AN OVERVIEW OF INNOVATIVE NANOENGINEERED BIOMATERIALS FOR MODERN THERAPIES

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ABSTRACT:

Nano-engginering enables for the precise manipulation and designing of biomaterials at the nanoscale for the novel applications in therapeutic, diagnosis, targeted drug delivery, implants and tissue engineering. Nanotechnology offers unparalleled atomic-level precision, making it possible to create materials with extremely specific and desirable features. Materials with this degree of control over their synthesis have extremely specialized and adjustable characteristics. Having at least one dimension in the nanoscale, which permits distinct physical and chemical properties, is a common characteristic of nanomaterials. Nano-engineered materials have special optical, magnetic, and electrical capabilities, among other characteristics. The physicochemical properties of nanoparticles are notably different from those of macroscopic materials due to their greater surface-to-volume ratio, which results in novel and increased capabilities. Applications for the special qualities of nanoscale materials can be found in a wide range of industries, including targeted gene and medication delivery, biotechnology, and electronic storage systems. This review will look at the vast number of nanomaterials that biomedical engineers can work with, emphasizing how they can be used to solve a variety of biomedical problems.

Keywords: Biomaterials, Nano-engineered, biomedical Applications, targeted delivery, nanoparticles

INTRODUCTION:

Nanomaterials are substances that have been reduced in size to a range of approximately 1 to 100 nanometers. Examples of nanomaterials include nanocrystals, which consist of a quantum dot surrounded by semiconductor materials; nanoscale silver; dendrimers, which are repetitively branched molecules; and fullerenes, which are carbon molecules shaped like hollow spheres, ellipsoids, or tubes.

Nanomaterials divides into several groups according to their form and chemical composition.[1]

A nanomaterial can be any of the four categories listed below, depending on how many dimensions are outside of the nanoscale,

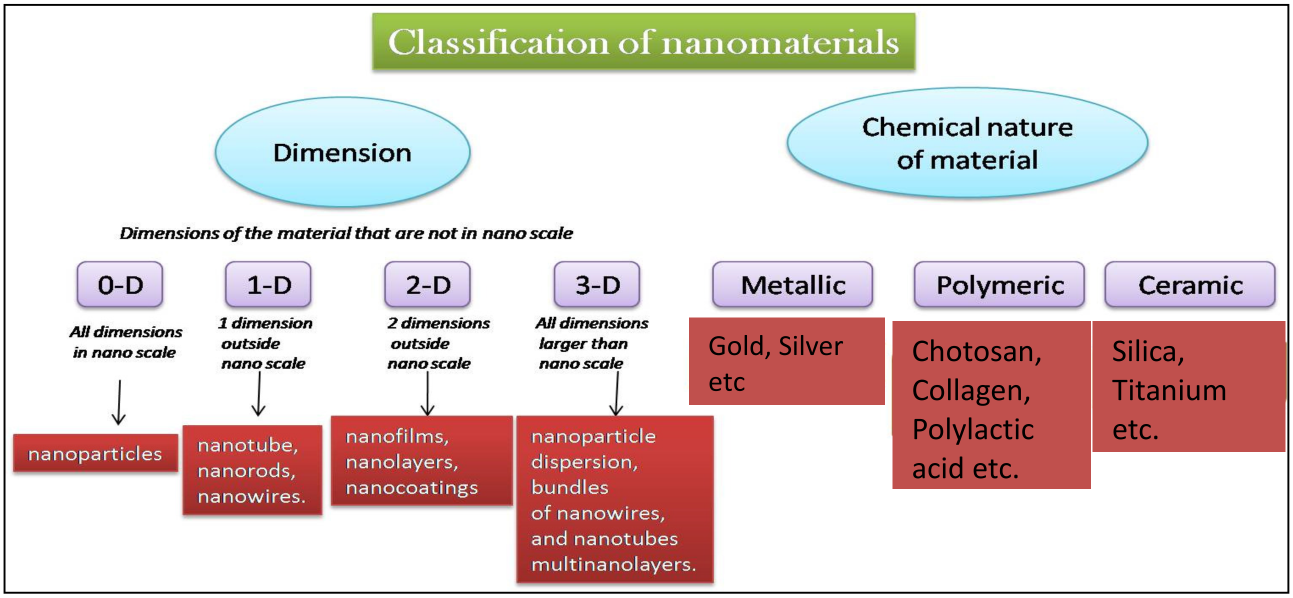

Fig. 1 Nanomaterials Classification

1) **Zero-dimensional (O-D):** Zero-dimensional materials—those with all of their dimensions at the nanoscale, or smaller than 100 nm—are categorized as 0 D nanomaterials. Such materials exhibit no delocalization and total electron confinement. The most common kind of 0-D nanomaterial is in the form of nanoparticles. Nanoparticles exist in a range of sizes and shapes and can be composed of one or more chemical components.[2]

2) **One-dimensional (1-D):** One-dimensional materials, or 1-D nanomaterials, that have a single dimension that are not nanoscale, resulting in needle-shaped materials. These materials include nanowires, Nano rods, and nanotubes. Reduction of the bulk crystalline material into the nano

form causes delocalization along the axis and 2-D electron confinement, which have a substantial impact on the material's quantum characteristics.[3]

Single-walled carbon nanotubes (SWNTs) and multi-walled carbon nanotubes (MWNTs) are two distinct types of carbon nanotubes (CNTs) that were discovered in 1990. Carbon nanotubes are used in a variety of sectors, such as energy research, field effect emitters, composite materials, and nanoelectronics, because of their unique physical and chemical properties.[4]

