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# Theranostics: An Emerging Concept of Nanomedicine

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**Abstract:** ***The field of nanotechnology plays an important role in medical and pharmaceutical science. Nanomedicine deals with new technologies for developing customize or personalized drug delivery system. In the last decades there is development of nanomedicine in the treatment of cancer which only consist of therapeutic modalities so some limitations may arises regarding actual diagnosis of disease. So there is need of imaging along with its therapy hence Nuclear medicine is one of the advanced concept in field of nanotechnology which also include the concept of theranostic. Theranostics is type of nuclear medicine which is combination of both therapy and diagnostic. This is concept which monitor pharmacokinetic and pharmacodynic of drug in the body. In this review we presents brief overview of different theronostic techniques for the treatment of different diseases specially for cancer.***

**Keywords:** nanomedicine, nuclear medicine, cancer, molecular imaging, theranostic

## 1. Introduction:[1, 2,3]

Cancer is reported to be emerging as a major public health concern in India. It was found that expenditure on cancer treatment is become highest. From last decade new technology is arises in the treatment of cancer i.e. nanoparticulate drug delivery system, the use of NDDS found to be great success in the treatment of cancer.[1]

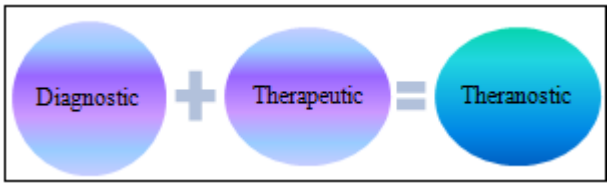
The average particle size of nanoparticle is 1-100nm which exhibits unique properties as well as it possess optiml surface characteristic so it can be proven as more effective than other drug delivery system. It may show following advantages:

- Increase the drug dissolution rate
- Enhance drug absorption
- Increase bioavailability
- Improve tissue selectivity
- Improve the efficacy of drug having narrow therapeutic window and low bioavailability.
- Drug resistance
- Enhanced permeability and retention effect[2]

Beside all these application there are some limitations of nanomedicine that it can be only applicable for therapeutic purpose so there is major need of technique which can give single platform to diagnostic and therapeutic agent because of this diagnosis and therapy of life theatning diseases like cancer, AIDS and cardiovascular disease takes place in early stage which help to avoid further complications. This technique is named as theranostic refers to simultaneous application of therapeutic and diagnostic.[3]

## 2. Theranostics:[4, 5]

Theranostic is defined as it is material which is combination of two modalities i.e. therapy and medical imaging which helps to monitor pharmacokinetics and pharmacodynamics of the drug in the body.




**Objective:**

- To make advanced technology in the field of nanomedicine.
- To diagnose the disease at its early stage.
- Sensitive diagnosis
- Accurate targeting
- Effective and controlled delivery of material
- Intracellular diagnosis
- Therapeutic monitoring[4]

Nanotheranostic is bifunctional in nature which can help to diagnose the diseased condition and delivery of the drug to specific cell with the help of biomarker. It consist of two parts:

***Diagnostic Agent*:** flurocent dye, quantum dots, MRI, radionuclides, iron oxide and computed tomography

***Therapeutic Agent*:** protein, peptide and genetic material. This system is mainly focused on cancer treatment but long with this it may useful in the treatment of autoimmue disorder i.e. type I diabetes mellitus, cardiovascular disorder, nerves disorder and inflammatory diseases. Recently it was found that theranaustic technique also useful in the alzimer disease.[5]

### 2.1 Therapy:[6, 7, 8]

#### 2.1.1 Photodynamic Therapy:

It is based on the principle of photosensitizing agent which absorbs the photons and react with neighbouring hydrophobic agent and give therapeutic effect.

In the treatment of cancer, photosensitizing agent absorbs incident light of specific wavelength and produces reactive

oxygen species so that cells get undergo apoptosis or nechrosis.

In the theranostic, photosensitizing agent are conjugate with various polymer metallic and carbon based nanoparticles. The photosensitizers absorbs light and produces ROS and kills the cancerous cells.

The main advantage of this is specific for only cancerous cell.[6]

#### 2.1.2 Photothermal Therapy

This is based on the principle of generation of heat to destroy tumor cells, for this purpose photothermal agents are used as they absorbs energy and get excite from ground state to excited state and further return to the ground state during this period they release energy in the form of kinetic energy which is responsible for the production of heat which help to disrupt cell membrane and degradation of protein takes place.

