Frontiers in Nanotechnology

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Nanotechnology advances for biomedical applications

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Nanotechnology has recently emerged as a revolutionary force in the field of biomedical science, offering innovative solutions to complex challenges in diagnostics, drug delivery, tissue engineering, and disease therapeutics. The current sources of nanotechnology and their implications on biomedical applications have been discussed in this review. Nanomaterials are widely used in medical applications because these materials possess some peculiar physicochemical properties. Particularly in cancer, infectious diseases, and chronic diseases, because of its size, available surface area, and responsive surface, it has enhanced therapies, better medication delivery, and superior targeting of medications. Nanotechnology allows the design of drug delivery systems that have advanced carriers that release drug formulations in response to specific stimuli in the neighborhood. Nanotechnology has also increasingly contributed to early disease diagnosis by combining it with diagnostic equipment. These innovations have prophesied non-invasive diagnostics that accelerate and enhance the diagnosis of diseases at the molecular level. Regenerative medicine has benefited from nanotechnology through the design of nano scaffolds that promote tissue regeneration and support stem cell therapies. In addition, the start of the application of nanomaterials in immunotherapy has provided novel directions in the development of antigen-directed vaccines and immune modulation. Despite the vast potential, the translation of nanotechnological innovations from laboratory research to clinical applications encounters difficulties with cost, safety, adaptability, and approval from regulatory bodies. In addition, the review addresses the potential future paths of nanotechnology in biomedicine, including the integration of artificial intelligence, the development of multifunctional nanodevices, and the promise of theranostics. Nanotechnology has the enormous possibility to transform healthcare in the future by offering accurate, individualized, and successful therapies for a variety of illnesses.

KEYWORDS

biomedicine, drug delivery system, immunotherapy, nanoparticles, regenerative medicine

1 Introduction

Nanotechnology (NT), a field encompassing biology, chemistry, physics, engineering, and material science, has progressed considerably beyond the idea Richard Feynman proposed in his 1959 speech, "There's Plenty of Room at the Bottom," on manipulating individual atoms and molecules. Finally, Eric Drexler, credited with developing NT, came up with a more detailed account of the subject in his book The Engines of Creation. NT involves the study of events or processes that occur at the submicroscopic level of matter or materials, whereby there is a progression in scale from millimeter to millisecond, and new properties arise from quantum effects or interactions at surfaces (Conte et al., 2024). On this size scale, materials show characteristics that are removed from their macroscopic analogs and have new and novel optical, electrical, and mechanical properties. By employing top-down and bottom-up strategies, the researchers build complex nanostructures benefiting from such properties (Zain Ul Abidin et al., 2024).

The uses of NT are found in virtually all fields. In medicine, NT allows for the administration of medications to certain organs or tissues, enhancing therapeutic activities where they are needed most. In electronics, it leads to the creation of improved miniaturization, thus resulting in small, enhanced efficiency products. In the context of materials science, NT has opened up a new way to create lightweight yet strong materials. In diagnostics, NT has touched many fronts, with greater sensitivity, specificity, and precision being key revolutionary areas. Engineered nanoparticles (NPs) display elevated potentials to serve as imaging probes for ultrasound, magnetic resonance imaging (MRI), and computed tomography scan (CT), helping to improve tissue visualization (Habeeb et al., 2024). Nanobiosensors are also important in early disease diagnosis via biomolecule recognition. In the area of diagnostics, miniaturized structures and components at the nanoscale range have revolutionized point of care, for instance, DNA nanodevices for the detection of genetic mutation and lab-on-chip for viral detection (Thwala et al., 2023).

Molecular-based NT or nanobiotechnology is an interdisciplinary research that makes use of chemical and physical means to develop functional materials of nanometre dimensions. In the last 30 years, NT has become important because of the distinctive chemical, magnetic, electrical, and optical characteristics of nanomaterials (NMs) (Sindhwani and Chan, 2021). Compounded with biotechnology, NT opens opportunities in biosensing, diagnostic tools, medical images, and so on. NPs like organic/inorganic ones, metal oxide, and metal are produced using methods ranging from conventional chemical production to environmentally friendly processes. Green synthesis techniques are particularly appealing due to their lower toxicity, cost-effectiveness, and environmental compatibility (Radulescu et al., 2023).

Apart from liposomes and a few commercial nanomedicines like Abraxane (130 nm) and Myocet (180 nm), NPs typically have a size limit of 1–100 nm. The catalytic efficiency, chemical reactivity, and thermal properties of NPs are all improved by their large surface area-to-volume ratio. By altering NPs' size, shape, and surface characteristics, their interactions with biological systems are optimized, opening up new uses in controlled administration of medicines, imaging, and diagnosis. Because of their regulated release and biocompatibility, nano-liposomes, for example, are frequently utilized for specialized drug administration in cardiovascular and cancer treatments (Yetisgin et al., 2020). Nevertheless, several issues in NT applications prevent it from being scaled up for commercial purposes. NMs production in relatively large quantities requires both economic solutions and the ability to adjust and attain uniform particle sizes while maintaining dependable surface characteristics. Purposes of characterization typically do not match or can be incompatible with traditional laboratory methods for industrial production. In approaches such as these, quick and low-cost yet accurate means of assessing critical properties such as particle size and the behavior of the surface are required. Overcoming these difficulties is important for the application of NMs in actual commodities for biomedical uses, such as wound maturation, medication, and tissue restoration (Szczyglewska et al., 2023).

NPs design innovation enhances therapeutic index and decreases systemic toxicity (Rosic et al. (2024); Salahshour et al. (2024) describes how bioinks from NMs could be used to mimic natural extracellular matrices, which facilitates cell viability and differentiation. Such scaffolds provide reliable mechanical strength and architecture required in the fabrication of artificial organs by the combination of nanobiomaterials and bioprinting technology in regenerative medicine and artificial organ generation, such as the problem of vascularization and the complexity of the scaffold. The nanocarriers are aimed at increasing efficiency in delivery and reducing immunogenicity by signaling modulation to enhance cardiac regeneration and manage inflammation after injury (Erdil, 2024). The bilosomes are lipid-based vesicles which are resistant to unfavorable gastrointestinal conditions and help to increase the bioavailability and targeted delivery of drugs (Banoon et al., 2025). It underlines the property of bilosomes to decrease systemic toxicity and increase adherence to the treatment in patients to new developments in the bilosome design, such as the active targeting and controlled release by means of surface modifications. This bilosomes are promising as multifunctional nanocarriers in oral cancer therapeutics and overcome the difficulties associated with gastrointestinal delivery of drugs. The properties of the silver NPs have high antimicrobial properties against pathogens and high cytotoxic effects on cancer cells lines (Keskin et al., 2025). Such biogenic production is a more sustainable substitute to chemical synthesis: it has less impact on the environment to increase their efficacy and safety in biomedical uses.

NT has also extended improvements in biosensors that rely on structures like nanotubes, nanofibers, and nanorods for new transduction strategies (Welch et al., 2021). This capability has broadened to biomolecular interactions for the creation of functional materials, nanomachines, and perhaps even future nanorobots. These sub-cellular devices have exceptional possibilities of treating diseases and overcoming health issues related to aging (Giri et al., 2021). In addition, NT has been able to systematically alter nanostructures to serve as essential components for biomedical devices due to the nature of biological systems being nanoscale. Representing the dynamic field of nanomedicine, NT indicates that it will be capable of changing current treatments, identification of diseases, and prevention. They extend from improving antioxidant treatments in cancer therapies to the creation of nanoelectrodes for body-touching devices and biomedical imaging (Pei et al., 2022). Yet there is still insufficient information on designing, synthesizing, and characterizing NPs for mass application in biomedical practices. Various uses of NT in the biomedical sector are detailed in Table 1.

The purpose of this review is to discuss the application of NT in biomedical areas and focus on how research here may help to tackle a few of the issues facing modern healthcare. It aims to provide the reader with a concise overview of the status of NT in today's world with an emphasis on its application in the pharmaceutical area, tissue engineering/contacting, diagnostics and preventive measures. Further, the review will discuss limitations related to NT, such as biocompatibility, scalability issues and regulatory compliance issues of NT, but at the same time point towards the future of NT research and development. This type of review attempts to draw the cascade

TABLE 1 Nanotechnology applications in the medical field.

S. No.	Nanotechnological applications	Description	References
1	Drug delivery system	Drugs can be delivered precisely to specific locations with NPs, increasing their effectiveness and lowering adverse consequences	Vaishampayan et al. (2023)
2	Chemotherapy	Tailored therapy for cancer cells is possible by loading NPs with therapeutic substances like gene therapies or chemotherapeutic medications	Avula and Grodzinski (2022)
3	Targeted therapy with nanorobots	Small nanorobots can be designed to carry out certain medical duties, like dispensing medication or clearing clogs	Zhang et al. (2022)
4	Diagnostic NPs	Highly effective healthcare diagnostics are made possible by the engineering of gold NPs or quantum dots (QDs) that can recognize and measure target molecules	Shen et al. (2020)
5	Wound healing	Wound dressings and coatings made of nanofibers can hasten wound healing	Sharifi et al. (2021)
6	Regenerative medicine	Nanomaterials can promote tissue repair as well as regeneration	Dirisala et al. (2022)
7	Cancer diagnostics	Technologies based on nanotechnology have an outstanding range of sensitivity and specificity for identifying cancer biomarkers	Ou et al. (2023)
8	Early disease detection	Through biomarker analysis, nanosensors can identify diseases in their earliest phases, possibly allowing rapid treatment and better results	Dessale et al. (2022)
9	Biosensors	Nanofabricated sensors, like glucose monitoring equipment for diabetes treatment, can identify biomarkers linked to disease and track situations in real time	Mbunge et al. (2021)
10	Imaging agents	NPs can improve the contrast of medical imaging procedures like positron emission tomography (PET) scans, CT scans, and MRIs	Singh and Amiji (2022)
11	Dental applications	Dental reconstructive materials like nanocomposites contain nanomaterials	Wang et al. (2023)
12	Artificial organs	Designing and creating artificial organs with better functioning qualities can be aided by nanotechnology	Kumari et al. (2022)
13	Tissue engineering	Artificially created tissues and scaffolds to support tissue regeneration and repair can be created using nanomaterials like nanofibers and nanocomposites	Dessale et al. (2022)
14	Drug discovery	High-throughput screens and drug design techniques are made possible by nanotechnology, which speeds up the search for novel medicinal molecules	Khan et al. (2022)
15	Antibacterial coatings	To prevent infections, medical devices like catheters can integrate nanoscale antibacterial compounds	Amiri et al. (2022)

of recent progress and ongoing developments to recognize the revolutionary potential of NT in shaping medical science.

2 Properties of NMs relevant to biomedicine

The success of NMs in biomedical applications lies in their distinct properties. Surface chemistry allows drug functionalization, ligand targeting, or imaging agents, enabling specified interactions with biological tissues (Diez-Pascual and Rahdar, 2022). Optical properties, such as fluorescence and plasmon resonance, are critical for imaging and diagnostic tools. Their electrical and thermal conductivity facilitates the development of electroactive scaffolds and hyperthermia-based cancer treatments. Furthermore, NMs exhibit mechanical properties, like flexibility and resilience, making them suitable for implantable devices. They are biocompatible and their shapes afford easy incorporation into biological systems due to morphology that mimics many biological molecules and structures, in addition to size-dependent properties that are beneficial in cellular uptake and biodistribution. Such diverse applications place NMs on the cutting edge of advancements in medicine and enhance their capability to effectively provide for multiple issues of healthcare. However, their long-term viability, stability and effects on the environment continue to be contested as issues for future analysis (Diez-Pascual and Rahdar, 2022). The key elements that should be considered while choosing NMs in the biomedical sector are shown in Figure 1.