Biomedicine has also shown a great deal of interest in CNTs. Many CNT-based biosensors with different sensing techniques have been developed to treat cancer, distribute medications, and detect different biological chemicals.[5]

3) **Two-dimensional (2-D):** These materials have the appearance of plates because two dimensions do not extend to the nanoscale. Two-dimensional nanomaterials may include nanofilms, nanolayers, and nano-coatings. Along the plane, electrons are delocalized, while electron confinement occurs throughout the material's thickness.[2]

4) **Three-dimensional (3-D):** Bulk materials with no dimensions at the nanoscale are called three-dimensional nanomaterials. They either have a nanocrystalline structure or are made up of tiny components. Nanoparticle dispersions, nanotubes, and bundles of nanowires or nanofibers are examples of three-dimensional nanomaterials.[6] They also comprise multi-nanolayer materials like layered and matrix-reinforced nanocomposites, in which the reinforcing phase has a nano diameter and the nanocomposites' dimensions transcend the nanoscale.

Biomedical sectors such as burn and wound care, tissue engineering, organ repair, and regenerative medicine—which treat osteoporosis and other disorders—have found several uses for nanofibers. Because of their greater surface area, drugs, proteins, and cells can cling to nanofibers more easily than they do to bulk materials. It can be produced in the form of complex macro-scale structures. While electrospinning is the most commonly used method for creating nanofibers, self-assembly and force-spinning have also been documented as viable approaches. [7]

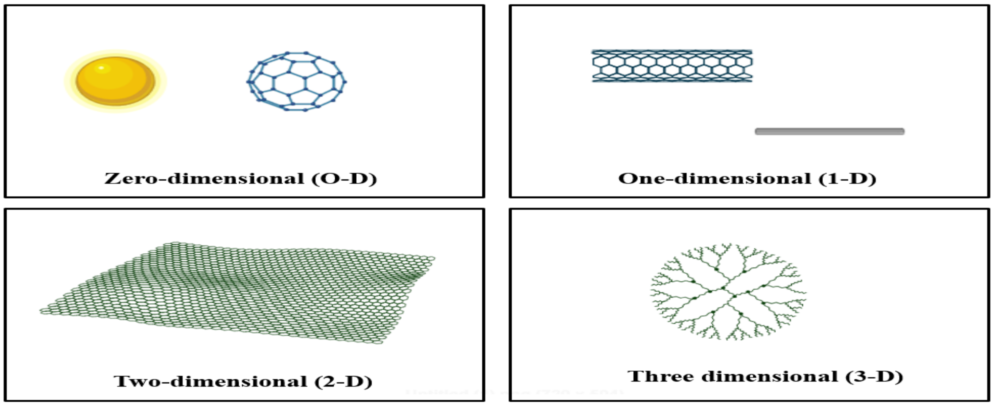

Fig. 2 nanomaterials based on Dimension

Nanomaterials can be broadly classified into four groups based on their chemical composition: metallic, ceramic, polymeric, and nanocomposites. Nanocomposites consist of porous media, colloids, gels, and copolymers and are composed of a blend of metallic, ceramic, and polymeric nanoparticles. [8]

(i) **Metallic nanomaterials** - With their distinct electric, magnetic, optical, and catalytic qualities, metallic nanomaterials and metal nanoparticles have become a novel class of substances with applications in chemistry, physics, material sciences, biology, and medicine. They are generated by reducing bulk crystalline metallic salts of Ru, Pt, Ag, Au, and so on to their nanoform.[9]

Gold nanoparticles can have a wide range of chemical functional groups added to them to facilitate conjugation with target antibodies, ligands, and pharmaceuticals. This allows for a multitude of potential biotechnological applications.[10] and customized drug administration in addition to target analyte pre-concentration, innovative methods for distributing genes and medications. Moreover, several biological imaging modalities, such as MRI, CT, PET, ultrasound, SERS, and optical imaging, have been developed using gold nanoparticles.[11]

Both biological (plants, bacteria, yeast, algae, and fungi) and chemical (sonolysis, thermolytic reduction, sun irradiation, laser ablation, etc.) techniques can be used to create these.[12]

(ii) **Polymeric nanomaterials** - The biodegradable polymers poly (D,L-lactic acid) (PLA), poly (D,L-lactic-co-glycolic acid) (PLGA), and poly (ε-caprolactone) (PCL) as well as their copolymers that are diblocked or multi blocked with poly (ethylene glycol) (PEG) are included in polymeric nanomaterials. Numerous synthetic and natural polymeric materials have been documented for usage in biomedical applications. One such application is the delivery of curcumin to malignant cells using mPEG-PA.[13]

(iii) **Ceramic nanomaterials** - Because ceramic nanoparticles can tolerate harsh environments that metals cannot, including high loading rates, high temperatures, wear, and chemical attack, they have gained a lot of interest as possible building materials. Materials made of titanium, silica, copper, and other materials are examples of ceramic nanomaterials.[14]

(iv) **Nanocomposite** - These are multiphase solids, where each phase has one, two, or three dimensions less than 100 nanometers (nm), or they are formations with recurring distances between phases that are nanoscale.[15] This term can refer to copolymers, colloids, porous media, and gels in the broadest sense; however, its most common meaning is a solid mixture made up of a bulk matrix and one or more nano-dimensional phases that have different properties because of structural and chemical differences. Polymeric nanocomposites, such as collagen, polylactic acid, and chitosan, were used in medical settings for wound dressing and pharmaceutical adhesive applications.[16]

