

## Review Paper:

# Cancer Diagnostics and Therapeutics: Recent Advances in Nanomedicine

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## Abstract

The recent developments in the field of nanomedicine have transformed the conventional therapeutic approaches to diagnose and treat cancer which was restricted earlier to radiation, chemotherapy, and surgery. Through packaging of the drugs within sterically stabilized, long-circulating nano vehicles and its further surface-modification with ligands to precisely target cellular/molecular components involved in the disease can curtail its concomitant side effects due to the direct administration of systemic drugs.

In this review, we try to summarize recent studies based on currently employed nanomedicine such as quantum dots, metal nanoparticles, polymeric nanoparticles, liposomes etc. for cancer diagnosis, treatment and prevention.

**Keywords:** Cancer, Nanomedicine, Diagnosis, Treatment.

## Introduction

According to WHO, cancer is one of the dominant causes of morbidity and mortality worldwide. Environmental factors triggering the mutation of genes that code for the critical cell-regulatory proteins are one of the major reasons for the occurrence of cancer. Statistical studies show that more than 11 million people are diagnosed with cancer each year and also account for about 7 million deaths/year (12.5% of deaths worldwide), making this disease a crucial factor in worldwide mortality. It is speculated that by 2030, this global burden will grow to 21.4 million. Despite tremendous efforts to treat cancer, there has been only a minimal actual improvement in cancer therapeutics over the past 50 years.

Moreover, the early and efficient detection of cancer is another problem since there is only a low concentration of cancer biomarkers in the early phase of tumor progression. In this context, nanomedicine, a branch of nanotechnology, gained a lot of attention in the treatment of cancer. "Nanomedicine" is developed by merging many disciplines including biological, physical, chemical, mechanical, material, and clinical sciences<sup>19</sup>.

Using nanoscale engineering, it is possible to develop an entirely novel therapeutic and diagnostic procedure through the supramolecular assembly of simpler components. Consequently, nanomedicine is formed as a side shoot of

nanotechnology. This acts through molecular-scale medical intervention for treating a disease or repairing damaged tissues. The precisely targeted delivery of specific nanoparticles to the malignant cells allows its efficient local interaction with affected cells. It forces them to enhance the production of the corresponding biomarkers significantly. Detection of biomarkers thus becomes much easier, and the early detection of cancer prevents the hurdles of burdensome treatments, thereby increasing the chances of recovery.

In the case of nanotherapeutics, sufficient progress in cancer treatment was achieved by site-specific drug delivery to cancer tissues. For example, the harmful effects of conventional chemotherapeutics in killing the normal healthy cells during the chemotherapy can be significantly reduced through the administration of folate and transferrin-mediated nanotherapeutics, which are specifically aimed to target cancerous cells. This property is mainly associated with increased permeability of the blood vessels at the locus where the tumor resides.

Brain tumors significantly limit the effectiveness of conventional chemotherapy by its unique anatomical, physiological, and pathological features. In this context, nanoparticle-based drug delivery systems could address the critical challenges in transporting a sufficient amount of therapeutic agents into the brain tumor areas while minimizing the potential side effects<sup>10</sup>. Another great challenge in treating cancer was the development of multidrug resistance in chemotherapy. This can be alleviated by the development and usage of various nanomedicines like solid lipid nanoparticles (NPs), mesoporous silica NPs, nanoparticulated chemosensitizer, nanoparticulated poloxamer, polymeric NPs and magnetic NPs<sup>2</sup>. Several nano carrier-based drugs are commercially available on passive targeting tumorous cells through a process known as enhanced permeability and retention<sup>58</sup>.

Here drug delivery system should have the ability to retain the anticancer drug with desired concentration in the blood and then allow a sudden or sustained drug release at the targeted cancer cells or organs. Nano-based drug targeting should be passive or active. Nano carrier-based passive targeting can exploit "enhanced permeability and retention effect" (EPR) in the tumor microenvironment because they can extravasate into the tumor tissues via the leaky blood vasculature and can localize and accumulate in the tumor micro-environment. Here the nanocarriers or nanoparticles did not need any type of surface modification<sup>53</sup>.

Nanomedicine based active targeting imparts specificity by the interaction of different ligands such as transferrin, folic acid, enzymes, engineered antibodies, and biological organic molecules like proteins and carbohydrates. Herein, the nanoparticles endowed with ligands are proficient at binding with specific receptors that are overexpressed on the tumor surface and prevent the non-specific uptake of nanoparticles by cells.

Thus, it can remarkably upgrade the therapeutic effectiveness of nanomedicine in the treatment of cancer metastasis<sup>55,22</sup>. Multifunctional nanomedicine shows considerable promise as a futuristic medicine that enables the early detection of cancer cells, accurate cancer imaging, and its treatment, such as intrinsic and targeted therapy with minimal toxicity. Analysis of different approaches of nanomedicine will help to optimize biomedicine systems associated with nano-oncology. The current review attempts to evaluate the role of various nanoparticles used in different biomedicine approaches, which will provide an attractive impact in the field of nano-oncology. It is proved that time responsive delivery owing to internal stimuli (e.g. pH, temperature, enzyme, redox, and H<sub>2</sub>O<sub>2</sub>) and external stimuli (e.g. magnetic, photo, and ultrasound) of nanotherapeutics by surface modification of tumor cell-specific ligands ensure active targeting to tumors<sup>40</sup>.