3 Nanomaterials in biomedical applications

NPs and other nanostructures with a size of 1–100 nm are unique since they can pass cell membranes and cause characteristic

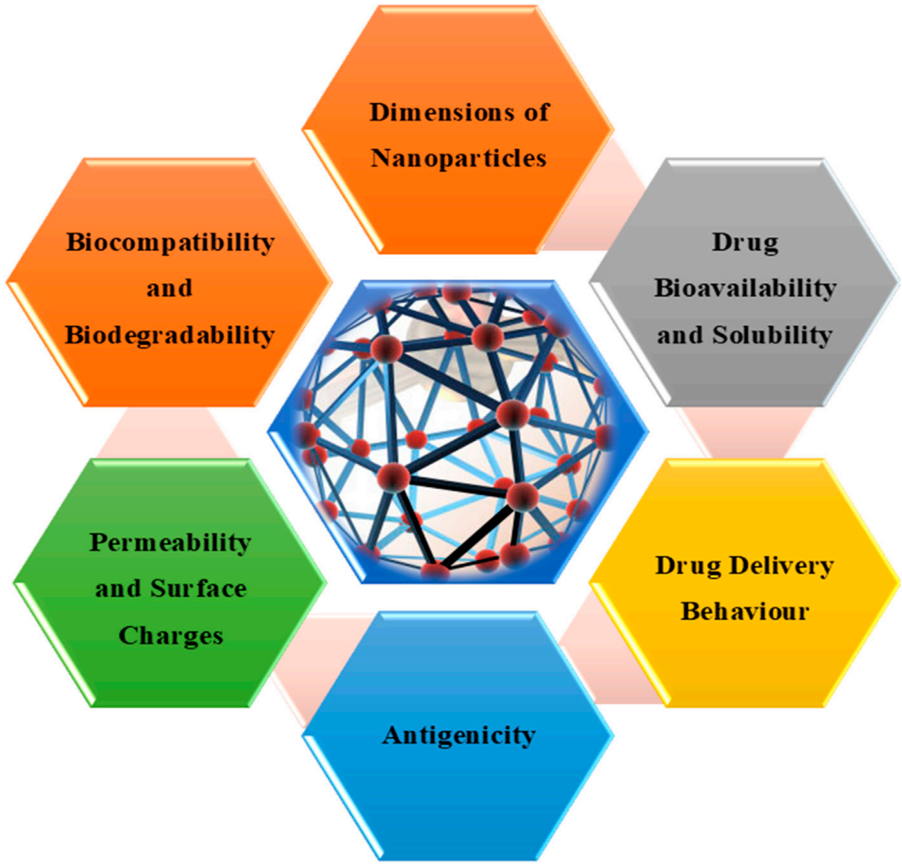

FIGURE 1
Key factors for considering nanomaterials in the health sector.

reactions within cells, affecting both the cell structures and organelles. Nanostructures have a built-in ability, or what might be referred to as inherent functions, which makes them essential in many biomedical fields, including improved imaging, photothermal therapy, contrast chemicals for imaging and medication delivery devices. A variety of nanostructures and their applications in the healthcare industry are shown in Table 2.

Regardless of the area of interest or research in NT, there are some common nanostructures on which NT focuses. A few of the significant types are NPs, dendrimers, nanowires, CNTs, nanoprobes, QDs and NDs. Therefore, it is relatively easy to get NPs across microscopic pores and membranes due to their size and different properties. These particles can also be classified according to their composition and they have been divided into lipid, metal, polymeric, ceramic, and semiconductor NPs. Metal precursors are used to create metal NPs. Specifically, these exhibit unique optoelectrical capabilities. Ceramic NPs, which are inorganic and nonmetallic, come in a variety of amorphous, crystalline, hollow, and solid forms (Bhardwaj et al., 2023). In this regard, they improve photocatalyst efficacy and facilitate dye photodegradation and imaging. Because semiconductor NPs combine the properties of metal and non-metal NPs, they can be used in a variety of fields like electronics and photo-optics. Polymeric NPs are organic particles that can be encased within molecules or act as matrix particles, which are typically solid and can attach to molecules to be transported (Mitchell et al., 2021). The moieties of lipid nanoparticles are lipids. Their dimensions range from 10 to 100 nm, and they are typically spherical. It has a solid lipid core that makes it relatively easy to transport any lipophilic compounds.

CNTs are nanoscale, tubular structures manufactured from graphite planes. These have terminal parts which are open but will be closed by fullerene caps. It exhibited the highest tensile strength among all natural materials possible for construction. They are good for the reception of magnetic radiation and at the same time possess properties of heat conductivity and catalytic activity. Based on the purity, length, diameter, special surface area, and amorphous carbon, their properties exist. These elongated tubes are part of the fullerene nanotube family and have a rather cylindrical form. CNTs also include fullerenes, which are spherical and cylindrical structures known as Buckyballs. CNTs are used in contemporary technical healthcare systems because they can influence elements that were previously unaddressed. Although the nature of the process is yet unknown, they can diffuse relatively effortlessly through slightly permeable membranes of cells. Proteins, peptide molecules, nucleic acids, antibiotics, and other tiny chemical medicines can all be transported by them to certain locations. Within these CNTs, these tiny molecules may be encapsulated, adsorbed, or covalently bound. They can covalently or noncovalently bind proteins less than 80 KDa. Cells absorb these through the endocytosis process. X-ray imaging serves as another

TABLE 2 Nanostructures and their applications in the biomedical field.

Nanostructure	Applications in the health sector	References
QDs	Beneficial for intracellular monitoring, therapeutic delivery of medications, real-time *in vivo* biological imaging, disease control, diagnostics and delivering siRNA for RNA interference	Iravani (2014)
NPs	Utilized in diagnostic imaging, as sensors, catalysts and antimicrobial agents and antifungals	Anjum et al. (2021)
Nanocapsules	Utilized to increase the absorption of medicinal products and improve the solubility of weakly soluble medicines for specialized drug delivery, especially in the treatment of cancer	Deng et al. (2020)
Nanofilms	Serve as necessary chemical, biological and nanomechanical sensors in electrochemical equipment; they are employed in controlled medication release systems and they are utilized as nano patches to seal incisions following open surgery	Anjum et al. (2021)
Polymeric NPs	Used in controlled drug release, vaccine delivery, tissue engineering, and as carriers for proteins and nucleic acids. These particles offer advantages like biocompatibility and versatility in formulation	Mitchell et al. (2021)
Liposomes	Drug delivery devices that can hold both hydrophilic and hydrophobic medications, shield medications from enzymatic and chemical deterioration and encapsulate anti-tumoral medications	Anjum et al. (2021)
Dendrimers	Utilized for ophthalmic disease treatment, transferring genes, antibacterial and anticancer medications, diagnostic applications and enhancing vaccine formulations by serving as antigen carriers	Sztandera et al. (2024)
Carbon nanotubes (CNTs)	Employed as vectors for gene delivery, to transport fibrinogen and bovine protein to cells and to treat breast cancer, osteoporosis and fractured bones	Anjum et al. (2021)
Nano-diamonds (NDs)	For use in screening and therapy, preliminary cancer detection and the treatment of breast and brain tumors; used to treat bone damage by targeted medication administration	Chauhan et al. (2020)
Magnetic NPs	Utilized as biosensors, in MRI, for drug administration and in cancer treatment (magnetic hyperthermia). Magnetic fields can be used to direct magnetic NPs to particular bodily areas	Anjum et al. (2021)

application for CNTs (Soni et al., 2020). A laser infrared beam was used to heat one of the CNT solutions to 158°F in about 2 minutes. As CNTs can absorb near-infrared radiation, laser beams cannot harm the cells that contain them. Lasers, more particularly, could instantly kill off cancer cells. It is, however, important to note that dendrimers are biodegradable nanopolymers whose structures are naturally occurring. They are macromolecular nanostructures with globular shapes in three dimensions due to the formation of many branching layers. NPs, particularly those with sizes ranging between 1 and 10 nm, which are globular and lipophilic with the ability to cross cell membranes, are perfect models for use in healthcare in drug and gene delivery systems (Sztandera et al., 2024). The structure of a dendrimer has three main parts: a core, which is an atom or a molecule with multiple reactive sites, branching units linked covalently to the core, and numerous terminal functional groups at the end of the branching units. Physical and chemical interactions are involved between dendrimers and drug molecules. The existence of voids in the carrier, which have vacant interior structures to engage with the active ingredient molecules through hydrophobic interactions, is what causes the physical connections (encapsulation of the medication). These interactions happen through chemical interactions that may result from electrostatic interactions or by forming covalent linkages with the dendrimers. The dendrimer's surface is coated with the active group, like p-aminobenzoic acid or polyethylene glycol (PEG), to facilitate covalent binding. Following this, the medications can effectively form a covalent link with the dendrimers (Sztandera et al., 2024).

NDs represent a type of nanopillar produced from a single diamond crystal in which carbon atoms are arranged according to sp3 hybridization. They are roughly 4–5 nm in size. In addition to their great heat conductivity and biological compatibility, NDs are extremely rigid and chemically quiescent (Hyder et al., 2024). They feature a huge surface area and a customizable surface that allows for the conjugation of gene and drug functions. The visualization of internal structures through fluorescence can be attributed to their use for diagnostic imaging. All these properties of NDs are attributed to the synergistic effect between the properties of the diamond matrix and the NPs. The structure of NDs comprises an inner diamond core formed by C-sp3 hybridization and an outer graphitic shell where carbon atoms are formed by C-sp2 hybridization, and functional groups are at the terminal of dangling bonds. Chemical vapor deposition, elevated temperatures, excessive pressure, and explosive detonation are among the methods used to create NDs (Chauhan et al., 2020).

QDs are man-made particles in the size dimension of 1.5–10 nm. They can be referred to as miniature; their semiconductor nature makes them capable of transporting electrons (Payal and Pandey, 2022). The functionality of the QDs means that when a sample of them is exposed to UV light, the electrons within the QDs become energized and emit light when the electrons get back to their less energetic state. The emission intensity of QDs varies with the size of the QDs, as these QDs emit light of different colors. Heavy metal-derived QDs like cadmium are extremely toxic and carcinogenic; hence, the health sector cannot employ them regularly. However, carbon and graphene QDs are reasonably stable, environmentally friendly, and have a wide range of uses in the medical field. Polymeric sheets with a significant surface area and exceptionally small thickness of a few nanometers (10–100 nm) are called nanofilms. Stacking several layers of oppositely charged entities leads to the formation of multilayer, but very thin, biofilms. For depositions, cohesive layers are placed one at a time. Layer deposition strategies include spinning, emersion, electromagnetic deposition, and fluidic assembly. The liposomes are spherical vesicles composed of one or multiple lipid bilayers separated by aqueous spaces (Tiwari et al., 2023). Its size ranges from a few nanometers to several micrometers. Both hydrophilic and lipophilic

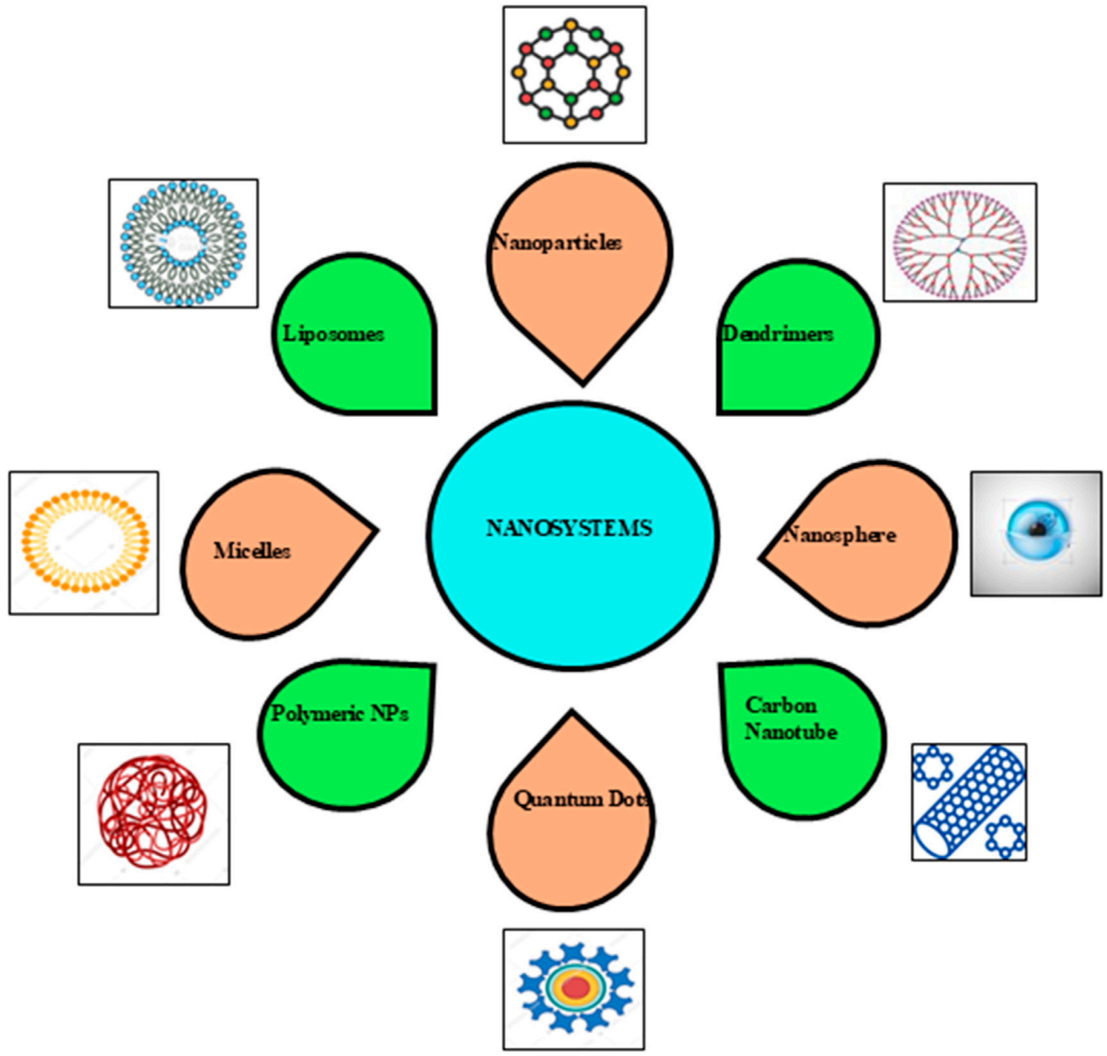

FIGURE 2
Different types of nanosystems used in the medical field.

