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Cancer Nanotechnology: Nanotechnology-Based Drug Delivery Approaches For Cancer

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ABSTRACT

Cancer continues to be one of the deadliest diseases and a leading cause of death globally. Detecting it early and providing prompt treatment are crucial strategies in combating cancer. Over the last few years, progress has been made across the nanomedicine landscape, in particular, the invention of contemporary nanostructures for cancer diagnosis and overcoming complexities in the clinical treatment of cancerous tissues. Nanomedicine is a prominent area of nanotechnology research that applies nanoscale techniques to create precise medical solutions for diagnosing, preventing, and treating diseases. Nanotechnology offers targeted release of drugs that maximizes the therapeutic index and minimizes system toxicity. Because of its wide-ranging uses, nanotechnology holds great potential for identifying cancer cells, detecting cancer biomarkers, and providing effective treatment. Nanomedicines improve drug bioavailability and reduce systemic toxicity, offering more effective and precise cancer therapies. This review offers an in-depth analysis of different approaches in nano-delivery systems for chemotherapy drugs. It highlights how nanoparticle-based carriers enhance drug targeting, improve therapeutic effectiveness, and reduce side effects by selectively delivering anticancer agents to tumor tissues. This review discusses the ability of nanotechnology to overcome drug resistance mechanisms, thereby paving the way for the development of more effective and safer anti-tumor drugs.

Keywords: *Nanotechnology, Cancer, Nanoparticles, Treatment, Tumor, Nanomedicine, Drug targeting*

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1. INTRODUCTION

Cancer is a group of diseases characterized by uncontrolled growth of cells that can invade nearby tissues and spread to other parts of the human body, a process known as metastasis. A major cause of death and a burden on world health is cancer. By 2018, it was predicted that there would be 9.6 million cancer-related deaths and 18.1 million newly diagnosed cancer cases (Jin *et al*., Wang *et al*., 2020). Preventive measures play a crucial role in reducing cancer incidence and mortality. Cancer treatment includes surgical removal, chemotherapy, radiation, and hormone therapy (Sutradhar *et al*., Amin *et al*., 2014). Cancer symptoms, any sore that does not heal, Thickening or lump in the body, Obvious change in a wart or mole, Unexplained bleeding or discharge, Changes in bowel or bladder habits, Cough or hoarseness that does not go away, Unusual upset stomach or difficulty in swallowing (Goyal *et al*., Kumar *et al*., 2014). Cancer can be classified into various types based on the origin of the cells. Here are the main categories Carcinomas, Sarcomas, Leukemias, Lymphomas, Melanoma, Central Nervous System (CNS) Cancers, Germ Cell Tumors, Myeloma. Here are numerous other specific cancer types categorized by location or cell type, including: Thyroid Cancer- Liver Cancer- Kidney Cancer.

The progress of nanotechnology-based screening techniques has led to target-based drug development regimens which increase the survival rate of cancer patients (Vlad *et al*., Kubelac *et al*., 2015). Therapeutic agents are becoming highly specific and have a high affinity for various molecular targets, depending on the malignancy's genotype and phenotype (Herbrink *et al*., Nuijen *et al*., 2015). Treatments for cancer include adjuvant/neo-adjuvant surgery, radiation, and a variety of combination chemotherapy medications. Unwanted side effects are the primary disadvantages of chemotherapy. Therefore, intensive research is carried out to develop novel therapeutic formulation using specific nanoparticles for targeted delivery in order to avoid the cytotoxic effects on healthy cells (Banu *et al*., Sethi *et al*.,2015). Nanoparticle-based drug delivery systems show remarkable progress due to their ability to have a "controlled-release reservoir", which can safely deliver therapeutic agents to injury sites or specific cells (Fujita *et al*.,2015, Kleinstreuer *et al*., 2013). For safe use in medicine, nanoparticles must be biocompatible, that is, able to integrate within a biological system without causing immune response or negative side effects when the construct is directly released either into the tumor or into the bloodstream (Wilczewska *et al*., Niemirowicz *et al*., 2012). Nanoparticles must also provide controlled drug release, increase the therapeutic agent's protection and circulation time and thus decrease toxicity to healthy cells (Shahin *et al*., Soudy *et al*., 2013). This can lead to enhanced permeability and retention (EPR) effect (Lee *et al*., Yip *et al*., 2015).

Nanoparticles are used in medicine to improve bioavailability, (Jain *et al*., 2014, Tomuleasa *et al*., 2014) to enhance the delivery of therapeutic agents (Kim *et al*., Djazayeri *et al*., 2011) or to develop novel imaging techniques, (Ajnai *et al*., 2014; Tomuleasa *et al*., 2014) in order to assure the control of biological systems for single molecules or groups of molecules (Wang *et al*., Chen *et al*., 2011). A wide range of nanostructures such as liposomes, nano-diamonds, quantum dots, peptides, cyclodextrin, carbon nanotubes (CNTs), graphene and metal-based nanoparticles are used for diagnostic or therapeutic purposes (Song *et al*., Tarrant *et al*., 2015). Nanoparticles have the potential to improve the effectiveness of treatment, decrease the severity of adverse effects on healthy tissues, and promote the accumulation and diffusion of pharmacologically active medications at the location of tumor cells. It is feasible to combine medicinal and diagnostic substances into a single nanoparticle because of the inherent characteristics of nanoparticles (Baetke *et al*., 2015, Irimie *et al*., 2015).

Nanoparticles loaded with numerous anti-cancer medications, including carboplatin, doxorubicin, paclitaxel, rituximab, lestauritinib, and tyrosine kinase inhibitors, has the ability to treat a variety of cancers with a higher therapeutic efficacy than free chemotherapeutics. For most cases, a single targeted therapeutic agent may not be sufficient, and therefore, nanoparticles are designed to assure an efficient delivery (Jurj *et al*.,2017).

Delivery systems used in cancer research

This section highlights the ideal delivery systems used in cancer therapy, such as vectors, solid lipid nanoparticles (SLNs), Polymeric Nanoparticles (PNPs), liposomes, hybrid systems, dendrimers and Carbon Nanotubes (CNTs). This section's main objective is to outline the designs of delivery systems and highlight their advantages and impacts in the medical domain for the diagnosis and treatment of cancer.