Nanomaterial based technology is making it possible to diagnose and detect variety of disorders such as cancer and infectious diseases with potential applications in biomedicine. It also aided in the development of novel medications and drug delivery systems based on genes or proteins. When nanomaterials are used in biomedicine, different nano devices must be designed and developed to interact more precisely with the intended tissue of the body in order to exert their effect. Thus, with fewer negative consequences, these kinds of substances and devices may be developed into biomedical applications that are particular to cells and tissues.[17]

Biomedical applications are using a wide range of nanomaterials, such as hydrogel, polymeric nanoparticles, carbon nanotubes, silica, magnetic, and metallic nanoparticles. Different nanomaterials are distinguished by their massive surface area, unique shape and size, and unique optical and magnetic characteristics. [18]

Because of their remarkable optical and electrical properties, high stability, biological compatibility, adjustable shape and size dispersion, and ease of surface functionalization with a range of biomolecules, gold nanoparticles are a great option for biomedical applications. Numerous investigations and studies in the fields of biology and medicine have concentrated on these qualities.[19]

GNP in diagnostics:

Gold nanoparticles were used in bioimaging and visualization techniques to identify various biological and chemical agents. In 1880, alcoholism was treated with intravenous injections of colloidal gold solution. Further development in 1927 uses colloidal gold solution to relieve cancer patients' discomfort who are incurable. The gold isotope (198Au) colloidal solution proved therapeutically effective in the treatment of cancer.[20] Applications for colloidal gold that have emerged more recently include electron transport in bio macromolecules and catalytic processes, endocytosis, cell motility research, and PCR efficiency.[21]

Using colloidal gold in membrane assays, diseases caused by parasites, viruses, and fungi have been diagnosed, early pregnancy, blood group identification, myocardial infarction diagnosis, and hepatitis B detection. Currently, GNP-assisted immune chromatographic analysis is utilized for the quick diagnosis of tuberculosis, as well as the environmental and biological liquid detection of pesticides, antibiotics, and poisons.[22]

Nanoscale gold has been effectively employed in the creation of plasmatic biochips and biosensors. These devices are primarily utilized in medicine (drug screening, antibody and antigen analysis, infection diagnosis), biology (fast environmental monitoring, solution assays, and disperse systems), and chemistry (assays, rapid environmental monitoring, and disperse systems).[23]

Various GNP-assisted biosensors have been created for the immunodiagnosis of HIV infections, tick-borne encephalitis, papillomas, and Alzheimer's disease. Due to GNPs' exceptional ability to maintain their optical qualities in cells for extended periods, photo thermal therapy has been developed as a biomedical application of GNP in chemotherapy-resistant malignancies.[24] In addition to their usage in diagnostics and cell photothermolysis, GNPs are being utilized more frequently in direct therapeutic applications, such as the management of rheumatoid arthritis.

One of the main factors in the pathogenesis of tumor growth is intense angiogenesis, which is the production of new capillaries in organs or tissues.[25] It was discovered that the GNPs interacted with glycoproteins that bound heparin, such as basic fibroblast growth factor and vascular permeability factor/vascular endothelial growth factor. When combined with anticancer medications, GNP mediates angiogenesis, including that which occurs in tumor tissues, and inhibits tumor activity by altering the shape of the molecules. This provides an alternative and highly successful method of treating cancer by targeted drug delivery.[26]

Silver Nanoparticles:

Silver can inhibit a broad range of germs and bacterial strains that are commonly encountered in industrial and medical processes. Topical ointments and lotions containing silver to prevent burns and open wound infections are among the most popular and well-known uses of silver and silver nanoparticles.[27]

Wounds induce disruptions in the anatomic and cellular continuity of tissues, which impacts physiological activities. As a result, wound healing is a biological reaction that is complex and crucial to the restoration of bodily functioning and tissue integrity. delayed recovery time often leads to bacterial infection and nutritional deficiencies hence the principle objective is to minimize the patient's pain and discomfort while healing the wound as quickly as possible.[28]

Because of their special optical characteristics connected to surface plasmon resonance and antibacterial qualities, silver nanoparticles are becoming more and more significant in biological applications these days.[29] Bacterial invasion at the wound site delays the healing process and causes the inflammatory phase to become chronic, limiting the regeneration phase. Silver nanoparticles loaded with guar gum alkylamine (GGAA) result in to development of new nanocomposite for skin wound healing application. Furthermore, silver nanoparticles can deliver therapeutic molecules to specific locations within the body, increasing the effectiveness of medications while reducing negative effects. Additionally, they are essential to diagnostic technologies because they allow for the sensitive detection of biomolecules and disease indicators using a variety of optical and electrochemical techniques.[30]

Chitosan Polymeric Nanoparticles:

Chitin is a naturally occurring biopolymer consisting of βlinked N-acetyl glucosamine (NAG) units. These units form a three-dimensional α-helical shape that is stabilized by hydrogen bonding between molecules within the molecule.[31] The primary sources of chitin production are the crustacean cuticles, particularly those of prawn and crab shells, as well as other food sector leftovers. chitosan is a polysaccharide derived from chitin deacetylation and composed of glucosamine and N-acetyl glucosamine.[32]