elements and behaviors can be captured by them. They are therefore regarded as the most efficient drug delivery mechanism. Their similarity to the body's membranes, which help to improve medication administration (*in vitro*), is another reason for this. They can supply a lot of medications because of their size as well. Figure 2 lists the primary healthcare fields where NT-mediated nanosystems are contributing positively.

3.1 Nanotechnology for drug delivery systems

In recent years, the utilization of NT has greatly contributed to the enhancement of medication delivery systems; this has enhanced the development of sophisticated drug carriers like NPs that need to be directed to specific sites in the body. The system assists in enhancing the outcomes of therapy, decreasing the side effects, and enhancing the bioavailability of drugs. In the application of NT, the materials utilized have to be compatible with biological systems and must degrade naturally, hence being safe and effective in transporting drugs to the targeted locations (Prakash, 2023; Afzal et al., 2022). Different types of drug delivery systems are depicted in Figure 3.

Polymeric NPs like PEG, chitosan (ChNPs), polyacrylic acid (PAA), polycaprolactone (PCL), and polylactic acid (PLA) have emerged as promising candidates due to their biodegradability and biocompatibility. However, the synthesis of these NPs normally comes with chemical or solvent reinforcements that are environmentally sensitive and can hamper the process of fabrication. PEGylated formulations and other polymeric NPs are more complex and time-consuming in the processing steps to provide the above-stated therapeutic advantages (Prakash, 2023). To overcome such limitations, lipid-based NPs, particularly liposomes and nanoliposomes, have drawn much attention. These lipid-based systems can be prepared more easily, have good biocompatibility and biodegradability, and afford a straightforward means for drug delivery. Methods such as thin-film dispersion have proved that liposomes can enhance the

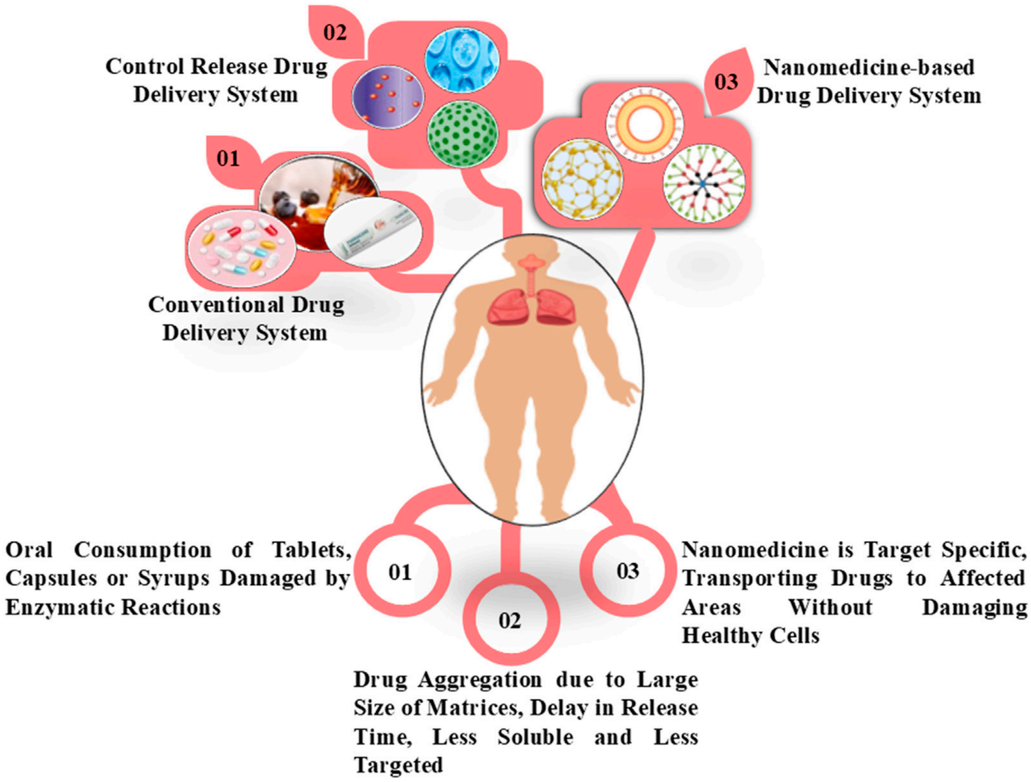

FIGURE 3
Various types of drug delivery systems.

solubility and bioavailability of drugs. Advanced targeting of liposomes is also possible by coating the liposomes with mannose–cholesterol or by varying the molecular weights of PEGs. Further, there have been attempts to develop liposome–peptide hybrids that provide improved solubility of drugs in water, better dispersion, slow-release properties, and favorable pharmacokinetics. These peptide-lipid NPs with improved stability and bioavailability are capable of entrapment of therapeutic agents, such as hydrophobic as well as hydrophilic drugs, imaging agents, and photosensitizers, to be developed as effective drug delivery systems (Anjum et al., 2021).

Conventional techniques of NPs formation in the biomedical field are classified into top-down approaches like milling and lithography, in which mass material is reduced towards the size of the nanoscale, and bottom-up approaches like chemical vapor deposition and sol-gel methods, in which an amalgamation of NPs occurs atom by atom or molecule by molecule (Karnwal et al., 2024). Such methods are developed to yield biocompatible and functionalized NPs intended for drug delivery, diagnosis, and imaging (Figure 4). Recent drug delivery systems using NT in areas of dendrimers, polymeric NPs, and inorganic NPs have also been developed and enhanced. Dendrimers are polymeric nanostructures featuring a highly branched architecture; the size and the functional groups can be directly regulated, allowing for the multi-ordination of a target drug or ligand. This enables increased solubility, bioavailability, and localized drug delivery, which is very important for a long-term illness. Polymeric NPs like PLGA biodegradable matrix can exhibit controlled release of the drug, and by surface coating with PEG, there is enhancement in circulation time and better targeting of the desired site (Zeb et al., 2022).

Additional inorganic NPs with optical and electrical properties for medication delivery and diagnostic applications include gold NPs and mesoporous silica NPs (Shah et al., 2022). NT has also made breakthroughs in drug delivery systems by providing a high level of effective and innovative approaches. NPs are small and are energy-centered particles, making it easier for them to penetrate the tissue and show better distribution of drugs with low side effects in the body. Pharmaceutical NPs can enhance the solubility, stability, and bioavailability of the drug and can be applied in the cure for diseases, including cancer, neurological disorders, and infections. Medical nanorobots for delivering drugs into the body by moving through blood vessels and releasing active substances only in the affected areas represent one of the most promising directions of NT in the treatment of diseases, especially cancer, when targeted drug delivery decreases negative side effects on healthy tissues (Giri et al., 2021). Despite this, DNA NT has brought another aspect to drug delivery. DNA nanostructures, which can form complex three-dimensional shapes through self-assembly, possess high specificity for drug delivery and display low toxicity compared to traditional chemotherapy drugs. DNA-based systems can be effectively incorporated with drugs like doxorubicin, increasing the cellular uptake and effectiveness of the drug. DNA NT will have the best application in drug delivery systems in terms of programming nanostructures for cancer treatment or gene therapy, so that drugs are more effectively targeted and less toxic.

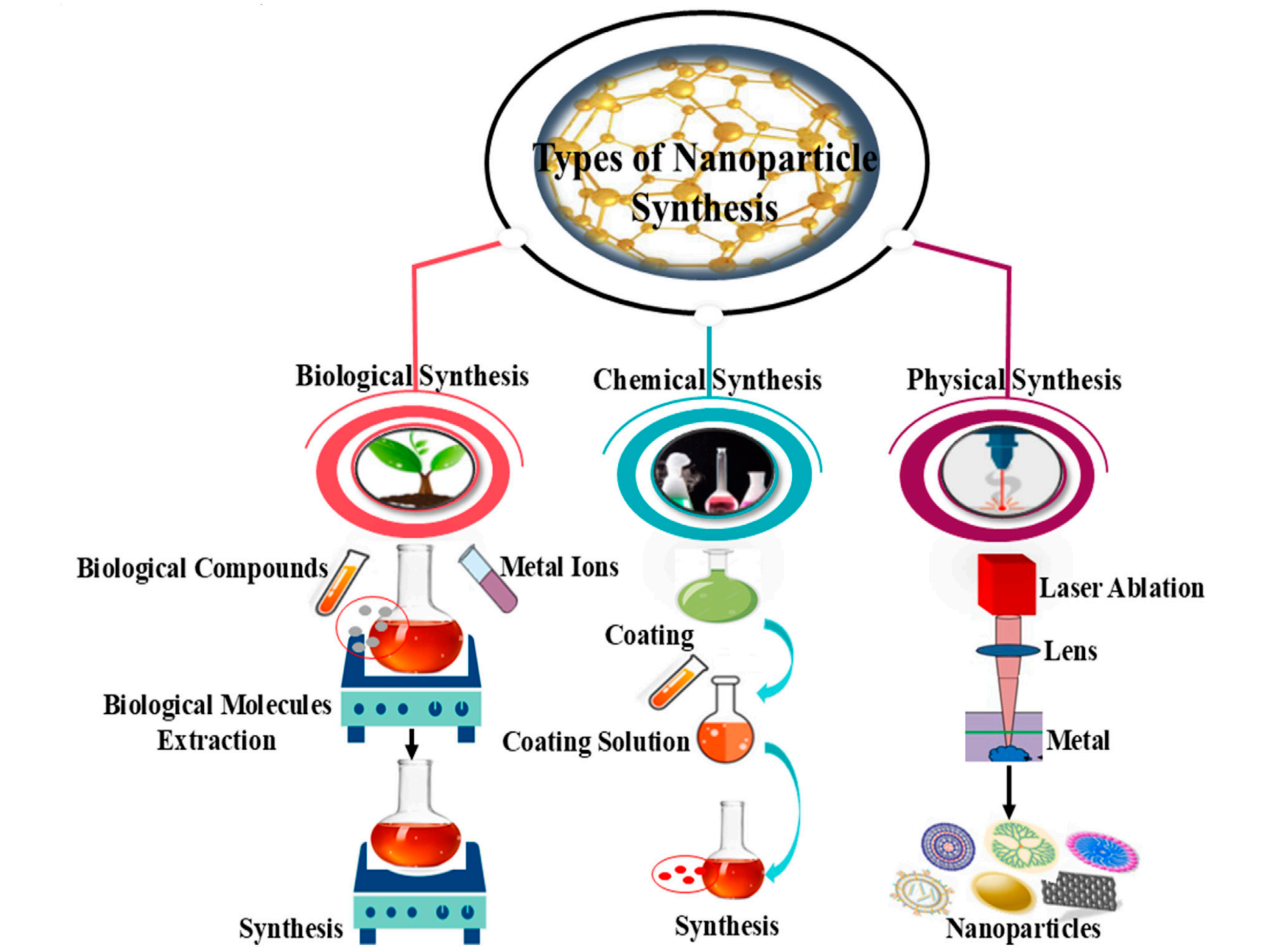

FIGURE 4
Nanomaterial synthesis methods.