2. NANOTECHNOLOGY TECHNIQUES USED IN CANCER TREATEMENT

Liposomes:

In simple terms, liposomes are spherical structures with a lipophilic layer situated between two hydrophilic outer layers. Multilamellar vesicles (MLVs) are liposomes that include multiple concentric bilayers of lipid. Liposomes are typically classified into small unilamellar vesicles (SUV), large unilamellar vesicles (LUV), MLVs, and multi-vesicular vesicles (MVV) (Schilt *et al*., Berman *et al*., 2016). MLVs have two or more concentric lipid bilayers organized like an onion skin, 1–5 µm primarily encapsulate lipid-soluble pharmaceuticals, while ULVs have one lipid bilayer, 50–250 nm contains a big aqueous core and are appropriate to entrap hydrophilic medications. They can fuse with tumor cells and enter the extracellular matrix via endocytosis to release drugs (Mukhtar *et al*., Bilal *et al*., 2020). Since these formulations will avoid: I) first pass metabolism; II) undesirable gastrointestinal (GI) effects; and III) poor GI tract absorption, the parenteral route is the most effective method for administration of liposomal drug delivery. Furthermore, parenteral administration results in a higher bioavailability and increased efficacy, compared to oral or rectal administration (Barani *et al*., Bilal *et al*., 2021).

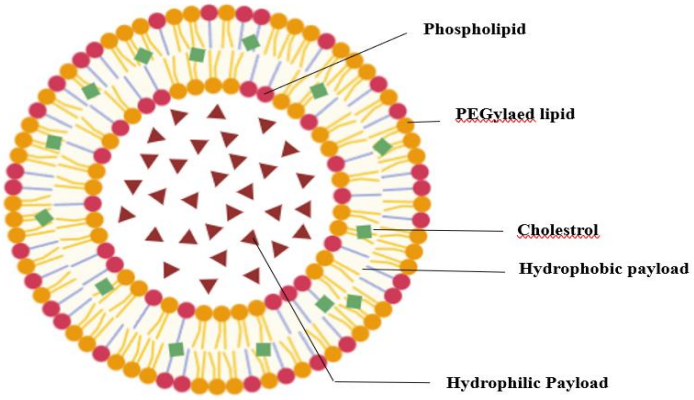

Fig. 1: Structure of Liposome

These are biodegradable and clinically renowned delivery nanosystems that are extensively employed to entrap a large number of hydrophilic and hydrophobic bio pharmaceuticals, such as proteins, peptides, RNAs, and small molecules without altering their properties (Barani *et al*., Bilal *et al*., 2021). Liposomes are unique in having characteristics such as low intrinsic toxicity, weak immunogenicity, and biological inertness. Liposome provide an excellent platform for drug delivery such as doxorubicin, paclitaxel, and nucleic acid as well by demonstrating higher anti-tumor efficacy and enhanced bioavailability (Gavas *et al*., Quazi *et al*., 2021).

Liposomes and Cancer: Liposomes have the inherent capacity to target cancer. Endothelial cells that are connected by tight junctions enclose the capillary walls of all healthy human blood arteries. The big blood particle is prevented from escaping the channel by these tight connections. Tumor vessels lack this kind of organization, making them "leaky" in terms of diagnosis. The improved permeability and retention effect are terms used to describe this capability. Liposomes of size less than 400 nm, can rapidly enter tumor sites from blood, but these are then kept in bloodstream by endothelial wall in healthy tissue (Hamad *et al*., Harb *et al*., 2024).

Nanoemulsion:

Nanoemulsions are colloidal particle systems of submicron diameters that carry drug compounds. Their size ranges from 10 to 1,000 nm. These carriers are solid spheres with a negatively charged surface, amorphous, lipophilic in nature. Site specificity can be improved by using magnetic nanoparticles. As a medication delivery mechanism, they reduce toxic reactions and side effects while increasing the drug's therapeutic efficacy. The term "nano emulsion" which is a fine oil/water or water/oil dispersion stabilized by an interfacial layer of surfactant molecules with droplet sizes ranging from 20 to 600 nm.

There are three types of nanoemulsion which can be formed:(a) oil in water nanoemulsion in which oil is dispersed in the continuous aqueous phase, (b) water in oil nanoemulsion in which water droplets are dispersed in continuous oil phase, and (c) bi-continuous nanoemulsions (Barani *et al*., Bilal *et al*., 2021). Nanoemulsions are superior in efficacy and stability, and a serial of routes they can use to administer (Gavas *et al*., Quazi *et al*., 2021).

Advanced melanoma can be treated with a nanoemulsion that contains rapamycin, bevacizumab, and temozolomide. In contrast to liposomes, nanoemulsions undoubtedly possess superior properties, including stability, optical clarity, and biodegradability. However, there are challenges to clinical applications of these nanoemulsions as these involve high temperature and pressure and instruments such as homogenizers and microfluidizers that are expensive (Jaiswal *et al*., Dudhe *et al*., 2015).

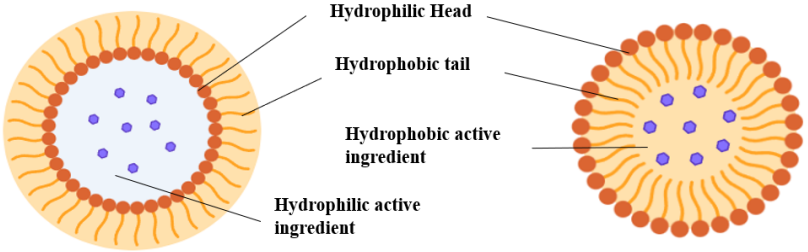

Fig. 2: Structure of Nanoemulsion (A) O/W Nanoemulsion (B) W/O Nanoemulsion

Nanoemulsions have several advantages over most lipid-based nanomaterials and nanoparticles: optical clarity, thermodynamic stability, large surface area, convenience in manufacture, biodegradability, and ideal drug release profile (Gavas *et al*., Quazi *et al*., 2021). Nanoemulsions can deliver large concentrations of chemotherapeutic medications to malignant tissues without harming systemic circulation cells and organs. They have consistently showed great deal of promise for cancer treatment medication delivery. The pain associated with the intravenously administered drugs can be minimised by the lipid emulsion by exposing the tissue to lower concentration of the drug and by avoiding a tissue irritating vehicle (Cheng *et al*., 2021).

