Nanomaterialsin Medical Applications

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ABSTRACT:

The nanomaterials are the materials within the nano dimension (1–100 nm scale) have remarkably new characteristics which may influence the changes of device structures, and systems with novel properties and functions.They may have potential applications in many sectors, e.g, healthcare, electronics, transportation, energy harvesting, space exploration etc. In healthcare sector, it has the possibilities to develop drug delivery, gene therapy, diagnostics, and many areas of research and development. In recent years nanomaterialshave been applied to human health with promising results, especially in the field of cancer treatment. It focuses on developing new methods of preventing, diagnosing and treating various diseases. These materials show very high efficiency in destroying cancer cells and drug delivery trials. So the nanomaterialsin the form of nanorobotmay be used as an alternative to traditional cancer therapy, mostly due to the fact that they allow cancer cells to be targeted specifically. Other potential applications of nanotechnology in medicine may include cell repair, blood clotting, immune properties development and subsequently to deliver vaccine antigens. A nano-knife may be used as an almost non-invasive method of destroying cancer cells with high voltage electricity. Carbon nanotubes are already a popular way of repairing damaged tissues and might be used to regenerate nerves in the future. There are endless applications of these materials. The main objectives of this article are to outline the potential uses of nanomaterialsin medicine and suggest their future prospects.

Keywords: Cancer, Healthcare, Nanomedicine, Nanorobot,Nanotechnology

I. INTRODUCTION:

The word ‘nano’ has come from a Greek word meaning ‘dwarf’ or something very small and depicts one thousand millionth of a meter (10^{-9} m). A single human hair has 60,000 nm thickness and the DNA double helix has a radius of 1 nm. A virus is of typically 100 nm in size.Nanotechnology is one of the most promising technologies in this century. It is the ability to convert the nanomaterialsinto many useful applications by observing, measuring, manipulating, assembling, controlling and manufacturing matter at the nanometer scale. The materials with nanodimenions(usually 1 ~ 100 nm) are called nanomaterials (NMs). There are potential medical applications of NMs due to their good biocompatibility, mechanical, optical, electrical and chemical behaviors. Nanoparticles (NPs) with suitable diameter range have been reported to be able to enter blood circulation system.30 There are reports that the NM-based therapeutics have great potential in the treatment of tumors, diabetes, infection, neurodegenerative disease, and inflammation.

Different physical and chemical properties of NMs,due to the presence of different functional groups, are suitable of their applications in biodistribution, cellular processes, and cytotoxic effects. For example, the size of the NM affects cellular entrapment by facilitating or inhibiting polymerization. The shape of NMs also influences organ and cellular tropism. Spherical NMs promote phagocytosis of macrophages, but disk-shaped

structures do not. By tailoring these aspects, specific properties of NMs can be used to design new biomedical applications, which include various clinical and research activities and modulation of processes in target cells.38 Based on nanotechnology, various NMs have been developed, such as iron oxide NPs, gold NPs (AuNPs), cerium oxide NPs, carbon-based materials, polymeric NPs, and quantum dots (QDs). NMs have shown great potential in cancer treatment; its early detection, diagnosis, imaging, and treatment are possible due to these materials. Their specific physical, chemical, and biological properties and unique structure, allow them to manipulate to work at the molecular level. The NMs are antigenic or medicinally active, and can stimulate a strong immune response in the body.There are couple of examples of the NMs those can kill or inhibit pathogenic cell types by exploiting their autoimmunity or cellular toxicity.Many NMs are used nowadays as the potential antitumor drugs. The most of the NMs developed so far for medical applications are of metallic type as they are prepared by relatively easy processes; however, there may few non metallic or polymeric types materials used in this area.

II. METALLIC NANOMATERIALS (MNMS)

The MNMs used in medical applications are of fine metal or metal oxide nanocrystals. As they have some unique properties, they are used to interact directly with cell membranes and intracellular structures. TheMNMs mostly used in different medical applications are iron oxide, gold NPs, and cerium oxide NPs, etc.

