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Emerging Opportunities and Challenges of Nanoparticles in Nanomedicine

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Highlights

- The use of NPs in nanomedicine reveals new developments.
- Organic and inorganic nanoparticles reveal tremendous opportunities for nanomedicine.
- The use of NPs in Nanomedicine in lung, heart, brain, and kidney treatments gives positive results.

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Abstract

Nanomedicine encompasses a wide range of utilizations, including medical biological devices, nanoparticles (NPs), nanoelectronic biosensors, and possible future applications of molecular nanotechnologies, such as biological machines. Understanding toxicity and environmental impact problems is a current challenge in nanomedicine. The advancement of NPs in nanomedicine foresees emerging opportunities that may change healthcare by enhancing pharmaceutical effectiveness. This review may reveal novel and improved biomedical significance by delving deeper into advanced growth methodologies and NP applications in nanomedicine. NPs' outstanding physical and chemical characteristics have advanced medical, diagnostic, and screening techniques. The present review offers a current overview of organic and inorganic nanoparticles, highlighting recent advancements, obstacles, and potential applications for nanomedicine. Also, the focus of this review is on a fundamental concept that underlies the creation of novel and successful therapies using NPs in the field of nanomedicine for the human body's lungs, heart, brain, and kidneys. This extensive and insightful information source would be beneficial to the advancement of nanomedicine.

1. INTRODUCTION

Nanomedicine hopes to provide a useful selection of equipment for clinical use and research in the near future [1]. According to the national nanotechnology initiative, innovative commercial uses for the pharmaceutical industry will include in vivo imaging, novel therapeutics, and enhanced drug delivery systems [2]. The economy is anticipated to be significantly impacted by the nanomedicine sector's continued growth. Through the use of NPs, nanotechnology enables the targeted delivery of medications to particular cells. By simply applying the active ingredient to the diseased area and using the smallest dose necessary, the overall amount of medication consumed, and adverse effects can be considerably reduced.

Targeted drug distribution aims to reduce therapeutic side effects while concurrently reducing drug intake and treatment costs [3]. The goal of drug delivery is to increase bioavailability at particular locations and sustain it for a specified period of time. This may be accomplished by the use of nanoengineered devices that target certain molecules. Smaller, less intrusive devices that may be embedded throughout the body and faster times for biological reactions are two advantages of adopting nanotechnology for medical technologies [4]. Compared to standard medication delivery methods, these technologies are swifter and more perceptive. The successful delivery of the drug to the desired area of the body, the efficient encapsulation of the drug, and the successful release of the drug all contribute to the efficacy of drug delivery by nanomedicine [5].

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Nanomedicine is the application of NPs in medicine [6]. It can be given new functions by interacting with biological molecules or structures. NPs, being comparable in size to various biological molecules and structures, can find application in both in vivo and in vitro biomedical research [7]. The combination of biology and NPs has produced a variety of useful technologies, including analytical instruments, contrast agents, diagnostic tools, physical therapy applications, and medication delivery systems. NPs offer a cutting-edge platform [8] for existing engineering disciplines like chemistry, physics, biology, medicine, neurology, and information and communication engineering, resulting in a new multidisciplinary study field. It's aroused a lot of interest in various synthesis techniques, and they've got a number of uses in energy, the environment, electronics, and medicine [9]. Despite significant progress and the introduction of many marketed NPs, nanoscience, and technology-based commodities in these fields, they continue to face a slew of new challenges in areas critical to basic public needs.

Day by day, gold is becoming increasingly interesting in the chemistry, biochemistry, biophysics, radiation medicine, and nanoscience communities [10]. Some of the metal dioxide materials have several advantages over the comparable ultraviolet protection properties of bulk materials [11, 12]. As the particle dimension decreases, it gains cosmetically desirable whitening. A nanofiber can make clothes wrinkle-free or stain-resistant. In the textile industry, cleaning at low temperatures is less common. It can be utilized to incorporate carbon into the membrane, providing the wearer with full-body conservation from electrostatic charges. Analog instruments are replaced by digital optoelectronic devices with enormous bandwidth and capacity, such as photonic crystals and quantum dots. It offers the propagation of a certain wavelength of photons instead of electrons.

Quantum phenomena can be used to perform different operations in advanced computation [13]. The essential utilization of NPs in photocatalytic devices within catalysis ranges between fuel cells and catalytic converters. It is very crucial for the production of chemicals. Platinum has been considered for the next generation of converters. In the industrial sector [14], TiO2 nanotubes are potentially utilized as photocatalytic materials. Agriculture is the backbone of developing nations; the majority of the population depends on it for a living. The nanomaterial can help understand the biological structure of various crops. Thus, it potentially enhances yields or nutritional values as well as provides appropriate conditions for monitoring environmental conditions that deliver nutrients.

The emergence of nanotechnology as an enabling NP has opened avenues for innovative applications in the biomedical sector [15]. The five qualities of the principle—long blood circulation, effective tumor accumulation, deep matrix penetration, increased cell internalization, and accurate drug release—offer a viable platform for improving modification properties such as size, surface charge, ligand receptors, and stability. The working framework is advancing a toxicology technology characterization technique for determining toxicity phenomena in this arena [16]. Due to their biocompatibility, oxide NPs is widely used in the biomedical sector. The requirements for the materials utilized in different biomedical instruments are increasing with the continuous aging of the population. The copper oxide may restrict development, enhance oxidative stress, and cause potential cancer cells to die off, thus acting as an antibacterial agent [17]. Early diagnosis is an important idea in the treatment of devastating diseases and potentially prevents them [18]. The novel treatment option is dominated by a new imaging agent for diagnosis. Nanomedicine is allowing for new possibilities in implantable delivery techniques that are superior to current medication delivery methods. A comprehensive summary of the most thoroughly studied NP is due to the enormous quantity of research papers and the speed with which the published data is continuously updated [19]. The review addresses the developments, difficulties, and future prospects of the most innovative and challenging uses of NPs in contemporary nanomedicine. Finally, a summary of food and drug administration (FDA) approved and commercialized nanomedicine is covered. NP toxicity studies are crucial for the efficient use of NPs; nevertheless, this subject is outside the scope of the research and calls for explanations in future reviews. This review updates readers on regularly used organic and inorganic NPs while highlighting current advancements, difficulties, and potential utilization.

2. DEVELOPMENT OF NANOPARTICLES

The broad range of synthesis processes, extraction from various sources, production from different elements within nontoxic environments, simple handling, physicochemical modification, and development of their compounds with multiple specimens have led to their large-scale production and applications in various sectors [20]. Thermodynamic and kinetic equilibrium approaches are used to carry out physical and chemical processes. The development rates of NPs are very important in physical and chemical synthesis processes, and they are used for different purposes [21]. Metal NPs and their oxides can be created using specific physical and chemical techniques. These techniques have been refined through extensive research and testing, allowing for exceptional control and customization of the physiochemical properties of the nanostructures. However, these processes have a number of drawbacks since they consume hazardous chemicals, create dangerous byproducts, and demand a lot of energy [22]. It is crucial for the continued advancement of an environmentally benign method of producing metal and metal oxide NPs. Any nanostructured material is formed in one of two ways. The top-down strategy is one of them, while the bottom-up approach is the other [23]. The term "top-down approach" describes the process of gradually reducing a material's mass to the nanoscale. It also goes by the name of lithography. This method for creating semiconductor nanostructures is a direct result of improvements in standard microelectronics manufacturing's spatial resolution. It entails systematically removing every nearby unmasked specimen while masking selective nanoscale portions of a semiconductor thin film with a different large lateral extent. Semiconductor nanostructure materials now have minimum feature dimensions below 100 nm as a result of the application of photolithography and electron or x-ray beam lithography together. The production of 10 nm diameter quantum wires and a dot is still limited by the capabilities of a lithographic process. On the other hand, the bottom-up approach starts at the atomic or molecular level and involves the self-assembly of devices. The mechanisms of spontaneous self-assembly are another term for it. Using this method, there is an impressive amount of research being done on semiconductor nanostructure development. Early in the 1990s, semiconductor quantum dots (QDs) were created by using spontaneous formation [24]. At first, this outcome was thought to be the product of a flawed film advancement strategy. By adopting this method to create the QDs, various pathways for the growth of atomic-scale clusters of semiconductor components have recently been discovered. Each of these methods directly contributes to stress. Considerable research has focused on understanding the external uncertainties caused by stress that may result in the development of nanostructures in semiconductor materials. The Stranski-Krastanov growth mode [25] has been identified as the process responsible for the creation of QDs.

