Utilisation of nanotechnology in cancer treatment

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Abstract- **Nanotechnology is a science that has novel approaches to enhance the potential of drug delivery systems at the molecular level (1 to 100 nanometers). The development of nanotechnology is based on the use of small molecular structures and particles as tools for delivering drugs. Nonocarriers Such liposomes, polymeric micelles, carbon nanotubes, dendrimers, and quantum dots of gold nanoparticles have been mostly used in cancer treatment. Nanotechnology in cancer treatment improves pharmacokinetics and reduces the systemic toxicities of traditional cancer treatments. Nanotechnologies and nanomedicines are concerned with cancer treatment at the molecular level as detection of cancer cells, malignant tumors, and they provide great targeting drug delivery with minimizing unwanted toxicity.**

Keywords: **Nanotechnolog, Nanoparticles, Cancer treatment, Nanomedicine, Drug delivery, Targeted therapy, Controlled release.**

Introduction:

About 10 million people die from cancer each year, making it a major public health concern with an incidence and mortality that are both rising quickly globally1.2. Because of its current great efficiency, chemotherapy is one of the most widely used anti-cancer therapies.3, 4, Practical constraints have been brought about by its lack of selectivity for tumor cells and difficulties in delivering drugs to the tumor location efficiently. Furthermore, multi-drug resistance presents a further challenge to effective treatment.(5)The nonspecific distribution of conventional chemotherapeutic medications causes them to impact both healthy and malignant cells in the body, leading to dose-related side effects and insufficient

amounts of medication that reach the tumor. Effective anticancer therapy is seriously hampered by non-specific drug distribution, which causes major difficulties. Furthermore, the incidence of resistance phenomena lowers the effectiveness of cancer treatments. Many ligand-targeted treatment approaches, including as drug immunoconjugates, radioimmunotherapeutics, and immunotoxins, are being developed to address the lack of specificity of traditional chemotherapeutic medicines.(4)Nanotechnology is any artificially created technology at the nanoscale that has use in the modern world. Rearranging and rearranging matter in sizes ranging from 1 to 100 nm is what it comprises. Both on a larger and nanoscale, differences in the characteristics of matter were observed. characteristics are constant at first, but as the size drops below 100 nm, negative effects on characteristics are observed. The physical and chemical features of nanoparticles can be used for new and profitable purposes that benefit society. Two primary approaches are encompassed by nanotechnology: top-down and bottom-up. When there is no atomic-level control, the top-down method reduces bigger structures into smaller components.(1) Recent years have seen a significant increase in interest in the use of nanotechnology in the healthcare industry. Nowadays, there are a variety of time-consuming and highly expensive therapies available. Nanotechnology can be used to generate therapies that are more faster and less expensive. Furthermore, using nanotechnology to medicine has additional benefit. Through the application of nanotechnology, a medication may be precisely targeted, increasing its effectiveness and decreasing the likelihood of adverse effects. Although there are numerous medications available to treat cancer, which is one of the most common illnesses, employing a nanotech-based strategy boosts activity while significantly lowering negative effect profile . Our goal in this study is to talk about the nanotech-based strategy, namely the application of NPs and their many forms in the delivery of anticancer drugs.(6) Nanotechnology is any technology that is created at the nanoscale and has application in the modern world. It involves rearranging and rearranging materials with a size range of 1 to 100 nm.(7) Both the bigger and nanoscales were thought to have different characteristics of matter. While qualities are constant at this early stage, drastic changes in attributes were seen as the size drops below 100 nm. Nanoparticles' physical and chemical characteristics can be used for new and profitable purposes that benefit society.(8,9) Two primary approaches are covered by nanotechnology: top-down and bottom-up. If atomic-level control is not available, the top-down method reduces bigger structures into smaller components. It provides lithographic and non-lithographic technologies for the formulation of micro- to nanoscale components. Materials created by atomic and molecular elements through chemical synthesis, roll-to-roll processing, self-assembly, etc. are included in the bottom-up methodology.(10)