(i) Iron oxide

Medical applications and biotechnological advances, including magnetic resonance imaging, cell separation and detection, tissue repair, magnetic hyperthermia and drug delivery, have strongly benefited from employing iron oxide nanoparticles due to their remarkable properties, such as superparamagnetism, size and possibility of receiving a biocompatible coating [1]. Iron oxide is a type of magnetic material that is used in cancer treatment and targeted therapy. Fe_3O_4-based magnetic NPs are recognized as promising hyperthermia-specific agents. , The magnetite (Fe_3O_4) nanoparticles are widely applied due to their biocompatibility, high magnetic susceptibility, chemical stability, innocuousness, high saturation magnetisation, and inexpensiveness. Magnetite (Fe_3O_4) exhibits superparamagnetism as its size shrinks in the single-domain region to around 20 nm, which is an essential property for use in biomedical applications [2]. According to a recent report, magnetic NPs with diameters ranging between several (~9 nm) and hundreds (~200 nm) of nanometers can circulate in blood vessels and undergo endocytosis into cells.Furthermore, Fe_3O_4 NPs can be functionalized using antibodies and achieve active targeted cancer therapy. There is a report of using a conjugated polypyrrole-Fe_3O_4 NPs to target and damage breast tumor cells in vitro. In fact, superparamagnetic iron oxide NPs have been recognized for clinical use in the form of ferucarbotran, ferumoxides, andferumoxtran. These NMs are highly biodegradable and biocompatible; the iron core is recycled into soluble ferritin iron or hemosiderin. Iron oxide NPs are also intensively used in imaging system as contrast agents in pathophysiological studies.

Multifunctional superparamagnetic iron oxide nanoparticles (SPIONs) are attracting an increased attention due to their magnetic properties, biocompatibility, and contrast imaging in biomedical applications such as cancer therapy and controlled drug delivery. SPIONs provide controlled release, can be directed toward affected site, track payloads via contrast imaging, heat the effected sites, and trigger the onset of drug release. Even though the concepts of hyperthermia were proposed over a century ago with considerable potential applicability the technique has still not been translated into routine clinical uses. The magnetic fluid hyperthermia (MFH) turned to be the most target specific method for localized remote heating system. MFH can revolutionize tumor treatment, along with radiotherapy or chemotherapy and/or as separate intervention. The precise control of the physico-chemical parameters of SPIONs is important for hyperthermia applications, as heat induced by SPIONs

is highly dependent on numerous factors. In this chapter, we review some of the recent technical advances and limitations in the SPIONs engineering for magnetic hyperthermia [3].Iron oxide nanoparticles are found very useful material for detecting morphological and physiological changes in vivo using magnetic resonance imaging (MRI) technique. Processes in the tissue where the blood brain barrier is intact in this way shielded from the contact to this conventional contrast agent and will only reveal changes in the tissue if it involves an alteration in the vasculature. This technique is very useful for detecting tumors and can even be used for detecting metabolic functional alterations in the brain such as epileptic activity [4]. Magnetic Quantum Dots (MQDs) derived from iron oxide nanoparticles and QDs possess excellent superparamagnetic and fluorescent properties, respectively making them multifunctional nanoprobes because of their; (a) strong magnetic strength with tunable functionality, such as rapid and simple magnetic separation, (b) intense and stable fluorescence from QDs combined with tunable biological functionality upon QDs bio-activation, and (c) imaging/visualization by simple ultraviolet light exposure. These excellent features of MQD nanoprobes enable them to be used for magnetic resonance imaging (MRI) as contrast agents, nano-diagnostic systems for Point-of-Care (PoC) disease diagnosis, theranosticsnanorobots and in other bio-medical applications. Most of MQDs are derived from iron based MNPs because of their abundance, superparamagnetic properties, low cost and easy to synthesize. In this review, we present different methods employed for chemical synthesis of MQDs derived from iron oxide MNPs, their major chemical compositions and important parameters, such as precursor compositions, quantum yield and magnetic properties. The review also summarizes the most frequently used MQDs in applications such as bio-imaging, drug delivery, biosensor platforms and finally ends with future prospects and considerations for MQDs in biomedical applications [5].Here, the oleate-capped iron oxide nanoparticles (OIONPs) were synthesized by the high-temperature method first; after then, the poly(acrylic acid)-capped iron oxide nanoparticles (PIONPs) were obtained via a ligand exchange reaction between OIONPs and sodium poly(acrylic acid). The physicochemical properties of PIONPs were evaluated by Fourier-transform Infrared Spectroscopy (FT-IR), X-ray Diffraction (XRD), Scanning Transmission Electron Microscopy (STEM), Dynamic Light Scattering (DLS), and zeta potential. The FT-IR analysis confirmed the successful ligand exchange on the surface of iron oxide nanoparticles. STEM images displayed that the prepared PIONPs were monodisperse spherical nanoparticles. The PIONPs were stable in ultrapure water and could be kept for 5 weeks without aggregation [6].

