Nanotechnology: optimal applications in anti-cancer drug medicine treatment and diagnosis

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Abstract:

The scientific field devoted the importance of studying nanotechnology, which characterizes nanoparticles and their multi-purpose functions, especially nanomedicine techniques. The review focused on newer technologies in biomedical applications as a drug vector in cancer treatment. To occupy the center stage on most of the biological vectors of drugs for the treatment of cancer. Practically, chemical treatments have harm as they target cancerous and non-cancerous cells alike, the solubility is almost non-existent, and the inability of chemotherapy to penetrate cancerous cells, which opens the way for this technique with clear prospects for the aforementioned purpose. The ability to selectively deliver nano-drugs to targeted cancer cells in an optimal manner and to avoid non-specific interactions with healthy cells. The current review focuses on ways to improve the size, shape, and properties of nanomaterials that can be exploited in cancer therapy. The successful treatment of nanocarriers for cancer can be designed for the future as nanotherapies.

Introduction

One of the most recent and pioneering medical applications that bear several directions in cellular therapy is nanotechnology (Yan, *et al*., 2019 ; Al-saidi *et al*, 2022). There are countless studies, whether by industrial methods or by green methods, using organic compounds. (Proteins, sugars, lipids, Pac-Tria, fungi, and viruses) (de Marco *et al*., 2019), inorganic substances (Ag, Au, Ti, Zn, Co, etc.) and also by volcanic eruptions and weathering. NPs are synthesized by physical, chemical and biological methods. The physical and chemical methods are very expensive (Khan *et al*., 2022). Biological methods for the synthesis of NPs will help remove harsh processing conditions, by allowing synthesis at physiological pH, temperature and pressure and at the same time at minimal cost (Lade & Shanware, 2020). A large number of microorganisms have been found to be competent to synthesize inorganic NPs, both inside and outside the cell (Sumanth, et al., 2020).

The completely new and improved properties within the range of 100 nanometers (nanometers) or less have entered the present application of the widest sections and this is what distinguishes them from the properties of larger particles (Chaturvedi & Dave, 2020 ; Hassan *et al*, 2022). They are usually produced based on specific properties including size, shape, distribution and surface morphology. These applications showed characteristic colors and properties with the variation of size and shape, which can be utilized in bioimaging implementation (Wang *et al*., 2020).
Nanotechnology is the main support in dealing with materials and creating structures and systems at the atomic and molecular level (Ariga, 2021) ; Dastani, 2019). This

technology contributes to giving the material unique properties at sub-atomic scales to create unique or improved materials and products (Aljamali *et al*., 2021).
In the second half of 1980s to the early 1990s a number of important discoveries and inventions was made, which created an essential impact on the further development of nanotechnology (Zin *et al*., 2021). Since then, a considerable intensification of nanotechnological researches and designs is underway, the number of publications on nanotechnological subjects increases sharply, practical application of nanotechnology expands; project financing in nanotechnology increases significantly, as well as the number of organizations and countries involved in it (Wanget *et al*., 2019).
In 2001 the National Nanotechnological Initiative (NNI) of the USA was approved. The principal idea of this program was formulated as follows: "National Nanotechnological Initiative defines the strategy of interaction between federal departments of the USA for the purpose of prioritizing nanotechnology development, which should become a basis for the economy and national security of the USA in the first half of the 21st century» (Forestal et al., 2022 ; Hartshorn & Morris 2019).
Recently, several synthesis methods have been developed to lay the basic building block for introducing it within the scope of practical implementation and manufacturing more unique and exciting materials instead of incorporating the use in the traditional form whose particle size is less than 100 nm to successive luminal fields of interest due to its wonderful properties with multiple applications compared to its bulk counterparts. Research on particle size, shape, and surface properties of a material is one of the major important areas of properties of NPs for targeted applications in broad fields of science (Dutta et al., 2021; Guo & Jin, 2019).
"Biolab" is the green way to manufacture pure materials using a bio-reducing medium that is sustainable, economical, easy to use, fast and environmentally friendly with the efficiency to produce pure metal and metal oxide particles at the nanometer scale using a biomimetic approach. (Fein, 2020),

Microorganisms, such as bacteria, fungi, yeast, plant extracts and waste materials acted as eco-friendly factories for the synthesis of nanomaterials with prepared applications (Kaur *et al*., 2022). Professionally, the synthesis of nanomaterials on the green method has become the latest in the availability of the aforementioned biological sources, in addition to reducing the use of toxic chemicals. These microorganisms involved in the synthesis of these nanomaterials also demonstrate the size, shape, and functional groups involved in the synthesis and application of nanomaterials (Kumar *et al*., (2021).