Gold Nanoparticles:

Gold nanoparticles are the key focus of biomedical research due to their physical–chemical properties such as shape, surface area, amphiphilicity, carrier capabilities and biocompatibility (Mukhtar *et al*., Bilal *et al*., 2020). Gold nanoparticles (AuNPs) are an intriguing system with unique properties for a range of therapeutic uses. Desirable characteristics like biocompatibility, ease of modification into different forms and sizes, and integration with different functional moieties urge researchers to focus on their applications for tumor therapy and detection. Similar to other inorganic nanostructures, AuNPs are susceptible to oxidative stress-induced cytotoxicity. AuNPs also possess a set of advanced features, including mono dispersity, adjustable core size, easy fabrication, low toxicity, surface plasmon absorption, large surface area, binding capacity to various biomolecules and light-scattering and diagnostic properties (Sánchez-López *et al*., Guerra *et al*., 2019).

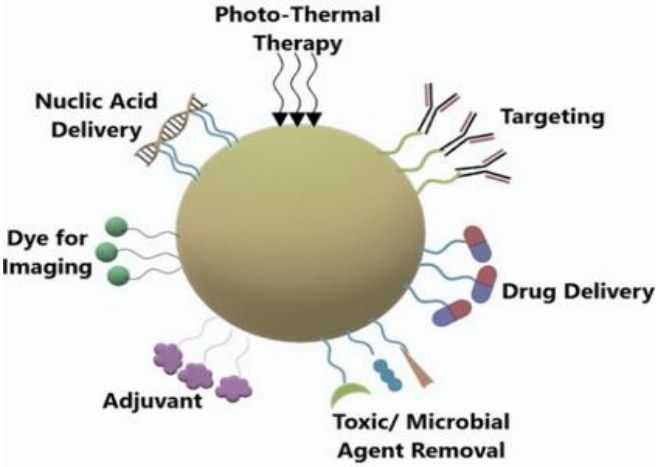

Fig. 3: Structure of Gold Nanoparticle

Similar to liposomes, tumor-specific antibodies can bind to the gold particles' surface to specifically target cancer cells. Utilizing the EPR effect following intravenous injection, the about 10-nm-wide nanoparticles gather in the tumor cell microenvironment while ignoring the other tissues. The ligands on gold particles enter cancer cells by binding to their receptors. After the gold nanoparticles have gathered, the tumor site can be targeted by an infrared laser. The gold particles are excited by this light energy, which causes them to get so hot that gaseous bubbles start forming until the cell can no longer withstand it and lyse. This is quite a physical method of cancer treatment for those tumors that cannot be removed surgically (Zhu *et al*., Zhang *et al*., 2022). Moreover, gold nanoparticles exhibit a low cytotoxicity to the normal cells, increase the lifespan of the cargo in the bloodstream enable easy size control, improve surface chemistry increase therapeutic effects, increase accumulation of drug into the cancer cells and improve pharmacokinetic effects and biodistribution (Mukhtar *et al*., Bilal *et al*., 2020).

Exosomes:

Most cells secrete exosomes, which are extracellular vesicles that range in size from 20 to 150 nm and are enclosed in a lipid bilayer membrane. Exosomes were previously thought to play a role in waste transport within the cell; however, recent research has revealed that exosomes represent the state of the secretory cell and play an important role in cell–cell communication by regulating the role and function of the recipient cell, and contributing to the biological processes of various diseases, including cancer (Kalluri *et al*., LeBleu *et al*., 2020).

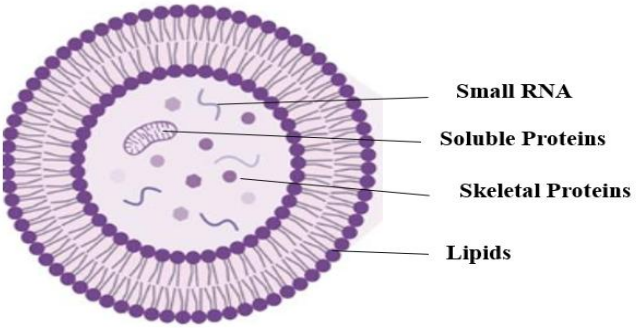

Fig. 4: Structure of Exosome

The components of exosomes, which are membrane vesicles, are in charge of a number of physiologic and pathological activities. Originally, they were used to determine the presence or frequency of specific illnesses in the human body, such as cancer. Exosomes, which are parts of the body, were later investigated as drug delivery vehicles because they were recognized to have several benefits, including improved circulation time and non-immunogenicity. Exosomes were created by Tian *et al*. to carry DOX (doxorubicin), and they showed good target and delivery to BC cells that were positive for αv integrin. When administered intravenously, DOX-loaded exosomes target tumor tissues and prevent tumor growth without having harmful side effects (Patel *et al*., Li J *et al*., 2024). Hadla *et al*. used exosomes loaded with DOX (exoDOX) to treat human breast cancer cells and the result showed that compared with free DOX, exoDOX enhances the cytotoxicity of doxorubicin and avoid drug accumulation in the heart (Gavas *et al*., Quazi *et al*., 2021). Cell-to-cell communication inside the tumor microenvironment determines the course of cancer. Exosomes control the surrounding cell's metabolic status in the tumor environment (Liu *et al*., Shi *et al*., 2021). Exosomes can be administered to the immune cells in the tumor's microenvironment to induce an anti-tumorigenic activity through immune activation, or they can be given directly to cancer cells to inhibit tumor progression. Exosomes also enhance pro-tumorigenic functions by suppressing the immune system (Sergazy *et al*., Seydahmetova *et al*., 2025).

Metallic nanoparticles:

Nanoparticles have special electrical, optical, magnetic, catalytic, and advantageous biological properties, especially metallic NPs. Metallic NPs are a type of inorganic nanomaterials that are composed of titanium, silver, gold, ruthenium, zinc, selenium, iron, copper, gadolinium or hafnium, have been used for cancer treatment (Jurj *et al*., Braicu *et al*., 2017).