(ii) Gold NMs

Functionalized gold nanoparticles with controlled geometrical and optical properties are the subject of intensive studies and biomedical applications, including genomics, biosensorics, immunoassays, clinical chemistry, laser phototherapy of cancer cells and tumors, the targeted delivery of drugs, DNA and antigens, optical bioimaging and the monitoring of cells and tissues with the use of state-of-the-art detection systems [7]. In recent years gold NMs (AuNMs) have shown important potential in various biomedical and research applications, such as catalysis, bioanalysis, and imaging. The preparation technology is simple, and it is easy to control the size and shape of AuNMs. It has been reported that AuNMs can selectively and specifically recognize tumor cells. Studies reported in the literature have shown that AuNMs are easily functionalized, increase the time of circulation, and are stable in systemic circulation. In addition, AuNMs have low toxicity and protect drugs from potential transformation in tissues and organs. Perhaps the most important property of AuNMs is their ability to destroy tumor cells. Thus, such AuNMs as AuNPs and gold nanocages are a promising tool for selectively killing tumor cells through photothermal (PT) damage.AuNPs can enhance the apoptotic effect of tumors, which makes it possible to decrease radiation doses, thereby reducing side effects on surrounding normal tissues.

AuNPs can also enhance the effect of radiotherapy, which has been verified in vivo and in vitro in animal models of tumors.AuNPs are commonly used as nanobioconjugates. The functionalization of NPs (eg, with polyethylene glycol [PEG] or antibodies) allows the nanobioconjugates to remain in the bloodstream and preferentially accumulate in cancer tissue. These nanobioconjugates have the ability to penetrate the cell nucleus, increasing the likelihood that the active cytostatic substance acts directly on DNA. Studies reported in the literature have shown that multifunctional AuNPs can be used both to image and medical treatment.If a high-frequency electrical current passes through the electrode and creates heat that destroys cancer cells. AuNPs have been used in this field widely, making it possible to destroy the cells efficiently. The optical properties of nanoshells can be utilized in ablation techniques. The nanoshells coated with gold, absorbsspecific wavelengths of light. Citrate-coated gold has been shown to have antitumor properties. A novel gold nanocages ~45 nm in edge length are reported to show potential for inhibition of targeted cancer cells. The AuNMs as reporters have been broadly applied into lateral flow immunechromatographicalassay (LFICA) and enzyme-linked immune sorbent assay (ELISA), which is a well-established technology for analysis of the target analytes in food safety, clinical diagnosis, environmental monitoring, and medical science and so on. Au based nanomaterials (AuNMs) are known to possess many attractive features such as unique electrical, optical and catalytic properties as well as excellent biocompatibility. [8]

Due to their unique optical and physicochemical properties, gold nanoparticles have gained increased interest as radiosensitizing, photothermal therapy and optical imaging agents to enhance the effectiveness of cancer detection and therapy. Furthermore, their ability to carry multiple medically relevant radionuclides broadens their use to nuclear medicine SPECT and PET imaging as well as targeted radionuclide therapy. In this review, we discuss the radiolabeling process of gold nanoparticles and their use in (multimodal) nuclear medicine imaging to better understand their specific distribution, uptake and retention in different in vivo cancer models. In addition, radiolabeled gold nanoparticles enable image-guided therapy is reviewed as well as the enhancement of targeted radionuclide therapy and nanobrachytherapy through an increased dose deposition and radiosensitization, as demonstrated by multiple Monte Carlo studies and experimental in vitro and in vivo studies [9].Gold nanoparticles (AuNPs) have been shown to be useful as carriers of various anticancer drugs as well as diagnosis platforms. In this review, we discuss the synthesis and physiochemical properties of AuNPs. We also highlight the photothermal and photodynamic properties of AuNPs and relevant applications in therapeutic studies. Furthermore, we review the applications of AuNPs in cancer treatment as and their underlying anticancer mechanisms in multiple types of cancer [10].The color changes of the gold nanoparticles embedded in a porous hydrogel show the concentration changes of substances in the body to allowconstant monitoring of disease progression and therapeutic success, and with the potential to extend the lifetime of implantable sensors. The research group of CarstenSönnichsen has used gold nanoparticles as sensors to detect proteins in microscopic flow cells for many years. The nanoparticles react to alterations in their surrounding by changing color and act as small antennas for light, as they strongly absorb and scatter it and therefore appear colorful. In this study, to stopthe particles moving away or being degraded by immune cells, they were embedded in an innovative porous hydrogel with a tissue-like consistency. After being implanted under the skin, tiny blood vessels and cells grow into the pores to allow the sensor to integrate in the tissue and not be rejected as a foreign body [11].