Nanotechnology racing

In the current century, nanotechnology is the turning point in technological medicine in particular and the technical advance of various fields in general. Where it started from the pathological diagnosis, especially the scaling of the diseased condition and its treatment (Huang *et al*., 2018 ; Thangadurai,. 2020) , which called on governments to develop strategies and organizational plans to keep pace with the fierce competition between governments to take the closest position to the fore in the hierarchy of advancement (Adir *et al*., 2020).

In the second half of the eighties to the early nineties, a number of important discoveries and inventions were made, which created a fundamental influence on the further development of nanotechnology. Since then, a significant intensification of nanotechnology (Riaz *et al*., 2021).

Research and designs are in progress, the number of publications on nanotechnology topics is increasing sharply, and the practical application of nanotechnology is expanding; Funding for projects in the field of nanotechnology is increasing significantly, as well as the number of organizations and countries participating in it (Vurro et al., 2019; Falchi, et al., 2018).

In 1991, the first Nanotechnology Program of the National Science Fund was started in the USA (Doubleday & Viseu, 2019).

In 2001 the National Nanotechnology Initiative (NNI) of the USA was approved. The main idea of this program is formulated as follows: “The National Nanotechnology Initiative defines the strategy of interaction between the federal departments in the United States of America for the purpose of giving priority to the development of nanotechnology, which should become the basis for the economy and national security of the United States of America in the first half of the twenty-first century (Merzbacher, 2020).

During 1996-1998, prior to the approval of the NNI, a special commission of the American Center for Global Technology Assessment monitored and analyzed the development of nanotechnology in all countries and published survey newsletters on the basic trends of development and scientific, technical and management achievements (Fogelberg, 2019). experts in the United States. In 1999, the Interbranch Group Session on Nano-sciences, Nanoengineering and Nanotechnology (IWGN) took place, with the result that research in the field of nanotechnology for the next ten years was anticipated. In the same year, the conclusions and recommendations of the IWGN were supported by the Presidential Council on Science and Technology (PCAST), as the NNI was formally approved in 2000 (Ryzhenkov & Inshakova, 2019). From 1987 established research in nanomaterials to the most technologically booming years 2006 to 2020, catalytic research in nanotechnology was one of the four most priority programs (Sanchez, et al., 2018).

Activation of NPs for high-throughput biomedical applications. Attracting the most efficient number of scientists to the field of advanced sciences with nanotechnology, for practical, especially medical, practical briefing (Chen *et al*., 2022) The unique chemical and physical properties have stimulated a growing interest in the field of nanoscience to synthesize NPs from various materials including noble metals such as Ag, Au, Pd, Pt, magnetic materials (such as Co, CoPt, CoFe2O4, Fe3O4, FePt) and semiconductors (such as CdSCdSe and ZnS) (Nouri, 2022).. and InP, PbS, Si and TiO2) and their possible combinations (Giri et al., 2022). NPs are specifically and comprehensively used as parameters, drug vector, trace agents, genetic vector, diabetes, cancer, hyperthermia therapies, contrast agents in magnetic resonance imaging (MRI) etc (Malik & Mukherjee, 2018). for applications. The use of NPs medically depends on several things, they must have certain criteria such as fluorescent staining, have no cytotoxicity, non-specific reactivity to plasma proteins, evasion of the endothelial re-epithelial system (RES) depending on the application, under physiological condition, they must also It has good colloidal stability in a wide range of pH, and these are the most important things that are highlighted in the pharmaceutical production and the practical application of any medical drug, whether it is of a therapeutic, preventive or diagnostic quality at the physiological or molecular level (Khalili *et al*., 2022); (Pang *et al*., 2020).