Targeted addition also uses NT to enhance the delivery of hydrophobic drugs that are normally dangerous when disseminated throughout the entire body. NPs, for example, can afford sustained and targeted delivery, making it possible to deliver therapeutic agents right to the required organs. Altering the size, geometry, and/or surface chemistry of the NPs increases drug targeting and therapeutic efficacy while decreasing toxicity. Drug-carrying nano vectors can be functionalized with ligands such as peptides, antibodies, and folic acid to help them attach only to targeted cells (Foglizzo and Marchiò, 2022). This is most important in cancer treatment, where the nanovectors can contact cancer cells and be safely cleared from the body without affecting the normal tissues. Another added advantage to these drug delivery systems is that several ligands can bind to a single NPs, enhancing the selectivity of these systems. The anticancer mechanism of NPs is illustrated in Figure 5.

NPs are also being applied in slow-release drug delivery systems that have longer-lasting therapeutic benefits than other conventional approaches. There was evidence that insulin incorporated with polymeric NPs can have a better and longer duration of action than free insulin. NPs can also be applied to gene therapies, which allow for targeted plasmid DNA delivery and for the genes to continue being expressed in cells. By controlling the size and surface chemistry of NPs, it is possible to target tissues or organs for a specific disease, such as tumors, which have permeable pores in their blood vessels. NPs laden with drugs can be released at tumor sites by a process known as the enhanced permeability and retention (EPR) effect. The application of NT for drug delivery discusses the significant improvement and transformation of the existing technologies. Advanced characterization of new NPs with remarkable targeting opportunities, controllable release characteristics, and better solubility profiles has greatly improved the effectiveness of the drug therapies, with less harm to the patient. Some of the drawbacks of NT include: scalability, reproducibility, and biocompatibility, yet NT-based drug delivery systems have a wide prospect. Further investigation of liposomes, dendrimers, and DNA nanostructures will persist because it opens a way for developing more efficient, targeted medicines in the future (Egwu et al., 2024).

3.2 Nanotechnology in diagnostics

NT is drastically transforming healthcare diagnostics by improving the efficiency of medical diagnostics. Nanodevices help to diagnose diseases at an early stage, providing information about

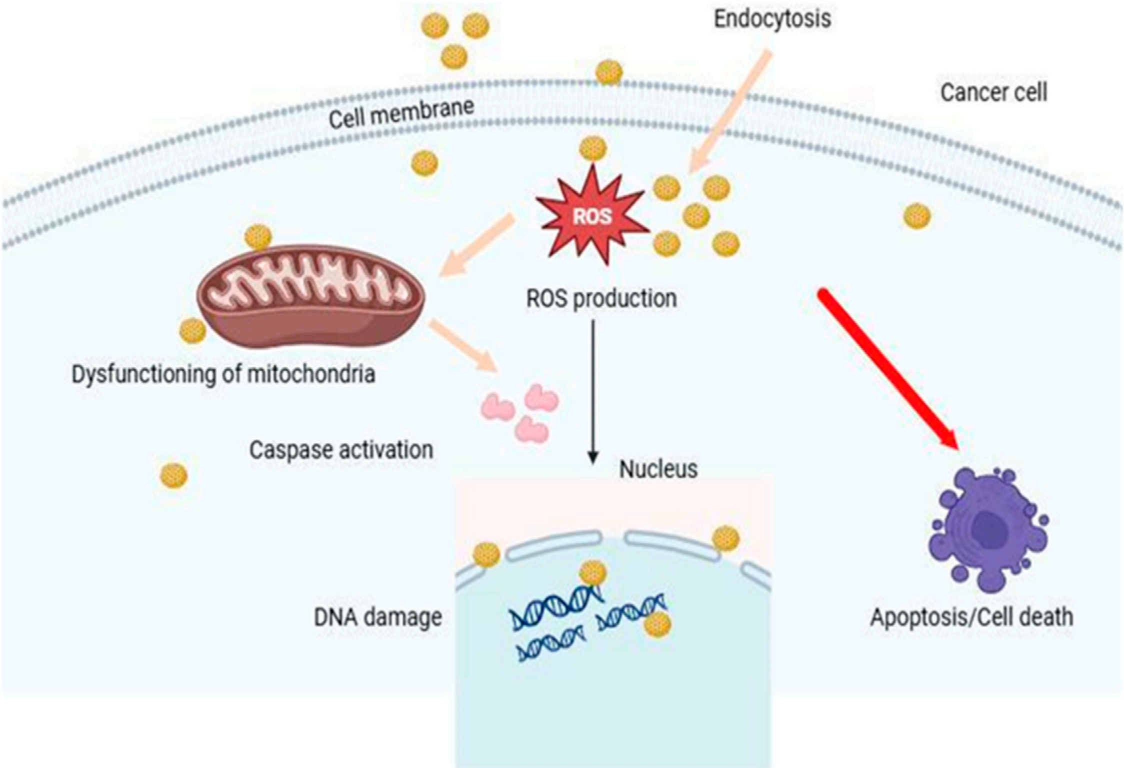

FIGURE 5
Anticancer activity pathway of nanoparticles.

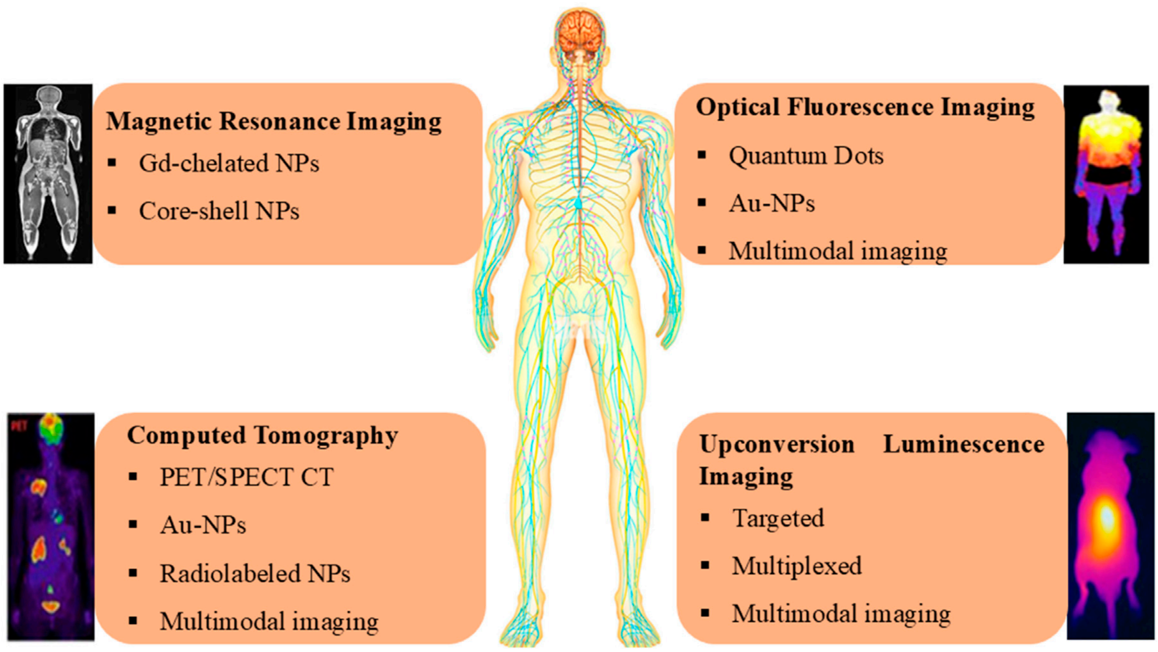

FIGURE 6
Nanoparticles in MRI, CT, and PET scans for disease detection.

diseases on the cellular and molecular levels. Huge benefits include functional imaging, where NPs enhance methods such as MRI, CT, and PET scans for disease detection (Figure 6).

NT also focuses on quick and accurate point-of-care tests to diagnose infections, tumors, and many other diseases, so that treatments can start early. For early disease diagnostic applications, biosensors and microfluidic devices in combination with NMs are indispensable. A nanoscale biosensor can be created to detect biomolecules that are in very low concentration in blood and urine, while microfluidic devices can accurately identify certain cells and genetic materials to give a diagnosis. Another advancement in the sequencing technique is nanopore sequencing, which is used for accurate detection of sequences, in particular DNA/RNA, for the diagnosis of genetic disorders. Portable diagnostic tools are improving through *in vivo* devices for the early identification of diseases such as tumors (Gomez-Marquez and Hamad-Schifferli, 2021).

Advanced methods of nanoengineering also advance diagnostic imaging and increase the accuracy of these methods. Gold NPs, QDs, and magnetic NPs are often used for biosensors since they have optical and electronic characteristics. Nanoengineering also improves ultrasound and optical imaging, with microbubbles, nanodroplets, and gold nanorods enhancing imaging sensitivity and resolution. Lab-on-a-chip technology integrates these advancements, creating small, multi-functional devices for rapid diagnostics with minimal samples. Lab-on-a-chip devices can diagnose conditions like cancer, infections, and genetic disorders and improve drug delivery systems. The combination of NT and lab-on-a-chip technology is transforming healthcare by enabling faster, more accurate diagnostics and personalized treatment. However, challenges related to biocompatibility, stability, and cost-effective production remain (Surappa et al., 2023).

3.3 Nanotechnology in regenerative medicine

NT has significantly advanced tissue engineering and regenerative medicine by providing tools and materials that mimic the natural cellular and tissue environment at the nanoscale. This interdisciplinary field integrates engineering principles with life sciences to create substitutes capable of restoring, maintaining, or enhancing tissue function (Altyar et al., 2023). The integration of NT enhances the properties of biomaterials, improves interactions with cells, and offers precise control over tissue regeneration processes. One key application of NT in tissue engineering is the development of biomaterials with customized characteristics. NMs, such as NPs and nanofibers, can mimic the structure and composition of the extracellular matrix found in natural tissues, providing mechanical support, promoting cell attachment, and facilitating nutrient transport essential for tissue growth. When poly(lactic-co-glycolic acid) (PLGA) or collagen nanofiber scaffolds are produced, they can effectively control the attachment, proliferation, and differentiation of cells in repairing complex structures like bone and cartilage (Figure 7) (Zhao et al., 2021).

Targeted drug molecules or particles are provided by NPs in a way that makes treatment more effective. Furthermore, the nanostructured scaffold resembles the architecture of bone tissue, facilitating new bone formation (Dirisala et al., 2022). Further development in the usage of nanoscale in the fabrication of 3D prints allows for highly personalized bone implants. Studies on biomineralization aim to develop nanostructured bone graft substitutes with properties that integrate seamlessly with body tissues, revolutionizing bone repair. NT is also being used for artificial joints and nanoscale collagen-mimicking coatings, which stabilize bone formation by osteoblasts (Liang et al., 2024). Regenerating nerve tissues remains a significant challenge, but NT offers solutions by providing materials with suitable physicochemical properties for neural regeneration. Inorganic NMs such as metallic, silica, and magnetic NPs, as well as organic NMs like polymeric NPs and nanofibers, have shown promise in enhancing neuronal cell recovery, attachment, and expansion. These advancements could lead to breakthroughs in treating nerve damage and facilitating neural regeneration.

NT has made significant strides in wound healing. NPs loaded with antibacterial agents or antibiotics, as well as nanofibers embedded with bioactive molecules, have demonstrated effectiveness in promoting skin regeneration and preventing infections. Electrospun nanofibers, known for their high surface-area-to-volume ratios and tunable porosity, are being developed for applications like antibacterial mats, rapid hemostasis patches, wound dressings, and scaffolds for skin regeneration (Keirouz et al., 2020). The principles of quality-by-design (QbD) are being applied to ensure NMs meet healthcare standards, minimizing side effects and maximizing patient satisfaction. NT is transforming tissue engineering and regenerative medicine by enabling the creation of biomimetic materials, advancing cellular manipulation techniques, and improving targeted drug delivery systems. Its applications span bone and nerve regeneration, wound healing, and more, offering innovative solutions for previously challenging medical issues. Continued interdisciplinary collaboration and adherence to quality standards will further enhance the development of NT-based regenerative therapies, shaping the future of medicine.