History of Nanotechnology:-

Emerging science and technology are frequently the result of human imagination and dreams. Born out of such ideals is nanotechnology, a frontier of the twenty-first century. Understanding and manipulating matter at sizes between 1 and 100 nm, where special phenomena allow for new uses, is known as nanotechnology.1. While human exposure to nanoparticles has always existed, the industrial revolution saw a sharp rise in this exposure. Nanoparticle research is nothing new. The chemistry Nobel laureate Richard Zsigmondy initially put up the idea of a "nanometer" in 1925. He was the first to use a microscope to measure the size of particles like gold colloids and he also created the word "nanometer" specifically for the purpose of defining particle size. The inventor of modern nanotechnology is physicist Richard Feynman, winner of the 1965 Nobel Prize in Physics. He first proposed the idea of atomic-level matter manipulation in a talk titled "There's Plenty of Room at the Bottom" at the 1959 American Physical Society conference at Caltech. This innovative concept opened up new avenues for thought, and Feynman's theories have since been validated. He is regarded as the founding father of contemporary nanotechnology because of these factors.

The term "nanotechnology" was first used by Japanese scientist Norio Taniguchi, over 15 years after Feynman's presentation, to characterize semiconductor processes that took place on the order of a nanometer. He promoted the idea that materials may be processed, separated, consolidated, and deformed by one method in nanotechnology.(13). Michael Faraday investigated the creation and characteristics of colloidal suspensions of "Ruby" gold in 1857. They are among the most intriguing nanoparticles due to their distinct optical and electrical characteristics. Faraday gave an example of how gold nanoparticles may create solutions with diverse colors. in specific lighting circumstances [18]. Figure 1 summarizes how nanotechnology has advanced as a result of the benefits of nanoscience.(11)