The analysis of cell-associated nanoparticles can be mainly done through microscopic and flow cytometric methods (qualitative analysis). New applications of mass spectrometric (MS) methods such as laser ablation ICP-MS (LA-ICP-MS), time-resolved ICP-MS (TR-ICP-MS), nano secondary ionization mass spectrometry (nano-SIMS), and mass cytometry (MC; mainly flow cytometry combined with time of flight mass spectrometry, ToF-MS) provide the quantitative data for the nanoparticle – cell interactions more precisely<sup>24</sup>.

### **Polymeric nanoparticles for cancer therapy**

In recent years, researchers have sought to develop cancer therapeutics involving drug delivery by a combination of nanotechnology and polymer chemistry<sup>18</sup> which has received great attention for its ability to improve the efficacy of these therapeutics. Several natural and synthetic biodegradable polymers including polyethylene glycol, starch, alginate, cellulose, hyaluronic acid, chitosan, gelatin, dextran, poly aspartic acid<sup>29</sup>, polylactic acid and poly (lactide-*co*-glycolide) have been investigated for their potential to synthesize polymer nano-therapeutics. Polymer nanoparticles will exhibit different properties such as biodegradability, biocompatibility, hydrophobicity, high surface to volume ratio, enhanced colloidal stability etc. and make them key candidates for cancer treatment.

The smaller diameter and excellent biocompatibility of polymer nanoparticles will help the targeted delivery of tumor-specific drugs and will allow these therapeutic agents to circulate in the bloodstream for a longer time. The

biocompatible and/or biodegradable property of the polymer nanoparticles will help to satisfy the requirement of the Food and Drug Administration (FDA). A combination of polymer nanoparticles with other biomolecules such as DNA (Polyplexes), micelles etc. bearing hydrophobic drugs helps to contribute a lot to nanomedicine. In most cases, the drug will be dispersed within the polymeric nanoparticle or attached to the polymeric backbone, and the nanopolymer-drug conjugates considered for biomedical applications are prepared using water-soluble polymers that provide prolonged therapeutic effects.

Nanospheres are the spherical polymer nanoparticles having the size range from tens to hundreds of nanometers consisting of synthetic/natural polymer (collagen, albumin, dextran) or amphiphilic copolymer characterized by amorphous or crystalline nature. The drug used for tumor targeting and treatment is either dissolved, entrapped, attached or encapsulated throughout or within the polymeric matrix and showed improved stability by preventing enzymatic and chemical degradation.

At the same time, the hydrophobic surface of nanospheres is highly susceptible to opsonization and clearance by the reticuloendothelial system. The nanospheres developed from albumin, starch, gelatin, polypropylene dextran, and polylactic acid are biodegradable. Nanospheres can deliver the concentrated dose of the drug to the tumor targets through enhanced permeability and retention effect or active targeting with the help of ligands attached to its surface.

Herein, site-specific targeting of nanospheres will reduce the toxicity by preventing drug exposure to healthy tissue. Out of the different strategies adopted to regulate the physicochemical properties of NPs, stimuli-responsive multistage nanocarriers were found to change their sizes in response to the local environment. Moreover, it represents a promising strategy in which multiple functionalities can be integrated into a single delivery system so that they can surpass multiple delivery barriers present<sup>59</sup>.

### **Nano dendrimers**

Nano dendrimers are highly branched and monodispersed macromolecules with nanometre scale-dimensional architecture emanating from it. Three components - a central core, an interior dendritic structure (the branches), and an exterior surface with functional surface groups are their main features. Here the polymer growth occurs in an outward direction starting from the central core molecule layer by layer using a series of polymerization reactions. Nano dendrimers are amenable to modification on their attached surface groups and can be tailored for specific therapeutic applications. Diagnostic agents are usually attached to these surface groups by chemical modification. The surface group will also affect the solubility and chelation ability, while the varied cores impart unique properties to the cavity size, absorption capacity and controlled release characteristics.

Earlier studies revealed that nano-dendrimers have remarkable molecular monodispersity with suitable pharmacokinetic properties which are responsible for its various applications in the bio-medical field. Certain major biomedical applications of nanodendrimers include different modes of therapies (photodynamic therapy, neutron capture therapy), systemic drug delivery with cleavable chemistry for drug dissociation<sup>31</sup>, imaging etc. Elham<sup>1</sup> gave an account of special properties like high solubility, reduced systemic toxicity, and selective accumulation of the drug in solid tumors exhibited by drug-dendrimer conjugates. Researchers have developed "avidimers"<sup>33</sup> which are dendrimers functionalized with small targeting ligands and are able to target tumor vasculature using a methotrexatepolyamidoamine (PAMAM) bioconjugate platform<sup>41</sup>.