The periodic morphology gradually replaces the flat structure that originally characterized the formation of strained thin films. Following that, the capacity to release tension outperforms the additional surface power needed to cause QDs to develop. The bottom-up technique has recently become more noticeable in technical applications, while the top-down strategy is quickly becoming out of date. By adopting a straightforward chemical solution technique, the bottom-up strategy is able to create device-quality material that is far more affordable than the top-down approach. Moreover, it offers a technique for uniformly ascending chemical mixtures. The chemical synthesis process will yield a novel whose self-assembly will enable power and time-saving strategies, which is a fundamental aspect of NPs research [26, 27]. The hydro- and solvothermal reactions are primarily involved in the chemical solution pathway [28]. These procedures are essential in a variety of scientific fields where fundamental or applied material research is conducted. These processes have advanced more recently, especially with the development of nanostructured materials. The relative amount of precursor consumed throughout the nucleation and growth stages for a specific amount of precursor added to the reaction medium will determine the ultimate NP size [29]. Particle growth is limited to the point when the molecular precursor has been fully consumed. The slow nucleation leads to the creation of a population of relatively larger particles due to the low concentration of embryonic seeds it produces. Although slow nucleation consumes the same amount of precursor as fast nucleation, it ultimately results in the production of small particles.

By analyzing the effects of various parameters, the electrochemical process for developing NPs is a critical strategy for achieving high performance and stability in energy devices [30, 31]. To create ZnO NP, a number of biological synthesis techniques have been employed. Waste materials were used to carry out these processes. The mediation of plant parts like roots, shoots, leaves, and stems as well as the mediation

of microbes including fungi, algae, viruses, actinomyces, and bacteria [32]. It is vital to create environmentally safe NPs that don't release hazardous substances. The intracellular or extracellular processes of many microbes, including fungi, algae, viruses, actinomyces, and bacteria, can be exploited to synthesize various nanostructured materials. This sort of synthesis procedure appears to be a beneficial method for biological nature that is also environmentally friendly and green. Examples of organisms that engage in biological synthesis processes include bacteria, algae, fungi, and plants. Large-scale NP generation by plants results in the discovery of additional pollutants. Plant materials like fruits, seeds, stems, leaves, and roots, among others, are used to make nanostructures [33]. Metal ions are involved in the process, and depending on the biological medium used, they either undergo oxidation or reduction. Due to the fact that each autotrophy comprises a different set of molecules that are responsible for the reaction, the precise mechanisms underlying the process of biologically synthesizing NPs have not been extensively explored yet. It is understood that the metallic substance's nucleation starts the process, and then NP development starts in the mixture, where it forms the precipitate.

Plant extracts are commonly used as reducing and stabilizing agents in the production of NPs. Low toxicity, low cost, and environmental friendliness are only a few advantages of using plant extracts in the manufacturing of NPs [34]. Plant extracts contain various phytochemicals such as flavonoids, phenols, terpenoids, alkaloids, and tannins that can act as both reducing agents and stabilizers during the synthesis process. These phytochemicals can reduce metal ions, leading to the formation of NPs, while simultaneously preventing their agglomeration. The creation of nanostructures from these extracts involves the reduction of metal ions in the solution. The plant extracts are added to the metal ion solution, and the reduction reaction occurs in their presence. The extract functions as a reducing agent to reduce metal ions and simultaneously stabilizes the resulting NP. By altering the concentration of the extract, the concentration of the metal ion solution, and the duration of the reaction, the size, shape, and morphology of the NP can be regulated. For the creation of nanostructured materials, plant extracts from numerous plants, including green tea, ginger, neem, turmeric, and grapefruit, have been employed. One instance is the utilization of neem extract to synthesize ZnO NPs [35] that fall within a size of 25.51 nm and the use of green tea extract to create Ag NPs [36] with a size range of 8–68 nm. Many uses for the resultant NP in industries like medicine, catalysis, and electronics have been discovered. Furthermore, the organic substances in plants and microbes play a role in stabilizing, or capping, the NP as they attach to the surface of the nanostructures. This prevents aggregation and eliminates the need for additional stabilizing chemicals [37]. Plant extracts appear to be the superior biological media for reproducing this process in a lab setting because they are more stable, decrease metal ions more quickly, and are simpler to scale up than microorganisms [38, 39]. As they have demonstrated greater efficacy in synthesizing NPs than microbes, plants have been the primary focus of research on the biosynthesis process [40].

3. TYPES OF NANOPARTICLES

The different types of NPs have played a significant role in the advancement of nanotechnologies [41]. For improvements in drug delivery that can save lives as well as increasing productivity across a variety of fields. As nanotechnology develops, more useful NPs will be created and produced for application in the engineering and medicinal industries. The capacity to adapt their functions for a variety of applications, high surface energy, and large surface areas are just a few of the characteristics that set nanostructures apart from bulk materials. The classification of NPs can be based on several factors, such as their size, morphology, physical characteristics, and chemical properties [42]. Often, the classification of these materials determines their function.

3.1. Organic Nanoparticles

Polymeric nanostructure: Depending on the technique used for preparation, polymeric nanostructure materials have an organic base. Its structures resemble nanospheres or nanocapsules. Nanocapsules possess a core-shell configuration, while nanospheres exhibit a matrix-like structure. In polymeric nanocapsules, active substances are enclosed within a polymer shell, while in polymeric nanospheres, they are evenly dispersed throughout the structure. Polymeric nanostructures have a number of benefits, including controlled release, drug molecule protection both inside and outside the body, and the potential for precision

targeting, imaging, and therapy combined. Medication administration and diagnostics are two uses for polymeric nanostructures. Drug delivery techniques based on polymeric nanostructures are also exceptionally biocompatible and biodegradable [43].

Lipid nanostructure: Lipid nanostructures typically have a diameter between 10 and 100 nm and are spherical in shape. They have a matrix of lipophilic compounds that are soluble and a solid lipid core, and the exterior core is stabilized by emulsifiers and surfactants. The biomedical industry employs lipid nanostructures, which are used in the biomedical industry as drug carriers and to release ribonucleic acid during the treatment of cancer [44].

Viral-based nanostructure: The term "viral-based nanostructures" refers to a broad category of naturally occurring NPs generated from mammalian, plant, and bacteriophage viruses. The use and advancement of viral nanostructures and their genome-free equivalents, virus-like particles (VLPs), is a swiftly growing field of study. To achieve tissue selectivity, VLPs can be genetically attached to target ligands as well as incorporate a variety of active components. VLPs are produced using biocompatible, biodegradable ingredients by scalable fermentation or molecular farming. These features have resulted in numerous applications, such as imaging and theranostics, cancer treatments, immunotherapies, vaccines, antimicrobial therapy, cardiovascular therapies, and gene therapies [45]. To bring these treatments to the clinic, enough research must be done consistently as the utilization of VLPs as instruments for drug delivery evolves. This review highlights some of the cutting-edge studies being conducted in the field of VNP medication delivery that are working toward this larger objective.