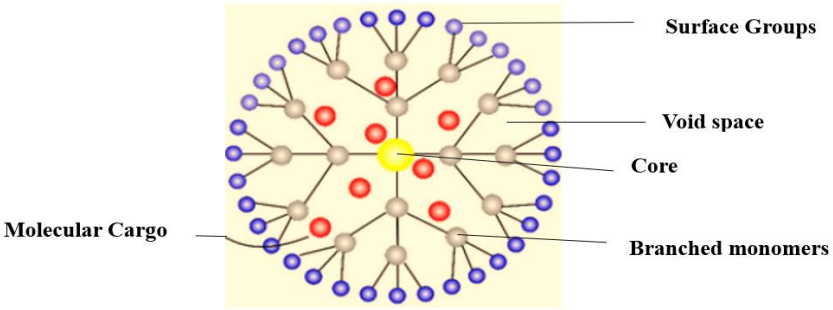

Fig. 5: Structure of Metallic Nanoparticle

Metallic nanoparticles have been shown in various studies to be efficacious against human leukemic monocyte tumor cells as well as liver, breast, colon, and prostate cancer cells. Metallic NPs are usually coupled with a targeting compound or molecule and are loaded with chemotherapeutic drug to increase therapeutic efficacy (Al-Samydai *et al*., Abu Hajleh *et al*., 2024).The ability of metallic nanoparticles to deliver anticancer medicines selectively to the tumor location while preventing off-target damage makes them particularly suitable for treatment of cancer utilizing targeting ligands. Furthermore, by using active or passive targeting, multifunctional metallic nanoparticles can identify and target the diverse population of malignancies. In this way, metallic nanoparticulate drug delivery systems are thus utilized for confiscating anticancer drugs exclusively in the tumor cells, thus reducing the accumulation of drugs in the healthy organs (Kumar *et al*., Shukla *et al* 2023).

Rokade *et al*. formulated the phytogenic platinum nanoparticles (PtNPs) and palladium nanoparticles (PdNPs) incorporating Gloriosa superba tuber extract (GSTE), the developed NPs revealed potent cytotoxicity against MCF-7 cells

in-vitro (Patel *et al*., Li J *et al*., 2024).

Extracellular vesicles:

EVs are lipid-bilayer-contained vesicles that are released into the extracellular environment by nearly all cells and are present in all somatic fluids, including the urine, saliva, blood, and cerebrospinal fluid. EVs are divided into three subtypes based on their size distribution and techniques of biogenesis: apoptotic bodies, vesicles or micropaticles, and exosomes (Kumar *et al*., Shukla *et al*., 2023).

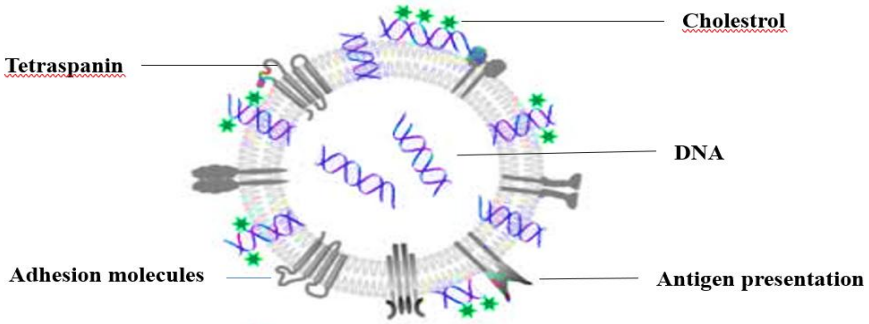

Fig. 6: Structure of Extracellular Vesicle

Bilayer phospholipid vesicles, or EVs, are usually between 50 and 1000 nm in size. Different cell types continuously release EVs, which vary in size, origin, and content. Based on the origin, EVs are classified into three major groups: exosomes, microvesicles and apoptotic bodies (Gavas *et al*., Quazi *et al*., 2021). EVs are membrane-coated nanoparticles made of proteins, lipids, DNA, and RNA that are expelled from a small number of body cells. EVs also frequently use transcytosis to cross the blood-brain barrier. EGFR protein is expressed by EVs, which are present in the serum of glioma patients. Therefore, EGFR in EVs can be found to accurately diagnose the tumor's malignancy (Mukhtar *et al*., Bilal *et al*., 2020). Their cell surface can be altered to target a particular cell type, and they can carry a range of payloads due to their inherent biocompatibility. EVs can reduce the toxic effects on cells due to chemotherapy medications on healthy cells (i.e., the nonspecific cytotoxicity of chemotherapy treatments) by targeting certain cell populations. Additionally, both hydrophilic and hydrophobic medications can be loaded into EVs. EVs are comparatively more stable than liposomes and synthetic polymer-based nanoparticles because of their composition. In contrast to modified liposomes, exosomes may carry CD47 to shield them from phagocytosis, which keeps more exosomes in circulation. Because of their stability, exosomes with therapeutic short interfering RNA that targets cancer cells that express KRAS are more effective than liposomes with the same RNA payload. One very important aspect of EVs that could solve a major problem in brain cancer treatments, is that they are able to pass through many physiological barriers within the body, including the blood–brain barrier (BBB) (Walker *et al*., Busatto *et al*., 2019).

Chitosan Nanoparticles:

The primary component of crab, lobster, and shrimp shells, chitin, is deacetylated to produce chitosan, a naturally occurring carbohydrate polymer. Chitosan is thought to be appropriate for use in pharmaceutical applications because of its lower cost, better biocompatibility, minimal toxicity, and chitinase-mediated degradation in the body. As chitosan dissolves in acidic water-based solutions at ambient temperature and doesn't require heat or hazardous organic solvents, it is frequently used to create nanoparticles under mild circumstances. A broad category of drugs can be incorporated into chitosan DDS, including small molecules, proteins, and poly nucleotides (Cheng *et al*., Li M *et al*., 2021). Chitosan is able to release the encapsulated drug in a controlled manner. The free amine groups on chitosan also provide ionic crosslinking ability (Elumalai *et al*., Srinivasan *et al*., 2024). Chitosan nanoparticles offer many advantages due to their better stability, low toxicity, simple and mild preparation methods, providing versatile routes of administration and has gained more attention as a drug delivery carrier (Nagpal *et al*, Singh *et al* 2010). Chitosan nanoparticles have been extensively studied for their use in cancer treatement. Chitosan nanoparticles can target tumors on specific organs through passive targeting (also known as enhanced permeability and retention (EPR) effect, active targeting, and physical targeting through stimuli-sensitive targeting (Jain *et al*, Kumar *et al*., 2020). In the passive drug delivery, CS NPs assemble in cancer cells due to their natural pathophysiological and physicochemical characteristics and EPR effect; however, in the active drug delivery, these NPs could substantially internalize into the cancer sites by ligand-mediated processes (Nagpal *et al*., Singh *et al*., 2010).