**Liposomes for cancer therapeutics:** Liposomes are phospholipid based nanosized drug carriers (50-500 nm), which can entrap drugs with various solubility (hydrophilic, hydrophobic and amphiphilic drugs) and have been used for the treatment of different diseases such as cancers, lymphomatous meningitis, tuberculosis and fungal infections<sup>53</sup>. Liposomes offer the advantages that they are non-toxic, high drug loading capacity, improved therapeutic drug index, enhanced stability, and are non-immunogenic for systemic and non-systemic administrations. Liposomes can be used for targeted drug delivery to areas where energy sources such as high-intensity ultrasound, microwaves, radio frequencies are necessary. For hyperthermia, thermosensitive liposomes are used which allow the release of encapsulated drugs at these specific areas<sup>5</sup>.

Moreover, recent reports reveal that liposomal formulations of doxorubicin (DOX) have been on the market for cancer therapy<sup>46</sup>. Doxil, a pegylated liposome loaded with active agent doxorubicin, was clinically used to treat multiple types of cancer, especially ovarian cancer. The protective coating of Doxil will increase the blood-residence time by preventing its destruction by the immune system. Daunoxome is another type of liposomal formulation containing an aqueous solution of daunorubicin citrate used as a first-line therapy against Kaposi's sarcoma-associated with HIV<sup>9</sup>. Liposomal formulations are also associated with severe side effects due to their accumulation in skin tissue.

**Aquasomes (carbohydrate-ceramic nanoparticles):** Aquasomes are self-assembled three-layered nanocarrier systems comprised of a solid phase nanocrystalline core coated with oligomeric film. Sometimes, they are surface-functionalized with biochemically active molecules with or without modification<sup>47</sup>. This surface functionalization will help them to evade the defense mechanism by our immune system and also prevent the degradation by other environmental challenges, thereby enhancing their retention capacity in the blood. The hydrophilic nature of aquasomes enables them to protect and preserve biologically active molecules and also helps to maintain structural and

conformational integrity and the biochemical stability of bio-active compounds.

The increased surface to volume ratio of aquasomes may result in its increased degree of surface exposure and this property of aquasomes is exploited in targeting fragile biomolecules like peptide and protein hormones, enzymes, antigens and genes. The layered structures of aquasomes are self-assembled by non-covalent and ionic bonds. Different properties of aquasome like its excellent surface chemistry, structural stability, biodegradability etc. allow the efficient loading of drugs through ionic, non-covalent, van der Waals, and entropic forces.

The delivery of a drug by aquasome was attained through a combination of processes like specific targeting, molecular shielding, and sustained release process<sup>47</sup>. *In vivo*, biodegradation of aquasomes was achieved by monocytes and osteoclast. The phagocytosis of aquasomes was categorized into two i.e. 1) aquasomes taken up alone followed by its dissolution in the cytoplasm after the disappearance of phagosome membrane and 2) dissolution after the formation of heterophagosome<sup>37</sup>.

### Quantum dots

Quantum dots (QDs) are nanosized semiconductor crystals measuring only a few nanometers which are about the same size as a protein molecule or a short sequence of DNA. QDs with novel optical and electrical properties developed as a new strategy for nanomedicine with particular emphasis on diagnostics and therapy. In the presence of a light source, these quantum dots emit specific colors of light depending upon their size (band shift) and they are found to have size-tunable light emission (Figure 1).

They also offer superior signal brightness, high surface to volume ratio, resistance to photobleaching, and broad absorption spectra for simultaneous excitation of multiple fluorescence colors. These properties are responsible for many of its medical applications including cell labelling, biosensing, *in vivo* imaging, bimodal magnetic-luminescent imaging, *in vitro* diagnostics and as a gene-silencing tool (siRNA) etc. They are also involved in tumor or vascular imaging that can be approved for human clinical use.

For the identification of biomarkers in cancer stromal cells, Chunwei et al<sup>16</sup> developed a promising quantum dot-based tool, which is a probe-based multiplexed molecular imaging method.