3.2. Inorganic Nanoparticles

Carbon-based nanostructure: There are two main types of carbon-based nanostructures; fullerenes and carbon nanotubes (CNTs). Their strength, which is 100 times greater than steel, makes them suitable for structural reinforcement applications. Carbon nanotubes come in two varieties: single-walled (SWCNTs) and multi-walled (MWCNTs). Because they are non-conductive across the tube yet thermally conductive along its length, CNTs are special in a way. Fullerenes are a type of carbon allotrope characterized by their hollow cage structures comprising sixty or more carbon atoms. Buckminster fullerenes, which form the structure of C60, resemble a hollow football and consist of carbon units shaped like pentagons and hexagons. These carbon-based NPs possess desirable commercial properties, including electrical conductivity, high strength, structure, and electron affinity [46].

Ceramic nanostructure: Phosphates, carbonates, oxides, and carbides make up the inorganic solids that make up these nanostructures. Ceramic NPs are used in biological imaging, drug administration, photocatalysis, and dye photodegradation because of their great heat resistance and chemical inertness [47]. Nanostructure materials serve as efficient drug delivery systems due to their precise properties, including controllable size, surface area, porosity, and surface-to-volume ratio. Ceramic nanostructure materials have been successfully utilized to transport medications for several illnesses, including cancer, glaucoma, and bacterial infections.

Metal nanostructure: Metal precursors are used in the production of the metal nanostructure, which can then be produced chemically, electrochemically, or photochemically. Chemical reducing agents are used in chemical procedures to reduce metal-ion precursors in solution and produce metal nanostructure materials. These resulting nanostructures possess a high surface energy and can adsorb small molecules. The detection and imaging of biomolecules, as well as applications in the environment and bioanalysis, all make use of metal nanostructure material [48]. Au nanostructures are used to coat the sample before scanning electron microscopy (SEM) examination, thereby enhancing SEM and producing exceptional electron microscopy images.

Semiconductor nanostructure: Groups II–VI, III–V, or IV–VI of the periodic table contain semiconductor nanostructure materials and have characteristics similar to those of metals and non-metals. These feature broad bandgaps that, when tuned, exhibit various characteristics. Semiconductor nanostructures are made of a variety of substances, including Si and Ge from group IV, as well as GaN, GaP, InP, and InAs from

groups III–V, and ZnO, ZnS, CdS, CdSe, and CdTe from groups II–VI. Applications for semiconductor nanostructures include photocatalysis, electronics, nanophotonics, and water splitting [49].

4. NANOPARTICLES IN NANOMEDICINE

NPs are under investigation in the field of nanomedicine for a range of purposes such as drug delivery, imaging, and diagnostics [50]. NPs have the potential to be extremely useful in nanomedicine [51]. They can adroitly bear and convey biological materials to targeted sites through imaging probes and therapeutic agents. They can influence a specific tissue, organ, or hidden cell. One of the key advantages of using NPs in medicine is their ability to target specific cells or tissues. By attaching molecules to the surface of the NPs that bind to specific cells, such as cancer cells, the NPs can be directed to those cells and deliver drugs or other therapeutic agents directly to the site of the disease. This can increase the effectiveness of the treatment while reducing side effects. The utilization of NPs for drug delivery has a tremendous influence on different areas of nanomedicine [52]. Nanomedicine refers to the use of NPs for medical purposes. It is defined as the use of engineered nanocarriers to diagnose, screen, monitor, prevent, and cure diseases starting at the molecular level. We will eventually achieve this phenomenon for medical purposes [53, 54]. Drug delivery and imaging have both utilized a variety of materials. NPs have the ability to penetrate biological barriers, including the blood-brain barrier, which is an added benefit of using them in medicine. It can be a significant obstacle to delivering drugs to the brain. NPs can be designed to pass through these barriers and deliver drugs or other agents directly to the brain. In addition to drug delivery, NPs are also being investigated for use in medical imaging and diagnostics. It can be designed to interact with magnetic fields or emit/absorb certain wavelengths of light, enabling their use in imaging modalities such as optical imaging and magnetic resonance imaging (MRI) [55]. However, there are still many challenges to overcome before NPs can be widely used in medicine. These include ensuring the safety of the NPs and their long-term effects on the body, as well as developing methods for large-scale production of the NPs. Despite these challenges, the potential benefits of using NPs in medicine make them an exciting area of research with the potential to revolutionize the field of healthcare. Liposome, dendrimer, nanotube, micelle, nanogel, quantum dot, nanocrystal, polymer, and polymer-metal are the types of NPs. Reduced toxicity, high specificity, controlled drug release, enhanced delivery, diverse routes of administration, and dose reduction are benefits of NPs [56].

Nanomedicine has the potential to completely transform healthcare by offering better, more individualized, accurate, and effective therapies for a variety of medical diseases. The development of many types of NPs with a variety of uses has been assisted by advancements in materials engineering and characterization methods. The use of nanotechnology in illness prevention, diagnosis, and treatment has various advantages over traditional pharmacological therapy [57]. Nanotherapeutics have the ability to administer more focused and precise therapies, reduce side effects, and improve patient outcomes, which has the potential to transform the field of medicine. NPs have the capacity to target therapeutic molecules and improve medication selectivity, which results in increased bioavailability, better patient adherence, and, eventually, lower drug doses. Moreover, nanotechnology makes it possible for poorly soluble chemicals to be administered effectively through the right pathways, which lowers their toxicity and increases their effectiveness. Due to their multimodality, nanocarriers are particularly notable for their capacity to simultaneously transport numerous therapeutic and diagnostic substances. Targeted drug delivery, imaging, sensing, and therapy are all possible uses for NPs in nanomedicine [58].

4.1. Drug Delivery

NPs have surfaced as a hopeful drug delivery platform in the field of nanomedicine [59]. It can be engineered to carry drugs and other therapeutic agents directly to the site of the disease, improving the efficacy and reducing the toxicity of the drugs. NPs can be designed to possess particular qualities that enable interaction with biological systems in a controlled manner. For example, the NP's exterior can be coated with molecules that target specific cells or tissues, allowing the NPs to selectively deliver drugs to those cells. The extent, shape, and charge of the NP can also be carefully controlled to optimize its interaction with the body and the drug being delivered. The capacity of NPs to shield drugs from degradation or clearance is one of their main benefits for medication delivery by the body before it reaches

the site of action. The NPs can also increase the bioavailability of the drug, allowing for lower doses to be used while still achieving the same therapeutic effect [60]. In addition, NPs can offer sustained drug release for an extended duration, minimizing the requirement for frequent dosing and enhancing patient adherence. Chronic conditions can especially benefit from this, such as cancer, where long-term treatment is often required. Regardless of NPs potential benefits as a drug delivery system, there are still challenges that need to be addressed. For example, the safety and biocompatibility of the NPs need to be thoroughly evaluated, and the manufacturing process must be scalable and cost-effective. Nevertheless, the utilization of NPs in drug delivery exhibits significant potential for enhancing the treatment of various diseases. Figure 1 illustrates drug delivery systems for diagnosing and treating different diseases.