The ionic ligands

It is one of the most important chemical conditions to allow NPs to continue pairing. The physiological salt concentration should be around 100 mM (Fu *et al*., 2019; Zhang *et al*., 2021). as free ions may be lost during steric re-conjugation and NPs such as citric acid/citrate or phosphoric acid/phosphate can easily lose protons and exhibit a pH-sensitive property such as protonation/deprotonation affecting The surface charge that leads to the salting out of the NPs (Guru Prasad, 2019) ; Mertins, 2020). However, this strategy in stereochemical recombination is not valid for biomedical application. It is an alternative strategy for ionic stability of NPs to prevent aggregation by giving a physical barrier to superior NPs (Zhao et al., 2020). This kind of performance can be achieved by coating the bonding envelope on the NPs or embedding the NPs within appropriate polymer or inorganic matrices (Shi et al., 2022). This allows the NPs to come into contact and aggregate which helps in increasing the hydrodynamic radius of the NPs and thus makes it suitable for in vivo applications with a longer turnover time in the bloodstream (Zhou et al., 2021). To achieve NPs for desired applications, considerations must be taken of several important properties of synthesized NPs such as:

1. Ionic stabilization
2. Steric stabilization
3. Polymeric ligands
4. Small-molecule ligands
5. Phase transfer (PT)
6. Ligand exchange
7. Ligand addition
8. Effects of the ligand shell
9. Type of biofunctionalization
10. Type of coupling strategies for biofunctionalization (Duan et al., 2018 ; Aslam et al., 2021).

The choice of method for preparing the nanomaterial determines the advantages that the particles will have, such as increased surface-to-volume ratio as well as magnetic properties, and depending on the cellular targets, medical purpose or any interesting application they will be categorized into different engineered nano-systems (Dinesha et al., 2021; Hakke et al., 2021).

Cancer medication by type I (magnetic NPs (MNPs))

The topic of concern now in the biomedical application of cancer is the structuring of NPs with magnetic properties to possess excellent stimulation of biological response, which was the focus of interest as the first proposed for biomedical application. Their inclusion in the treatment pathways of various diseases highlights the growing trend towards integrating new biotechnologies into health-care (Mertz et al., 2020).; He et al., 2021).

The primary function of Superparamagnetic NPs (SPNs) is to produce a localized thermal effect that leads to the breakdown of bacterial biofilms and cancer cells. Furthermore, through architectural disruption of bacterial membranes, S. pneumoniae can sensitize bacterial cells that are resistant to antibacterial compounds (Dong et al., 2019 ; Liu et al., 2019).

The magnetic property of NPs is to overcome the light, and MNP can convert external electromagnetic energy into controlled heat circulating in most directions of biology and medicine due to the property of local temperature control in nanoscale by remote control method (Nawaz et al., 2018). This is due to the nature of biological molecules such as DNA and transmembrane proteins that have similar stereotyped structures that influence MNPs to specifically catalyze or activate target molecules in a sensitizing manner at the molecular level. MNPs have been extensively studied specifically for the type of cancer using heat therapy (Mikocziova et al., 2021). The architecture of cancer cells is degraded by the heat emitted by the MNPs which is a cascade of shocks and the generated heat can stop the cancer cells and return to their state for anticancer activities (Cardoso et al., 2018). This remarkable potential has made it a strong candidate for clinical applications specifically for prostate cancer and gliomas without serious side effects. Recently, researchers in biomedical applications have begun to automatically use MNPs as inducible components of various biological systems such as cell signal trafficking, cargo delivery by magnetically actuated NPs, to heat-sensitive activation of transmembrane receptors by NPs, and production of proteins by gene expression studies (Shrestha et al., 2022).;(Zhong *et al*., 2022).