Nanofibers-based chitosan derivatives such as carboxymethyl, carboxyethyl and hexanoyl chitosan has been utilized extensively in the biomedical field. Hexanoyl chitosan nanofibers in chloroform solvent are resistant to lysosome hydrolysis and have anti-thrombogenic properties, they can be used in a variety of medical applications.[33] The high moisture retention, gel-forming ability, and antibacterial properties of hexanoyl chitosan nanofibers make them an excellent biomaterial for a variety of tissue engineering applications. Tissue engineering uses living cells whose extracellular environment has altered to create biological replacements that may be implanted into the body Cell adhesion and proliferation were enhanced by an electrospun water-soluble carboxymethyl chitin (CMC)/PVA scaffold, that's why tissue engineering applications utilized it. Recent work has combined chitosan with nano silver to create novel scaffolding for wound healing and its antibacterial effect against E. Coli and S. aureus.[34]

In conjunction with polylactic acid and alginates, chitosan is a potentially effective carrier for the regulated administration of anti-HIV and anti-cancer medications. Drug delivery uses water-soluble carboxymethyl chitin (CMC) including lamivudine for antiretroviral therapy and curcumine for cancer treatment.[35]

Recent advances in nanotechnology leads to development of various nanomaterial for biomedical application such as diagnostics and imaging. One interesting type of nanomaterial is magnetic iron oxide nanoparticles since it has a long blood half-life, is biocompatible, and has minimal toxicity, among other qualities.[36]

Due to their large surface area, iron oxide nanoparticles can be used to deliver therapeutic agents, create a nanostructured electrode for implantable micro batteries (e.g., cochlear implants), and cross-link functional groups to tumor-targeting ligands such as antibodies or peptides for diagnostic imaging (magnetic resonance imaging).[37]

Precipitation-based synthesis is the most widely used technique for producing iron oxide nanoparticles. While iron oxide nanoparticles have been shown to be a viable tool for medication delivery and cancer detection since 2006, a significant barrier to their utilization in therapeutic applications as they quickly aggregate and precipitate, especially in physiological fluids when there is no surface coating, and unstable in aqueous systems. Thus, IO nanoparticles must be coated or encapsulated in liposomes, and chitosan for there in vivo applications. [38]

Owing to their unique magnetic properties super para magnetic iron oxide nanoparticles (SPION) makes them appealing materials for a range of biological uses, including targeted drug delivery to cancer cells and other disease areas, heat therapy to kill cancer cells, and use of contrast substances in magnetic resonance imaging.[39]

Nanofibres:

In recent year nanofibers drew a lot more interest because of their distinctive qualities and intrinsic functionalities. Nanofibers comes under the class of one dimensional nanomaterials. Nanofibres made from the biocompatible and biodegradable material shows greater potential in biomedical and healthcare industry because of its porosity and large surface area, which allow cell adhesion and attachment sites for various biomolecules such as proteins, DNA etc. [40]

One of the most crucial fields of biomedicine is drug delivery. Electro spun nanofibres help to encapsulate drug molecules and preserve their integrity and bioactivity. The drug's release is dependent on the polymer fibre breaking down, which is easily controlled.[41]

Most of the drugs are weak organic acid or bases and get deactivated when comes in extreme acidic or basic environment results in to low bioavailability at the site of action. To overcome this problem core shell electrospun fibers were widely used in that the drug molecules can be encapsulated until needed at the site of action and in this way efficacy of drug molecule can be maintained. This form of drug therapy can be used in treatment of cancer and AIDS.[42] Tissue engineering helps to regenerate different tissues, including skin, cartilage, and bone, and it also helps to restore normal function. In addition to having therapeautic application, tissue is either grown in patient or grown outside followed its transplant. Tissue engineering can have diagnostic application where tissue grown outside the body followed by invivo study such as its uptake, metabolism and toxicity testing.[43]

Electrospinning is the efficient method for preparation of artificial scaffold by the use of various natural and synthetic polymers. These electrospun nanofibers are used to repair, replace and enhance the properties of the tissues. The natural polymers which are mainly employed to support the extra cellular matrix includes the collagen and glycosaminoglycans, collagen gives tensile mechanical properties at the level of single fiber but having poor bulk quality taking this in consideration synthesis of collagen with poly l lactic acid gives desirous properties required for bone tissue regeneration.[44]

The mechanical and electrical properties of electrospun fibres are important in tissue engineering, in this core shell nanofibres are employed which not only encapsulate the bioactive molecule but also it will modify the surface characteristics of electrospun nanofibres. Collagen-coated poly ε caprolactone nanofibers are used for skin tissue engineering. Electrospinning of Hyaluronic acid and poly ethylene glycol diacrylate fibres are being used for soft-tissue scaffold materials in 3D cell cultures.[44]

Electrospun nanofibers can also be used in wound care applications. The important feature of electrospun nanofibre for wound dressing is it should be non-toxic and non-antigenic. Derivatives of chitosan possesses antibacterial and antifungal activity, possess effective resistance to both gram-positive and gram-negative bacteria. Electrosunnanofibre of chitosan/collagen composite is widely used in wound dressing due to its beneficial effects such as it stimulating cell migration and proliferation and aids in the healing of wounds. [45]

Carbon nanotubes (CNT):

The demands placed on the biomedical sector today are incompatible: patients want better healthcare, while healthcare providers seek increasingly cost-effective diagnostics and treatments which has led to the creation of a variety of devices for theranostic applications. The biomedical sector must therefore overcome the issue of creating tools and materials that are advantageous to both.[46]

Carbon nanotubes (CNTs) have remarkable mechanical, electrical, thermal conductivity, and physical properties that contribute to their promise in biomedicine. These are carbon atom allotropes with a diameter of 1 nm and a length ranging from one 1–100 m.