(iii) Cerium oxide nanoparticles

Promising results have been obtained using cerium (Ce) oxide nanoparticles (CNPs) as antioxidants in biological systems. CNPs have unique regenerative properties owing to their low reduction potential and the

coexistence of both Ce^{3+}/Ce^{4+} on their surfaces. Defects in the crystal lattice due to the presence of Ce^{3+} play an important role in tuning the redox activity of CNPs. The surface Ce^{3+}:Ce^{4+} ratio is influenced by the microenvironment. Therefore, the microenvironment and synthesis method adopted also plays an important role in determining the biological activity and toxicity of CNPs. The presence of a mixed valance state plays an important role in scavenging reactive oxygen and nitrogen species. CNPs are found to be effective against pathologies associated with chronic oxidative stress and inflammation. CNPs are well tolerated in both in vitro and in vivo biological models, which makes CNPs well suited for applications in nanobiology and regenerative medicine. [12] Cerium oxide nanoparticles (CONPs) are highly unique catalytic antioxidants with scavenging capacity across a broad spectrum of agents, including reactive oxygen species (ROS) and reactive nitrogen species (RNS). The nanoparticle format imparts elevated surface oxygen vacancies that support potent scavenging of oxidants, while CONP's capacity to cycle between the Ce^{3+}/Ce^{4+} states results in a theoretically inexhaustible catalyst. Because of these highly favorable features, CONP has tremendous potential to serve as a redox-modulating therapeutic for various biomedical applications [13]. Cerium oxide NPs include a cerium core surrounded by an oxygen lattice. In normal cells, these NPs have an antioxidant and cytoprotective role under neutral pH. In an acid medium, which is one of the characteristics of tumorcells, these NPs show prooxidant and cytotoxic effects. Pei et al studied the antitumor effects of cerium oxide NPs in in vitro models, and the results showed that cerium oxide NPs inhibited the growth of tumor cells. There has been another report indicating that a high concentration (10 μg/mL) of cerium oxide NPs can suppress tumor-cell migration and inhibit tumor-cell proliferation.Cerium oxide (CeO_2) nanoparticles and silver-doped cerium oxide were produced via a green bioprocess by water extract of Salvia seeds as a capping agent without using any alkaline agent. Various procedures such as FT-IR, FESEM, EDX, TGA/DTG, and XRD were applied for the structure determination and morphology of synthesized nanoparticles. The outcomes show that synthesized nanoparticles have a uniform spherical morphology and a size average of 62 nm. The in vitro cytotoxicity effect of silver nanoparticles was investigated on the EPG human gastric cancer cell line which was detected in the treated EPG human gastric cancer cell to be up to 62.5 mM. Also, the synthesized nanoparticles were used to study antibacterial activity against pathogenic bacteria (Staphylococcus aureus and Pseudomonas aeruginosa) [14].Diabetic wounds represent a significant healthcare burden and are characterized by impaired wound healing due to increased oxidative stress and persistent inflammation. It was shown that CNP-miR146a synthesized by the conjugation of cerium oxide nanoparticles (CNP) to microRNA (miR)-146a, improves diabetic wound healing. CNP are divalent metal oxides that act as free radical scavenger, while miR146a inhibits the pro-inflammatory NFκB pathway, so CNP-miR146a has a synergistic role in modulating both oxidative stress and inflammation. In this study, we define the mechanism(s) by which CNP-miR146a improves diabetic wound healing by examining immunohistochemical and gene expression analysis of markers of inflammation, oxidative stress, fibrosis, and angiogenesis. We have found that intradermal injection of CNP-miR146a increases wound collagen, enhances angiogenesis, and lowers inflammation and oxidative stress, ultimately promoting faster closure of diabetic wounds [15].