NPs like Carbon nanotubes, calcium nanoparticles, graphite, and polymeric NPs (such as chitin and chitosan) have improved cancer diagnosis and treatment because of their enormous size, charge on their surface, and shape. These NPs help with drug delivery and cancer cell detection by functionalizing with a variety of biological molecules, including antibodies. Chitin has the potential to function as an anticancer agent and a medication delivery mechanism. It has been

proved that chitin can inhibit the overexpressed chitinase-3-like protein-1 (CHI3L1), which causes breast cancer cells to produce proinflammatory mediators. Moreover, the synthesis of vascular endothelial growth factor C (VEGF-C), associated with tumor angiogenesis, can be downregulated with chitin (Narmani *et al*, Jafari *et al*., 2021).

Dendrimers:

Another type of nanocarrier is a dendrimer, which has a spherical polymers core with branches spaced regularly. As the linearity increase in the diameter of dendritic macromolecules, they become more inclined toward the globular shape (Svenson *et al*., Tomalia *et al*., 2005). Dendrimers are usually synthesized by two methods, first is a divergent method in which dendrimers can be grown outwards from a central core and the second method is the convergent method by which the dendrimer is synthesized from the margin inwards, ending at the core (Tomalia *et al*., Baker *et al*., 1986). Dendrimers exhibit a variety of chemical structures and characteristics, such as basicity, charge, hydrogen bonding ability, etc., which can be altered by altering the groups on the dendrimer surface or by increasing dendrimer formation. Antineoplastic agents are typically covalently attached to the peripheral groups of dendrimers to form dendrimer-drug conjugates. As a result, each dendrimer molecule can have multiple medication molecules connected to it, and the type of connections can influence how these therapeutic molecules are released. Due to unambiguous properties and multiple linkage groups, polymer size, charge, biologically related properties such as lipid bilayer interactions, cytotoxicity, internalization, blood plasma retention time, biodistribution, and filtration dendrimers have become a potential nanocarrier (Hawker *et al*., Frechet *et al*., 1990).

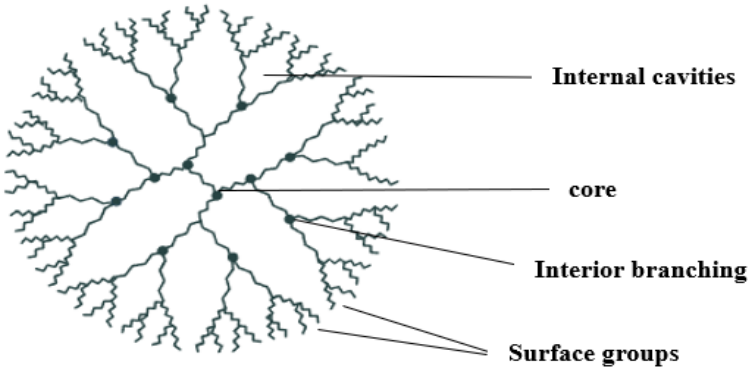

Fig. 7: Structure of Dendrimer

Fréchet and Szoka's work is illustration of architecturally-optimized dendritic drug delivery system here an asymmetric doxorubicin-functionalized bow-tie dendrimer was made by PEGylation of one side of a 2,2- bis(hydroxymethyl) propionic acid dendrimer (G3) and on other side linked the drug by acyl hydrazone linkage (G4) the whole system contains 8–10% doxorubicin (Lee *et al*., Gillies *et al*., 2006). Following the injection of the entire medication and the dendritic system into BALB/c mice with s.c. C-26 colon cancer, it was discovered that the dendritic doxorubicin complex was absorbed at a higher rate than doxorubicin alone. It was unexpected that all of the mice survived and that the tumor entirely disappeared after 60 days of doxorubicin-conjugated dendrimer treatment for malignant mice. On the other hand, mice given doxorubicin alone shows no change in tumor size. In another study, it was found that cancer cells which express more folic acid receptor can be foil by folic acid conjugated dendrimers (Wiener *et al*., Konda *et al* 1997). The ability of the dendrimer to combine with DNA in clusters, such as the DNA-Polyamidoamine cluster, or DNAPAMAM, provides an additional benefit. This combination effectively destroys cancer cells with high levels of folic acid receptor expression. While dendrimer-antibody conjugates do not bind with normal cells, they do bind with prostate-specific membrane antigen-positive (LNCaP.FGC) cells. Additionally, tumor cells absorbed the conjugation at a significantly higher rate than unconjugated dendrimer. Another class of dendrimer i.e. glycodendrimers is glycopeptide dendrimers conjugated to the anti-mitotic agent colchicine and dendrimers that incorporate sugar moieties into their construction (Woller *et al*., Cloninger *et al*., 2001).

Nanoshells:

Nanoshells are a class of nanoparticles with a thin metallic shell enclosing a dielectric core. Nanoshells absorb light, producing intense heat that can kill cells-specifically tumor cells-while sparing healthy cells. As a result, using it to treat oral cancer may be advantageous. Additionally, regulated site-specific drug administration into periodontal gum tissues can be facilitated using nanoshells. Nanoshells consist of a semiconductor encased in a gold shell. They can be exposed to radiation once they get to the cancer cells. The heat produced by these irradiations kills the cancer cells. Ventral tumors in mice have been successfully treated with this method (Paolo D *et al*., 2004). With a biodegradable polymer core and mixed lipid monolayer shell, a system of folic acid-conjugated nanoparticles was developed for targeted delivery of docetaxel (Mohanraj *et al*., Chen *et al*., 2006).

Cancer treatment employs gold-shelled nanoparticles that are sphere-shaped particles with silica cores and gold shells (Yanv *et al*, Xu H *et al*., 2004. In an ectopic tumor model, laser-activated gold nanoshell thermal ablation provides a specific and successful method for ablating prostate cancer. Only due to the absorption and scattering that takes place for plasmonics is it possible to treat cancer. Depending on the size and shape of the particles, imaging procedures that are adjusted to the proper wavelength can see the gold-plated nanoparticles when they scatter. Photothermal ablation takes place during absorption, heating the nanoparticles and the area around them to temperatures high enough to destroy the tumor cells. This is achieved with least possible damage to cells in the body due to the usage of the "water window" (the spectometric range between 800 to 1300 nm). As the human body is mostly water, this optimizes the light used versus the effects rendered (Yanv *et al*, Xu H *et al*., 2004).

