendrimers, polyerosomes, polyplexes, polymer hybrid systems and polymer conjugates was investigated. The polymers used to make such nanocarriers may either occur naturally or are of synthetic origin. Such polyfimeric NP's are capable of ferrying a wide range of drugs at target sites in a controlled manner for a sustained period of time to provide enhanced antitumor efficacy with minimal systemic side effects. These nanosystems too protect drugs from their rapid degradation during systemic circulation and liver clearance. Network of the kidney and reticuloendothelial which further enhances drug stability and target specificity. Many polymer based NPs have been approved for clinical use<sup>5</sup>.

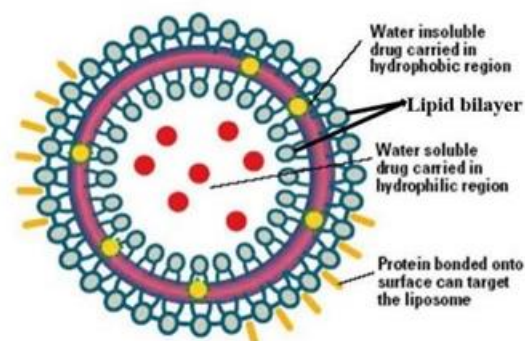
#### Tools of nanotechnology

- Liposomes
- Polymer micelles
- Dendrimers
- Carbon nanotubes
- Quantum dots

#### Liposomes

Liposomes as closed spherical vesicles are composed of a lipid bilayer that encapsulates an aqueous drug storage cycle. Liposomes, forming lipid bilayers through hydrophobic interaction are known to be excellent sites for delivery of hydrophobic and hydrophilic drugs.

#### General structure of liposome



#### 1. Liposomes

Liposomes in particular demonstrate great persistence in the blood. It allows the delivery of drugs to target tissues with success. Different lipids have different chain lengths of fatty acids, different head groups and varying fusion temperatures. The US FDA has also approved Industrial liposomes. Doxorubicin encapsulated liposomes (Doxil), which have important antitumor activity against a wide variety of cancers are the best example of this.

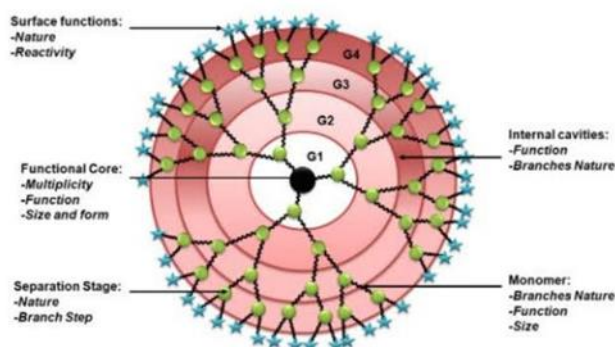
Liposomes of less than 400 nm size can easily reach blood tumor sites but these are held in healthy tissues by bloodstream endothelial layer. Thus liposomes act to deliver the drug by diffusion rather than direct cell fusion. This expertise is regarded as enhancing permeability and retaining effect<sup>19</sup>. Examples of liposome-mediated drug delivery are doxorubicin (Doxil) and daunorubicin (Daunoxome), currently on the market as delivery mechanisms for liposomes. Liposomal doxorubicin polyethylene glycol (PEG)ylated (Doxil1, Caelyx1; Alza Pharmaceuticals, San Bruno, CA, USA) The most extended circulation has been reached so far, with a terminal half-life of 55 hours in humans.

#### Dendrimers

Dendrimers are distributed as highly branched artificial macromolecules with tree-like structures, three-dimensional molecules that have molecular weights defined, and trapping properties of host guests.

The size ranging from 1 to 10 nm can be synthesized with dendrimers with various chemical structures and functional groups. The generation determines the size and shape of dendrimers via a series of repeated chemical synthesis at the middle. The most useful character of dendrimers is the branches that can provide drug substances with large surface area and target molecules. Meanwhile, the surface functionalities of the core, internal

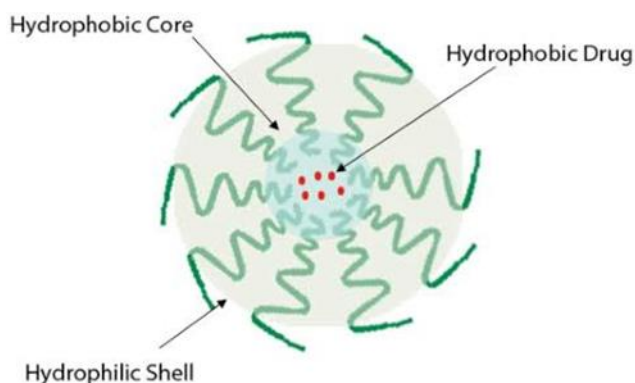
branching, and chemical composition play an important role in reactivating the macromolecule. Dendrimers are small spheres that have been deliberately designed to have several loose ends that may be connected to other molecules, such as a targeting agent that can identify and distinguish a cancer cell from a healthy cell, or a drug that destroys cancer cells<sup>19</sup>.