In the cancerous condition, the heat is only develop in the cancerous cell as it possess less vasculature hence this technique is selective for only cancerous cell.[7]

#### 2.1.3 Hyperthermia Treatment

This treatment is based on the principle of elevated body temperature. Once the body temperature gets elevated the cancerous cell may get destroy without affecting normal cells as the nanoparticles possess some biomarkers which only attached to the cancerous cell. The killing of cell takes place only at temperature range between $40^0$C to $45^0$C .

Magnetic nanoparticle in the cancer therapy act on the principle of hyperthermia as they enhance magnetic property by the application of the magnetic field while gold nanoparicle show their property by the laser application.[8]

## 3. Molecular Imaging in the Cancer Theranostics:[9,10]

It is technique which uses in the diagnostic imaging which helps for characterization, visualization and to measure the biological processes at the molecular and cellular level in humans.

Molecular imaging is a technique which is one of the helpful technique to the physician to identify diseased state, to study the different stages of disease during its period.

To image tumor cells different radiopharmaceuticals can be used for the purpose of molecular imaging . PET and SPECT are the type of radiopharmaceuticals which are used in the cancer imaging with best diagnostic accuracy.

PET and SPECT are both working on the emission of the positron and gamma emitting radionuclides respectively for the generation of the signals. But this system also possess following disadvantages:

a) The production is depend upon the presence of cyclotrone.
b) Radiolabelled compound with long half life are required.
c) It is expensive process.[9]

In the current study it was found that these modalities may render allocation of molecular data to a specific anatomical structure. This system also possess poor resolution.

There are different modalities that can be used for the purpose of molecular imaging demanding for targeted cell become visible i.e. fluroscence imaging and MRI.

MRI is based on the principle of manipulation of the inherent nuclear moment of endogeneous nuclei.

There are three magnetic labels are used for in vivo MRI

a) Gadolinium based contrast agent
b) Hyperpolarized molecule
c) Iron oxide magnetic nanparticle[10]

## 4. Theranostic Nanomedicine:[11-19]

Nanotheranostic is advanced feature of nanotechnology in the treatment of life threatening disease such as cancer, AIDS, autoimmune diseases.

Nanomedicine are emerging platform for the incorporation of theranostic agent which can be useful to the delivery of drug as well as imaging and also monitor the therapeutic response. Nanoparticle based theranostic are still in the early stage of development.

### 4.1 Metallic Nanomaterials for Theranostic

#### 4.1.1 Iron Oxide Nanoparticles

During the last decade, iron oxide nanoparticles show potential applications in biomedical field as well as pharmaceutical field.

Iron oxide nanoparicles useful as MRI contrast imaging, enhance the drug delivery and gene delivery and hyperthermia, in the magnetic hyperthermia iron oxide nanoparticles generate heat due to application of external high frequency magnetic field. The generated heat kills the cancerous cell.

Application of iron oxide nanoparticles are as follows:

- They are biocompatible
- They possess property of superparamagnetism
- They have high saturation magnetization
- They show low coparatively low toxicity.
- They are only magnetic nanopaticles which are approved by FDA.[11]

#### 4.1.2 Gold Nanoparticles

Gold nanoparticles having the unique property of surface plasmone resonance. When electromagnetic radiations falls on the metal surface which is plasmonic, it produces coherent oscillation of free electron gas on the surface. Because of this there is formation of dipole moment with the direction of electric field.

The amplitude of the oscillation in SPR reaches maxium at a particular frequency and induced strong absorption and scattering of the incident light which help in the molecular imaging. Larger size nanoparticle show greater scattering as compared to small sized nanoparticles.

In the treatment of cancer, gold nanoparticles are found to be best option as they are safe, specific and effective delivery of single stranded RNA.

Gold having affinity to the thiol and amine group hence there is utilization of the bifunctional moiety is possible.

These nanoparicles are preferentially used in the photothermal therapy.[12]

**4.2 Carbon Based Nanoparticles:**

Carbon shows excellent mechanical strength, electrical, thermal conductivity and good optical properties hence it is proved to be better option for biomedical purpose.

Carbon have large surface area which provide higher drug loading.

**4.2.1 Carbon Nanotube**

These are cylindrical carbon structure having electrical and optical properties. Because of good optical properties it show optical transition in the NIR region which make potent imaging of cancerous cell.

These are preferentially used as carrier of drug also helpful in the gene delivery as they protect from the enzymatic degradation rather than this they also efficient in the transfection. Carbon nanotubes are used in the photothermal therapy.