Carbon nanotubes are classified into two categories based on how the graphene cylinders are arranged. Single-walled (single layer) and multi-walled nanotubes (each with roughly 50 layers,). [47]

In radiation oncology, CNT is used to treat malignant tumors. Conventional radiation and chemotherapy kill both the cancer and healthy cells, which can have a variety of negative effects. CNT-based miniature x-ray machines are primarily used to deliver precise doses of radiation directly to a target location without endangering nearby healthy tissues. The advantages of CNT-based machines include quick reaction times, fine focus points, low power consumption, extended lifespan, and inexpensive costs. [48]

CNT as a biosensor: biosensor is a device which convert biological response in quantifiable electrical signal. CNT employed piezoresistive sensors are extensively employed in theranostic applications, including inhalers, kidney dialysis machines, breathing equipment, hospital beds, eye surgeries, and patient monitors. DNA sequencing of the body is another method utilised by CNT-based biosensors to identify the faulty gene linked to cancer.[49]

CNT based chemical sensors are also used in analysis of blood gases,salt concentration such as sodium, potassium and for determination of blood ph and glucose. CNT can serve as carrier in systems for the targeted delivery of medications[50]

Graphene:

Graphene is a material with exceptional electrical, optical, and mechanical capabilities that is made up of individual carbon atoms organised in a honeycomb configuration. First study in 2008 on graphene for biomedical applications, explored the further development for widespread applications ranging from biocompatible scaffold for cell culture, antibacterial material and cell imaging, Graphene and its derivatives have demonstrated exceptional promise in a variety of fields, including nanoelectronics, field effect transistors, engineering of nanocomposite materials and in different biomedical applications such as in targeted therapy of cancer, drug delivery and in gene therapy. Its excellent property in fluorescent resonance energy transfer makes it useful in various biosensing applications. [51]

Drug delivery: graphene oxide, which is created when graphite is oxidised, is a useful nanocarrier for applications involving the transport of drugs and genes. Graphene's high surface area and abundant oxygen-containing groups make it biocompatible and enable chemical conjugation to carry drugs or DNA. Graphene oxide's reactive OH and COOH groups enable conjugation with a variety of biomolecules, including $Fe3O4$ nanoparticles, quantum dots, DNA, protein, and biotargeting ligands, making it valuable for a range of biological and medicinal applications.[52]

To treat cancer, a combination of medications is administered to overcome drug resistance in cancer cells. In cancer therapy, graphene oxide is employed as a nanocarrier to provide regulated loading and distribution of various medicines. In addition to being utilised in cancer treatment, graphene oxide is a useful nanocarrier for the delivery of the anti-inflammatory medication ibuprofen.[53]

Gene therapy:

Gene therapy is a potential technique to treating numerous diseases caused by genetic disorders, such as Parkinson's disease, cystic fibrosis, and cancer. It uses genes or short oligonucleotide sequences as therapeutic agents instead of traditional drug therapy.[54] This method is frequently employed to treat genes that are faulty and contribute to the development of disease. In gene therapy, a "vector" that carries DNA encoding a therapeutic protein is used to move the DNA within cells. To increase the transfection efficiency and to reduce the toxicity of polymer, graphene oxide (GO) conjugated with positively charged polyethylene amine is used in gene therapy applications It enables the electrostatic contact caused by the cationic polymer to cause plasmid DNA to condense onto the surface of GO. Recent application of graphene oxide include functionalization with chitosan in gene as well as in drug delivery.[55]

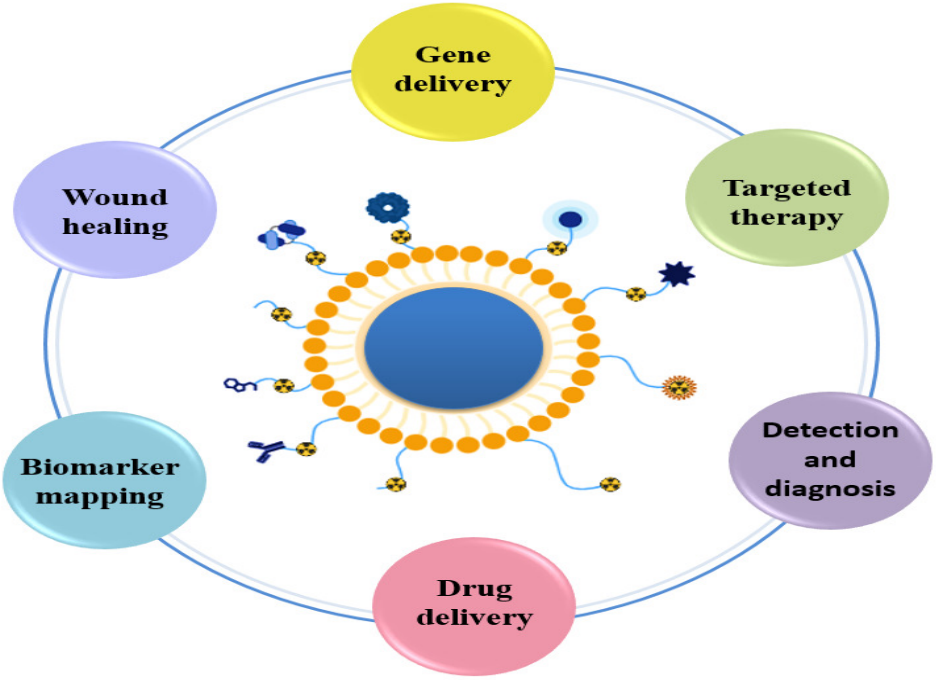

Fig. 3 Applications of Nanomaterials

Photothermal therapy:

Besides gene therapy and chemotherapy, phototherapy is another approach to treat various diseases. Phototherapy include phototherma therapy and photodynamic therapy, which utilizes light irradiation at raised temperature to destruct the abnormal tissues. The concept underlying photothermal and photodynamic therapy is that when photosensitizers (PSs) are exposed to the right kind of light, free radicals or reactive oxygen species are produced, which causes permanent damage to cancer cells.[56]

PEGylated nanographene oxide loaded with doxorubicine is utilised to provide heat and medication to the tumorigenic zone to enable combination chemotherapy and photothermal treatment in one system to cure cancer.[57]

Biosensing:

Several graphene derivatives, including graphene oxide, pristine graphene, doped graphene and chemically reduced graphene, are extensively employed in a variety of biosensing applications. A variety of graphene oxide-based biosensors have been created to detect different biomolecules, including DNA, ATP, amino acids, and dopamine. FRET-based biosensors have been developed for the detection of DNA and other biomolecules, owing to the fluorescence quenching ability of graphene.[52]

In anticancer therapy, a range of compounds can be conjugated with graphene oxide due to its larger surface area; for photodynamic treatment (PDT), graphene oxide conjugated with sulphonic acid and folic acid loaded with porphyrin photosensitizers was employed to treat diseases including cancers due to its low toxicity and high stability under physiological conditions. Through hydrophobic interactions, GO was loaded with a chlorine photosensitizer, which dramatically increases the accumulation of photosensitizers in tumor cells and has a stunning photodynamic effect on cancer cells.[58]

Conclusion

The present review focused on use of various nanomaterials which may give breakthrough for the development of nano as well as biosensors in diagnosis. However more comprehensive studies are required for assessing their contribution for safe and effective use in the field of nanomedicine.

REFERENCES

[1] J. K. Patel, A. Patel, and D. Bhatia, "Introduction to nanomaterials and nanotechnology," in *Emerging technologies for nanoparticle manufacturing*, Springer, 2021, pp. 3–23.

[2] A. Behera and A. Behera, "Nanomaterials," *Adv. Mater. An Introd. to Mod. Mater. Sci.*, pp. 77–125, 2022.

[3] B. Wang, D. Xue, Y. Shi, and F. Xue, "Titania 1D nanostructured materials: synthesis, properties and applications," *Nanorods, Nanotub. Nanomater. Res. Prog.*, pp. 163–201, 2008.

[4] D. Tasis, N. Tagmatarchis, A. Bianco, and M. Prato, "Chemistry of carbon nanotubes," *Chem. Rev.*, vol. 106, no. 3, pp. 1105–1136, 2006.

[5] T. Rasheed, A. A. Hassan, F. Kausar, F. Sher, M. Bilal, and H. M. N. Iqbal, "Carbon nanotubes assisted analytical detection–Sensing/delivery cues for environmental and biomedical monitoring," *TrAC Trends Anal. Chem.*, vol. 132, p. 116066, 2020.

[6] C. A. Amarnath, S. S. Nanda, G. C. Papaefthymiou, D. K. Yi, and U. Paik, "Nanohybridization of low-dimensional nanomaterials: synthesis, classification, and application," *Crit. Rev. solid state Mater. Sci.*, vol. 38, no. 1, pp. 1–56, 2013.

[7] A. A. Nayl *et al.*, "Recent progress and potential biomedical applications of electrospun nanofibers in regeneration of tissues and organs," *Polymers (Basel).*, vol. 14, no. 8, p. 1508, 2022.

[8] S. Pandya *et al.*, "Nanocomposites and IT'S application-review," *Int. J. Pharm. Sci. Res.*, vol. 4, no. 1, pp. 19–28, 2013.

[9] H. Bönnemann and K. S. Nagabhushana, "Metal nanoclusters: synthesis and strategies for their size control," *Met. nanoclusters Catal. Mater. Sci.*, vol. 2, pp. 21–48, 2008.

[10] I. Ielo *et al.*, "Synthesis, chemical–physical characterization, and biomedical applications of functional gold nanoparticles: A review," *Molecules*, vol. 26, no. 19, p. 5823, 2021.

[11] Y. Wu, M. R. K. Ali, K. Chen, N. Fang, and M. A. El-Sayed, "Gold nanoparticles in biological optical imaging," *Nano Today*, vol. 24, pp. 120–140, 2019.

[12] M. Rani, J. Yadav, S. Chaudhary, and U. Shanker, “An updated review on synthetic approaches of green nanomaterials and their application for removal of water pollutants: Current challenges, assessment and future perspectives,” *J. Environ. Chem. Eng.*, vol. 9, no. 6, p. 106763, 2021.

[13] H. Danafar, “MPEG–PCL copolymeric nanoparticles in drug delivery systems,” *Cogent Med.*, vol. 3, no. 1, p. 1142411, 2016.