3.4 Nanotechnology for precision medicine

NT has rejuvenated the idea of precision medicines due to the high level of precision within short-term treatments. Employing molecular and electronic materials and devices at the nanoscale level allows the creation of systems that can deliver drugs, imaging agents, or genetic materials directly to the target diseased cell, tissue, or organ. Liposomes, dendrimers, polymeric NPs, and inorganic NPs could be modified on their surface with ligands to interact with biomarkers over-expressed on diseased cells. It thereby minimizes off-target effects and increases the treatment's effectiveness. In addition, due to their size, the delivery systems can be designed with stimuli-responsive properties in terms of pH, temperature, or enzymatic activity, which means that the action of delivering the encapsulated therapeutic agent will only take place at the target tumor site, thereby avoiding side effects (Figure 8) (Alghamdi et al., 2022; Bigham et al., 2024).

3.5 Personalized therapeutics using nanoscale systems

Since individualization of treatment is the basic principle of the precision medicine approach, nanoscale systems are in high demand for it. These systems can be specifically designed based on the molecular and genetic characteristics of specific patients and hence offer disease management for conditions as they exist in a

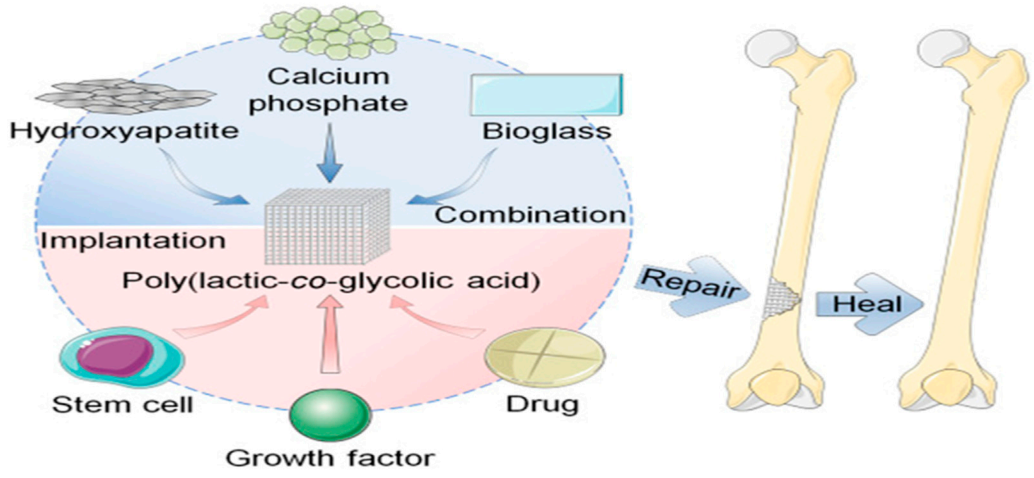

FIGURE 7
PLGA-based bone-substitute materials used in the treatment of bone defects (Reproduced with permission from Zhao et al., 2021).

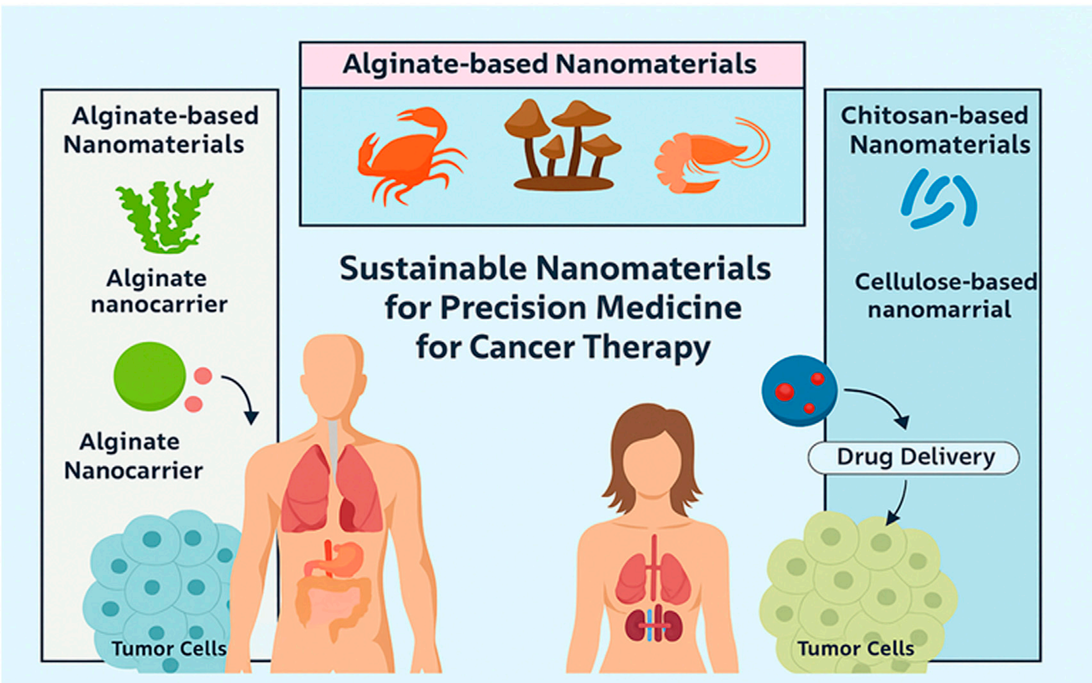

FIGURE 8
Different types of nanomaterials in targeting cancer sites (Bigham et al., 2024).

particular patient (Puccetti et al., 2024). A therapeutic agent in which NPs are used to carry a payload can target specific mutations in cancerous cells, as seen in genomics. Likewise, nanocarriers can incorporate small interfering RNA (siRNA) or components of CRISPR-Cas to knock down or modify, respectively, pathogenic genes. Other imaging NPs are also used to track treatment responses in real time, as treatment plans can be adapted as necessary. It is now possible for clinicians to use NT to take the practice of medicine to a new level of precision that results in enhanced positive impacts on patients while reducing those negative impacts associated with the administration of medications (Alghamdi et al., 2022).

3.6 Integration of nanotechnology with genomics and proteomics

Demonstrating the application of NT in conjunction with genomics and proteomics has paved the way for further

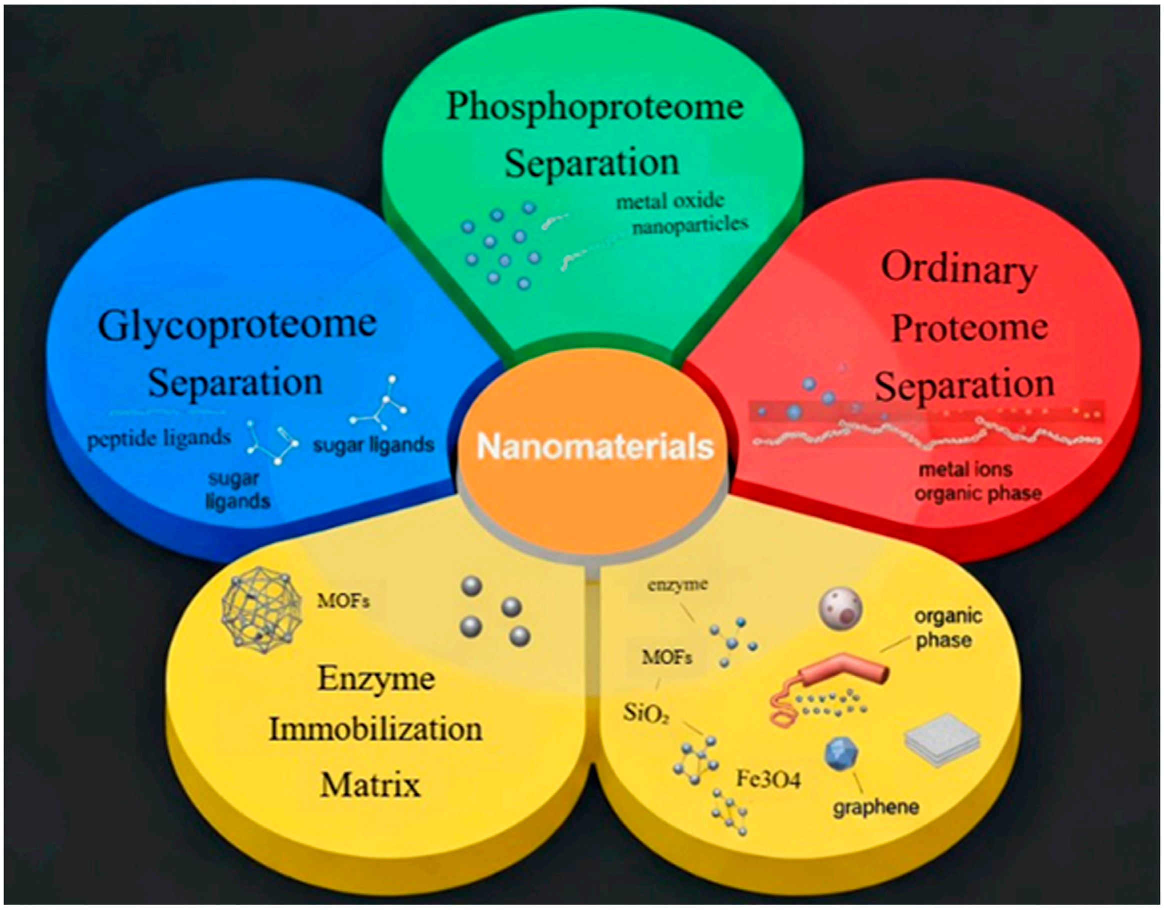

FIGURE 9
An overview of nanomaterials in proteomics (Sun et al., 2019).

innovation in the treatment of diseases at the molecular level. NT improves the methods of identification and characterization of molecular and cellular biomarkers, leading to early diagnostics and targeted therapy. For instance, nanosensors are being developed to detect unique DNA or RNA sequences with great precision and assist in the early diagnosis of inherited diseases and cancer genes. Another area that has been supported by NT includes proteomics, which is centred on the identification and analysis of expressed proteins in complicated biological matrices. Furthermore, NT-based platforms, including lab-on-chip systems, allow high-throughput and prompt processing of genomics and proteomics for better understanding and targeting drug discovery at the molecular level (Figure 9). The amalgamation of these technologies points to the massive role NT is going to play in the revolution of precision medicine (Sun et al., 2019; Arias-Hidalgo et al., 2022).

3.7 Nanotechnology in immunotherapy

Immunotherapy has been advanced by NT in that it effectively provides precise instruments with which to manipulate immune responses and interact effectively with the immune system (Akkın et al., 2021). Current nanosystems include liposomes, dendrimers, polymeric NPs, gold NPs, CNTs, and nanodots designed to deliver antigens, adjuvants, and immunomodulatory agents selectively to immune cells for reduced side effects. These NPs can be size-limited to the micro and nanoscale with specific shapes, surface charged, and functionalized to be not recognized by the immune system, efficiently absorbed by cells in the body, and can provide long-term delivery of the therapeutic agents. In vaccines, NT increases the ability of antigens to be presented and enhances powerful immune responses. NPs copy the pathogens in the sense that both particles present the antigens and adjuvants so that they are easily recognized by the dendritic APCs. For instance, lipid NPs are an essential component of all currently licensed mRNA vaccines, including both the COVID-19 vaccines, because they shield mRNA from degradation and facilitate delivery to target cells (Yasamineh et al., 2022; Ou et al., 2023). Apart from the common vaccinations, special nano vaccines are being designed and synthesized to fight against cancers by building immunity to search and kill tumor-producing cells (Figure 10).

In autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis, nanosystems appear to be an effective tool in the development of immune tolerance. Understanding and harnessing the potential of NPs to deliver tolerogenic agents, such as regulatory cytokines or autoantigen peptides, to APCs, thereby reshaping the T-cell responses for the prevention of autoimmunity, is feasible. Also, due to their ability to

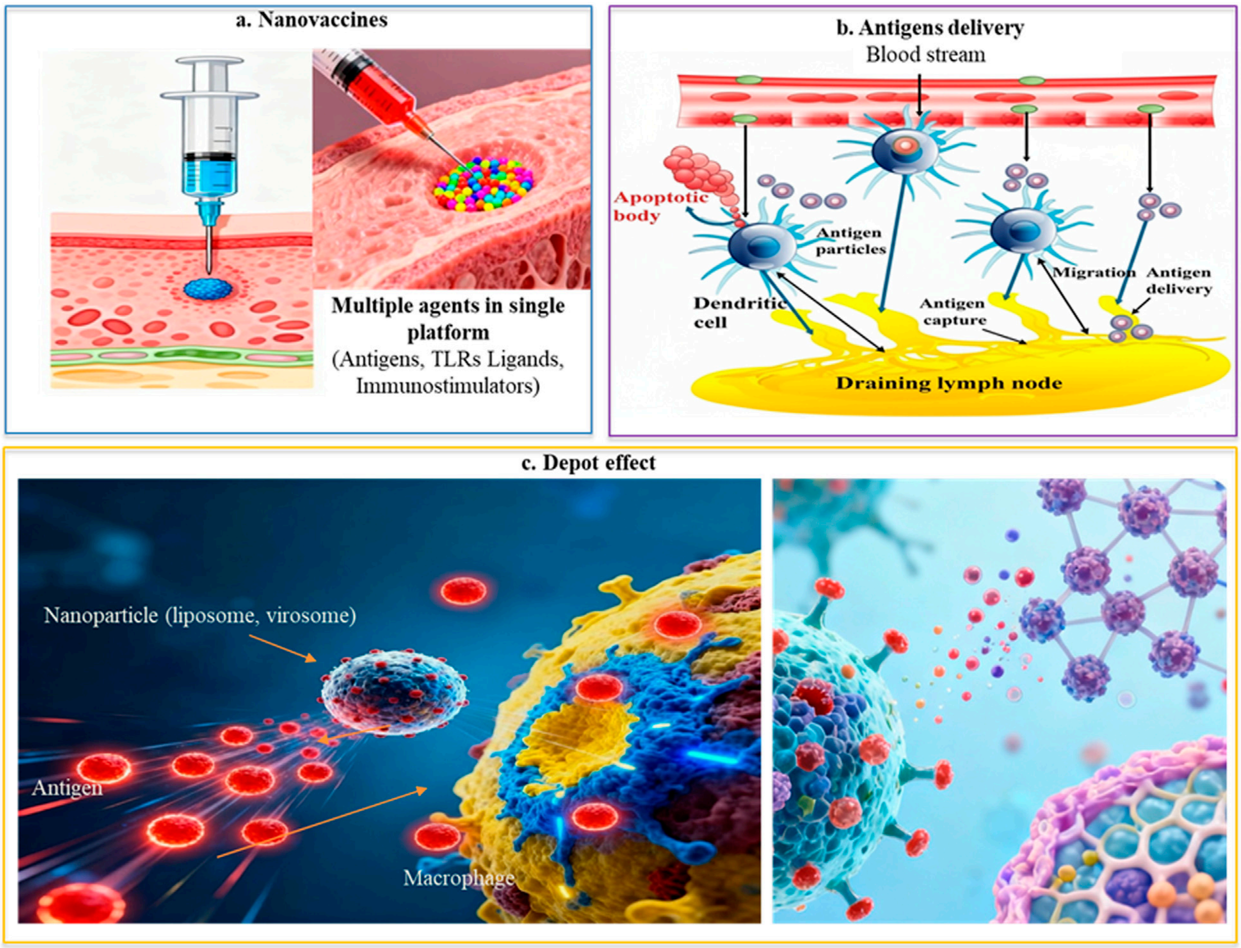

FIGURE 10
Role of nano-based vaccines in immune reaction (Yasamineh et al., 2022).

encapsulate and deliver immunosuppressive drugs to the site of inflammation, their systemic toxicity will be reduced. Polymeric NPs have been synthesized for the targeted delivery of the anti-inflammatory drugs dexamethasone or the anticancer drug methotrexate to minimize their related toxicity. Especially in the COVID-19 period, nanomedicine has been used in bio-diagnosis and treatment, therapeutic interventions, and vaccine delivery. It is easier to connect the Coronavirus and the NPs due to their comparable sizes and functionality versatility. Since virus particles and NPs are in the same size range, they can interact with each other properly. Functionalization of NPs involves an interaction of the NPs with specific functional compounds that allow them to be attached to viruses such as SARS-CoV-2 (Croitoru et al., 2024). This feature allows NPs to be involved in detection, treatment, and shielding from the virus. In diagnostics, NPs are engineered to adhere to particular areas of the virus and generate observable signals, including color alteration or light emission, to expedite and make the test more delicate. Through these advancements, it has become easier and more efficient to diagnose diseases using equipment such as biosensors with QDs. In pharmacological applications, NPs function as carriers where antiviral therapeutic agents are loaded and then released at targeted sites, increasing therapeutic efficiency and minimizing toxicity. Filtering face shields and masks with NPs that immobilize the virus have also been created to improve healthcare workers' and citizens' protection.

In this novel strategy of vaccine development, NT has provided solutions for stability and delivery systems, which have come up with inventions such as microneedle patches and nasal sprays that bring convenience in vaccines and offer better yields. Lipid NPs that are part of a core platform of mRNA vaccines have shown their capabilities when it comes to condensing and delivering genetic material to primary cells. NT is also used in vaccine production to facilitate scale-up and enhancement of its function. This is particularly important in instances where resources are limited (Fries et al., 2021). In addition, nanomedicine has also helped in the development of antiviral drugs using systems such as liposomal, polymeric NPs, metallic NPs, and micellar. Nanosystems in general enhance drug delivery, inhibit virus-receptor interactions and viral proliferation, and amplify effective pharmacological concentration. Nevertheless, some issues, including possible cytotoxic effects on normal cells and difficulty in purging sufficient amounts of the product, should be solved for its more effective use in practice. In conclusion, the current paper affirms that NT has been particularly useful when combating the current pandemic and can be useful in further advancements in diagnosing and treating bacterial and viral infections in the future. The customization of nanomedicine within personal health operational tools and medicinal products establishes nanomedicine as a revolutionary innovation in medicine. Nano-based drugs and antiviral technologies remain innovative in their progression, for the protection of medical staff and to enhance the experiences of the patients (Kirtane et al., 2021). Further development of these technologies will go together with the reduction of toxicity of such technologies, as well as additional analysis of their applicability as far as other new world threats that are to appear in the future are concerned.

3.8 Biosafety and biocompatibility of nanomaterials

One of the main challenges of NM use in medicine is biosafety and biocompatibility because of such factors as physicochemical properties that may cause negative toxicological outcomes. NMs, owing to their size, morphology, and reactivity, can cause several adverse effects in biological systems such as cytotoxicity, oxidative stress, inflammation, and Immunogenicity. These toxicological concerns, therefore, require a thorough risk analysis to compare their effects on man and the environment in the short run and the long run. To reduce biotoxicity and increase the compatibility of NPs with biological tissues, common approaches are their surface functionalization, for example, by using biopolymers, polypeptides, or biomimetic layers. Approaches involving functionalization include: PEGylation or the use of zwitterionic coatings to reduce the immunogenicity of particles and increase circulation time. Furthermore, legal and normative frameworks for biomedical NT from organizations such as the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Organization for Standardization (ISO) set out principles of safe design, testing, and commercialization of nanomedicines that are critically important. These guidelines emphasize thorough preclinical and clinical evaluation, standardized toxicity testing, and the consideration of ethical implications. As the field advances, ongoing research and updated regulations will be essential to balance innovation with safety in the use of NMs for healthcare (Li et al., 2023). Table 3 lists the use of nanotechnology-based medical devices approved by the FDA.

4 Toxicology and safety analysis of nanotechnology

The negative consequences of NT are alarming for mankind, animals, and the ecosystem. Although the toxicity attributed to these assemblies is still unknown, the scientific community is still not very clear as to the extent to which they expect the application of NT, particularly in the field of medicine, which is a very sensitive area of healthcare (Noga et al., 2023). Some nano-based products have been launched in previous years, but due to the side effects reported by the people, they were shortly withdrawn from the market. Therefore, the risk assessment of nanomedicine is essential, and this area needs to be assessed soon. The requirement is to focus on experiments for the further protection of NPs, dosing adjustment, and effective usage. NT, as a miraculous technology itself, can be applied to the sensors or markers for biological, chemical, and other environmental enhancements. This means that toxicity profiling of consumer products should be done. Various NMs, such as liposomes, cubosomes, solid lipid NPs, and dendrimers, present in skin care and dental products, must be evaluated separately, and the side effects of these products must be identified to develop more enhanced, efficient, and safer nanoemulsions shortly. In the same vein, the problem of bioaccumulation and persistence is associated with NT (Rathnasinghe et al., 2024).

NMs take a long time before they degrade and can accumulate in life forms. This can, in turn, produce several undesirable implications for human health, as well as for ecosystems (El-Kady et al., 2023). Furthermore, in healthcare facilities where these materials are used, the personnel may be susceptible to existing NM exposure either through the respiratory, dermal, or oral routes. Measures needed to be taken so that one does not come into contact with these materials or chemicals; hence, handling practices needed to be put in place. However, using NMs in medicine creates other important issues like the right of informed consent, privacy, fairness to access healthcare in the future, and so on, and their potential risks to sensitive populations. Yet, there is a need to respond to these ethical concerns to establish and apply the ethical norms of NMs use in healthcare.

Several measures can be taken to establish the safe and appropriate use of NMs in medical science; Firstly, research and development of the NMs for medical application should undergo extensive risk analysis. This should entail assessments of the risks and dangers that are associated with the given NM before they are employed in applications in the medical practice. Likewise, sufficient legal structures should be established to govern the correct application of NMs, including in production, processing, and usage. This comprises the assessment of their safety, how they should be classified, and their utilization and impact on health systems scrutinized. Further, the methods for testing the safety and efficiency of NMs for biomedical applications can be standardized. This, in a way, includes common procedures in toxicity testing, characterization, and the quality of the product. In addition, efficient measures should be taken to prevent the staff from exposure to NMs in the workplace. This includes engineering controls, personal protective equipment, and training and education for the employee. Furthermore, it is crucial to clarify the possible risks and opportunities connected to the usage of NMs due to the possible negative consequences and suspicious perceptions among consumers, the healthcare system, patients, and the public (Li et al., 2023). The task that lies down here is to define the experimental focus within the scope of NPs' safety, dosing, and utilization. The miracles of the NT itself can be employed in the development of sensors and markers in biological, chemical, and environmental recoveries (El-Kady et al., 2023). Harmful composition identification should be recommended to be done on consumer goods, particularly. Cosmetics and pharmacological products incorporated with various nonmaterial liposomes, cubosomes, solid lipid NPs, and dendrimers have to be examined individually, and side effects have to be studied so that better and side-effect-free nano-emulsions can replace them in the future. Checking possible risks, applying correct legislation and measures

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TABLE 3 List of nanotechnology-based medical devices approved by FDA (Reproduced with permission from (Ma et al., 2024).