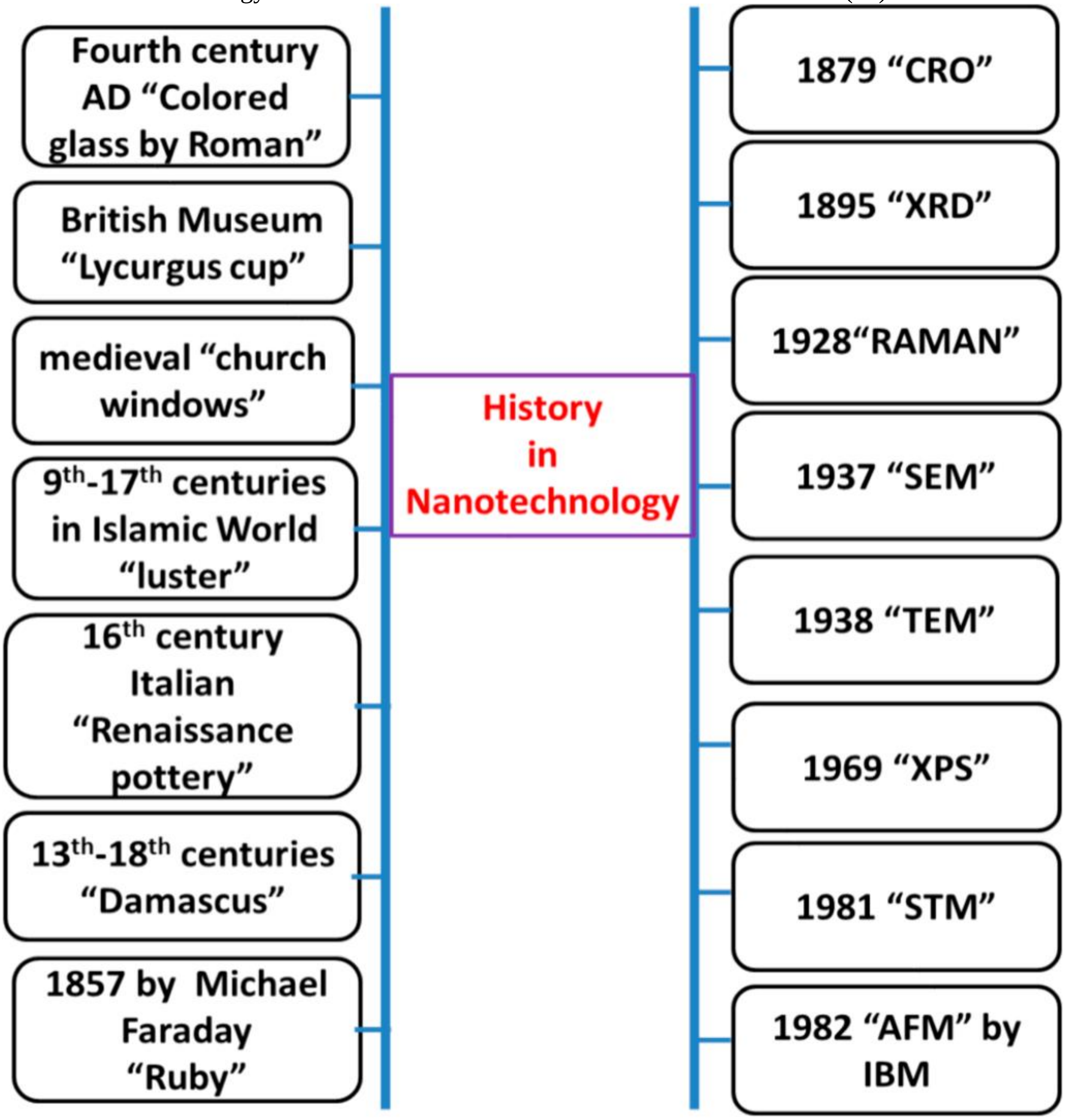

Figure 1: Nanotechnology Advances

One of the most intriguing instances of nanotechnology in antiquity was displayed by the Romans in the fourth century AD, when they used nanoparticles and structures.

The Lycurgus cup, housed at the British Museum, is a remarkable example of the achievements made in the ancient glass industry. This is the first known instance of dichroic glass. Dichroic glass refers to two distinct varieties of glass that exhibit color changes under specific lighting conditions. This indicates that the Cup has two distinct colors: when light shines through the glass, it appears reddish-purple, and when it is green in direct light.(12)

Figure 2. The Lycurgus cup. The glass appears green in reflected light (**A**) and red-purple in transmitted light (**B**). Reproduced with permission from reference

cancer and its causes:-

There are various factors that can lead to cancer in different parts of the body. For example, tobacco use accounts for 22% of deaths, while poor diet, obesity, inactivity, and excessive alcohol consumption account for 10% of deaths. Other factors include specific exposure to ionizing radiation, environmental pollutants, and infections. Hepatitis B, hepatitis C, human papillomavirus infection, helicobacter pylori, immunodeficiency virus (HIV), and Epstein-Barr virus are among the illnesses that cause around 15% of cancer cases worldwide. These are the ones that alter the genes, at least in part.(15)

Table 1: Some of the Factors Causing Cancer(14)

Name of cancer	Causes
1.Brain Cancer	Ionizing radiation [Strong], Chromium [Good], methylene chloride [Good]
2. Melanoma	UV radiation [Strong]
3. Thyroid Cancer	Ionizing radiation [Strong], ethylene thiourea (ETU) [Good]
4. Bone Cancer	radium [Strong], Pesticides [Good]
5.Colo-rectalCancer	1,1-dichloroethane [Good], alachlor [Good], Aromatic amines [Good], Chlorination by-products [Good]. [Good], Solvents [Good]
6. Prostate Cancer	Agent Orange [Good], Aromatic amines [Good], methyl bromide [Good], Organ chlorine pesticides [Good], PAHs [Good], Pesticides [Good], Solvents [Good]

7. Leukemia's benzene [Strong], Ionizing radiation [Strong], Agent Orange [Good], carbon tetrachloride [Good], Chlorinated solvents [Good], Metal dusts [Good], Pesticides [Good], Secondhand smoke [Good], trichloroethylene (TCE) [Good]
8. Liver Cancer aflatoxin B1 (Aflatoxins) [Strong] androgens [Strong], ethyl alcohol (ethanol) [Strong], Hydrocarbons [Strong], N-nitrosodimethylamine [Strong], arsenic [Good], captafol [Good], PCBs [Good].

A precancerous lesion usually develops into a malignant tumor over the course of several stages, during which time normal cells can turn into tumor cells and cause cancer.

The issue In 2020, cancer will be the primary cause of mortality globally, accounting for around 10 million fatalities (1).

In terms of new cancer cases in 2020, the most prevalent were: There were 2.26 million instances of breast cancer, 2.21 million cases of lung cancer, 1.93 million cases of colon and rectum, 1.41 million cases of prostate cancer, 1.20 million cases of non-melanoma skin cancer, and 1.09 million cases of stomach cancer.