Thermal magnetization NPs in drug delivery

Several decades ago, after a series of experiments, and after using several experiments to stimulate and release loaded particles under controlled physiological conditions, including pH, ionic levels, glucose levels, changing enzyme levels, different thiol states, and hypersensitive or different immune stimuli. molecular bonds. Under these conditions, MNPs induce effective target drug delivery by modulating bi-molecular interactions such as contraction, contraction, and cleavage of target molecules (Singh et al., 2022 ; Gulfam *et al*., 2019). With this intriguing new approach, many new molecules such as siRNA, aptamers, chemotherapeutic agents, antibodies, and cell membrane escaping peptides can be used in various applications and have a future for remotely controlled cellular activities by designing MNPs with novel characteristic properties (Dong *et al*., 2019 ; Subhan & Torchilin, 2020)..Expand its potential to the whole body to provide appropriate therapy for different biological systems, and spherical therapy for the biological system. In terms of therapies, NPs play a potentially large role (Tabish *et al*., 2020).

NPs can also be designed to deliver selective drugs and genes to target organs or tissues, thus reducing the exposure of healthy tissues to drugs or genes. Moreover, some nanomaterials are used in heat therapy (Raj et al., 2021). Several classes of NPs, namely liposomes, magnetic and metalloids, are currently under clinical trials for cancer thermotherapy (Tan *et al*., 2020) Magnetic NPs (MNPs) are designed to be heated under a high-frequency magnetic field to induce cancer cell death. Research is progressing further in the fight against cancer by targeting cancer stem cells (CSCs) (Dong et al., 2019). Infect, CSCs can not only play a major role in cancer initiation, development and drug resistance, but chemotherapy drugs may increase the fraction of CSCs in a tumor, allowing these cells to survive and evade distant sites (Zhou et al., 2021).

In this battle against CSCs, MNPs have shown encouraging results. For example, the magnetic hyperthermia transduced by superparamagnetic iron oxide NPs (SPION) in the alternating current magnetic field reduced or eliminated CSC population (Najafi *et al*., 2019). The combination therapy of monoclonal antibody and paclitaxel loaded iron oxide magnetic NPs against cancer stem-like cell activity in multiple myeloma, led to significant reduction of tumor growth in a preclinical study (Iannazzo et al., 2020).

NPs have a large and obvious role in therapies. This is done by designing NPs as drug and gene-selective transporters to target organs or tissues, without exposure to healthy tissues of drugs or genes (Filipczak et al., 2021). As well as the use of some nanomaterials in heat treatment. Several classes of NPs, namely liposomes, magnetic and metalloids, are currently under clinical trials for cancer thermotherapy (Tan et al., 2020). Magnetic NPs (MNPs) are designed to be heated under a high-frequency magnetic field to increase the rate of cancer cell death. Research is progressing further in the fight against cancer by targeting cancer stem cells (CSCs) (Dong et al., 2019). Indeed, CSCs are not only involved in cancer initiation, development and drug resistance, but chemotherapy drugs may increase the fraction of CSCs in a tumor, allowing these cells to survive and evade distant sites. In this fight against CSCs, MNP has shown encouraging results. For example, the magnetic temperature of superparamagnetic iron oxide NPs (SPION) in the alternating current magnetic field reduced or eliminated CSC counts. Combined treatment of monoclonal antibodies and paclitaxel-loaded iron oxide magnetic NPs against CSC activity in multiple myeloma, significantly reduced tumorigenicity.

The objective of applying nanotherapy in medicine is to improve detection as well as increase the effectiveness of cancer medicine and reduce the systemic toxicity associated with this treatment (Soltani et al., 2021). It is important that the therapeutic agents arrive and can be concentrated at the target sites. Another advantage of nanomedicine in cancer treatment is personalized medicine where we can review the treatment results in the patient and plan the next treatment or decide to repeat the same treatment session (personalized medicine) (Milewska et al., 2021). Innovative, multifunctional hybrid NPs combine therapeutic and visualization capabilities for future use in simultaneous magnetic resonance imaging and treatment strategies based on targeted drug design, magnetic hyperthermia, or magnetic mechanical actuation (Montiel Schneider et al., 2022).