[14] K. L. Arun, M. Udhayakumar, and N. Radhika, “A Comprehensive review on various ceramic nanomaterial coatings over metallic substrates: applications, challenges and future trends,” *J. Bio-and Tribo-Corrosion*, vol. 9, no. 1, p. 11, 2023.

[15] A. Faghri and Y. Zhang, *Transport phenomena in multiphase systems*. Elsevier, 2006.

[16] A. Biswal, S. S. Purohit, and S. K. Swain, “Chitosan based composite scaffolds in skin wound repair: A review,” *J. Drug Deliv. Sci. Technol.*, p. 104549, 2023.

[17] J. Jagur-Grodzinski, “Polymers for tissue engineering, medical devices, and regenerative medicine. Concise general review of recent studies,” *Polym. Adv. Technol.*, vol. 17, no. 6, pp. 395–418, 2006.

[18] K. Zhu, Y. Ju, J. Xu, Z. Yang, S. Gao, and Y. Hou, “Magnetic nanomaterials: Chemical design, synthesis, and potential applications,” *Acc. Chem. Res.*, vol. 51, no. 2, pp. 404–413, 2018.

[19] J. Yao, M. Yang, and Y. Duan, “Chemistry, biology, and medicine of fluorescent nanomaterials and related systems: new insights into biosensing, bioimaging, genomics, diagnostics, and therapy,” *Chem. Rev.*, vol. 114, no. 12, pp. 6130–6178, 2014.

[20] M. Laprise-Pelletier, T. Simão, and M. Fortin, “Gold nanoparticles in radiotherapy and recent progress in nanobrachytherapy,” *Adv. Healthc. Mater.*, vol. 7, no. 16, p. 1701460, 2018.

[21] W. Zhou, X. Gao, D. Liu, and X. Chen, “Gold nanoparticles for in vitro diagnostics,” *Chem. Rev.*, vol. 115, no. 19, pp. 10575–10636, 2015.

[22] V. Gubala, L. F. Harris, A. J. Ricco, M. X. Tan, and D. E. Williams, “Point of care

diagnostics: status and future," *Anal. Chem.*, vol. 84, no. 2, pp. 487–515, 2012.

[23] G. A. Lopez, M.-C. Estevez, M. Soler, and L. M. Lechuga, "Recent advances in nanoplasmonic biosensors: applications and lab-on-a-chip integration," *Nanophotonics*, vol. 6, no. 1, pp. 123–136, 2017.

[24] L. Dykman and N. Khlebtsov, "Gold nanoparticles in biomedical applications: recent advances and perspectives," *Chem. Soc. Rev.*, vol. 41, no. 6, pp. 2256–2282, 2012.

[25] M. Papetti and I. M. Herman, "Mechanisms of normal and tumor-derived angiogenesis," *Am. J. Physiol. Physiol.*, vol. 282, no. 5, pp. C947–C970, 2002.

[26] P. Zanjanchi, S. M. Asghari, H. Mohabatkar, M. Shourian, and M. Shafiee Ardestani, "Conjugation of VEGFR1/R2-targeting peptide with gold nanoparticles to enhance antiangiogenic and antitumoral activity," *J. Nanobiotechnology*, vol. 20, no. 1, p. 7, 2022.

[27] S. Agrawal, M. Bhatt, S. K. Rai, A. Bhatt, P. Dangwal, and P. K. Agrawal, "Silver nanoparticles and its potential applications: A review," *J. Pharmacogn. Phytochem.*, vol. 7, no. 2, pp. 930–937, 2018.

[28] H. Sorg, D. J. Tilkorn, S. Hager, J. Hauser, and U. Mirastschijski, "Skin wound healing: an update on the current knowledge and concepts," *Eur. Surg. Res.*, vol. 58, no. 1–2, pp. 81–94, 2017.

[29] N. Chouhan, *Silver nanoparticles: Synthesis, characterization and applications*, vol. 1. IntechOpen London, UK:, 2018.

[30] O. A. Sadik, A. O. Aluoch, and A. Zhou, "Status of biomolecular recognition using electrochemical techniques," *Biosens. Bioelectron.*, vol. 24, no. 9, pp. 2749–2765, 2009.

[31] D. Elieh-Ali-Komi and M. R. Hamblin, "Chitin and chitosan: production and application of versatile biomedical nanomaterials," *Int. J. Adv. Res.*, vol. 4, no. 3, p. 411, 2016.

[32] M. Yadav, P. Goswami, K. Paritosh, M. Kumar, N. Pareek, and V. Vivekanand, "Seafood waste: a source for preparation of commercially employable chitin/chitosan materials," *Bioresour. Bioprocess.*, vol. 6, no. 1, pp. 1–20, 2019.

[33] K. Azuma, S. Ifuku, T. Osaki, Y. Okamoto, and S. Minami, "Preparation and biomedical

applications of chitin and chitosan nanofibers," *J. Biomed. Nanotechnol.*, vol. 10, no. 10, pp. 2891–2920, 2014.

[34] L. A. L. Fliervoet and E. Mastrobattista, "Drug delivery with living cells," *Adv. Drug Deliv. Rev.*, vol. 106, pp. 63–72, 2016.

[35] T. Fazal *et al.*, "Recent developments in natural biopolymer based drug delivery systems," *RSC Adv.*, vol. 13, no. 33, pp. 23087–23121, 2023.