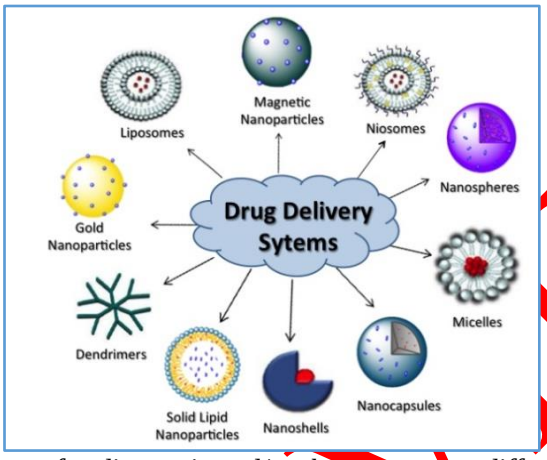

Figure 1. *Drug delivery systems for diagnosis and/or therapy across different diseases [61], Reprinted with permission; ©2016 Bentham Science Publishers, https://doi.org/10.2174/1570159X14666151230124904*

Chronic obstructive pulmonary disease (COPD) and asthma are the two most common respiratory diseases. As pollution levels rise and air quality declines, the prevalence of these diseases increases in the population. As a result of this growing burden, researchers are attempting to create new medications and diagnostics for better illness management. Research is being scaled down to the nanoscale in order to advance an acceptable approach for treating and curing respiratory disorders. These respiratory disorders affect a vast population, including people of all ages, from newborns to the elderly. Recently, significant progress has been made in the advancement of NPs for the medication of chronic obstructive lung infections such as asthma [62]. Antibiotic-conjugated particles accumulate in the lumens of macrophages and neutrophils in the alveoli. Drugs can be released into the airways through antibiotic-conjugated NPs with sizes ranging from 1 to 5 nm [63, 64].

To treat respiratory conditions like cystic fibrosis, chronic obstructive pulmonary disease (COPD), and asthma, pulmonary drug administration is a way to give drugs directly to the lungs [65]. The medication is inhaled using this mode of drug administration, whether it is an aerosol, powder, or gas. The possibility of inhaler overuse, the challenges of synchronizing inhaler use with breathing, and the risk of lung irritation or allergic reactions are a few drawbacks to the administration of pulmonary drugs. To guarantee the safe and efficient use of pulmonary drug administration for the treatment of respiratory disorders, it is crucial to cooperate closely with a healthcare professional.

Researchers have turned to NPs in nanomedicine as a result of the expansion of nucleic acid-based therapies, which have needed better delivery. Day by day, formation into NPs has been the favored technique for distribution to the necessary biological compartments in diverse treatments [66]. The backbone of approved nucleic acid delivery medications has been lipid NPs (LNPs), which are made up of lipids in addition to their nucleic acid payload. Different functions in nucleic acid delivery are played by cationic or ionizable groups included in NPs. Complex negatively charged nucleic acids for effective encapsulation, particle formation, and cellular absorption are all made possible by their interaction with the negatively charged head groups of the endosomal lipid membrane. Since cationic groups cause immune activation and toxicity, it contains ionizable lipids that are primarily neutral at physiological pH but

positively charged at acidic pH. Lower endosomal pH causes the lipids to become charged, which encourages endosomal disruption. Throughout the coronavirus disease pandemic of 2019 (COVID-19), the use of lipid NPs for RNA delivery has greatly increased [67]. While there have been several successful attempts at integrating NPs into clinical practice, past failures, such as Bind Therapeutics' use of PEGylated Polylactic Acid (PLA-PEG) NPs [68] to encapsulate docetaxel chemotherapy, underscore the need to address outstanding issues. A tiny molecule was added to the PEG surface to enable it to bind to a membrane antigen unique to the prostate, allowing for selective accumulation in cancer tissues. Incorporating precision medicine principles, like utilizing NP imaging agents to showcase enhanced permeability and retention or considering susceptibility as a criterion for therapy selection in nanomedicine, could aid forthcoming endeavors. Because NP treatments need purity and homogeneity not just of their constituent chemicals but also of how these molecules are organized at the nanoscale, clinical scale utilization of NPs can present unique manufacturing issues. The utilization of self-assembling molecules to accomplish bottom-up NP synthesis instead of top-down, and the employment of microfluidics to ensure efficient mixing and continuous production are two instances of techniques that facilitate more scalable and consistent manufacturing. These processes must be used in the production of developing NP therapeutics in order to guarantee clinical success. The use of nanotechnology to augment the delivery of drugs to specific sites is referred to as nano-drug delivery [69], which is a relatively novel field that has witnessed numerous breakthroughs in recent years [70].

Doxil (doxorubicin hydrochloride liposome injection), a liposome-based drug delivery system [71], was initially accepted by the Food and Drug Administration (FDA) for the treatment of ovarian cancer. Ultimately, Vyxeos, a liposome-based medication for the treatment of acute myeloid leukemia (AML), received FDA approval. It simultaneously administers two chemotherapeutic medicines using liposomes. Since the initial liposome-based drug delivery device was approved in 1995, nano-drug delivery has advanced significantly. Researchers are continually coming up with novel and inventive ways to employ nanotechnology to enhance medicine delivery, and the area is constantly changing. Below is a timeline of some of the important occasions and developments in the development of legal nano-drug delivery systems. Designing NPs for better targeting and overcoming biological barriers has dominated cardiovascular nanomedicine research. In order to overcome problems with traditional pharmaceutical distribution, such as unfavorable systemic side effects, NPs are routinely injected into specific vessels for cardiac conditions like atherosclerosis, hypertension, and myocardial infarction. New nano-drug carriers can also be taken up preferentially by immune cells, aiming to control localized inflammatory processes and deliver a therapeutic payload to plaque. Innovative NP composition, formulation, and fictionalization design have improved the field in order to achieve therapeutic effectiveness [72]. This point of view seeks to assess these changes and provide fresh perspectives on how nanotechnology might most effectively help treat cardiovascular disease. Diverse researchers can provide their opinions on nanocomposites and nano coatings, as well as vascular, implantable, and wearable device technologies, which are new fields of technological inclusion and integration, in order to start conversations about where the field of study should focus. Furthermore, the researcher suggests that research should prioritize technological solutions for medication to aid in the prevention and treatment of cardiovascular diseases (CVD), which are responsible for a rising number of deaths globally [73]. Since many risk factors for CVD are avoidable, such as diets rich in saturated and trans fats and cholesterol, sedentary lifestyles, and the consumption of alcohol and tobacco, scientists should emphasize technological approaches for the early detection and management of these risk factors [74].

Nanotechnology-enabled advancements, such as enhanced wearable trackers that simultaneously monitor multiple heart parameters and track physical activity, sleep, and diet; portable exam kits that detect heart sound anomalies in patients; and sensors that aid in medication adherence, could all play a part in achieving this objective. Nanotechnology may have a huge impact on the advancement of technology and sensitivity because of its exclusive capacity to change the structure at the nanoscale. Advanced NP-based sensors [75] will aid in earlier disease detection and ongoing symptom monitoring, while remote-controlled nanoscale switches or manipulation will aid in disease prevention. Sustained and controlled release of molecules or agents with targeted activities can be advantageous for the treatment and restoration of damaged heart tissue. It is thought that treating CVDs is the most expensive condition to treat because it requires developing and making available all the technologies and devices.

The generation, characterization, and use of NP in the human immune system have made considerable scientific strides [76]. Traditional medicine, which was the only feasible option for treating sick individuals, offered better advantages by addressing the many problems caused by traditional therapy. Lower dosages, enhanced pharmacokinetics, and better-targeted effectiveness are a few of these. A few of these formulations have reached clinics and demonstrated promise in raising the survival rates of patients with terminal illnesses. The relationship between NPs and the innate and adaptive immune systems is still unknown and under investigation. The lymphatic system guides NPs within an identifiable size range that is taken up by the innate immune system to these sites [77]. NPs interact as immunostimulation and immunosuppression in the immune system [78].

Two TCR (T-cell receptor) approaches are identity cell immunostimulation followed by T-cell priming, which causes antigen-presenting cell (APC) immunosuppression [79], which raises T and B-cell counts and activity, and medication release into tumor cells. Murine models exhibit negative effects in these regions in vivo, which can inhibit natural killer cells. These cells were inhibited by negatively charged SiO2, which also decreased the release of proinflammatory cytokines and the activity of natural killer cells, which prevented the inflammatory responses seen in these mice. In addition to controlling cellular immunity, ZnO NPs also promote antioxidant and anti-inflammatory agents [80]. Having enough zinc in the human diet is essential for maintaining good health and optimal immune system operation. Seafood, steak, pig, poultry, beans, nuts, and whole grains are excellent sources of zinc.