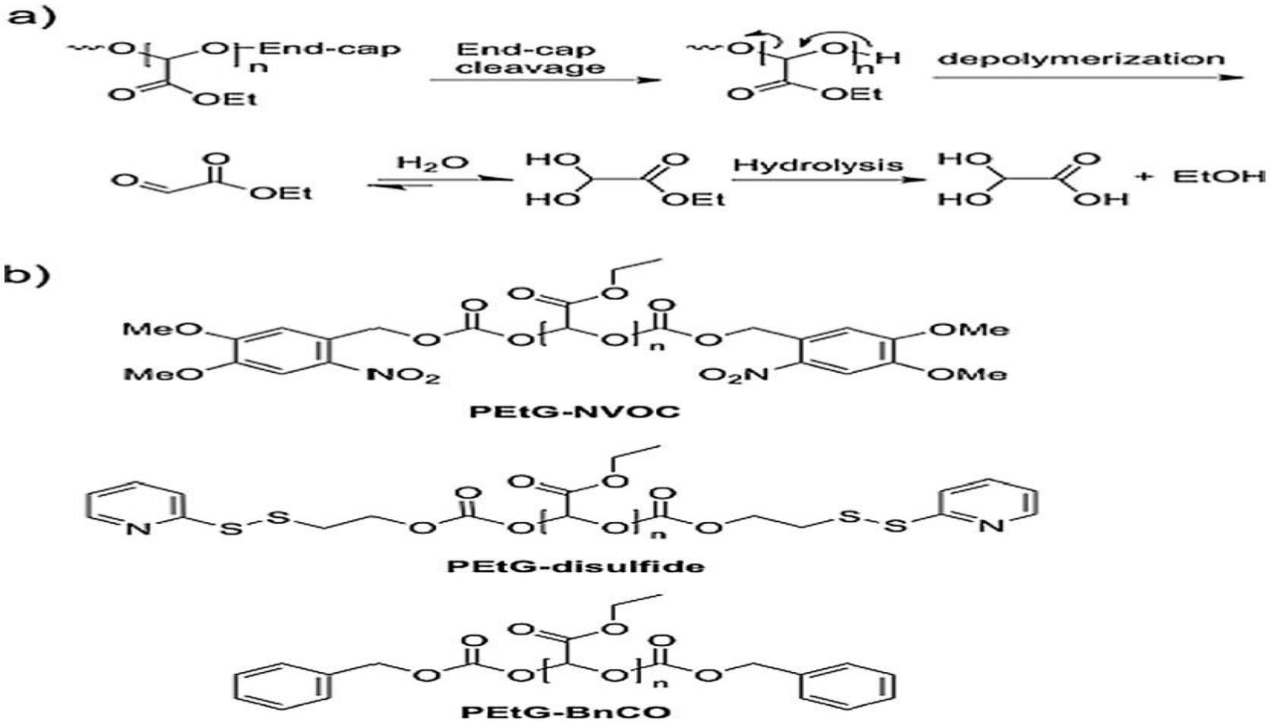
SPIONs are used in medical imaging, tumor targeting, drug delivery, and cancer treatment. The sizes, shapes, and surface properties of SPIONs can be engineered to improve targeting efficiency, drug delivery, MRI contrast, responses to external magnetic fields and reduce their toxicity as well as nonspecific cellular uptake. Successful application of MRI and some clinical findings from SPIONs could pave the way for advanced therapeutic use in clinical applications (Palanisamy & Wang, 2019).

Combustible polymers

Over the past few decades, there has been much research on the controlled release of medications employing drug delivery systems. Drug delivery methods can increase the bioavailability, specificity of targeting, solubility, or dispersibility of hydrophobic medications, resulting in fewer negative side effects. Due to their ability to be manipulated to assemble into a range of nanostructures, including vesicles, micelles, and solid core particles, polymers have been extensively investigated for drug administration. (Al-Musawi et al., 2020 ; Dong et al., 2019).