Nanomedicine can employ various pathways for cellular entry, which involves penetration, endocytosis, and semi-endocytosis, and in the case of endocytosis, different mechanisms were available including phagocytosis and pinocytosis through clathrin-dependent and clathrin-independent pathways. QDs are more likely to utilize caveolae-mediated endocytosis, which is clathrin-dependent pinocytosis. It is reported that folate conjugated fluorescent

QDs are targeted towards tumor cells by means of receptor-mediated endocytosis.<sup>44,51,57</sup>

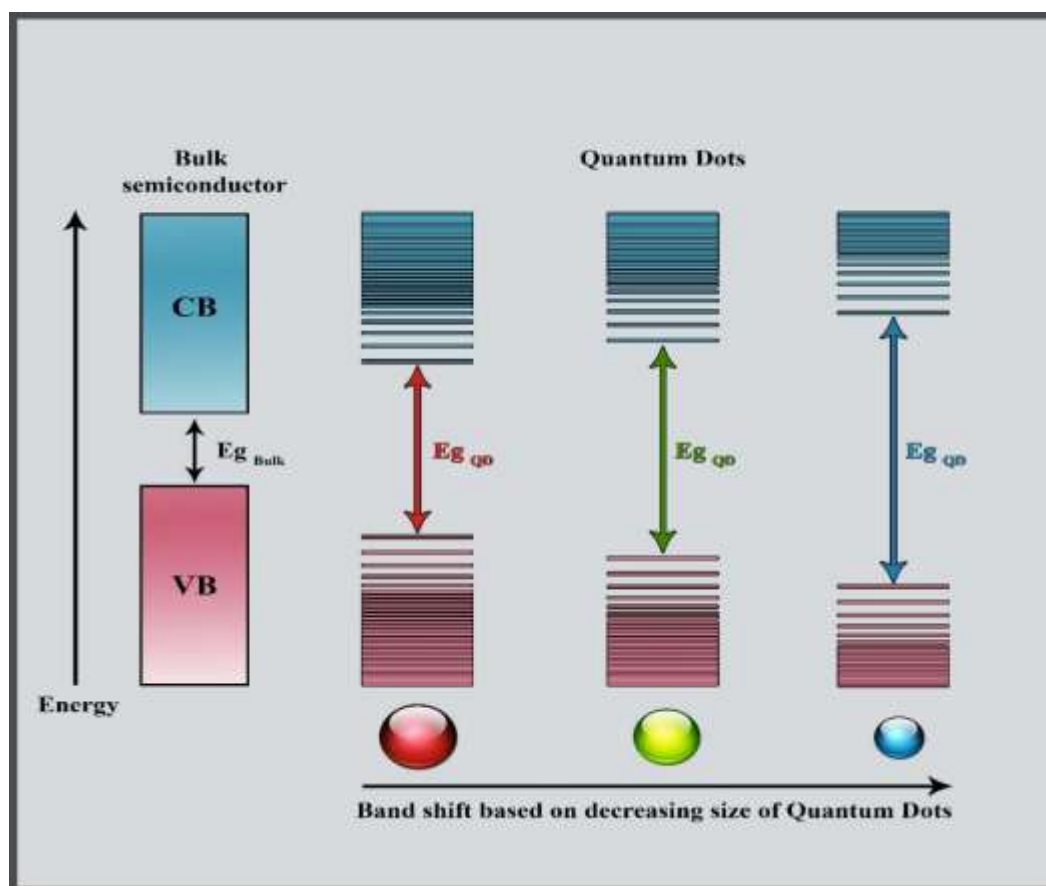
QDs can be surface functionalized with different compounds. For example, biotin antibody complexes with streptavidin functionalized Quantum Dots are used for *in vivo* cell labelling of membrane receptors, immune filtration assays etc. (Figure 2). Here the antibody will not be cleaved and retains the whole molecule attached to the quantum dot surface. The targeted delivery of QDs and QD conjugates is an indispensable necessity for selective imaging and effective therapy of cancer (Figure 3).

Receptors that are overexpressed in malignant conditions form ideal targets for delivering the drug in cancer cells. The various mechanisms for transporting and delivering QDs inside cells include both physical and biochemical techniques. Biochemical processes such as peptide, antibody and secondary antibody-based drug targeting are found to be the most promising tools for selective labelling of cancer cells with QDs. In contrast, physical techniques such as electroporation and microinjection have practical limitations in *in vivo* applications. QDs are a hopeful substitute for conventional fluorophores and photosensitive drugs and can be used in *in vivo* imaging and photodynamic therapy of cancer<sup>8</sup>.

Quantum dot-based theranostic drug delivery was newly developed to study the mechanism of drug delivery inside the cell<sup>4</sup>. QD-based micelle conjugated with anti-epidermal growth factor receptor (EGFR) nanobody (Nb) is reported to exhibit anticancer property due to the presence of an entrapped anticancer drug aminoflavone (AF)<sup>54</sup>.

QD bioconjugates can be delivered to tumors *in vivo* by both active and passive targeting mechanisms, although passive targeting is much slower and less efficient than active targeting. In the passive targeting mechanism, QD bioconjugates accumulate preferentially at tumor sites due to enhanced permeability and retention effect. This effect can be attributed to the fact that angiogenic tumors (i) produce vascular endothelial growth factors, which are responsible for enhanced permeability, (ii) lack an effective lymphatic drainage system, which results in QD bioconjugates accumulation.

On the other hand, in the active targeting mechanism, antibody-conjugated QDs are employed where the antibody gets attached to their specific tumor biomarkers such as prostate-specific membrane antigen present on the tumor cells at the target site.