4.2. Imaging

NPs have emerged as a useful tool in a variety of applications in nanomedicine, including imaging and biosensing [81]. NPs possess distinct biophysical properties that enable contrast enhancement in biomedical imaging, and their customization at the molecular level allows for tissue-specific diagnosis. Subtle variations in the size or composition of NPs can significantly alter their optical, magnetic, or electrical properties, providing a unique method of multiplexing. Figure 2 demonstrates the integration of imaging and nanomedicine in atherosclerosis.

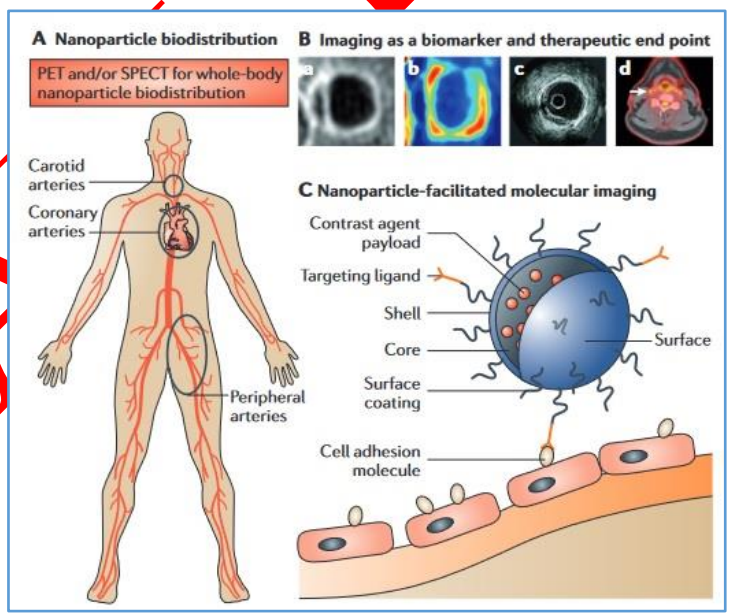

***Figure 2**. Integration of ımaging and nanomedicine in atherosclerosis [82], Reprinted with permission; © 2011 Macmillan Publishers Limited, https://doi.org/10.1038/nrd3578*

The real-time monitoring of the drug delivery process and therapeutic effects using a variety of imaging modalities, such as fluorescent (FL) imaging, magnetic resonance imaging (MRI), computed tomography (CT), photoacoustic imaging (PAI), positron emission tomography (PET), and electron microscopy, is crucial to ensuring the best performance of the proposed nanomedicine [83]. Moreover, it is crucial to

develop nanomedicines that effectively fulfill drug delivery requirements. Cancer remains a leading cause of mortality worldwide, causing millions of deaths annually. According to global cancer observatory (GLOBOCAN) 2020 estimates by the International Agency for Research on Cancer, approximately 19.3 million new cancer cases and nearly 10.0 million cancer-related deaths are expected in the near future. The role of imaging in the targeted delivery of nanomedicine for cancer therapy was discussed in detail by P. Li et al. [84].

NPs are also being explored as imaging agents in nanomedicine. Because of their small size, NPs can possess distinct optical and magnetic characteristics, making them advantageous for imaging purposes. Moreover, NPs can be customized to interact with particular biological molecules or tissues, allowing them to be used to target specific targets in the human body. For example, NPs can be coated with molecules that bind to cancer cells, making them useful for cancer imaging. NPs can also be tailored to emit or absorb light of precise wavelengths, enabling their application in optical imaging methods such as FL imaging, photoacoustic imaging, and two-photon microscopy. Conversely, magnetic NPs can be utilized for magnetic resonance imaging (MRI) [85]. Magnetic NPs can be coated with molecules that bind to specific tissues or cells, making them useful for targeted imaging. Magnetic NPs can also be used to image biological processes such as blood flow and protein-protein interactions. Another advantage of using NPs for imaging is their ability to enhance contrast. By altering the size and surface properties of the NPs, the contrast between different tissues or structures can be improved, allowing for better resolution and a more accurate diagnosis. Despite the potential benefits of using NPs for imaging, there are still challenges that need to be addressed. For example, the safety and biocompatibility of the NPs need to be thoroughly evaluated, and the imaging performance of the NPs needs to be optimized. However, utilizing NPs as imaging agents presents significant potential for enhancing the diagnosis and treatment of various diseases. Many supramolecular nanomedicines are in clinical use, and a considerable number are making steady progress in human research, indicating their promise for identifying and treating brain cancer [86, 87].

By utilizing their distinctive qualities, such as improved payload bioavailability via controlled pharmacokinetics and pharmacodynamics and superior distribution at the site of two problems, nanomaterials are rapidly showing promise to solve our brain tumor features and tumor-specific drug activity. One of the toughest obstacles in treating these tumors is getting medications to the brain tumor site with therapeutic concentration while avoiding the blood-brain (tumor) barrier. Recent research has linked the injection of drug-loaded NPs to magnetic resonance imaging and near-infrared imaging, allowing for target imaging with these novel theranostics.

4.3. Diagnostics

The goal of early diagnosis has been to arrest and manage these health conditions as soon as possible. Despite the challenges we face, recent scientific progress has greatly improved our diagnostic capabilities. The emergence of nano-diagnostics as a new branch of laboratory medicine has enabled the early detection of diseases before symptoms arise, enhanced imaging of internal body structures, and simplified diagnostic procedures [88]. Ongoing research in nano-diagnostics includes the development of microchips, biosensors, nano robots, single-cell structure identification, and micro electromechanical systems. J. Gomez-Marquez et. al. [89] illustrates a comprehensive overview of current nanotechnological advances in medical diagnosis and explores the potential for improved healthcare delivery in the future. Deconstructing nanotechnology into toolkits and protocols instead of more traditional, fully integrated devices has the potential to have a greater impact. R. Khademi et. al. [90] reviewed preclinical research on nanotechnology-based diagnostics and therapies for acute lymphoblastic leukemia in their study.

In response to specific triggers, different types of nanogates can release pharmacological agents into particular environments; some of these compounds can be employed on both tumor and normal cells due to minute variations. Targeting or sensing ligands are advantageous in this situation because they can specifically bind to malignant cells that overexpress particular receptors. Small drugs that are free can enter malignant cells via passive transmission across the cell membrane, where they interact with membrane proteins like drug efflux pumps, resulting in suboptimal levels in the target cell [91]. On the other hand, NPs can get around this resistance mechanism by delivering therapeutic agents directly into cancer cells

without relying on specific receptors or channels. Increased membrane fluidity implies increased drug permeability, which can be influenced by lipid packing density and velocity. Specific micro-environmental factors in the target region, such as changes in pH and enzyme activity, as well as external stimuli like heat, light, electric or magnetic fields, or ultrasound, can promote the release of drug content from carriers. Targeted gene therapy boosted the stability and concentration of targeted gene therapy drugs, which improved their anti-leukemic potency. Ruolin Wu et. al. [92] discuss the use of nanomedicine for the treatment of renal cell carcinoma (RCC), with a focus on exploring the potential of nanotechnologies in RCC management and their translation into clinical practice. With the increasing knowledge and application of nanotechnologies, there is a promising potential for the development of new and effective treatments for renal cancer.