They also possess some limitations are as follows:

- Insolubility
- Toxicity
- Agglomeration
- Induced inflammation[13]

**4.2.2 Grapheme Oxide:**

It show higher NIR light absorption, it is used as photothermal agent. Grapheme oxide used for combinational therapy which is tagged with folic acid and loaded with doxorubicine for chemotherapy.[14]

**4.3 Polymer Based Nanoparticles:**

For the theranostic purpose, synthetic and natural polymers are used for the delivery of gene, drugs and diagnostic agent. In the theranostic the polymer should be functionalize with the diagnostic and therapeutic agents by chemical conjugation or copolymerization.

Different polymers such as PLGA, PLA-TPGS, PLGA-PEG, PEG and HPMA are used in the theranostic technique.[15]

**4.3.1 Dendrimes**

Dendrimes are type of spherical polymeric nanomedicine consist of braches of polymer. Their size is about 10- 100 nm. They are insoluble in water.

Dendrimers are found to be highly integrated nanomedicine and provide multiple function i.e. targeting, imaging and therapy.

Dendrimers can be used as imaging agents for fluorescence imaging, MRI, X-ray, computed tomography and nuclear medical imaging.

These are mostly used in the treatment of cancer with the help of photothermal therapy, beside that they also successful in the hepatic cancer.

The function of dendrimers can be enhanced by combining them with magnetic nanoparticles.[16]

**4.3.2 Liposomes**

Liposomes consist of phospholipids and cholesterol bilayer same as like living cell. These are biocompatible, nontoxic and biodegradable type of nanomedicine. they are spherical vesicle having unilamellar and multilamellar structure.

They saturated passively into the tumor cell and give EPR effect. Due to biodegradable polymer they can also help in the delivery of gene.

But there is some problem with liposomal drug delivery system that it can be easily recognized by reticuloendothelial system to avoid this it should coated with polymer i.e. polyethylene glycol which also help to keep the drug for longer time in the blood circulation. It also help to facilitate MRI contrast agent accumulation at target site.

Advantages of polymeric liposome:

- Lower toxicity
- Prevent from drug leakage
- Protein absorption
- Expose biotin for cancer cell uptake[17-19]

**4.3.3 Micells**

Micells are colloidal in nature consist of hydrophobic core and surrounding of it is hydrophilic in nature. The cohesive force is present between the drug and polymer. The stability of micells is depends upon the cohesive force.

Therapeutic and diagnostic agents are loaded into the hydrophobic core while hydrophilic shell consists of targeting moiety. For diagnostic purpose magnetic nanoparticles are loaded in the hydrophobic core.

In order to monitor drug action towards the cancerous cell, micells which are to be administer can also visualize by NIR optical imaging.[20]

**4.4 Quantum Dots**

Quantum dots are prepared from the semiconductor material. Semiconductor having property of luminescenc which provide platform for the imaging. This is system which help to deliver therapeutic drugs, protein, peptides and gene.

Quantum dots are used for highly sensitive cellular imaging, the major use of quantum dots for targeting tumor cells by two mechanisms i.e. active targeting and passive targeting.

Quantum dots work on the principle of the photodynamic therapy, when incident light falls on them the

photosensitizing agent absorbs the light and reach to excited state. Quantum dots containing oxygen species get excite to its triplet electronic state after absorbing specific amount of light and cause cell death.[21]

## 5. Future Perspective:[22-23]

Now a days nanoparticulate drug delivery system prove as efficient system of drug delivery. Numerous research have done on the modification of nanotechnology.

In this review we mention the theranostic technique which is also one of the modification of the nanotechnology in that there is fusion of therapeutic and diagnostic as name indicate.

Iron oxide nanoparticles are preferentially used as theranostic agent, they are biologically safe as they help in the synthesis of hemoglobin after their degradation or entered into the metabolic pathway.

The theranostic is found to be efficient and cost effective.

There are some issue arises with the heavy metals which are specifically used in the quantum dots.

There is need of further research wit respect to stability, biodistribution abd fabrication of theranostic system.[22-23]

## 6. Conclusion

Theranostic is combinational effect of the therapeutic and diagnostic, hence imaging of cell and delivery of therapeutic drug can takes place simultaneously.

Molecular imaging helps to give proper structure of cancerous cell and give idea about which treatment should be given to the patient in other words it can be said that theranostic tends towards the personalized medicine which give therapy to the patient according to their genetic variations, hence different patient with same disease get different therapy.

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