Bone regeneration is a crucial part in the treatment of periodontal tissue regeneration, in which new attempts come out along with the development of nanomaterials. Herein, the effect of cerium oxide nanoparticles on the cell behavior and function of human periodontal ligament stem cells was investigated. The cell cycle tests demonstrated that CeO_2 NPs not only had good biocompatibility, but also promoted cell proliferation. Furthermore, the levels of alkaline phosphatase activity, mineralized nodule formation and expressions of osteogenic genes and proteins demonstrated CeO_2 NPs could promote osteogenesis differentiation of the

nanoparticles. Then we chose electrospinning to fabricate fibrous membranes containing CeO_2 NPs. It was found that the composite membranes improved mechanical properties as well as realized release of CeO_2 NPs. Micro-CT and histopathological evaluations revealed that nanofibrous membranes with CeO_2 NPs further accelerated new bone formation. Those exciting results demonstrated that CeO_2 NPs and porous membrane contributed to osteogenic ability, and CeO_2 NPs contained electrospun membrane may be a promising candidate material for periodontal bone regeneration [16].Owing to the self-renewing reactive oxygen species scavenger capability of cerium oxide nanoparticles (nanoceria), in vivo radioprotective effects was tested on stem cells and tissue regeneration using low-dose irradiated planarians as model system. The treated planarians with nanoceria or gum Arabic, as control, and was able to generate the stem cell molecular markers and tissue regeneration capability, as well as cell death and DNA damage in non-irradiated and in low-dose irradiated animals. It enhances the use of nanoceria in the number of stem cells and tissue regenerative capability, and reduce cell death and DNA damage after low-dose irradiation, suggesting a protective role on stem cells [17].

(iv) Quantum dots

Semiconducting nanoparticles, more commonly known as quantum dots, possess unique size and shape dependent optoelectronic properties. In recent years, these unique properties have attracted much attention in the biomedical field to enable real-time tissue imaging (bioimaging), diagnostics, single molecule probes, and drug delivery, among many other areas. The optical properties of quantum dots can be tuned by size and composition, and their high brightness, resistance to photobleaching, multiplexing capacity, and high surface-to-volume ratio make them excellent candidates for intracellular tracking, diagnostics, in vivo imaging, and therapeutic delivery. [18,19].Another popular type of NM are QDs. QDs are very small nanocrystals that emit fluorescence when stimulated by a specific wavelength of light, and their diameter is approximately 2–10 nm. Their structure consists of an inorganic core and shell, which can be modified with biological molecules, such as PEG. Their emission and absorption properties can be controlled precisely by modulating their size and shape. The benefit of QDs for tumor therapy is attributed to their mechanisms of photosensitization and radiosensitization. With electronic energy levels in the 1–5 keV range, QDs can be used as photosensitizers for photodynamic treatments, which have become an approved therapy modality for some types of tumors. Because of their high electron and atom density, QDs act as radiosensitizers that absorb high-energy photons and cause localized or targeted damage to tumor cells.Physical and chemical preparation of QDs have prominent downsides, including high costs, regeneration of hazardous byproducts, and use of external noxious chemicals for capping and stabilization purposes. To eliminate the demerits of these methods, an emphasis on the latest progress of microbial synthesis of QDs by bacteria, yeast, and fungi is introduced. Some of the biomedical applications of QDs are overviewed as well, such as tumor and microRNA detection, drug delivery, photodynamic therapy, and microbial labeling. Challenges facing the microbial fabrication of QDs are discussed with the future prospects to fully maximize the yield of QDs by elucidating the key enzymes intermediating the nucleation and growth of QDs. Exploration of the distribution and mode of action of QDs is required to promote their biomedical applications [20].Quantum dot (QD), a unique nano-sized semiconductor material, has secured an enduring position as a promising nanosensor in today's industry for its various application areas. The control of particle sizes allows the bandgap of the QDs to be “tuned” to give desired electronic and optical properties such as broad excitation spectra and tunable emission spectra with a narrow bandwidth, which make them very special for various optical research and applications. The biggest societal problem now is water pollution due to water-dissolved hazardous metal ions (Cu^{2+}, Zn^{2+}, Co^{2+}, Pb^{2+}, and Cr^{3+}) from industrial wastages. QDs have justified themselves as selective nanosensors for the sensitive detection of metal ions. QDs are used as medical imaging