**Figure 1:** Band shift based on decreasing size of Quantum Dots (QDs) i.e. the bandgap ( $E_g$ ) of the semiconductor nanocrystal increases with decreasing size, while discrete energy levels also increases at the band-edges. This size based optical property of QDs is due to the quantum confinement effect.

VB: Valence band; CB: Conduction band.

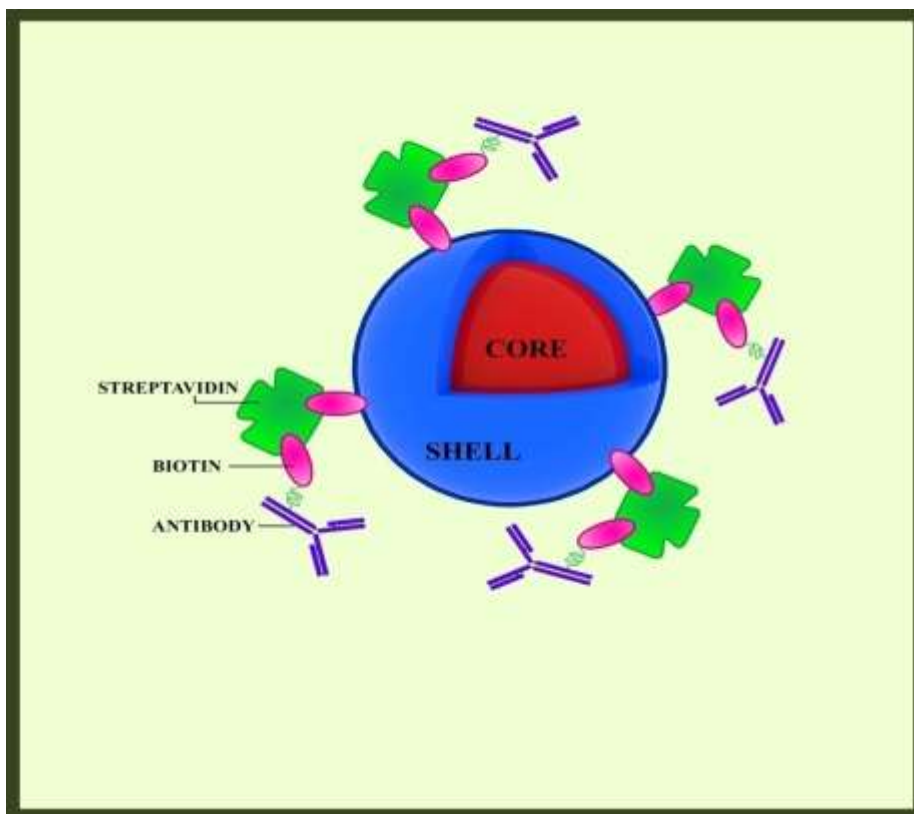


Figure 2: Schematic representation of Biotin-antibody complexes with streptavidin functionalized Quantum Dot.