Medical application/ specialty	Device/trade name	Applicant	Date of approval	Nanomaterial	Indication
Anesthesiology	UniPlex NanoLine cannula, PlexoLong-NanoLine set, StimuLong-NanoLine Set	Pajunk GmbH	01/12/2006	Nanoparticle-enhanced surface layer	Anesthesia conduction kits for temporary anesthetic delivery to peripheral nerve bundles during regional anesthesia
	SonoLong Sono, Curl Sono, NanoLine®	PAJUNK GmbH Medizintechnologie	03/01/2012	Polymer nanocoating	Anesthesia conduction kits for the delivery of continuous conduction anesthesia and/or analgesia of peripheral nerves
Clinical chemistry	Nanosep™ N10	Intercept, Ltd	04/26/1994	Nanoporous structure membrane	Clinical sample concentrator, for the concentration and purification of biological samples such as peptides, proteins, oligonucleotides, DNA, and RNA
	Nano-Check™ AMI 3 in 1 Cardiac Disease Test	Nano-Ditech Corporation	03/02/2006	Colloidal Au NPs	Immunoassay method, a one-step lateral flow immuno chromatography assay for the qualitative determination of three cardiac markers simultaneously in serum and heparin plasma
	Nano-Check™ AMI 2 in 1 Cardiac Marker, cTnI and Myoglobin	Nano-Ditech Corporation	10/20/2010	Colloidal Au NPs	Immunoassay method, to provide rapid and reliable results in diagnosing acute myocardial infarction (heart attack) by measuring the levels of cTnI and Myoglobin in the blood
	Nano-Check™ AMI cTnI Cardiac Marker Test	Nano-Ditech Corporation	10/20/2010	Colloidal Au NPs	A rapid immunoassay for the qualitative determination of cardiac troponin I (cTnI) in human serum and plasma specimens at cut-off, as an aid in the diagnosis of Acute Myocardial Infarction (AMI)
Dental	NanoTite PREVAIL, Certain, Parallel Walled, Tapered, External Hex	BIomet 3i, Inc	01/31/2008	Osseotite® nanoscale surface and nanocrystalline deposition of calcium phosphate	A root-form endosseous implant, for surgical placement in the jaw to support prosthetic attachments for single-tooth restorations, partially or fully edentulous spans, bridgework, and overdentures
	Renamel® NANO™ + plus	Cosmedent, Inc	02/24/2017	Multifunctional acrylic monomers and silicaceous nanofillers	Tooth shade resin material, designed for Class I-V dental restorations, direct veneering of anterior teeth, splinting and the repair of composite or ceramic restorations
	Nano composite	Cosmedent, Inc	04/16/2007	Light-cure nanocomposite	Tooth shade resin material, possesses the physical and mechanical properties to function in the oral cavity, mimicking the esthetic qualities of natural teeth
	DMRC NanoFlow; DMRC Nanocomposite; ebond; sure, etch gel; sure, etch liquid	Danville Materials, Inc	09/25/2012	Light-cure NPs	DMRC NanoFlow, a flowable composite for small cavities, repairs, linings, sealants and marginal repairs; DMRC NanoComposite, a universal composite for direct and indirect restorations; eBond, a bonding agent to enhance adhesion between composites and tooth structure; Sure, Etch Gel and Sure, Etch Liquid, both used to prepare tooth surfaces for improved bonding by creating micropores
	Prime & Bond® NT™ Dual Cure Nano-Technology Universal Dental Adhesive System	Dentsply International, Inc	02/23/2005	Nanofiller	Tooth bonding agent for bonding all indirect restorations, including metal, ceramic and composite crowns, inlays, onlays, veneers, bridge retainers and endodontic posts to enamel and dentin without light
	Nanocomposite Restorative Kit	DMG USA, Inc	05/30/2008	Light-cure nanocomposite	Tooth shade resin material, designed for restorative procedures to repair and restore the function and aesthetics of teeth affected by cavities or other forms of dental damage

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TABLE 3 (*Continued*) List of nanotechnology-based medical devices approved by FDA (Reproduced with permission from (Ma et al., 2024).

Medical application/ specialty	Device/trade name	Applicant	Date of approval	Nanomaterial	Indication
	NanoCeram-Bright	DMP, Ltd	11/19/2010	Light-cure nano-hybrid composite	Resin material for anterior and posterior restorations, cervical caries, root erosion, wedge-shaped defects, veneering discoloured anterior teeth, splinting mobile teeth and repairing composite and ceramic veneers
	Nano Varnish, Plaquit, Lightpaint on Surface	Dreve Dentamid GmbH	04/05/2018	Light-cure NPs	Dental sealing lacquer for coating resin temporaries
	Nanotite™ Dental Implants	Implant Innovations, Inc	02/22/2007	Calcium phosphate nanocrystal	Dental implants with nanoscale calcium phosphate crystals on the surface
	Series of Nanova products for dental use	Nanova Biomaterials Inc	01/16/2018, etc.*	Hydroxyapatite nanofiber	Tooth bonding agents; sealant, pit and fissure, conditioner; tooth shade resin materials
	Nano-TiCrown™	Nano-Write Corporation	06/11/2003	Nanostructured titanium/titanium nitride material	Base metal alloy for making single-unit porcelain-fused-to-metal (PFM) prosthetics and custom dental prosthetics, such as porcelain-to-metal veneers
	Dimer Acid Derived Nano-hybrid Composite Restorative Material	Novocol, Inc	09/13/2007	Dimer acid derived nanohybrid composite	Tooth shade resin material, for class I, II, III, IV and V cavity classes
	NanoGen®	Orthogen, Llc	05/06/2011	Nanocrystalline calcium sulfate	Bone grafting material for bone regeneration, used alone, mixed with other bone filling agents to prevent particle migration, or as a resorbable barrier over other graft materials
	Pac-Dent Ceramic Nanohybrid Resin	Pac-Dent, Inc	07/26/2021	Ceramic nanohybrid	Tooth shade resin material, for fabricating permanent restorations such as inlays, onlays, veneers, and full crown restorations
	Nano-Bond II Adhesive System	Pentron Clinical Technologies	08/10/2007	Light-cure nanocomposite	Resin tooth bonding agent
	Sculpture® Plus Nano-Hybrid Composite	Pentron Laboratory Technologies	01/17/2003	Nanohybrid composite	Dental restorative material used to restore carious lesions, structural defects, or lost tooth structure
	CalApex Calplus, Cerafill RCS, Endoseal, Nanoseal S, Zical Ultra Paste, Zical Ultra Powder/ Liquid	Prevest Denpro, Ltd	05/23/2022	Ag NPs	Antibacterial root canal sealer fortified with nanosilver used in conjunction with gutta-percha for effective sealing root canals of permanent teeth
	Camouflage™ NanoHybrid Composite (Universal and Flowable)	Prismatik Dentalcraft, Inc	06/04/2014	Ceramic-filled nanohybrid resin composite material	Tooth shade resin material for Class I-VI cavities in anterior and posterior teeth, suitable for direct restorations, inlays, and onlays
	Capo Hybrid, Capo Slow Flow, Capo Flow, Capo Natural, Capo Universal, Nano Paq, Nano Paq Flow	Schütz Dental GmbH	10/24/2016	Light-cure nanocomposite	Tooth shade resin material for direct and indirect restorations, fissure sealing on premolars and molars, stump buildup, shape and colour correction
General & plastic surgery	Series of LigaSure™ products	Covidien	03/23/2021, etc.*	Nonstick nanocoating	Electrosurgical cutting and coagulation device and accessories, for open surgical procedures where ligation and division of vessels, tissue bundles, and lymphatics
	Medline ReNewal Reprocessed LigaSure Exact Dissector, Nano-coated (LF2019)	Surgical Instrument Service And Savings, Inc	04/29/2024	Nanocoating to reduce tissue sticking	Electrosurgical cutting and coagulation device and accessories
Immunology	Nanopia Wide Range C-Reactive ProTein (CRP) Reagent Kit	Clinical Data, Inc	02/09/2006	Antibody-coated latex particles	Quantitative latex agglutination immunoassay for measuring C-Reactive Protein (CRP) in serum or plasma, used to evaluate infection, tissue injury and inflammatory disorders alongside a complete clinical evaluation
Microbiology	Nano-Check™ COVID-19 Antigen Test	Nano-Ditech Corporation	01/23/2024	Au NPs	Simple point-of-care device, used as an immunochromatographic lateral flow assay for detection of SARS-CoV-2 nucleo protein antigens in human anterior nasal swab specimens

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Medical application/ specialty	Device/trade name	Applicant	Date of approval	Nanomaterial	Indication
Neurology	Series of Titan NanoLOCK products for neurology	Medtronic Sofamor Danek USA, Inc	09/29/2022, etc.*	Titanium nanoscale featured surface	Stereotaxic Instruments, to be used during preparation and placement of Medtronic implants during spinal surgery to assist in precisely locating anatomical structures in either open, or minimally invasive procedures
Orthopedic	Ascend VBR System, Ascend NanoTec VBR System	Alphatec Spine, Inc	10/06/2023	Hydroxyapatite nanocoating	Spinal intervertebral body fixation orthosis to replace a collapsed, damaged, or unstable vertebral body or for reconstructive decompression of the spinal cord and neural tissues in degenerative disorders
	Calibrate PSX Interbody System, Calibrate NanoTec PSX Interbody System	Alphatec Spine, Inc	07/13/2023	Hydroxyapatite nanocoating	Intervertebral body fusion device for spinal fusion from L1 to S1 in skeletally mature patients, treating symptomatic degenerative disc disease (DDD), degenerative spondylolisthesis, and/or spinal stenosis at one or two adjacent levels
	Series of IdentiTi Porous Ti Interbody Systems	Alphatec Spine, Inc	02/22/2024, etc.*	Hydroxyapatite nanocoating	Intervertebral body fusion devices for treating DDD and spinal instability in skeletally mature patients
	nanOss® Bone Void Filler	Angstrom Medica, Inc	02/03/2005	Hydroxyapatite nanocrystal	Resorbable calcium salt bone void filler device for non-structural bony voids or gaps in the extremities, spine, and pelvis
	Series of NanoBone® products	Artoss GmbH	04/23/2019, etc.*	Nanocrystalline osteoconductive hydroxyapatite	Resorbable calcium salt bone void fillers device for bony voids or gaps in the extremities, posterolateral spine, and pelvis
	EMPOWR Porous Femur with HAnano Surface™	Encore Medical, L.P	03/30/2021	Hydroxyapatite nanocoating	Knee joint patellofemorotibial metal/polymer porous-coated uncemented prosthesis for total knee arthroplasty, treating arthritis, avascular necrosis, joint configuration loss, deformities, fractures, and for salvage of failed surgeries
	NanoHive Medical Lumbar Interbody System	Ian Helmar	07/12/2023	Soft Titanium® lattice nanotextured surface	Intervertebral body fusion device for use in skeletally mature patients with DDD at one or two contiguous levels from L2 to S1
	Series of Titan NanoLOCK products for orthopedic	Medtronic Sofamor Danek USA, Inc	10/06/2022, etc.*	Titanium nanoscale featured surface	Intervertebral body fusion device for spinal fusion in skeletally mature patients with symptomatic DDD, degenerative spondylolisthesis, and/or spinal stenosis at one or two levels from L2 to S1
	Series of Nanova products for orthopedic use	Nanova Biomaterials Inc	05/05/2017, etc.*	Hydroxyapatite nanofiber	Metallic bone fixation appliances and accessories for securing soft tissue or bone-tendon-bone grafts during cruciate ligament reconstruction surgeries of the knee
	Series of Nanovis systems	Nanovis, Llc	06/02/2023, etc.*	Bio-ceramic nanotube surface	Intervertebral body fusion devices for immobilising and stabilising spinal segments as an adjunct to fusion in patients with DDD, spinal stenosis, spondylolisthesis, spinal deformities, trauma, tumours, pseudarthrosis, and failed fusions
	Series of nanOss™ products	Pioneer Surgical Technology, Inc	10/17/2014, etc.*	Nano-structured hydroxyapatite	Bone void fillers
	Series of SeaSpine Systems	SeaSpine Orthopedics Corporation	07/07/2021, etc.*	Titanium nanoscale featured surface	Intervertebral body fusion devices
	OsteoFlo® NanoPutty®-Quadphasic Synthetic Bone Graft	SurGenTec, Llc	08/14/2020	Hydroxyapatite NPs	Resorbable calcium salt bone void filler device
	Tyber Medical BioTy® Nanotopography Trauma Screw	Tyber Medical, Llc	06/20/2017 11/16/2016	Nanoscale featured surface	Metallic bone fixation fastener for bone reconstruction, osteotomy, arthrodesis, and joint fusion
Radiology	DRX-Revolution Nano Mobile X-ray System	Carestream Health, Inc	02/05/2018, etc.*	Carbon nanotube	Diagnostic mobile x-ray system with digital radiography (DR) technology, featuring a self-contained x-ray generator, image receptor(s), imaging

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Medical application/ specialty	Device/trade name	Applicant	Date of approval	Nanomaterial	Indication
					display, and software for acquiring diagnostic images outside a standard x-ray room
	Nanox.ARC	Nanox Imaging, Ltd	04/28/2023	Nano-cones field on a silicon chip	Tomographic X-ray system for producing images of the human musculoskeletal system from a single sweep, as an adjunct to conventional radiography for adult patients
	Nanox Cart X-ray System	Nanox Imaging, Ltd	04/01/2021	Nano-cones field on a silicon chip	Mobile X-ray system for radiographic examinations of hands, wrists, and fingers in adult patients, designed for use when transporting the patient to fixed equipment is not feasible
	Nanor® and Efficast/Nanor Hybrid Thermoplastic Materials	Orfit Industries N.V	09/26/2013	Hybrid thermoplastic NPs	Medical charged-particle radiation therapy system for retaining and reproducing a patient's position during radiation therapy
Toxicology	Nano-Check™ DAT 5 Multi-Drug Screening Test	Nano-Ditech Corporation	05/15/2005	Colloidal Au NPs	Qualitative immunoassay: a one-step, type II competitive immunochromatographic assay for detecting cannabinoids, opiates, benzoylecgonine, methamphetamine, phencyclidine, and their metabolites in human urine

as well as stimulating reasonable usage in the medical practice, NMs can be effectively and efficiently applied for diagnostics, medication delivery, and disease treatment.