Supermagnetic Nanoparticle:

Superparamagnetic nanoparticles (NPs) are oxides of iron or magnetite (Fe3O4) particles with a diameter of less than 10 nm. These superparamagnetic NPs, like other NPs, are being functionalized to enable targeted tumors. Such as iron oxide NPs can also be made by coating with aliphatic surfactants or liposomes resulting in magnetoliposomes (Kubo *et al*., Sugita *et al*., 2000). Magnetic NPs can be remotely activated using electromagnetic fields, and they can also be used to thermally treat cancers (Wust *et al*., Hildebrandt *et al*., 2002).

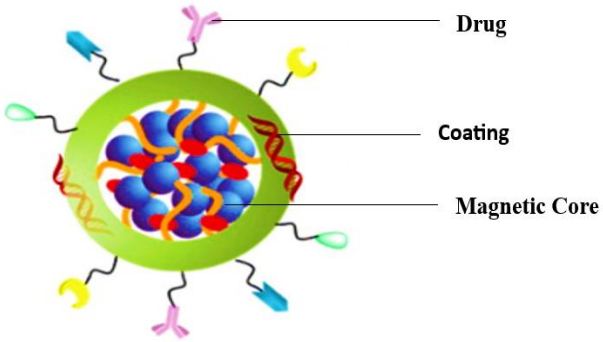

Fig. 8: Structure of Supermagnetic Nanoparticle

MNPs have become more widely used in a variety of medical applications, including biosensing, controlled release of drugs, MRI (magnetic resonance imaging) and the treatment of cancer caused by hyperthermia. To improve their acceptability for a particular target in the human body, a safe and biocompatible coating can be applied to modify the magnetic characteristics/properties and MNP effectiveness in vivo. The surface chemistry provided by this coating facilitates the incorporation of functional ligands. MNPs can become multifunctional by altering their surface chemistry. For instance, chemical modification provides multiplexed functionality such as combined hyperthermia-drug delivery and multimodal imaging (Wust *et al*., Hildebrandt *et al*., 2002).

Solid lipid nanoparticles:

These have rigid sizes that range from 1 to 1000 nm. Particles typically range in size from 150 to 300 nm (Muller *et al*., Shegokar *et al* 2011). Their solid matrix of SLNs (Solid lipid nanoparticles) allows them to restrict medication motility & offer better stabilization, allowing them to combine the benefits of polymeric nanoparticles, liposomes, and micronized emulsifiers (Kathe *et al*., Henriksen *et al*., 2014). Moreover, tests show that SLNs were highly advantageous in a variety of aspects such as the prevention of utilising organic solvent while manufacturing, possible scaling as well as the inclusion both of lipophilic and hydrophilic medicines in significant quantities (Teeranachaideekul *et al*., Muller *et al*., 2007). SLNs are formulated by substituting a solid lipid, or perhaps a mixture of solid lipids for the liquid lipid, or oil, in an oil-in-water emulsion. One crucial feature of SLNs is that they are solid at both room as well as temperature of body (Lima *et al*., Pizzol *et al*., 2013). These drug delivery systems consist of 0.1 to 30% (w/w) solid lipids distributed across an aqueous media. Higher purity triglycerides, free fatty acids, free fatty alcohols, complex glyceride blends, and also wax-generally well-known physiological lipids-are examples of solid form lipids that make up SLNs (Wissing *et al*., Kayser *et al*., 2004).

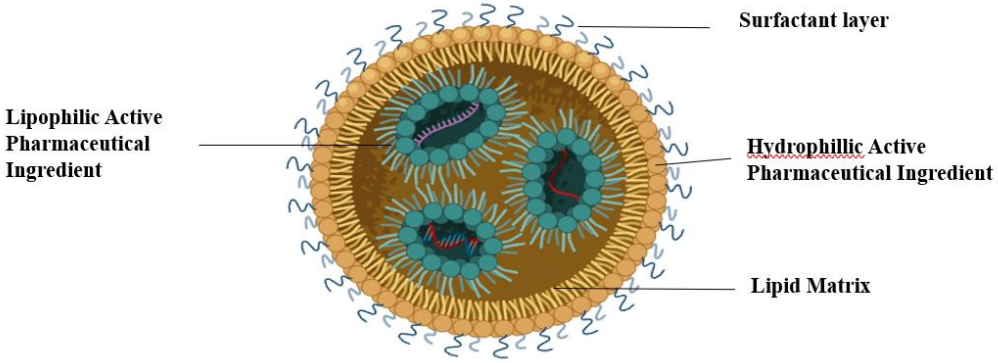

Fig. 9: Structure of Solid lipid nanoparticle

Polymeric nanoparticles:

Polymeric nanoparticles are defined as submicron colloidal nanoparticles and are used as carriers for different drugs such as chemotherapeutic drugs which are either adsorbed on the surface or encapsulated within the nanoparticles (Ahlawat *et al*., Henriquez *et al*., 2018). Various polymer types, including poly (lactic acid) (PLA), poly (ε-caprolactone) (PCL), poly (butyl-cyanoacrylate) (PBCA), poly (glycolic acid) (PGA), poly (amino acids), and poly (lactic acid) (PLGA), have been utilized in the formulation of nanoparticles (Elzoghby *et al*., El-Fotoh *et al*., 2011). All of them break down into lactic and glycolic acids, which then enter the Krebs cycle and leave the body as carbon dioxide and water. Polymeric micelles are composed of various amphiphilic polymers that preferentially self-assemble in an aqueous medium (Makadia *et al*., 2011). Polymeric micelles are made up of both hydrophilic and hydrophobic segments (Hussein *et al*., 2011). Polymeric nanoparticles can deliver not only small molecular weight drugs but also macromolecules such as genes and proteins (Tang *et al*., Lei *et al*., 2010). The most efficient nanotechnology platforms, polymeric nanoparticles, have become a flexible delivery mechanism for anticancer medications. One important advancement in nanotechnology is the active targeting of polymeric nanoparticles through surface modification with ligands that attach to target molecules on the surface of cancer cells or other bodily cells. Anti-cancer drugs, either individually or in combination with adjuvants or other anti-cancer drugs, can be loaded onto polymers (Kumar *et al*., Kulkarni *et al*., 2016).