tools for diseased cells like cancerous tumors, etc. due to their strong affinity toward a polar environment. This chapter covers the description of sensing and medical imaging applications of QDs for biomedical and sensing industries including some advances in this field [21].Quantum dots (QDs) as a new type of nano-structured luminescent materials has been widely used in biology, materials science, and physical optics. QD-based biosensors can be used for the rapid and accurate detection of biological macromolecules or inorganic molecules both in vivo and in vitro. To enhance their fluorescence properties and lower their biological toxicity, the surface of QDs needs to be modified. Currently, the surface modification technologies mainly include multidentate ligand, sulphydryl group coupling, amphiphilic molecules, cavity-chain, and dendrimer technology. Meanwhile, various biosensors have been developed by adopting different modification techniques to locate and track a variety of disease-specific biological molecules. Although enormous literatures have reported the biological applications of QD-based biosensors, few systematic reviews of surface modification technologies on QDs have been published. This paper reviews the surface modification technologies of QDs in biosensors and their medical applications [22].

III. NONMETALLIC NANOMATERIALS (NMS)

There are several different types of nonmetal NMs and carbon compounds are some of the most extensively studied. Several different "pure" carbon-based constructs have been studied, such as fullerenes and their derivatives, which are composed of carbon atoms arranged in a spherical shape, and carbon nanotubes (CNTs), which are most frequently studied in biological systems. Fullerenes and their derivatives are readily accessible to cells, and are conjugated with various therapeutic molecules because they have a unique nanostructure. In addition, the pure carbon composition of fullerenes gives them good biocompatibility. Moreover, carbon NMs have been linked with biological molecules and polymers, and so can be effectively used for antitumor applications in vivo. Therefore, functional fullerenes and their derivatives can be linked to a wide variety of active molecules to target tumor cells. Based on these experiments, fullerenes and their derivatives have become a new class of promising candidates for tumor treatments. C60 (or "bucky-ball" C60) is a hollow sphere with a diameter of 1 nm, and is made up of 60 carbon atoms. C60 is effective in terms of interactions with the immune system, and has dramatic potential as an antitumor drug. Compared with conventional antitumor chemicals, fullerenes and their derivatives are more efficient at inhibiting the growth of tumors. The result is not due to toxic effects on tumor cells, but the fullerenes, which have almost no toxicity in vivo or in vitro, have a strong ability to enhance immunity and protect normal tissues from tumor invasion.Endohedralmetallofullerenes (fullerenes encapsulating a metal atom) have shown dramatic potential for biomedical applications. The high antitumor activity may be because the water-soluble NMs can effectively trigger the host immune system to eliminate tumor cells and regulate the angiogenesis and oxidative defence system in vivo.

(i) Carbon nanotubes

CNTs are coaxial graphite layers with cylinders. CNTs are formed by polymerization of single carbon atoms under specific conditions. According to their structure, CNTs can be divided into two categories: single-walled CNTs (SWCNTs) and multi-walled CNTs (MWCNTs). The former is a single cylindrical carbon wall, and the latter is an MW cylinder nested in other cylinders. With the development of nanotechnology, integration of CNTs into tumor therapeutics is a rapidly advancing field. There are reports that CNTs promote the phagocytosis of dendritic cells at tumor sites, which produce more antigens to dendritic cells, significantly increasing the immunogenicity of proteins in the tumor. Similarly, inhaled CNTs can inhibit lung-resident dendritic cells and promote lung immune suppression. Regarding the direct therapeutic effect, CNTs can induce

tumor-tissue destruction by photothermal therapy (PTT), based on strong optical absorbance under near infra-red (NIR)-light excitation. Therefore, CNTs have attracted interest as efficient PTT agents for tumor treatments. Hyperthermia therapy is another type of optional solution for tumor treatment, especially for some solid malignant tumors, such as breast and liver tumors. CNTs are also used as PT tumor-ablation mediators. Due to the thermal conductivity and optical properties of CNTs, they have become mediators to optically stimulate NTs that are placed inside living cells and that kill tumor cells via local hyperthermia. SWCNTsare promising candidates as a PTT agent, because they also have high absorption in the NIR spectrum, which is ideal for inducing PT damage to tumor cells or tissues. Continuous NIR radiation can lead to cell death, because of excessive local heating of SWCNTs. MWCNTs also efficiently absorb NIR light and efficiently convert the absorbed energy into thermal energy. MWCNTs can be stimulated with NIR irradiation to damage tumorcell. CNTs make it possible to damage tumor cells noninvasively, and the potential applications for CNTs in tumor therapy have attracted much clinical interest. Therefore, CNTs can be considered another class of tumor PTT system, and are highly promising for clinical trials.