In 2020, these were the leading causes of cancer-related deaths: liver (830 000 deaths), stomach (769 000 deaths), colon and rectum (916 000 deaths), lung (1.80 million fatalities), and breast (685 000 deaths). Approximately 400 000 youngsters are diagnosed with cancer every year. The most prevalent malignancies differ throughout nations. In 23 nations, cervical cancer is the most frequent kind.

Nanotechnology for Detection of Cancer Cells or Circulating tumors cell(CTC):- Identification of Tumor Cells in Circulation

Almost 90% of deaths from solid tumors are caused by metastasis. A cancer cell from the original tumor first invades the surrounding tissue during metastatic dissemination. It then invades the microvasculature of the blood and lymph systems, survives, and moves through the circulation to micro-vessels in other tissues. Ultimately, these cells extravasate from the circulation and thrive in the remote milieu, which offers an appropriate foreign microenvironment for the growth of secondary tumors. Early detection of CTCs, or metastatic cancer cells in the circulation, can significantly affect the prognosis and diagnosis of cancer(16).

Because of their potential uses, CTCs have been thoroughly studied as a component of a liquid biopsy. One non-invasive technique for comprehending the molecular structure of malignancies is CTC detection. Notwithstanding this, CTC diversity and abundance are modest, creating technical challenges for CTC characterisation and separation. In recent years, researchers have concentrated on using nanotechnologies for the sensitive detection of CTCs; these technologies can aid in the characterization of cells and molecules, leading to a variety of clinical applications, including early disease detection, assessment of treatment response, and tracking the progression of the disease.(17)

The huge surface-to-volume ratio of nanomaterials makes them advantageous for CTC detection because it facilitates the adsorption of highly efficient targeting ligands that are able to identify certain chemicals on cancer cells. CTC separation benefits from excellent specificity and recovery as well as increased detection sensitivity.(17)

Drug Targeting Mechanism in Cancer Nanotechnology :-

Drug targeting methods come in two flavors: passive targeting and aggressive targeting. The rapidly expanding leaky vascularization and impaired lymphatic drainage that lead to the retention of nanoparticles and submicron particles in tumors are the causes of increased permeability and retention (EPR) based medication targeting in passive targeting. Drug delivery for this particular strategy in cancer treatment is being thoroughly researched using nanoscale drug carriers, such as liposomes, dendrimers, polymeric micelles, polymer-drug conjugates, and inorganic nanoparticles.(18)Since these nanoparticles are tiny (usually ranging from 1 to 200 nm), they are able to pass through hyper-permeable blood arteries and, through their enhanced photoluminescence (EPR) effect, preferentially aggregate at the tumor site.(19)

The active targeting strategy's fundamental mechanism is the interaction of a drug carrier loaded with a ligand with target cells' surface-exposed receptors, which promotes both the target cells' intracellular accumulation through receptor-mediated endocytosis and their accumulation within a tumor.(20) Normally, one or more types of particular receptors that are overexpressed in tumor cells can serve as target locations for active targeting by ligand-functionalized nanoparticles. Because of this, cellular targets are used in an active targeting strategy to identify the tumor and endothelial cells.(21,22)