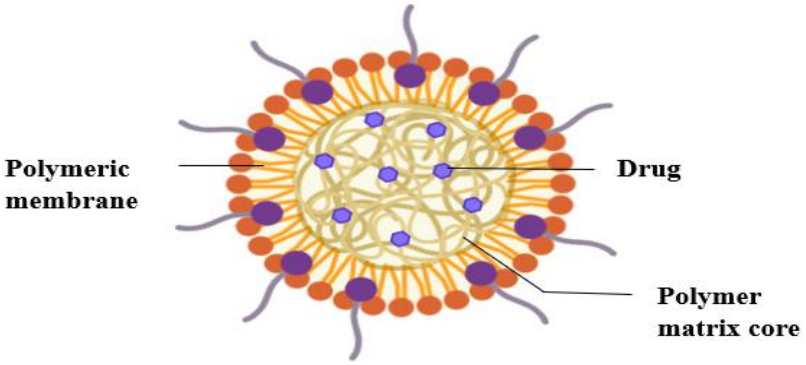

Fig. 10: Structure of Polymeric nanoparticle

Film hydration, emulsion and solvent-casting, dialysis, and dissolution are a few techniques utilized to create polymeric micelles. The thorough characterization of micelles involves the determination of critical micellar concentration (CMC), the drug payload, and its release (Tang *et al*., Lei *et al*., 2010). Polymeric micelles can pre-maturely diffuse drugs before reaching the target site. Drug release is an essential step in drug delivery, as an optimum drug concentration must reach the tumor site(s) to achieve an intracellular level that is efficacious (Yin *et al*., Shen *et al*., 2013).

Carbon nanotubes:

The fullerene family of carbon allotropes includes carbon nanotubes (CNTs), which are cylindrical in shape and made up of a hexagonal configuration of sp2-hybridized carbon atoms. Carbon nanotubes (CNTs) can be categorized into two types based on their diameter and structure: single-walled CNTs (SWCNTs) and multiwalled CNTs (MWCNTs).

The SWNTs are composed of monolithic cylindrical graphene, and the MWNTs are composed of concentric graphene (Sahu *et al*., Tiwari *et al*., 2023).

Through covalent and non-covalent interactions, CNTs exhibit the capacity to load drugs onto their surface or within their inner core. Carbon nanoparticles are effectively absorbed and transferred into the cytoplasm of the targeted cells without resulting in cell death because of their nanoneedle-like form. Carbon nanotubes also possess a property that allows them to absorb light from the near-infrared (NIR) region, causing the nanotubes to heat up by the thermal effect, hence can target tumor cells (Makki *et al*., 2024). Drugs like paclitaxel are built with carbon nanotubes and given in vitro as well as in vivo to treat cancer because of their appropriateness. As a carbon-based nanomaterial, CNTs can interact with immune cells and induce immune response, therefore elevate immunity to suppress tumor growth (Yuan *et al*., Zhang *et al*., 2019). Due to its hydrophobic nature, solubility in water, accumulation in internal organs, and slow rate of breakdown, CNTs have restricted applicability. To increase the systemic retention, circulation time and the solubility of CNTs, a hydrophilic biocompatible polymer with neutral charge such as PEG or polyethylene oxide is used (Huang *et al*., 2020).

Albumin nanoparticles:

Albumin is the most abundant protein in the plasma that is involved in many physiological processes, such as maintenance of osmotic pressure, transport of hormones, ligands, drugs, and neutralization of free radicals, among others (Miller *et al*., Jedrzejczak *et al*., 2001). It is a multifunctional protein that is highly stable, biodegradable, biocompatible and non-immunogenic (Zeeshan *et al*., Madheswaran *et al*., 2021). Albumin has numerous high-affinity hydrophobic binding sites that can bind a number of ligands and drugs (Wartlick *et al*., Michaelis *et al*., 2004). Thus, based on these aforementioned properties, albumin is commonly used as a nanocarrier (Zeeshan *et al*., Madheswaran *et al*., 2021). It has dense negatively charged areas that will induce a strong repulsive force towards negatively charged proteins, such as hemopexin, haptoglobin and transferrin, which increases its stability and half-life in the circulation (Hobbs *et al*., 1998; Chacón *et al*., 1999).

The majority of albumin nanoformulations are prepared by desolvation (Lei *et al*., 2021). Anti-cancer drug binding with albumin can be done via covalent and/or noncovalent conjugation (Quinlan *et al*., Martin *et al*., 2005). Albumin NPs can either actively or passively target cancer cells (Hobbs *et al*., 1998; Chacón *et al*., 1999). Binding of the NPs to the surface receptors on the cell that enter the cell during internalization is a component of active targeting. On the other hand, passive targeting has an EPR effect. Albumin NPs have certain drawbacks such as manipulation of particle size, shape, distribution, and stability poses major challenges (Hobbs *et al*., 1998; Chacón *et al*., 1999).

Quantum dots:

Quantum dots (QDs) are micro semiconductor crystals, shines when are stimulated by ultraviolet light. Quantum dots (QDs) are nanoscale nanomaterials that are said to be zero-dimensional because charge carriers are confined so tightly in three directions (Kumar *et al*., 2018). These are tiny semiconductor particles or nanocrystals that ranges from 2 to 10 nanometers in size. The ratio of the height of the surface to the volume of these particles gives the QDs the intermediate electron property which is between a mass semiconductor and a discrete atom (Bhattacharya *et al*., Preetam *et al*., 2024). The QDs ability to concentrate in a particular internal organ make them a viable defense against untargeted drug administration and may help prevent chemotherapy adverse effects. The structure of QDs, which is composed of a core, shell, and sometimes a surface coating, provides superior stability in terms of surface activation, chemical and photochemical behaviors, and quantum yield of photo luminescence. The core is made of semiconductor material (such as CdSe or CdTe) in a crystal structure that decides the excitation wavelengths and emission of fluorescence. That core is stabilized by the shell structure that surrounds it (Bhattacharya *et al*., Preetam *et al*., 2024).