Due to its propensity to magnify reactions to stimuli, CPs are very desirable for a variety of applications, including sensors. CPs are therefore very desirable for a variety of applications including sensors responsive plastics and coatings, lithography, and medication delivery because they have the capacity to enhance reactions to stimuli (Zhang & Travas-Sejdic, 2021). Few research has so far looked at CPs potential for drug delivery. To combat this, research of micelles made of poly (ethyl

glyoxylate) (PEtG)-PEG block copolymers was recently published. Ethyl glyoxylate is created when PEtG depolymers, and it is then hydrolyzed to produce ethanol and glyoxylic acid (Zeglio et al., 2019).
Glyoxylic acid is a metabolic intermediate that the liver can handle and should be safe in small doses. It was thought that initiating PEtG degradation would lead to drug erosive release from the PEtG domains and fast drug release, leaving drug-loaded PLA for sustained drug release (Fan, 2018). Due of its quick UV light response, 6-Nitroveratryl carbonate capped PEtG was chosen as the perfect model system.



(a) Depolymerization scheme for PEtG. (b) Chemical structures of thestimuli-responsive and control PEtGs. (Mishra et al., 2022).

Zwitterionic polymers

Additionally, nanoparticles have been created that exhibit a pH-dependent shift in surface charge. Zwitterionic polymers are one of the most often studied systems because they feature cationic and anionic groups that regulate surface charge in response to pH (Blackman et al., 2019). These zwitterionic polymers have a positive charge at an acidic pH and a negative charge in a basic pH. However, these zwitterionic polymers grow more hydrophobic and are generally neutral at neutral pH, with balanced populations of positive and negative components. But once within tumor cells, the equilibrium between positive and negative charges will be upset, leading to conformational changes that make it easier for the medicine to be released (Harijan & Singh, 2022); (Ching et al., 2020).
The carbonized zwitterionic polymer was combined with a photothermal dye (IR 825) to create the nanoparticles. These nanoparticles showed dimming of fluorescence before to aggregating in the tumor location as a result of the hydrophobic interaction with neutral pH and – stacking (Liu et al., 2013). The release of IR 825 and regained fluorescence were caused by the little pH shift in TME, which allowed the charge of the nanoparticles to be changed. These nanoparticles can be employed for photothermal treatment and diagnostics at the same time (Yang et al., 2019).

Electrochemical potential-responsive nanoparticles

Electrically triggered medication delivery devices have attracted increased interest recently in the context of cancer treatment. Utilizing materials whose dipole moment varies spontaneously or compounds that exhibit redox properties when an external current is introduced might accomplish this. Different electro-responsive materials, such as conducting polymers, metal nanoparticles, and nanocomposites, among others, are used to create electro-responsive drug delivery systems. The pace at which pharmaceuticals are delivered depends on the application and the conductive materials used (Das et al., 2020.; (Ji et al., 2019).

These electric signals may be produced and regulated easily, and they can also be used to induce the release of molecules at the target location in pulse, sustained, or on-demand fashion. Different factors, including charge density, electrodes, electrolyte concentration, hydrophilicity of the electro-responsive material, presence of ionisable molecules in the system, in-vivo pH, and aqueous medium composition, impact the electro-responsiveness (Dong et al., 2019 ; (HADI & ABOOD, 2022). The variation in thin film thickness affects the amount of loaded medicines. When the film is thin, the medication is released more quickly but is held in the film for a shorter period of time (Song et al., 2019). The capacity of a loaded drug will rise if the film thickness is greater, however since it is difficult to release the drug from the inner film, a large electric current must be provided (Puiggalí-Jou et al., 2019).

Due to the thin film's volume to surface ratio characteristic, nanoparticles are integrated into it to increase the loading capacity of drugs. Weaver et al. created dexamethasone-loaded polypyrrole nanocomposites using graphene oxide. Due to its great stability, graphene oxide serves as a nanocarrirer and increases the amount of drug put into nanocomposite film (Caldas et al., 2020 ; Bansal et al., 2020). The electrical reaction causes the medication to release from the thin nanocomposite layer. Paclitaxel-loaded magentoelectric nanoparticle ($CoFe_2O_4$@$BaTiO_3$) was used by Rodzinski et al. as a treatment for ovarian cancer. He showed how some of the nanoparticles detected in the target region compare to a current when d.c current is applied (Chauhan, 2022); (Lakshani Randitha, 2018). Many biological systems already have redox potential gradients in their intracellular and extracellular environments, thus if we use a weak redox conductive substance as a nanocarrier like DDS the efficiency (Casillas-Popova et al., 2022).