## 2. Dendrimers

### Polymeric Micelles

A micelle is characterized as a set of amphiphilic surfactant molecules; in the future of therapeutics, micelles prove to be a keystone.



## 3. Polymeric Micelles

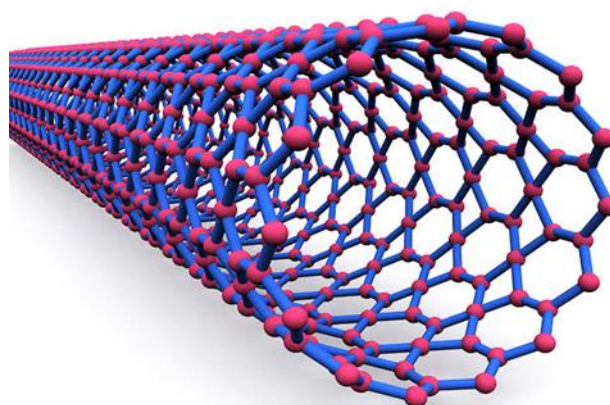
A micelle is characterized as a set of amphiphilic surfactant molecules; in the future of therapeutics, micelles prove to be a keystone. Paclitaxel, Genexol-PM (PEG-poly (D, L-lactide)-paclitaxel), the first polymeric micelle formulation, is a cremophor – EL – free polymeric micelle formulated paclitaxel. Several polymeric formulations of PEG-micelle have been used in clinical trials; for example, doxorubicin-loaded polymer micelle.

### Carbon Nanotubes

In the late 1980s, carbon nanotubes were first discovered as a distinct molecular type of carbon atoms that bond with each other through sp<sup>2</sup> bonds and present a hexagonal arrangement.

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hexagonal arrangement. Conceptually, when single or multiple sheets of graphenes formed by hollow.



## 4. Carbon Nanotubes

Nanotubes are presented as well as ordered. The cylinders are rolled in. The two types of carbon nanotubes are single and multiwalled carbon nanotubes. Carbon nanotubes in the family of nanotechnology platforms have been identified as a novel method for supplying anticancer drugs.

A part of this, to enter the cell membranes, carbon nanotubes must immobilize molecules such as proteins, DNA, and drugs. Heister has used an oxidized single walled carbon nanotube, consisting of a fluorescent marker and monoclonal antibody at non competing binding sites, to delivery anticancer drug doxorubicin. Nonetheless, the health of carbon nanotubes is concerned because of the fibre-like form of the wire. Recently the biological impacts (cytotoxicity, DNA damage, and inflammation) caused by multi-walled and single-walled nanotubes of different sizes were studied. Results show that long and thick multi-walled nanotubes of carbon are likely to induce severe biological effects and may result in increased cancer risk.

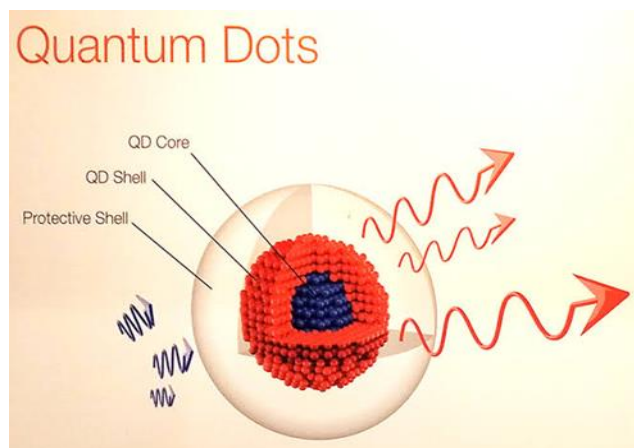
The remarkable ability of CNTs to penetrate cell membranes paves the way for their use as carriers for the delivery of therapeutic agents to the cytoplasm and also to the nucleus<sup>18</sup>.