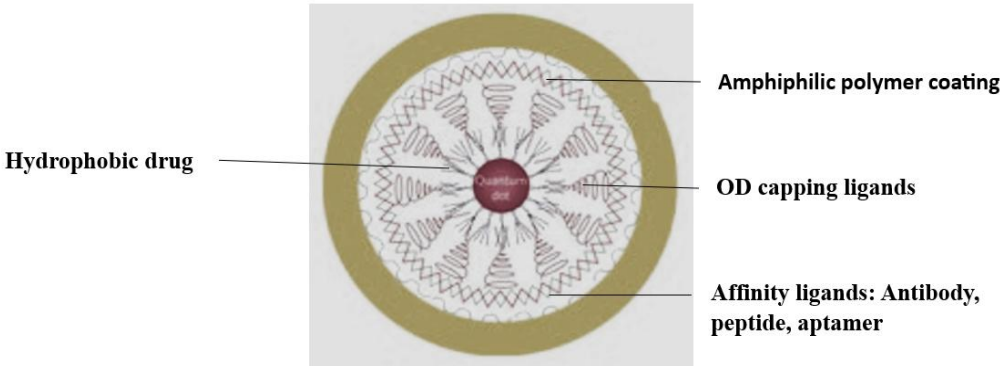

Fig. 11: Structure of Quantum dot

Phototherapy, tailored gene-drug delivery, bioimaging, early tumor detection and diagnostics, and drug administration are the main applications of QDs in cancer treatment. Because of their high cell absorption capability, low cytotoxicity, and excellent biocompatibility, QDs are also the best option for drug delivery. Quantum dots have several uses, such as cancer diagnosis, treatment, and detection (Huang *et al*., Tang *et al*., 2021).

Nanodiscs:

Apolipoprotein molecule interaction stabilizes the edge of nanodiscs (ND), which are disk-shaped, nanoscale phospholipid bilayers. ND are nanoscale (8–20 nm diameter) noncovalent assemblies organized as a disk-shaped phospholipid bilayer that is circumscribed by two or more amphipathic apolipoprotein molecules (Sweeney *et al*., Krueger *et al*., 2022). NDs can be used as vehicles for the delivery of bioactive agents because the bilayer component of ND offers an environment that can solubilize and sequester hydrophobic compounds. The presence of a sequence of amphipathic α-helices that align in a belt-like pattern, with their polar face facing towards the solvent and their hydrophobic face facing the phospholipid fatty acyl chains, is a crucial characteristic of the apolipoprotein component. The apolipoprotein component acts as a "scaffold" to preserve the integrity of ND particles and defines the disk boundary in this way. ND's third changeable component might be any hydrophobic molecule that can be firmly incorporated into the lipid environment of the ND bilayer (Dufourc *et al*., 2021). Therefore, the following characteristics set NDs apart from traditional liposomes or vesicles: 1] There is no aqueous core in NDs. 2] One of NDs' inherent structural components is scaffold proteins. 3] ND sizes vary between 8 and 20 nm, while liposomes have ND diameters between 60 and 250 nm. 4] NDs are completely soluble in aqueous media, in contrast to liposomes (Rajalakshmi *et al*., Eswar *et al*., 2024). Nanodiscs are very soluble in aqueous solutions because of this configuration. Membrane proteins can be maintained in solution without the need of detergents once they have been assembled into nanodiscs. Native cell phospholipids are used to create nanodisc structures surrounding membrane proteins, while synthesized polymers are used to break down cell membranes. The polymer serves as a stabilizer and solvent enhancer. Consequently, no extra detergent is needed (Sligar *et al*., Denisov *et al* 2021).

3. CURRENT INSIGHTS AND FUTURE PERSPECTIVES:

In the detection and treatment of cancer, nanotechnology is becoming more and more significant. Since NPs have a smaller size range than cells and cellular organelles, they can interact with particular cell characteristics and use active targeting to localize tumor cells (Elias *et al*., Poloukhtine *et al*., 2013). Safer and more effective derivatives for cancer management can be made available by enhancing the interactions between the physicochemical characteristics of the nanomaterials used in diagnosis and treatment. In conclusion, we aimed to draw attention to the main benefits of nanotechnology as well as its limitations when it comes to using it to treat cancer clinically. Furthermore, nanotechnology's therapeutic advantages and potential for further development may allow it to be used to treat a variety of illnesses. These can include rheumatoid arthritis and ischemic stroke, which call for the targeted administration of an appropriate pharmaceutical agent at the site of injury (Jin *et al*., Wang *et al*., 2020). Nanotechnology has emerged as an enabling technology for predictive oncology, which uses inherited and/or molecular markers to forecast the onset, course, and clinical results of cancer, as well as personalized oncology, which customizes cancer detection, diagnosis, and treatment based on each patient's unique tumor molecular profile. The US National Cancer Institute recently awarded funding to eight national Centers of Cancer Nanotechnology Excellence in recognition of its potential influence on cancer research. There are a number of study topics or avenues that hold great promise for the future, but they will need coordinated effort to succeed. The first involves the creation of nanoparticles that have one or more functionalities. Imaging (single or dual modality), therapy (one medication or a combination of two or more agents), and targeting (one or more ligands) are crucial features for cancer and other medical applications. Nanoparticles have demonstrated a promising future as a new generation of cancer treatments by offering the ability to develop and tune features that are not achievable with current therapeutic medication types (Misra *et al*., Acharya *et al*., 2010). Because of their chemical diversity, NPs can interact with external fields like as magnetic fields and NIR irradiation. This enables for very targeted interactions between external fields and tumor tissue, as well as possibly with single malignant cells in vivo. Because of their varied material composition, NPs can also cause external fields to change, improving contrast for imaging applications (Kim *et al*., Piao *et al*., 2009).

4. CONCLUSION

According to a 2021 WHO report, cancer still remains as the second leading cause of death globally. Various categories and uses of nanostructures for cancer control have been explained in this paper. Nanostructured carriers are highly versatile, flexible, and have many benefits that can improve the treatments and diagnostics of cancer. Nanomedicines have clear clinical advantage over conventional therapies used for cancer diagnosis and treatment. Nanoparticle based drug delivery has improved specificity, selectivity and sensitivity or provided whole new capabilities that cannot be achieved by the traditional/conventional systems. The ideal nanotherapeutic systems should be: (A) completely safe and biocompatible; (B) extremely stable and effective at maximizing drug loading; (C) simple to make and alter; and (D) capable of selectively targeting tumors and effectively facilitating endocytosis. Due to nano-immunotherapy personalized medicine is possible and inevitable in cancer treatment. The success of nanotechnology lies within incorporating the correct nanomaterials and reducing any possible side effectsIt is important to remember that before new nano-based products are authorized for clinical and commercial usage, risk assessment and identification are required. Nanosystem have scale up issue and too complicated for large-scale manufacturing. In this study, we have summarized various categories of nanomedicines for effective and safe diagnosis and treatment of cancer.

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