NIR light-based photo-responsive materials

Due to its numerous benefits, including its non-invasiveness, high spatial resolution, ability to regulate temperature, convenience, and ease of handling, light is utilized as an external stimulus in a variety of biological applications, including the delivery of drugs (Chen et al., 2021). Systems that use NIR to administer drugs have greater advantages than those that use other stimuli. Because NIR (750–1200 nm) is safer for cells and tissues than UV light and has better tissue penetration, it is a possible carrier for medication delivery to specific sites. In drug delivery systems, NIR light causes a variety of photoreactions, including photoisomerization, photolysis, photocoupling, photopolymerization, and photothermal (Dai et al., 2019).

Two photon absorption, upconverting nanoparticles, and photothermal mechanisms are the key foci of these photoreactions. Drug distribution by photochemical means (PCDD) is reliant on the speed of covalent cleavage caused by NIR light (Wang et al., 2022). PCDD needs enough energy to break covalent bonds, hence this technique

should include molecules that easily break when exposed to NIR light, such as ester, aldehydes, and carboxylic acids. Because of the vibrating action, the photo-thermal response mostly transforms light energy into thermal energy (Dong et al., 2019). The photo-thermal drug delivery system uses a variety of nanomaterials, including carbon-based nanomaterials, metal oxide nanoparticles, grapheme-based nanomaterials, and NIR absorption dyes (Sajjadi et al., 2021). Gold nanoshell-coated betulinic acid liposomes (AuNS-BA-Lips), created by Liu et al., exhibit regulated drug release with a synergistic impact of chemo-therapy and thermal-therapy, and can decrease tumor growth by up to 83.02% (Zhou et al., 2022 ; Abid Ali Baker et al., 2007).
When tested on U-87 MG cancer cells, a nanocomposite comprising spiropyran-functionalized amphiphilic polymers and upconversion nanoparticles (UCNPs) loaded with doxorubicin destroyed 60% of the cancer cells (Jin et al., 2021). Two photon fluorophores with two photon absorption have been reported by Jonas et al. They are suitable for FRET to photoisomerize azobenzene and mesoporous nanosilica and are loaded with the anticancer drug captothecin, which exhibits controlled release by two photon triggerred photoisomerzation and kills the cancer cells (Raza et al., 2019; Wang et al., 2022).

Nanoparticles-vehicles to target angiogenesis
It deals with the development of fresh blood vessels from older ones. Some tumor forms have a unique characteristic whereby they will not even grow to a size of 2 mm without angiogenesis (Silva et al., 2018). Inflammation, tumor recurrence, a high degree of metastasis, and a shorter life span are all associated with angiogenesis and are caused by the overexpression of angiogenic growth factors in an aberrant condition and the lack of angiogenic inhibitors (Okano et al., 2019).
Anti-angiogenesis treatment is based on the use of either medications that stop the growth of new blood vessels feeding the tumor or drugs that kill the tumor already present (Al-Ostoot et al., 2021 ; Al-Mayahi et al., 2008).
Endostatin, angiostatin, and TNP-470 are examples of NPs coated medications that must either block the stages involved in blood vessel development for tumor growth or destroy already existing blood vessels as part of the NPs directed antiangiogenesis chemotherapeutic mechanism based on delivered NPs (e.g., combretasta) (Liang et al., 2021 ; Baker et al., 2009).

Conclusions and future perspectives
Cancer treatment based on NPs is in in its infancy but has a lot of promise. By altering the approach of numerous therapeutic applications, nanotechnology has changed cancer therapy. This created a remarkable relevance for particularly identifying cancer kinds through the delivery of safe and effective systems and the tagging of active chemicals. To get around the drawbacks of traditional chemotherapies, certain formulations based on nanotechnology have been released on the market, and many more are now undergoing clinical studies. To increase a person's chance of survival, active or passive drug delivery devices can avoid the majority of chemotherapy adverse effects. A nanotechnology has also been deeply involved in nanomedicine as a result of the precise information about how NPs-mediated lingering safety problems including toxicity and immune response the prosperous.

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