### Quantum Dots (QDs)

Half-conductor QDs are emerging as a new form of fluorescent labels in biology and medicine. The broad absorption and narrow emission characteristics of QDs allow multiple performances. The high fluorescence quantum yield of the QDs, photo bleaching resistance, and special physical, chemical and optical properties make them strong candidates for molecular and cellular in vivo imaging fluorescent tagging.

The QD's also include a versatile nanoscale scaffold for the production of multifunctional nanoparticles for both imaging and therapeutic functions. QD's hold great promise for in vivo and intra-operational tumour imaging mainly because of their powerful fluorescent signals and multiplexing capabilities; That could allow high sensitivity

and selectivity to be achieved. Due to their substance formulations, QD's are subject to toxicological scrutiny; however, several groups have stated that QDs with biocompatible surface coatings such as PEG silica can be well tolerated by in vitro cells.



### 5. Quantum Dots

QD-based detection is fast, easy and cost-effective, enabling cancer markers to be screened rapidly at the point of care. QD's have special properties which make them suitable for detecting tumours. These include long term, solid and stable fluorescence; photobleaching resistance of high molar extinction coefficients; And highly sensitive detection because of their ability to absorb and emit light very effectively. Because of their large area-to-volume ratio, a single QD can be combined with different molecules, making QD desirable for use in the development of more complex multifunctional nanostructures.

#### Nanotechnology-based novel cancer therapy

- Gene therapy based on nanotechnology
- Photodynamic therapy based on nanotechnology
- Radiotherapy and radiofrequency therapy focused on nanotechnology
- Cancer theragnostics based on nanotechnology

#### Nanotechnology-mediated novel cancer therapy

Targeted therapy in cancer treatment has become highly common where only cancer cells are destroyed and normal cells are not affected. The advent of nanotechnology has brought new technologies and ways of treating targeted cancer. Nanoparticles' engineered properties open the door to new, non-invasive approaches for cancer therapies that were not previously feasible, such as advanced nanotechnology-based cancer therapy approaches, such as photodynamic therapy (PDT), radiotherapy and radiofrequency therapy, and theragnostics<sup>19</sup>.

#### Nanotechnology-based gene therapy

Gene therapy is based on the idea of the possibility of introducing different exogenous genes into the tumour cell genome to produce a tumoricidal effect. It represents one

of the fastest-growing fields of research on preclinical and clinical cancer. Although viral vectors have traditionally been the primary agents used for gene transfer to target cells, they carry serious immune hazards. And it has hosted volatile reactions. The viral vector-related problem is the question of toxicity, immune and inflammatory responses, gene regulation and targeting; but there is always a possibility that the virus will revive and cause disease.

The physical properties of nanoparticles, including their morphology, size, charge density and colloidal stability are important parameters for determining the overall efficacy of nanoparticles to act as potential non-viral gene delivery vehicles. Nanoparticles physical properties, including their shape, scale, charge density, and colloidal stability, are important criteria for evaluating the overall effectiveness of nanoparticles to serve as potential non-viral vehicles for the delivery of genes<sup>20</sup>.

#### Nanotechnology-based photodynamic therapy

PDT is an alternative to current adjuvant therapy which carries little morbidity associated with local or systemic treatment and is not susceptible to resistance growth. This requires a photosensitizing drug being administered. PDT is based on the activation of a photo sensitizer, which –if triggered by a particular light wavelength– Causes the release of reactive oxygen species that can directly kill tumour cells, as well as the tumour-associated vasculature, leading to tumour offence. Targeting is important in PDT, because radiofrequency ablation is a proven tumour destruction method that has historically required the insertion of samples into tumours; Nanotechnology however, enables non-invasive radiofrequency tumour ablation to evolve. In-vitro and in-vivo gold nanoparticles have been shown to enhance cancer cell destruction in a non-invasive radiofrequency region.

Cardinal et al., emphasized the possible use of gold nanoparticles for specific cancer cell targeting. They have used a new, non-invasive radio wave machine coupled with gold nanoparticle enhancer solutions in both in vitro and in vivo systems to thermally ablate tissue and cancer cells<sup>19</sup>.

#### Nanotechnology-based cancer theragnostics

The integration of diagnosis and therapy in a single process is an evolving biomedical approach known as theragnostics. The primary objective of theragnostics is to specifically target specific (diseased) tissues or cells to improve diagnostic and therapeutic precision. Biocompatible nanoparticles are currently under development as theragnostic agents for cancer that would allow non-invasive diagnosis and effective cancer therapy.