The kidney is a key organ that is essential to keeping the body balanced [93]. RCC, a common cancer of the urinary system, poses a serious threat to people's health. Cancer diagnosis and management have come a long way, but there are still several factors that might lead to treatment failure. First off, prompt diagnosis is hampered by the lack of readily available biomarkers. Second, it can be difficult to detect RCC early due to its diverse imaging appearance. Lastly, because kidney cancer has built-in drug resistance, chemotherapy has been ruled useless for treating it in clinical settings. The treatment of kidney cancer has changed dramatically in recent years, thanks to the development of nanotechnological techniques in pharmaceuticals.

Many advantages of nanotechnology over traditional techniques have led to a wide range of biological applications, including medication delivery, prevention, diagnostics, and treatment. Nanomedicine relies heavily on diagnostics for the early detection and diagnosis of diseases to improve patient outcomes. NPs can be designed to interact with specific cells or tissues and detect disease biomarkers or abnormalities, making imaging one of the most common diagnostic applications of NPs. Targeting ligands, such as antibodies or peptides, can be coated on NPs to bind specifically to cancer cells or diseased tissues. This enables the targeted delivery of contrast agents, which can improve the visibility of these tissues in imaging modalities such as MRI, CT, or fluorescence imaging [94]. Although whole-body imaging methods like MRI and CT have shown great clinical success due to their imaging depth and high resolution, they also have limitations, such as high and prolonged radiation exposure, which limits their applicability in real-time monitoring. NPs can also be functionalized with probes for biosensing applications to detect disease biomarkers or pathogens. The presence of the target molecule or pathogen causes a change in the NP's properties, such as their size, shape, or surface charge, which can be detected using various techniques, including colorimetry, fluorescence, or electrochemistry. Overall, the use of NPs in diagnostics in nanomedicine is a rapidly growing field, with many promising applications. By providing accurate and sensitive detection of diseases and biomolecules, NPs are helping to revolutionize the field of nanomedicine and improve patient outcomes. Table 1 contains a list of NPs that are increasingly being utilized in the field of nanomedicine, which involves the use of nanotechnology for medical purposes. The unique physical and chemical properties of NPs make them highly suitable for various medical applications.

Table 1. *A list of nanoparticle that are utilized in nanomedicine*

Nanoparticles	**Treatment**	**Active Drug**	**Commercial Name**	**References**
Liposome	Fungal infections	Amphotericin B	AmBisome®	[95]
PEGylated liposome	Breast cancer	Doxorubicin	Doxil®, Caelyx®	[96]
Lipid NPs	Fungal infections	Amphotericin B	Amphotec®, Abelcet®	[97]
Protein-based NPs	Viral infections	Paclitaxel	Abraxane®	[98]
Nanoemulsion	Eye inflammation	Difluprednat	Durezol®	[99]
Polymeric NPs	Kidney disease	Sevelamer	Renagel®	[100]
Nanocarrier	Cancer therapy	Pembrolizumab	Keytruda®	[101]

Au NPs, quantum dots (Q-dots), carbon nanotubes (CNTs), and dendrimers are some of the other most common NPs used in nanomedicine. Au is a biocompatible, highly stable particle that can be used for imaging, diagnostics, and targeted drug delivery. Q-dots are semiconductor NPs that can be used for imaging, diagnosis, and targeted drug delivery. CNTs are carbon-based cylindrical NPs that can be used

for drug delivery, imaging, and biosensors. Figure 3 demonstrates the use of gold-based nanoparticles in nanomedicine.

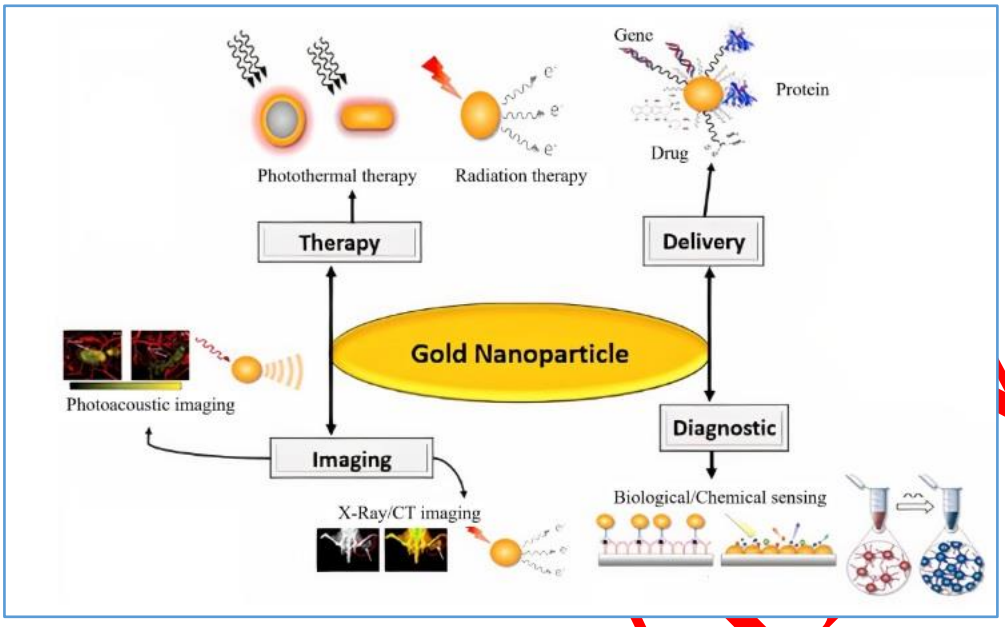

Figure 3*. Utilization of gold-based nanoparticles in nanomedicine [102], Reprinted with permission; Copyright and Licensing are available via the following link: https://www.frontiersin.org/articles/10.3389/fchem.2020*

Dendrimers are NPs that resemble heavily branched trees and can be employed as biosensors, imaging agents, and drug delivery systems. Targeted medication delivery, imaging, and diagnostics are just a few of the uses for NPs in nanomedicine. They are also being researched for their potential role in tissue engineering and regenerative medicine. To completely comprehend the effectiveness and safety of NPs in medical applications, however, more research is required.

5. CONCLUSIONS

The social acceptance of innovative nanotechnology in nanostructured materials is NPs' biggest hurdle. Long-term investments in commercial acceptability will be critical for material scientists and engineers in this area. The commercial aspect is posing several challenges to bringing in significant investment for the industry's progress. Incorporating cutting-edge items will be the most significant future trend for NPs. These will be critical for industry stakeholders, academics, scientists, and engineers to tackle complicated issues to meet the goal. According to the review study, plant extracts are recommended as the best biological medium for the formation of NPs because they are more stable, reduce metal ions more quickly, and scale up more easily than the microorganisms prevalent in the human body. Biocompatibility, stability, size, surface qualities, and targeting capabilities are a few of the many considerations when selecting the best NP for a given application in nanomedicine. NPs hold promise in nanomedicine, serving various roles in drug delivery, imaging, and diagnostics. Their unique properties enable targeted delivery, enhanced imaging, and sensitive diagnostics, offering the potential to revolutionize healthcare. Continued research may lead to more efficient treatments, precise diagnoses, and improved patient outcomes in medicine. It is advised to carry out more research on additional key NP kinds that might have application potential. The creation of NPs for diverse uses in the nanomedicine sector is the focus of this review. The reviews assembled here will address emerging opportunities for NPs in nanomedicine.

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CONFLICTS OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

[1] Xiao, S., and Chen, L., "The emerging landscape of nanotheranostic-based diagnosis and therapy for osteoarthritis", Journal of Controlled Release, 328: 817–833, (2020).

[2] Wang, L., Pan, H., Gu, D. Sun, H., Chen, K., Tan, G., and Pan, W., "A novel carbon dots/thermo-sensitive in situ gel for a composite ocular drug delivery system: characterization, ex-vivo imaging and in vivo evaluation", International Journal of Molecular Sciences, 22(18): 9934, (2021).