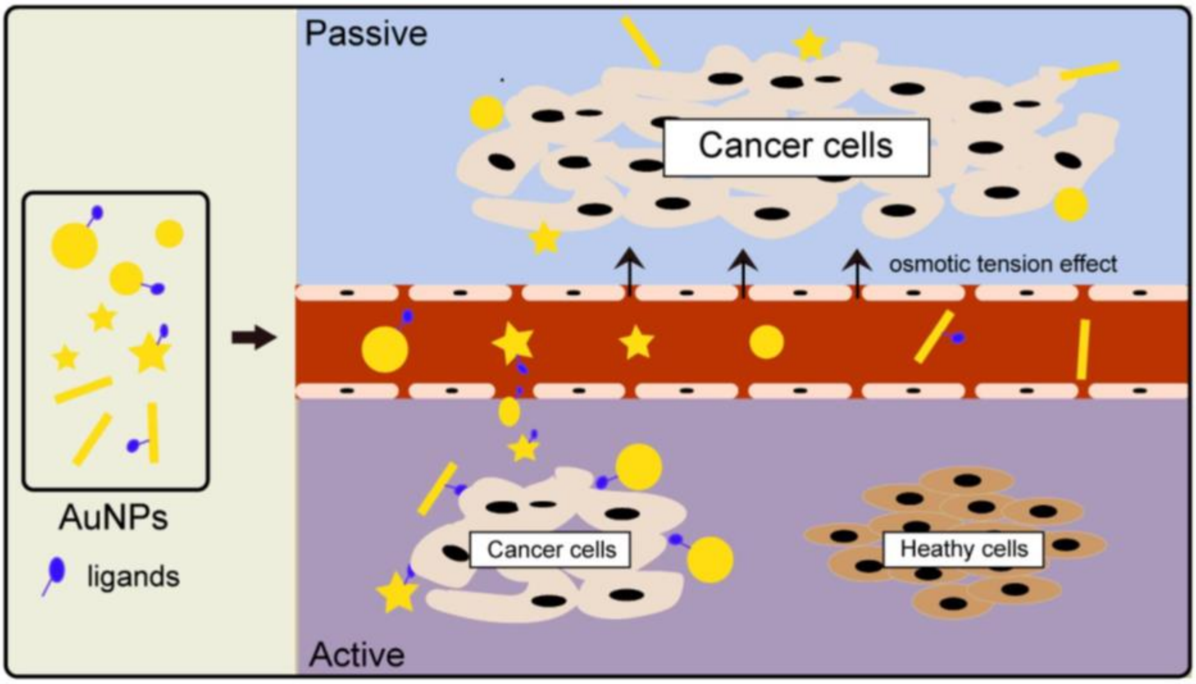

Figure 3. Various types of gold nanoparticles (different sizes, morphologies, and ligands) accumulate in tumor tissues by the action of osmotic tension effect (termed Passivetargeting) or localize to specific cancer cells in a ligand-receptor binding way (termed Active targeting).(23)

Nanotechnology Tools for Cancer Diagnosis and Therapy :-
Liposomes
One of the most researched nanomaterials is liposomes, which are tiny spheres made of water phase nucleus and phospholipid bilayer membranes, either naturally occurring or artificially synthesized. Liposomes occur naturally because phospholipids are amphiphilic.(24)
Hydrophilic medications are able to remain in the monolayer liposome while hydrophobic drugs develop in the multilayer liposome first[25]. By switching them from an acidic buffer to a neutral buffer, several medications might be included into liposomes. Liposomes can also be used to transport neutral medicines, however they are not easily released from within the liposomes because of their weak avidity for acidic environments [26]. Saturated medicines can also be combined with organic solvents to generate liposomes, which is another method of drug administration [24]. A vesicle of 4000 kDa, or 500 nm in size, may be able to enter the tumor through the pores in the arteries due to the EPR effect[26].

Polymeric Micelles
What's known as polymeric nanoparticles (PNPs) is the development of a solid micelle with a particle between 10 and 1000 nm in size[27]. PNPs, often referred to as polymer micelles, nanospheres, nano-capsules, or nanoparticles, were the first polymers to be identified for use in drug delivery systems.

PNPs are often employed in drug discovery processes and act as drug carriers for hydrophobic pharmaceuticals [28–30]. Because of the hydrophobic interactions in an aqueous solution, PNPs made of amphiphilic polymers with a hydrophilic and hydrophobic block may self-assemble quickly[30]. Because of a covalent link or a connection through a hydrophobic core, PNPs are able to bind and capture hydrophobic medicines. Therefore, these blocks are flipped to enable connections in order to carry the hydrophilic charged molecules, such as proteins, peptides, and nucleic acids.(28)

Carbon nanotubes
Carbon nanotubes (CNTs) may be divided into two types based on their diameter and structure: single-walled CNTs (SWNTs) and multiwalled CNTs (MWNTs)[31]. Concentric graphene makes up the MWNTs, whereas monolithic cylindrical graphene makes up the SWNTs[31]. Carbon nanotubes are a promising contender for extensive biological applications because to their physical and chemical characteristics, which include surface area, mechanical strength, metal properties, electrical and thermal conductivity, and so on[32]. Additionally, carbon nanotubes have the ability to

absorb light in the near-infrared (NIR) range. This allows the nanotubes to target tumor cells by heating up due to the thermal effect[33–34].