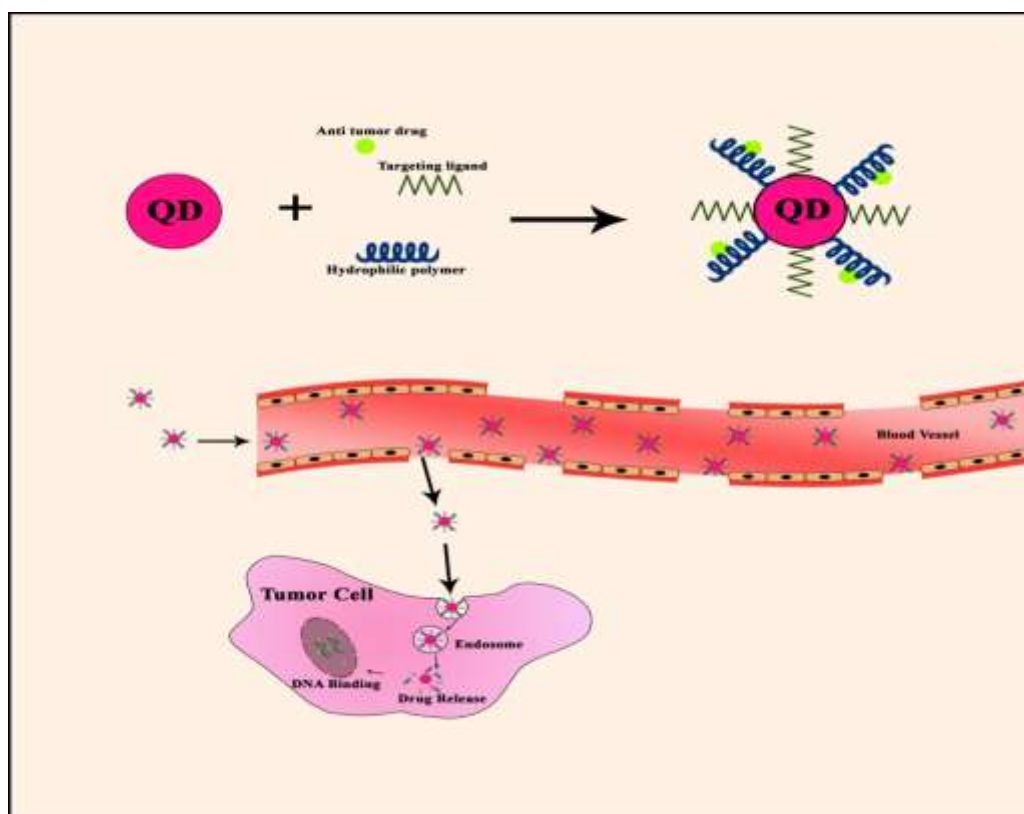


Figure 3: Quantum dot (QD) -based cancer therapy. The combination of different targeting ligands, imaging labels, therapeutic drugs, and many other agents can be used for targeted drug delivery to tumor cells. The enhanced permeability caused due to the vascular endothelial growth factors produced by the angiogenic malignant cells and retention due to lack of lymphatic drainage system cause QD bioconjugates to accumulate preferentially at tumor sites resulting in target specificity. There the QD conjugates are taken up by cellular endosomes followed by drug release inside the cellular micro environment.

## Metal Nanoparticles

Metal nanoparticles with improved characteristics such as high surface-to-volume ratio, broad optical properties, unique magnetic, thermal, catalytic and electrical property, facile surface chemistry and functionalization<sup>7</sup> may have the potential to address problems related to conventional chemotherapy. Conventional therapy may result in target non-specificity which may lead to many clinical outcomes like severe systemic toxic effects. Studies reveal that metal nanoparticle-mediated targeted delivery of drugs might significantly reduce the dosage of anticancer drugs with better specificity, enhanced efficacy and low toxicities. Metal nanoparticles are multifaceted agents with a variety of biomedical applications including different molecular diagnostic assays<sup>48</sup>, imaging, photothermal therapy, radiotherapy<sup>23</sup> drug and gene delivery<sup>42</sup> etc.

The highly tunable optical properties of noble metal NPs (e.g. gold, silver, copper or combination of these metal particles) make them suitable to accept wavelengths based on their shape (e.g. Spheroids, rods, triangle etc.), size (e.g. 1 to 100 nm), composition (e.g. core/shell or alloy noble metals) and dielectric environment<sup>28</sup>. In addition to this, the size of the nanoparticles enables them to interact with membrane proteins, enzymes, antibodies, peptides, DNA/RNA and other component of cells and allows the specific targeting of various tumor cells<sup>52</sup>.

Surface modification with biocompatible polymers (e.g., polyethylene glycol) helps to prolong their *in vivo* circulation of drug and its gene delivery applications<sup>20</sup>. Gold nanoparticles surface-functionalized with various biomolecules can be used for gene silencing, hyperthermia, radiotherapy, and drug delivery.

Recently Ru et al<sup>43</sup> studied the role of PEGylated hollow gold nanoparticles for combined X-Ray radiation and photothermal therapy for the treatment of cancer *in vitro*. It was also found that the modified particles help to develop an enhanced computed tomography (CT) imaging using breast tumor model.

Similarly, gold nanoclusters endowed with BSA and folic acids enhance the radiation efficiency for the treatment of intracranial glioma tumors<sup>27</sup>. PEG-coated AuNPs will retain in the blood vessels for a long time preventing the fast elimination of AuNPs from the body and allow the crossing of Blood Brain Barrier (BBB), thereby increase its therapeutic efficacy<sup>3</sup>.

L-DOPA-functionalized multi-branched gold nanoparticles also act as an efficient BBB penetrating nanomedicine for brain tumors as compared to the structurally similar gold nanoparticles functionalized with a non-targeting ligand. It was noted that brain macrophage could easily internalize L-DOPA functionalized gold nanoparticles without developing any inflammation<sup>21</sup>. CYT-6091 is an example of tumor necrosis factor (TNF)-alpha bound to PEG-coated gold

nanoparticles (~27 nm) developed by Cyt Immune Sciences, Inc. for therapy of solid tumors<sup>38</sup>.

Porcel et al<sup>39</sup> studied the combination of platinum nanoparticles with fast ions which play a key role in cancer therapy. Recently Manu et al<sup>35</sup> introduced a green chemistry approach to synthesize galactoxyloglucan functionalized AuNPs (PST-GNPs) with cancer-cell-specific toxic property.

Metal nanoparticles can efficiently convert photon energy or radio frequencies into heat using its nonradiative properties. This enables the damage of targeted cancer cells<sup>12</sup> by thermal effects like hyperthermia, coagulation, and evaporation<sup>14</sup>. Several types of metal nanoparticles exhibit the ability to develop heat at levels up to 70 °C through near-infrared light excitation or oscillating magnetic field stimulation<sup>13,25</sup>. The potential anticancer activity of metal nanoparticles mainly depends on several intrinsic and extrinsic factors.