[3] Meng, Q., Zhong, S., He, S., Gao, Y., and Cui, X., "Synthesis and characterization of curcumin-loaded pH/reduction dual-responsive folic acid modified carboxymethyl cellulose-based microcapsules for targeted drug delivery", Journal of Industrial and Engineering Chemistry, 105: 251–258, (2022).

[4] LaVan, D. A., McGuire, T., and Langer, R., "Small-scale systems for in vivo drug delivery", Nature Biotechnology, 21: 1184-1191, (2003).

[5] Shevchenko, K. G., Garkushina, I. S., Canfarotta, F., Piletsky, S. A., and Barlev, N. A., "Nano-molecularly imprinted polymers (nanoMIPs) as a novel approach to targeted drug delivery in nanomedicine", RSC Advances, 12: 3957–3968, (2022).

[6] Saeed, S., Khan, S. U., and Gul, R., "Nanoparticle: a promising player in nanomedicine and its theranostic applications for the treatment of cardiovascular diseases", Current Problems in Cardiology, 48: 101599, (2023).

[7] Magagula, S. I., Mohapi, M., Jafta, N., Mochane, M. J., Lebelo, K., and Lenetha, G. G., "Biopolymer-based biodegradable biomaterials for in vivo and in vitro biomedical applications", Polymeric Biomaterials for Healthcare Applications, 165–210, (2022).

[8] Naskar, A., and Kim, K. S., "Photo-stimuli-responsive CuS nanomaterials as cutting-edge platform materials for antibacterial applications", Pharmaceutics, 14(11): 2343, (2022).

[9] Gao, S., Li, Z., and Zhang, H., "Bioinspired green synthesis of nanomaterials and their applications", Current Nanoscience, 6(5): 452–468, (2010).

[10] Wu, D., Zhang, X. D., Liu, P. X., Zhang, L. A., Fan, F. Y., and Guo, M. L., "Gold nanostructure: fabrication, surface modification, targeting imaging, and enhanced radiotherapy", Current Nanoscience, 7(1): 110–118, (2011).

[11] Bhattacharjee, R., Kumar, L., Mukerjee, N., Anand, U., Dhasmana, A., Preetam, S., Bhaumik, S., Sihi, S., Pal, S., Khare, T., Chattopadhyay, S., El-Zahaby, S. A., Alexiou, A., Koshy, E. P., Kumar, V., Malik, S., Dey, A., and Proćków, J., "The emergence of metal oxide nanoparticles (NPs) as a phytomedicine: a two-facet role in plant growth, nano-toxicity and anti-phyto-microbial activity", Biomedicine and Pharmacotherapy, 155: 113658, (2022).

[12] Bhuiyan, M. R. A., and Mamur, H., "A brief review on the synthesis of ZnO nanoparticles for biomedical applications", Iranian Journal of Materials Science and Engineering, 18(3): 1–27, (2021).

[13] Akter, M., Khan, M. N. I., Mamur, H., and Bhuiyan, M. R. A., "Synthesis and characterisation of CdSe QDs by using a chemical solution route", Micro and Nano Letters, 15(5): 287–290, (2020).

[14] Chen, P. C., Chen, C. C., and Chen, S. H., "A review on production, characterization, and photocatalytic applications of TiO2 nanoparticles and nanotubes", Current Nanoscience, 13(4): 373–393, (2017).

[15] Remya, R. R., Julius, A., Suman, T. Y., Mohanavel, V., Karthick, A., Pazhanimuthu, C., Samrot, A. V., and Muhibbullah, M., "Role of nanoparticles in biodegradation and their importance in environmental and biomedical applications", Journal of Nanomaterials, 2022: (2022).

[16] Rai, M., Ingle, A., Gupta, I., Birla, S., Yadav, A., and Abd-Elsalam, K., "Potential role of biological systems in formation of nanoparticles: mechanism of synthesis and biomedical applications", Current Nanoscience, 9: 576–587, (2013).

[17] Kouhkan, M., Ahangar, P., Babaganjeh, L. A., and Allahyari-Devin, M., "Biosynthesis of copper oxide nanoparticles using lactobacillus casei subsp. casei and its anticancer and antibacterial activities", Current Nanoscience, 16: 101–111, (2019).

[18] Doroszkiewicz, J., Groblewska, M., and Mroczko, B., "Molecular biomarkers and their implications for the early diagnosis of selected neurodegenerative diseases", International Journal of Molecular Sciences, 23(9): 4610, (2022).

[19] Díez-Pascual, A. M., "Surface engineering of nanomaterials with polymers, biomolecules, and small ligands for nanomedicine", Materials, 15(9): 3551, (2022).

[20] Shoja Razavi, R., Reza Loghman-Estarki, M., Farhadi-Khouzani, M., Barekat, M., and Jamali, H. "Large scale synthesis of zinc oxide nano- and submicro-structures by pechinis method: effect of ethylene glycol/citric acid mole ratio on structural and optical properties", Current Nanoscience, 7(5): 807–812, (2011).

[21] Mughal, S. S., and Hassan, S. M., "Comparative study of AgO nanoparticles synthesize via biological, chemical and physical methods: a review", American Journal of Materials Synthesis and Processing, 7(2): 15–28, (2022).

[22] Rastogi, A., Singh, P. F., Haraz A., and Barhoum, A., "Biological synthesis of nanoparticles: an environmentally benign approach", Fundamentals of Nanoparticles: Classifications, Synthesis Methods, Properties and Characterization, 571–604, (2018).

[23] Biswas, A., Bayer, I. S., Biris, A. S., Wang, T., Dervishi, E., and Faupel, F., "Advances in top-down and bottom-up surface nanofabrication: techniques, applications & future prospects", Advances in Colloid and Interface Science, 170(1–2): 2–27, (2012).

[24] Eaglesham, D. J., and Cerullo, M., "Dislocation-free stranski krastanow growth of Ge on Si (100)", Physical Review Letters, 64: 1943–1946, (1990).

[25] Prieto, J. E., and Markov, I., "Stranski–krastanov mechanism of growth and the effect of misfit sign on quantum dots nucleation", Surface Science, 664: 172–184, (2017).

[26] Mamur, H., and Bhuiyan, M. R. A., "Characterization of Bi_2Te_3 nanostructure by using a cost effective chemical solution route", Iranian Journal of Chemistry and Chemical Engineering, 39(3): 23–33, (2020).

[27] Mamur, H., Dilmac, O. F., Korucu, H., and Bhuiyan, M. R. A., "Cost-effective chemical solution synthesis of bismuth telluride nanostructure for thermoelectric applications", Micro and Nano Letters, 13: 1117–1120, (2018).

[28] Liu, Y. K., Akula, K. C., Dandamudi, K. P. R., Liu, Y., Xu, M., Sanchez, A., Zhu, D., and Deng, S., "Effective depolymerization of polyethylene plastic wastes under hydrothermal and solvothermal liquefaction conditions", Chemical Engineering Journal, 446(4): 137238, (2022).

[29] Soltani, N., Saion, E., Erfani, M., Rezaee, K., Bahmanrokh, G., Drummen, G. P. C., Bahrami, A., and Hussein, M. Z., "Influence of the polyvinyl pyrrolidone concentration on particle size and dispersion of ZnS nanoparticles synthesized by microwave irradiation", International Journal of Molecular Sciences, 13(10): 12412–12427, (2012).

[30] Bhuiyan, M. R. A., Saha, D. K., and Firoz Hasan, A. S. M., "Effects of temperature on the structural and optical properties of $AgGaSe_2$ thin films", Journal of Bangladesh Academy of Sciences, 33(2): 179–188, (2009).

[31] Hoq, E., Bhuiyan, M. R. A., and Begum, J., "Influence of thickness on the optical properties of Sb doped ZnO thin films", Journal of Bangladesh Academy of Sciences, 38(1): 93–96, (2014).