[36] L. H. Reddy, J. L. Arias, J. Nicolas, and P. Couvreur, "Magnetic nanoparticles: design and characterization, toxicity and biocompatibility, pharmaceutical and biomedical applications," *Chem. Rev.*, vol. 112, no. 11, pp. 5818–5878, 2012.

[37] F. M. Kievit and M. Zhang, "Surface engineering of iron oxide nanoparticles for targeted cancer therapy," *Acc. Chem. Res.*, vol. 44, no. 10, pp. 853–862, 2011.

[38] A. Bumb *et al.*, "Synthesis and characterization of ultra-small superparamagnetic iron oxide nanoparticles thinly coated with silica," *Nanotechnology*, vol. 19, no. 33, p. 335601, 2008.

[39] null Wahajuddin and S. Arora, "Superparamagnetic iron oxide nanoparticles: magnetic nanoplatforms as drug carriers," *Int. J. Nanomedicine*, pp. 3445–3471, 2012.

[40] R. Rasouli, A. Barhoum, M. Bechelany, and A. Dufresne, "Nanofibers for biomedical and healthcare applications," *Macromol. Biosci.*, vol. 19, no. 2, p. 1800256, 2019.

[41] P. Wen, M.-H. Zong, R. J. Linhardt, K. Feng, and H. Wu, "Electrospinning: A novel nano-encapsulation approach for bioactive compounds," *Trends Food Sci. Technol.*, vol. 70, pp. 56–68, 2017.

[42] Š. Zupančič, "Core-shell nanofibers as drug-delivery systems," *Acta Pharm.*, vol. 69, no. 2, pp. 131–153, 2019.

[43] R. Cancedda, B. Dozin, P. Giannoni, and R. Quarto, "Tissue engineering and cell therapy of cartilage and bone," *Matrix Biol.*, vol. 22, no. 1, pp. 81–91, 2003.

[44] A. Rogina, "Electrospinning process: Versatile preparation method for biodegradable and natural polymers and biocomposite systems applied in tissue engineering and drug

delivery," *Appl. Surf. Sci.*, vol. 296, pp. 221–230, 2014.

[45] C. Ardean *et al.*, "Antimicrobial activities of chitosan derivatives," *Pharmaceutics*, vol. 13, no. 10, p. 1639, 2021.

[46] Z. Al-Dulimi, M. Wallis, D. K. Tan, M. Maniruzzaman, and A. Nokhodchi, "3D printing technology as innovative solutions for biomedical applications," *Drug Discov. Today*, vol. 26, no. 2, pp. 360–383, 2021.

[47] S. Nanot *et al.*, "Single-walled carbon nanotubes," *Springer Handb. Nanomater.*, pp. 105–146, 2013.

[48] V. Negri, J. Pacheco-Torres, D. Calle, and P. López-Larrubia, "Carbon nanotubes in biomedicine," *Surface-modified Nanobiomaterials Electrochem. Biomed. Appl.*, pp. 177–217, 2020.

[49] M. Sireesha, V. Jagadeesh Babu, A. S. Kranthi Kiran, and S. Ramakrishna, "A review on carbon nanotubes in biosensor devices and their applications in medicine," *Nanocomposites*, vol. 4, no. 2, pp. 36–57, 2018.

[50] V. Schroeder, S. Savagatrup, M. He, S. Lin, and T. M. Swager, "Carbon nanotube chemical sensors," *Chem. Rev.*, vol. 119, no. 1, pp. 599–663, 2018.

[51] M. J. Allen, V. C. Tung, and R. B. Kaner, "Honeycomb carbon: a review of graphene," *Chem. Rev.*, vol. 110, no. 1, pp. 132–145, 2010.

[52] S. M. Mousavi, S. A. Hashemi, Y. Ghasemi, A. M. Amani, A. Babapoor, and O. Arjmand, "Applications of graphene oxide in case of nanomedicines and nanocarriers for biomolecules: review study," *Drug Metab. Rev.*, vol. 51, no. 1, pp. 12–41, 2019.

[53] G. Gonçalves, M. Vila, M. Portolés, M. Vallet-Regi, J. Gracio, and P. A. A. P. Marques, "Nano-graphene oxide: a potential multifunctional platform for cancer therapy," *Adv. Healthc. Mater.*, vol. 2, no. 8, pp. 1072–1090, 2013.

[54] A. Yazdani, Z. Alirezaie, M. J. Motamedi, and J. Amani, "Gene therapy: a new approach in modern medicine," *Int. J. Med. Rev.*, vol. 5, no. 3, pp. 106–117, 2018.

[55] H. Bao *et al.*, "Chitosan-functionalized graphene oxide as a nanocarrier for drug and gene

delivery," *Small*, vol. 7, no. 11, pp. 1569–1578, 2011.

[56] R. Bhole, C. Bonde, P. Kadam, and R. Wavwale, "A comprehensive review on photodynamic therapy (PDT) and photothermal therapy (PTT) for cancer treatment," *Turkish J. Oncol.*, vol. 36, no. 1, 2021.

[57] M. Ashrafizadeh *et al.*, "Doxorubicin-loaded graphene oxide nanocomposites in cancer medicine: stimuli-responsive carriers, co-delivery and suppressing resistance," *Expert Opin. Drug Deliv.*, vol. 19, no. 4, pp. 355–382, 2022.

[58] Y. Li, H. Dong, Y. Li, and D. Shi, "Graphene-based nanovehicles for photodynamic medical therapy," *Int. J. Nanomedicine*, pp. 2451–2459, 2015.