This internal or intrinsic antitumor effect (antioxidant activity) will help the metal nanoparticles to prevent the tumor formation, its development and further progression of tumor<sup>3</sup>, while various extrinsic/external stimuli like infra-red or x-Rays, gamma rays and charged particles cause the production of free radicals which is fatal to cancer cells and also enhances the cytotoxic effect of ionizing radiations. Here the metal nanoparticles act as co-adjuvants<sup>17</sup>. Radiotherapy using metal nanoparticles (Gold nanoparticles) helps to increase the specificity of radiations to the targeted site which results in the reduced dose of radiations and ultimately helps to prevent the toxicity and damage to the healthy tissues<sup>26</sup>.

## Magnetic nanoparticles for cancer therapy

Recent developments in the field of oncology have shown remarkable progress with the use of magnetic nanoparticles (MNPs) in therapeutics. These nanoparticles possess many intrinsic magnetic properties such as tunable particle size, high surface energy, magnetic response, and superparamagnetism, which make them the most demanding contrast agents for magnetic resonance imaging (MRI) and induced magnetic hyperthermia. The magnetic nanoparticles are excellent materials for targeted drug delivery too.

Studies have proved that controlling the size and surface coatings of MNPs could reduce its toxicity and improve the magnetic behaviours of MNPs. Improving the drug loading capacity, increasing their specificity and affinity to target cancer cells, MNPs can be more suitable for clinical use with integrated imaging and multimodal therapy in the treatment of cancer which could create a profound impact<sup>36</sup> in future.

For most biomedical applications, the magnetic nanoparticles will mainly exist in the superparamagnetic state<sup>36</sup>. High surface to volume ratio of magnetic nanoparticles is fully exploited when they are used as drug

delivery agents and *in vivo* targeting of these drugs to the desired specific location is possible due to the presence of the external magnetic field. MNPs can be used in several different therapeutic methods such as chemotherapy, magnetic hyperthermia (MHT)<sup>56</sup>, photodynamic therapy (PDT)<sup>32</sup> and photo thermal therapy (PTT)<sup>49</sup>.

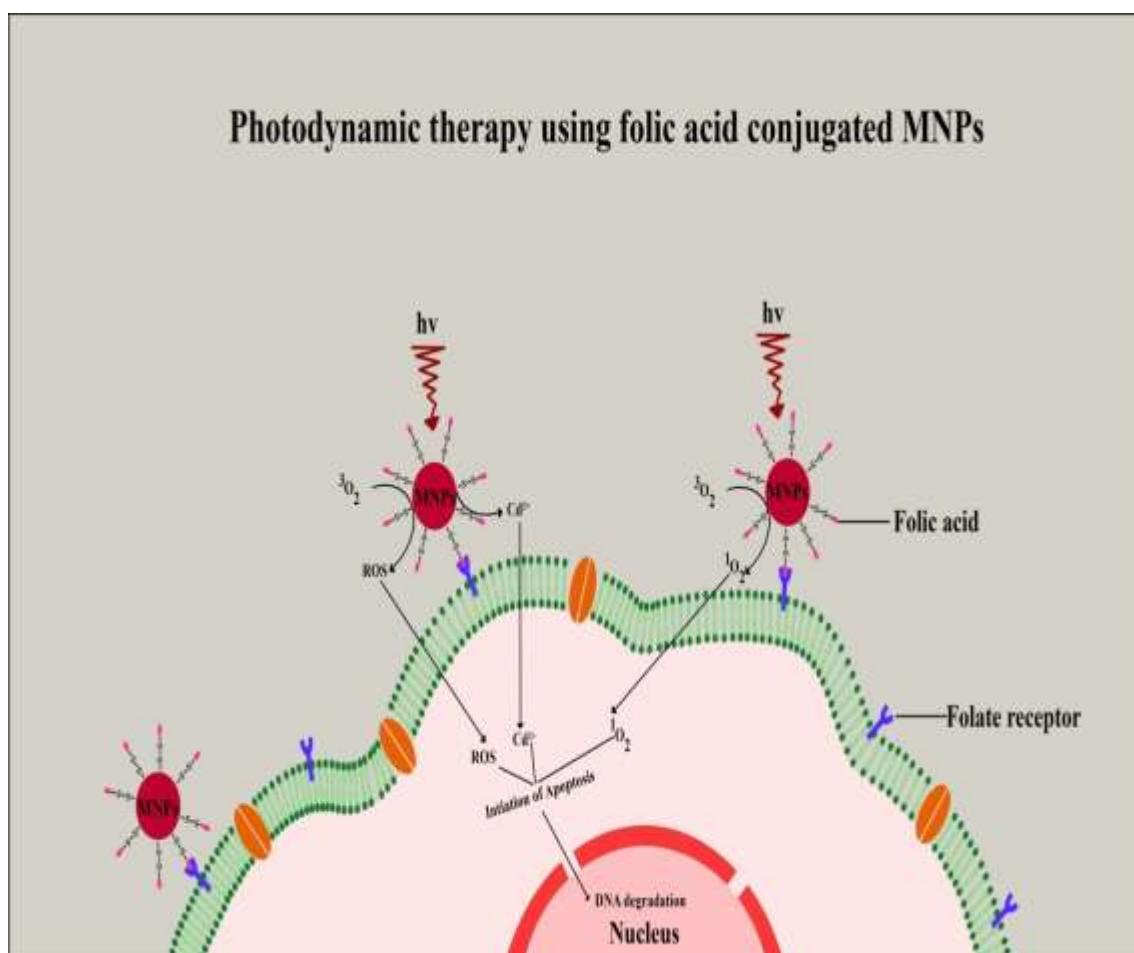
Though early detection of cancer can be achieved by MRI, individualized treatment combined with MRI can impart proper and increased efficacy treatment for cancer. The most commonly used magnetic nanoparticles are small iron oxide nanoparticles (~20 nm), which include magnetite ( $\text{Fe}_3\text{O}_4$ ) and maghemite ( $\gamma\text{-Fe}_2\text{O}_3$ ).