(ii) Graphene

Graphene is an emerging NM with single-layered carbon atoms in a two-dimensional honeycomb structure. Graphene has attracted great interest since its tremendous groundbreaking discovery in 2004.Graphene and its different subtypes, such as graphene oxide (GO) and reduced graphene oxide (RGO), have been extensively studied in the realm of nanomedicine, due to their exceptional physical, chemical, and mechanical properties.Graphene-based NMs have a well-described role in medical applications. Graphene-based NMs are used mainly for PTT. A report showed that Graphene-based NMs are highly efficient for tumor ablation under NIR-light irradiation [23], and GO-PEG was used for in vivo PTT [24]. It was found that the GO-PEG had no obvious side effects, and was safe during the treatment. Nanocomposite films of polysulfone (PSU) with different amounts (0.00–1.00 wt%) of a nanohybrid blend of graphene oxide (GO) and silver nanoparticles (AgNPs) obtained by a solution-blending method showed good properties. Tensile tests revealed that the PSU/GO-Ag nanocomposite films prepared have higher Young's modulus and tensile strength compared to the neat PSU films. The optimistic effects on the thermal stability, morphological structure as well as the hydrophilicity character of all the nanocomposite films was very clear furthermore, antibacterial testing results showed that the nanocomposite films prepared have a significant bactericidal capability, at very low GO-Ag loading (0.2 wt%), against both Gram negative (Escherichia coli) and Gram-positive (Staphylococcus aureus) strains. The characteristics of these nanocomposites based on the various results obtained in this study would give them a strong impetus for their use in many areas, particularly in the medical field [25].

nano-hydroxyapatite/Graphene Oxide were synthesized, and the composite were prepared in different ratios. The structural and morphological changes of synthesized nano hydroxyapatite, graphene oxide and reduced graphene oxide was investigated. Fourier Transform Infrared Spectrometer (FTIR) was used to investigate the chemical structural composition of the synthesized nano hydroxyapatite and its composite, which confirms that presence of presence of reduced graphene oxide, graphene oxide in the prepared composite. Field emission scanning electron microscopy (FE-SEM) analysis was employed to examine the surface morphology of the composite materials which confirms the presence graphene flakes and nanosized hydroxyapatite on the surface [26].Graphene and its derivatives, graphene oxide (GO) and reduced graphene oxide (rGO), are 2D carbon-based materials with remarkable physical, chemical and biological properties. Graphene sheets have high

specific surface area and mechanical strength. Moreover, they have been shown to influence the differentiation of stem cells and to improve properties of biomaterials [27].

Graphene oxide (GO) and hydroxyapatite (HAp) are frequently used as reinforcements in polymers to improve mechanical and biological properties. In this work, novel porous hybrid nanocomposites consisting of GO, HAp, and sodium alginate (SA) have been prepared by facile solution mixing and freeze drying in an attempt to obtain a scaffold with desirable mechanical and biological properties. The as-prepared porous GO/HAp/SA hybrid nanocomposites were characterized by SEM, XRD, FTIR, TGA, and mechanical testing. In addition, preliminary cell behavior was assessed by CCK8 assay. It is found that the GO/HAp/SA nanocomposites show improved compressive strength and modulus over neat SA and HAp/SA nanocomposites. CCK8 results reveal that the GO/HAp/SA nanocomposites show enhanced cell proliferation over neat SA and GO/SA nanocomposite. It has been demonstrated that GO/HAp20/SA holds promise in bone tissue engineering [28].

Agraphene-based biosensor for achieving a good sensitivity to detect hemoglobin and urine biomolecules of different concentrations.Graphene-based design results are analyzed in the form of absorption, sensitivity, and electric field. Metasurface in the form of a circle and split ring resonator is analyzed for detecting urine and hemoglobin biomolecules. The design results are also analyzed for different metasurface sizes. The thickness of different physical layers is varied to check its effect on absorption. The absorption response is reconfigured by changing the chemical potential of graphene material. The absorption response is tuned by changing the metasurface shape and size. The electric field intensity results are also matching with the obtained absorption response at a particular wavelength. The proposed design results are also compared with previously published similar designs. The high sensitivity obtained through this graphene-based biosensor can be applicable in medical applications for detecting hemoglobin and urine biomolecules [29].