Atomic Drops

Quantum dots (QDs) are nanocrystals, or tiny particles, of semiconductor materials that range in size from two to ten nanometers[36]. The QDs' intermediate electron property, which lies between that of a mass semiconductor and a discrete atom, is determined by the ratio of the height of the surface to the volume of these particles [89]. Numerous QD-based methods, including QD immunostaining and QD conjugate modification, have been developed throughout time. The speed and cost-effectiveness of QD conjugation significantly outperforms the monochromatic experiment thanks to the advancement in multiplexing capability [35].

Moreover, QD immunostaining is more accurate than conventional immunochemical techniques in low context and low protein expression levels. In When diagnosing cancer, QD immunostaining may be used to find different tumor biomarkers, including a cell protein or other elements of a mixed tumor sample[35].

Certain bodily sections can attract quantum dots, which then carry the medications to those areas. Because QDs may concentrate in a single internal organ, they may be able to prevent chemotherapy adverse effects and provide a possible defense against untargeted drug delivery. The most recent development in QD surface modification allows for the targeting of tumors and opens the door to new uses in cancer imaging and therapy. QDs mix with biomolecules, such as peptides and antibodies, in vivo. While QDs are used in some studies to flag cancer using prostate-specific antigen, others employ them to create immunological biomarkers that speed up the process and have a more steady light intensity than conventional fluorescent immunomarkers[36].

Nanoshells

Nanoshells, a type of dielectric core between 10 and 300 nanometers in size, are typically made of silicon and coated with a thin metal shell (usually gold) [36, 37]. These nanoshells convert plasma-mediated electrical energy into light energy and can be tuned optically through UV-infrared emission/absorption arrays. Nanoshells are desirable for their non-destructive imaging.(38)

Dendrimers

Dendrimers, branching and highly structured macromolecules, show promise in cancer research and therapy for a variety of applications.

Drug Delivery:- Dendrimers can encapsulate and transport anticancer medications to particular cells or tissues. Their structure allows for regulated release, which increases the therapeutic efficacy of the medications while reducing adverse effects.

Imaging: Dendrimers can be functionalized with imaging agents, allowing for accurate tumor visualization using techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET). This helps to diagnose and monitor cancer at an early stage.

Photodynamic Therapy (PDT): Dendrimers can be used as photosensitizer carriers. When exposed to light, these photosensitizers produce reactive oxygen species that preferentially kill cancer cells.

Gene Delivery: Dendrimers can be utilized to transport therapeutic genes to specific cells. This is useful in gene therapy techniques for cancer treatment, which seek to modify the expression of certain genes in order to suppress tumor development.

Theranostics: Dendrimers that combine therapeutic and diagnostic functions (theranostics) provide a versatile approach. They can administer medications while also offering imaging capabilities for real-time monitoring of therapy response.

Dendrimers' special features make them useful in the creation of targeted and individualized cancer treatments.(39,40)

Gold nanoparticles

Gold nanoparticles (GNPs) have potential in cancer research and treatment. They can be utilized in a variety of ways.

Diagnostic Imaging: GNPs improve procedures such as computed tomography (CT) and photoacoustic imaging. They enhance contrast, making tumors easier to identify and see.

Drug Delivery: GNPs can be functionalized to transport chemotherapeutic medicines directly to cancer cells. This focused medication delivery reduces harm to healthy tissues, increasing therapy efficacy while lowering adverse effects.

Photothermal Therapy: GNPs absorb light and convert it to heat, which is known as photothermal conversion. When GNPs are specifically transported to tumor cells and subjected to near-infrared light, they produce heat, killing the cancer cells while preserving healthy tissue.

Radiotherapy Enhancement: GNPs can improve the efficiency of radiotherapy. When paired with radiation, they increase the dosage supplied to cancer cells, which improves therapy results.