Nanobiotechnology holds immense promise for transforming healthcare by addressing complex biomedical challenges with unparalleled precision and predictability. Advancements in areas like immunotherapy and gene therapy highlight their potential to revolutionize therapeutics and diagnostics. Through collaborative efforts in academia and industry, nanobiotechnology is driving innovations in theranostics, emphasizing the need to prioritize applications that enhance efficacy, deepen scientific knowledge, and improve quality of life (Li et al., 2023). Precision medicine is one of the main uses, where nano-biosensors and nanocarriers allow for individualized treatments based on individuals' genetic identities, increasing effectiveness and lowering consequences. In regenerative medicine, NPs and nano scaffolds support tissue repair by delivering stem cells and therapeutic agents. Drug delivery systems, such as stimuli-responsive nanocarriers, ensure site-specific targeting, minimizing off-target effects and optimizing therapeutic outcomes. Nanobiosensors provide high sensitivity for early disease detection, improving patient outcomes and reducing healthcare costs.

Beyond medicine, nanobiotechnology addresses environmental and agricultural challenges. NMs can remove contaminants from water and soil, while biosensors detect contaminants at trace levels for timely intervention. In agriculture, NPs improve nutrient delivery and pest protection, and biosensors ensure food safety by identifying pathogens and contaminants. Future directions focus on nanoengineering for targeted drug delivery, ultra-sensitive diagnostic tools, and tissue engineering using nanoengineered scaffolds to mimic extracellular matrices. Overcoming challenges such as safety concerns, scalability, and regulatory hurdles is essential for widespread adoption. Harmonization among global regulatory bodies is critical to responsibly advancing this transformative technology. By addressing these challenges, nanobiotechnology and nanoengineering promise to revolutionize healthcare, environmental remediation, and agriculture, enhancing quality of life and creating a healthier planet for future generations.

5 Challenges in translation from bench to bedside

Translating NM-based innovations from bench research to clinical applications presents a multitude of challenges, many of which are technical, economic, and societal. There is a big challenge when it comes to the reproducibility and scalability of the synthesized NMs. Laboratory synthesis of NMs is relatively easy and well-controlled, but when the synthesis of a large quantity of NMs is desired, some characteristics of the NMs exhibit variations. Variations in the batch-to-batch particle size distribution, as well as in the surface morphologies of these materials, can have a profound impact on their uses and effectiveness in clinical situations. Reproducibility also arises as a problem since the slight differences in the synthesis parameters can give greatly different biological reactivity and curative effects, while attempts to standardize the necessary production parameters for applicability in practice can be very challenging.

Another issue of significant concern is the issue of cost and economic viability of NMs-based technologies. The production of high-quality NMs is associated with high costs, mainly due to expensive equipment, chemicals, and methods. When considering the translation of these materials to clinical practice, especially in low-resource regions, the cost of these materials forms a large part of the problem. Moreover, sequential production of such materials calls for corresponding research and developmental costs plus clinical services, including testing, that are costly. Thus, if efficient and inexpensive methods of synthesizing NMs are not developed, the practical application in the healthcare sector will be limited.

Lastly, ethical and societal consideration needs to be considered as to whether to apply NMs in clinical uses. As with other NMs, there are long-term toxicity, environmental disposal, and privacy issues related to the use of NMs in diagnostics and treatments that must be more fully explored. Ongoing research and development of NMs imply the possibility of their adverse effects on biological systems not predicted during the initial tests. Other ethical concerns include patient consent; a patient may never agree to receive implants with materials that have emergent side effects that are unknown to the patient. Furthermore, there may be issues with equity in these superior therapies to further ramp up inequality within healthcare hierarchies between people who can afford the new therapies and those who cannot. As NMs move closer to practical application, solid ethical principles for the use of these materials, as well as appropriate precautionary and legal measures, need to be developed to facilitate the ongoing incorporation of NMs into medicine.

6 Future perspective: unveiling the untapped potential of nanobiotechnology

In biomedicine, the future of NT is informed by trends such as artificial intelligence and machine learning; they facilitate modeling, enhanced NPs design, and individualized intervention. Machine learning makes it easier to study correlations in big data, leading to the determination of the best NPs characteristics for various applications in the nanomedical field. Well-designed, versatile nanodevices are also changing the profile of the field with theranostic applications that integrate diagnostics and treatment in a single construct. Responsive NT systems that change their responses according to changes that are influenced by the environment or the physiological characteristics of the body are opening the way to real-time surveillance and modality-specific treatments.

However, strong and effective policies are needed to protect consumers' interests and address the issues of safety, efficacy, and ethics of using nanomedicine. It is very important because several difficulties come with this approach, including toxicity, scale, and biocompatibility. The application of nanobiotechnology includes precision medicine, regenerative medicine, drug delivery, and environmental applications. Nanobiosensors and nanocarriers make all treatments more accurate and accessible, making therapies tailored to individual patients more effective with fewer side effects. Nanoengineered scaffolds can encourage tissue regeneration and can present solutions for wounds and degenerative diseases. NMs are also expected to remediate polluted environments and sense pollutants. NT will redefine medicine by enhancing diagnosis procedures, exploring new treatments, and developing distinct treatment plans. NPs in the drugs were another attribute that could improve the treatment efficacy of multifactorial diseases such as cancer and neurological diseases. Nanorobotics significantly provides unprecedented accuracy in surgical intervention and is a revolutionary dimension in the medical world. Such nanoscale robots should be able to navigate complex physiological environments, perform minimally invasive procedures and deliver drugs to specific tissues to the highest extent possible, minimizing collateral damage and complications of postoperative procedures. They are advanced in actuation, programmable materials and artificial intelligence (AI), which means real-time adaptive response to changing surgery. These technologies have been demonstrated to have potential in gastrointestinal surgeries and even neural surgery where the need to navigate extremely fine vascular and neural structures is critical to outcome and recovery. Nanomedicine applies the engineering versatility of nanoparticles to surmount the blood-brain barrier, which is a conventional barrier to drug delivery in neurodegenerative disease entailments to drugs such as Alzheimer, Parkinson, Anterior Diffusion diseases and ALS. To deliver functionalized nanocarriers, drugs, genes, antibodies or neurotrophic factors are encapsulated and released at the site of infection, reducing systemic toxicity and enhancing effective therapeutic action. Recent experiments have shown that amyloid-beta deposition can be reduced and pathological protein aggregation can be controlled specifically with such platforms. Besides providing personalized and disease specific therapy, these innovations also hold promise to provide better diagnosis and monitoring using nanosensors.

Moreover, the diffusion of NT-based imaging agents will enhance image resolution in diagnosis and treatment planning. But more than anything, incorporating NT in medicine comes with safety and ethical issues and national regulatory considerations like FDA clearances. Therefore, one can conclude that NT has the capability in the future to change the existing picture in the healthcare industry. In the future, therefore, consistency in standards across the world will help to fit the actual regulatory mechanisms that will enable the use of NMs in innovations without affecting the wellbeing of the users.

7 Safety, economic, and regulatory concerns

Safety is a fundamental issue since nanomaterials have physicochemical properties that are different from their bulk counterparts. Their nanoscale and highly reactive surface may generate unforeseen biological responses, which can cause toxicity, inflammatory reactions, and even carcinogenesis. There is also worry about NPs buildup in organs and long-term health risk, while pathways like oxidative stress, cell damage, and unwanted immune activation need to be extensively explored. NPs toxicity is material, size, and shape dependent, and so extensive preclinical and long-term safety assessments are needed. Regulation of biomedical NT in markets like the European Union and the United States, NT-based health products are traditionally examined under current drug and device laws, individually screened for safety, efficacy, and quality. Nonetheless, the absence of one integrated, NT-centric pathway leaves uncertainty, particularly for products that straddle drug, device, or biologic classification. Regulatory agencies require extensive documentation, which is usually in the electronic medium, and compliance with global standards, but lacking standardized NPs-testing protocols, approvals take longer, and entry into the market becomes more difficult. From a commercial and scaling perspective, the translation of nano-innovations generated in the laboratory to commercial health products is severely hindered. Reproducibility, large-scale production, and quality assurance challenges drive costs and increase the complexity of industrialization. However, innovations like high-pressure homogenization, microfluidization, and green synthesis technologies are reducing the cost and enhancing scalability, opening up nanomedicine. Addressing the dual objectives of affordability and high-throughput manufacturing, coupled with safety and efficacy, continues to be a determining factor for NT in healthcare to be adopted on a large scale.

8 Conclusion

Nanobiotechnology is revolutionizing healthcare in a way that presents new possibilities for optimized therapeutic applications with high accuracy and efficiency. Thus, NT facilitates the modification of the size, shape, and surface chemistry of nanocarriers to improve therapeutic profiles. Healthcare and medical uses of NT can go beyond the original ideas of diagnosing, curing, and preventing diseases. Given that the size of nanostructures is within the range of molecular and cellular dimensions, it is possible to influence their physical, chemical, and pharmacological properties and create new drugs and diagnostic techniques. In addition to drug targeting, NPs can modify drug properties by increasing their solubility, stability, and non-systemic bioavailability. It also includes sensors and devices derived from NT to facilitate constant patient condition checks and diagnosis in parallel with early treatment plans. The applications of new approaches and NMs, as well as devices, will further develop nanobiotechnology, meeting its present drawbacks and contributing to the advancement of healthcare in the future. In the future, such nanorobots may also move through the bloodstream, find and eliminate cancer cells, or deliver medications to affected tissues. As costs associated with the technology decrease, NT is expected to profoundly impact fields such as dentistry, healthcare, and overall human life. For a successful application, it is still crucial to address the toxicological hazards and concerns related to high dosages and overuse of NMs in medicine delivery and therapy. NT has had a significant impact on the biomedical field, leading to remarkable advances in the creation of functional NMs for medical purposes. Key properties of NPs, such as particulate shape, microstructure, diameter, and surface charge, play crucial roles in determining the effectiveness of designed NPs. These properties can be controlled through methods such as the seeding growth technique, and careful selection of materials and preparation tools is essential for optimizing NPs design. Characterization techniques are vital for gaining a comprehensive understanding of these properties, but sample preparation remains a challenge for some NPs. Researchers should focus on developing simple and efficient characterization methods to facilitate progress in this field. Finally, applying industrial concepts like QD to biomedical NM applications, along with fostering collaboration between industry professionals and NM researchers, will be key to scaling up the production and market availability of these innovative products.

The article addresses an extensive variety of NT uses, ranging from diagnostics to drug delivery, tissue engineering to regenerative medicine, immunotherapy to theranostics, and offers much depth for readers who wish to explore the subject. It emphasizes the distinctive physicochemical features of nanomaterials that facilitate better diagnostics, better drug targeting, and better therapies for diseases such as cancer and chronic ailments. The review does not ignore such key challenges as clinical translation, cost, safety, adaptability, and regulatory approval, showing even-handed reporting and a sense of reality regarding the field's status. The review does not discuss the detailed long-term environmental or biological impact of nanomaterials, which is crucial for practical application. This does not include a solution for production standardization and scalability challenges for large-scale use. The future of NT in healthcare is bright, with the potential to improve patient outcomes and revolutionize disease prevention and treatment approaches.

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LG: Conceptualization, Writing – original draft. SS: Writing – review and editing.

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Conflict of interest

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