IV. CHITOSAN NANOPARTICLES

Chitosan is a type of cationic oligosaccharide that is the major component of the exoskeleton of crustaceans and insects. Chitosan is a biopolymer containing β-(1,4)-2-amino-D-glucose and β-(1,4)-2-acetamido-D-glucose units. Chitosan NPs (ChNPs) are obtained by deacetylation, which removes an acetate moiety from chitin [30]. ChNPs are primarily degraded in the colon by the action of lysozyme and bacterial enzymes, and are finally eliminated in the feces. Chitosan is a natural polysaccharide that has excellent biocompatibility, biosecurity, biodegradability, and nontoxic characteristics.ChNPs are commonly modified with epichlorohydrin and PEG dicarboxylic acid.ChNPs also have dramatic potential for tumor therapy. ChNPs can directly affect the metabolism of tumor cells by inducing apoptosis and inhibiting cellular growth. Likewise, ChNPs play a role in increasing the immune function of the organism by facilitating the contact between the drug and the tumor-cell membrane. Reports show that ChNPs have high stimulatory activity on B and T lymphocytes and the humoral immune system, which can be activated at the same time.ChNPs also have a strong immunostimulating effect by increasing the activation and accumulation of polymorphonuclear and macrophage cells, and they induce cytokine production after intravenous injection. There is another example that indicates that ChNPs have their own antitumor effects [31]. ChNPs themselves have a positive charge; therefore, they can neutralize the negative charges on the surface of tumor cells, which has a tendency to contribute to their selective uptake. In this way, ChNPs can effectively inhibit proliferation of tumor cells by increasing the concentration of cytostatic agents at the tumor sites. All these attributes and examples show that ChNPs have great potential in tumor therapy.

CONCLUSION:

Over the last 20 years, NMs have come to play a significant role in commercial development. It has made many breakthroughs and new prospects for the world economy from advances in nanotechnology. With the potentially wide application of NMs in the future, NMs may be extensively used in various fields, especially medical applications. NMs can be used for clinical diagnosis and medical therapy, based on their size, biocompatibility, surface chemistry, relatively good stability, and adjustable toxicity in biological systems. It is highly expected that the application of NMs in the therapy will greatly improve current methods of cancer cell detection, imaging, and therapy, while reducing toxicity compared to traditional medical treatments.

However, there are several challenges in the field, and there are still controversies about the potential risk of nanomaterials. The most acute problems are potential chronic and acute toxic effects. There have been reports on the toxicity of NMs. NMs may be attached to the surface of biological membranes by adsorption or electrostatic interactions, and they can cause damage to cells by producing reactive oxygen species, leading to protein denaturation, lipid peroxidation, DNA damage, and ultimately cell death. For instance, NPs and CNTs can damage the respiratory and cardiovascular systems, and they can enter the central nervous system through the blood–brain barrier, resulting in a variety of nervous system diseases. In vitro studies have shown that CNTs can induce cell apoptosis, decrease cell viability, and disrupt the cell cycle and inflammatory responses. It has been confirmed that CNTs can damage lung tissue and that they are toxic to the immune system. Besides, the blood incompatibility of CNTs also limits their use in the clinic. Although many studies have shown that the functionalization of CNTs can improve their water-solubility, proof of their biocompatibility and safety is currently insufficient. There is a report that sugar-functionalized SWCNTs formed stable homogeneous aqueous solutions [32]. Thenoncovalent functionalized SWCNTs could also improve the water solubility of SWCNTs [33]. When QDs are applied in the body, their toxicity cannot be ignored, because they may contain heavy metals. It is necessary to carry out a detailed toxicity study to ensure safety prior to further applications in humans. Therefore, the long-term toxicity of NMs to living systems needs to be intensively studied. There is an article that analyzes the possible toxicological implications of NMs in nanomedicine [34]. Development of therapies is a multidisciplinary field, and with more in-depth research on immunology, molecular biology, and NMs, an ideal therapy or NM will eventually be produced for the medical applications. The conversion of nanotechnology to routine clinical practice will require a multidisciplinary approach guided by clinical, ethical, and social perceptions. In view of the significant research results being dedicated to the field, it may be expected that humans will greatly benefit from nanotechnology and NMs in the very near future.

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