These applications demonstrate the adaptability of gold nanoparticles in cancer research, providing diagnostic and therapeutic advantages.(41,42)

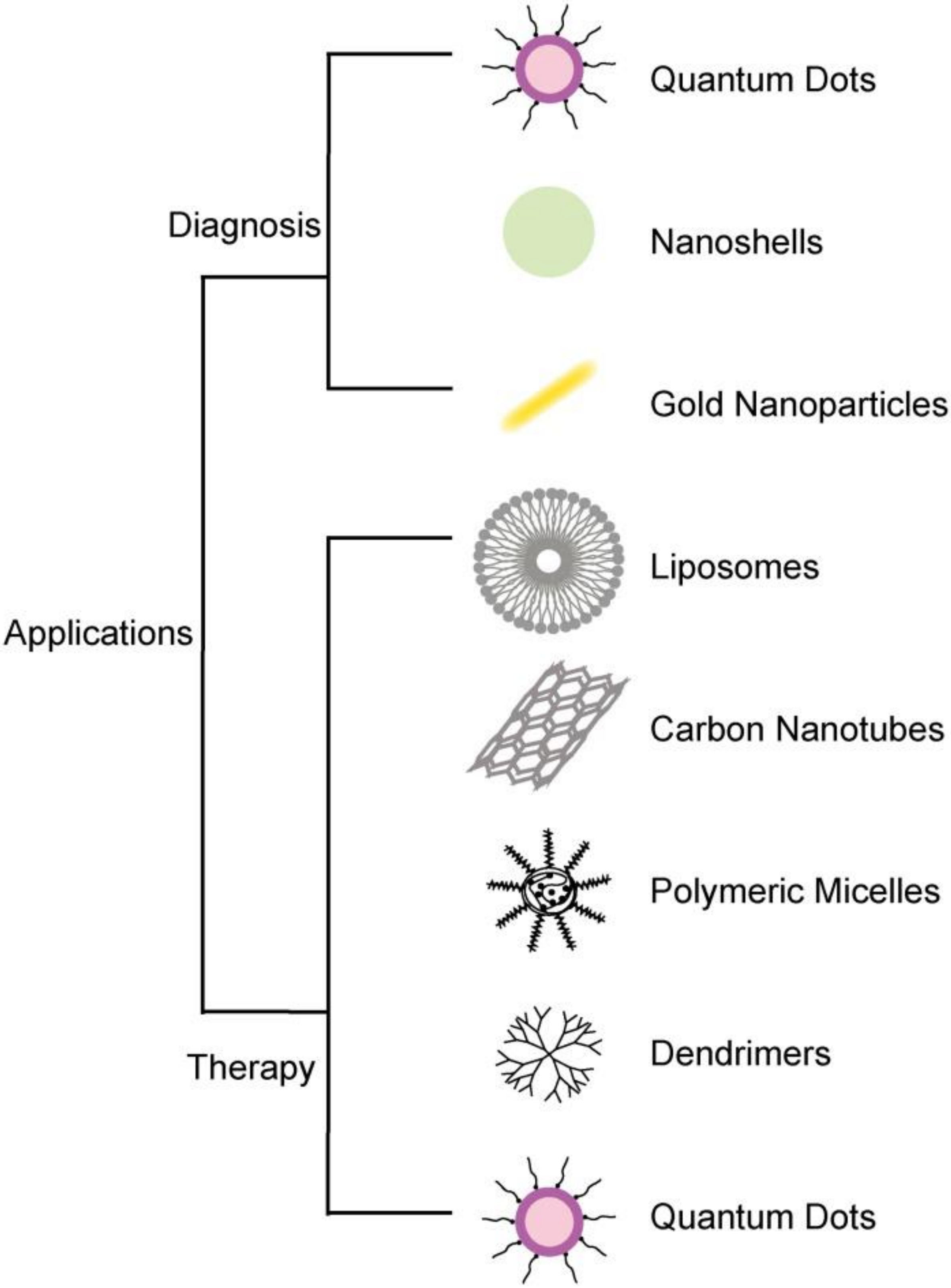

Figure 4. Application of nanomaterials in cancer diagnosis and therapy(23)

Conclusion:

In conclusion, nanotechnology has emerged as a promising and multifaceted tool in cancer therapy. Nanoparticles, including gold nanoparticles and dendrimers, offer unique properties that can be harnessed for both diagnostic and therapeutic purposes. These nanomaterials enable targeted drug delivery, enhance imaging techniques, and provide innovative approaches such as photothermal therapy and gene delivery. The ability to tailor nanoparticles for specific applications contributes to the development of more effective and personalized cancer treatments. While challenges remain, the progress in nanotechnology applications underscores its potential to revolutionize cancer therapy by improving treatment precision, minimizing side effects, and advancing early detection methods. Ongoing research and development in this field hold the promise of further innovations, paving the way for more efficient and tailored cancer care.

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