Such nanoparticles-mediated combination approaches aim to speed treatment, reduce diagnosis side effects and increase cancer cure rates. Lukianova-Hleb et al. have researched the optical generation and detection of plasmon nanobubbles (PNBs) around gold nanoparticles in individual living cells. Focusing on the tuning of PNB

properties in one cell and testing PNB multifunctionality. Several recent reviews addressed engineering designs, physiochemical features and biomedical applications of magnetic nanoparticles and they reported that magnetic nanoparticles may simultaneously serve as diagnostic molecular imaging agents and that drug carriers Shim et al. have achieved combined cancer diagnosis and therapy (theragnostics). In their research, they covalently coated non-interfering RNA-encapsulating polyplexes with small gold nanoparticles via acid-cleavable bonds to explore the potential for integrated stimulus-responsive multimodal optical imagery and stimulus-enhanced genesilencing<sup>19</sup>.

### Advantages and Challenges of Nanotechnology for Cancer Therapy:

Nanotechnology has many benefits in the treatment of cancer with a small size nanotechnology platforms can reach the tumour vasculature through EPR<sup>120</sup>. In addition, hydrophilic polymer/oligomer structure can provide a long half-life of circulation and extend the duration of tumour tissue exposure to anticancer agents; Whereas the addition of tissue recognition residues, such as antibodies, lectins and ligands that are unique to cancer cells, will allow nanotechnology platforms to target tumour cells.

A major challenge inadequate cancer therapy and combinations of multifunctional nanotechnology platforms and other therapies have been developed to resolve MDR cancer cells and have achieved substantial successes. However the creation and implementation of nanotechnology systems in cancer therapy, such as limited knowledge of cancer, remains a challenge. Cell physiology, limited variety and low functionalization of medical nanomaterials, and lack of clinical evaluation criteria. However with further developments in functionalization focused on a detailed understanding of the physiological characteristics of cancer cells, the Nanotechnology Platforms Promise that the practice of oncology would change substantially, allowing for easy and effective targeted therapy<sup>5</sup>.

### FUTURE DIRECTIONS

Nanotechnology has become an enabling technology for personalized oncology where cancer detection, diagnosis and therapy are adapted to each patient's molecular tumour profile and for predictive oncology where genetic and/or molecular markers are used to predict growth; Medical development and consequences of the diseases. The US National Cancer Institute recently established eight national centers of excellence in cancer nanotechnology in recognition of their potential effects on cancer research. Looking to the future, there are several large research directions that are particularly promising but that involves a concerted effort to be successful. The first is mono functional nanoparticles, or multiple functions, design and growth. Nanoparticles provide possibilities for the design and alteration of properties that are not possible with

other types of therapeutic drugs and they have a promising future as a new generation of cancer therapies.

Alternatively, the development of multifunctional nanoparticles could potentially make nanoparticles capable of simultaneous detection and destruction of cancer cells. Although some key concerns and many obstacles remain to the clinical production of nanoparticles, as there are more clinical evidence available, there is still greater awareness of nanotechnology. It will certainly lead to a more rational design of engineered nanoparticles with greater selectivity, effectiveness and safety. Yet current knowledge about nanocarriers health is inadequate. Pharmacokinetic activity of different types of nanoparticles requires thorough analysis and a database should be built on health risks associated with different nanoparticles.

### CONCLUDING REMARKS

The basic reason for using nanotechnology in oncology is because nanoparticles have mechanical, magnetic or structural properties that can not be accessed from larger molecules or bulk solids. These nanoparticles can be used when connected to tumour targeting ligands such as MAbs, peptides or small molecules. Tumour antigens (biomarkers) as well as high affinity tumour vasculatures and specificity. Nanoparticles have large surface areas and functional groups for multiple diagnostic and therapeutic anticancer agents in the size range of 5-100 nm diameter. Nanoparticulate bioaffinity samples for molecular and cellular imaging, nanoparticles guided for cancer therapy and nanodesicles integrated for early cancer detection. Nanoparticles have large surface areas and functional groups to combine multiple diagnostic and therapeutic anticancer agents in the 5-100 nm diameter size range. Recent progress has led to samples of nanoparticulate bioaffinity for molecular and cellular imaging guided nanoparticles for cancer treatment and integrated nanodesicles for early detection of cancer.

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