They are able to invade tumors and kill cancer cells by generating heat under magnetic fields. Chen et al<sup>11</sup> studied the possibility of using a reducible copolymer (polyamidoamine) self-assembled with superparamagnetic iron oxide nanoparticles (SPIONS) as a magnetic nanovector to deliver doxorubicin and other therapeutic drugs for cancer therapy. In another study, Manjili et al<sup>34</sup> used iron-gold core-shell as a contrast agent in radiation therapy of breast cancer. The magnetic mediators, due to their better temperature homogeneity and magnetic properties, have

applications in cancer hyperthermia treatment. Superparamagnetic iron oxide NPs<sup>30</sup>, various iron oxide-based NPs such as  $\text{MFe}_2\text{O}_4$  ( $\text{M} = \text{Co}, \text{Ni}, \text{Mn}, \text{Zn}, \text{Cu}, \text{Mg}$  etc.) and lanthanum strontium manganese oxide (LSMO) are among some of them. So far, magnetic iron oxide-based NPs dominate hyperthermia treatment in cancer as a heating mediator<sup>45</sup>.

The synergistic effect of iron oxide magnetic nanoparticle with photosensitizer (PS) molecule can be utilized for photodynamic therapy (PDT). PDT is a non-invasive treatment, and its treatment modality is purely based on the administration of a photosensitizer to the superficial tumor site. Irradiating with visible-near infrared light, it generates reactive oxygen species (ROS)/singlet oxygen, which cause fatal effects to the cancer cells in a moderate way.

But the short lifetime of ROS, the lack of selectivity of PDT and minuscule laser permeability etc. demand the necessity of new therapeutic strategy. The combination of magnetic iron oxide nanoparticle with photosensitizer is a new and promising PDT approach, which is able to compensate these encumbrances (Figure 4).



**Figure 4:** Photodynamic therapy using folic acid conjugated magnetic nanoparticles (MNPs). Folic acid specifically binds to folate receptors which are specialized markers that distinguishes cancer cells from normal cells. Folic acid conjugated with MNPs targets to the superficial tumor site and when irradiated with visible-near infrared light it generates reactive oxygen species (ROS)/singlet oxygen, causing deleterious effects to the cancer cells.

Choi et al<sup>15</sup> designed magnetic submicron cobalt ferrite particles conjugated with a photosensitizer containing folic acid-(FA) and hematoporphyrin (HP) used as effective anticancer agents for PDTPs-FAs in prostate cancer cells (PC-3 cells). In addition to this, magnetic nanoparticle clusters were reported for the photothermal ablation of cancer cells. Here the photothermal effect of the nanoparticle is utilized for cancer therapy<sup>50</sup>. Recently in Photodynamic therapy (PDT) mediated cancer treatment, using external beam irradiation and a nanoparticle scintillator as the transducer, the early prevailing shallow penetration issue has been resolved. Great success has been achieved by using nanoparticles as either a scintillator or as a photosensitizer to mediate energy transfer and radical production in PDT<sup>6</sup>.

## Conclusion

Nano based therapeutics has provided a robust system that may be used for treatment and diagnosis of cancer. Advances in nanotechnology proved that nanomaterials are highly potent soldiers for defeating cancer. With the use of various drug loaded nanodevices conjugated to ligand/antibodies, the possibility of simultaneous detection of multiple molecular targets/biological molecules in small tumor samples increased and nano-particles based *in vivo* imaging could allow simultaneous detection of cancer-related antigens.

Ongoing studies on its properties hold a futuristic relevant biomedical scenario for nanomaterials and the interplay of nanoparticles between therapy and diagnostics can contribute immensely to the theranostic platform in medicine in near future.

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