[32] Shah, M., Fawcett, D., Sharma, S., Tripathy, S. K., and Poinern, G. E. J., "Green synthesis of metallic nanoparticles via biological entities", 8(11): 7278–7308, (2015).

[33] Alshameri, A. W., and Owais, M., "Antibacterial and cytotoxic potency of the plant-mediated synthesis of metallic nanoparticles Ag NPs and ZnO NPs: a review", OpenNano, 8: 100077, (2022).

[34] Cuong, H. N., Pansambal, S., Ghotekar, S., Oza, R., Hai, N. T. T., and Viet, N. M., "New frontiers in the plant extract mediated biosynthesis of copper oxide (CuO) nanoparticles and their potential applications: a review", Environmental Research, 203: 111858, (2022).

[35] Koli, K., Rohtela, K., and Meena, D., "Comparative study and analysis of structural and optical properties of zinc oxide nanoparticles using neem and mint extract prepared by green synthesis method", IOP Conference Series: Materials Science and Engineering, 1248: 012065, (2022).

[36] Mobaraki, F., Momeni, M., Jahromi, M., Kasmaie, F. M., Barghbani, M., Yazdi, M. E. T., Meshkat, Z., Shandiz, F. H., and Hosseini, S. M., "Apoptotic, antioxidant and cytotoxic properties of synthesized AgNPs using green tea against human testicular embryonic cancer stem cells", Process Biochemistry, 119: 106–118, (2022).

[37] Singh, P., Kim, Y. J., Zhang, D., and Yang, D. C., "Biological synthesis of nanoparticles from plants and microorganisms, trends in biotechnology", 34(7): 588–599, (2016).

[38] Hussain, I., Singh, N. B., Singh, A., Singh, H., and Singh, S. C., "Green synthesis of nanoparticles and its potential application", Biotechnology Letters, 38: 545–560, (2016).

[39] Kharissova, O. V., Dias, H. V. R., Kharisov, B. I., Pérez, B. O., and Pérez, V. M. J., "The greener synthesis of nanoparticles", Trends in Biotechnology, 31(4): 240–248, (2013).

[40] Das, R. K., Pachapur, V. L., Lonappan, L., Naghdi, M., Pulicharla, R., Maiti, S., Cledon, M., L., Dalila, M. A., Sarma, S. J., and Brar, S. K., "Biological synthesis of metallic nanoparticles: plants, animals and microbial aspects", Nanotechnology for Environmental Engineering, 2: (2017).

[41] Alshareeda, A. T., Nur Khatijah, M. Z., and Al-Sowayan, B. S., "Nanotechnology: a revolutionary approach to prevent breast cancer recurrence", Asian Journal of Surgery, 46(1): 13–17, (2023).

[42] Saha, S., Bansal, S., and Khanuja, M., "Classification of nanomaterials and their physical and chemical nature", Nano-Enabled Agrochemicals in Agriculture, 7–34, (2022).

[43] Abd Ellah, N. H., and Abouelmagd, S. A., "Surface functionalization of polymeric nanoparticles for tumor drug delivery: approaches and challenges", Expert Opinion on Drug Delivery, 14(2): 201–214, (2017).

[44] Hald Albertsen, C., Kulkarni, J. A., Witzigmann, D., Lind, M., Petersson, K., and Simonsen, J. B., "The role of lipid components in lipid nanoparticles for vaccines and gene therapy", Advanced Drug Delivery Reviews, 188: 114416, (2022).

[45] Hajebi, S., Yousefiasl, S., Rahimmanesh, I., Dahim, A., Ahmadi, S., Kadumudi, F. B., Rahgozar, N., Amani, S., Kumar, A., Kamrani, E., Rabiee, M., Borzacchiello, A., Wang, X., Rabiee, N., Dolatshahi-Pirouz, A., and Makvandi, P., "Genetically engineered viral vectors and organic-based non-viral nanocarriers for drug delivery applications", Advanced Healthcare Materials, 11: 1–31, (2022).

[46] Dutta, V., Verma, R., Gopalkrishnan, C., Yuan, M. H., Batoo, K. M., Jayavel, R., Chauhan, A., Lin, K. Y. A., Balasubramani, R., and Ghotekar, S., "Bio-inspired synthesis of carbon-based nanomaterials and their potential environmental applications: a state-of-the-art review", Inorganics, 10(10): 169, (2022).

[47] Singh, A., and Amiji, M. M., "Application of nanotechnology in medical diagnosis and imaging", Current Opinion in Biotechnology, 74: 241–246, (2022).

[48] Xu, J. J., Zhang, W. C., Guo, Y. W., Chen, X. Y., and Zhang, Y. N., "Metal nanoparticles as a promising technology in targeted cancer treatment", Drug Delivery, 29: 664–678, (2022).

[49] Tan, Y., Xiong, M., Liu, Q., Yin, Y., Yin, X., Liao, S., Wang, Y., Hu, L., and Zhang, X. B., "Precisely controlling the cellular internalization of DNA-decorated semiconductor polymer nanoparticles for drug delivery", RSC Advances, 12: 31173–31179, (2022).

[50] Liu, R., Luo, C., Pang, Z., Zhang, J., Ruan, S., Wu, M., Wang, L., Sun, T., Li, N., Han, L., Shi, J., Huang, Y., Guo, W., Peng, S., Zhou, W., and Gao, H., "Advances of nanoparticles as drug delivery systems for disease diagnosis and treatment", Chinese Chemical Letters, 34(2): 107518, (2023).

[51] Mohammadzadeh, V., Barani, M., Amiri, M. S., Taghavizadeh Yazdi, M. E., Hassanisaadi, M., Rahdar, A., and Varma, R. S., "Applications of plant-based nanoparticles in nanomedicine: a review", Sustainable Chemistry and Pharmacy, 25: 100606, (2022).

[52] Nikzamir, M., Hanifehpour, Y., Akbarzadeh, A., and Panahi, Y., "Applications of dendrimers in nanomedicine and drug delivery: a review", Journal of Inorganic and Organometallic Polymers and Materials, 31: 2246–2261, (2021).

[53] Lu, H., Wang, J., Wang, T., Zhong, J., Bao, Y., and Hao, H., "Recent progress on nanostructures for drug delivery applications", Journal of Nanomaterials, 2016: (2016).

[54] Choi, Y. H., and Han, H. K., "Nanomedicines: current status and future perspectives in aspect of drug delivery and pharmacokinetics", Journal of Pharmaceutical Investigation, 48: 43–60, (2018).

[55] Bruno, F., Granata, V., Bellisari, F. C., Sgalambro, F., Tommasino, E., Palumbo, P., Arrigoni, F., Cozzi, D., Grassi, F., Brunese, M. C., Pradella, S., Stefano, M. L. M. D. S., Cutolo, C., Di Cesare, E., Splendiani, A., Giovagnoni, A., Miele, V., Grassi, R., Masciocchi, C., and Barile, A., "Advanced magnetic resonance imaging (MRI) techniques: technical principles and applications in nanomedicine", Cancers, 14(7): 1626, (2022).

[56] Ratemi, E., Sultana Shaik, A., Al Faraj, A., and Halwani, R., "Alternative approaches for the treatment of airway diseases: focus on nanoparticle medicine", Clinical and Experimental Allergy, 46: 1033–1042, (2016).

[57] Assolini, J. P., Carloto, A. C. M., Bortoleti, B. T. S., Gonçalves, M. D., Tomiotto-Pellissier, F., Feuser, P. E., Cordeiro, A. P., Hermes de Araújo, P. H., Sayer, C., Miranda Sapla, M. M., and Pavanelli, W. R., "Nanomedicine in leishmaniasis: a promising tool for diagnosis, treatment and prevention of disease – an update overview", European Journal of Pharmacology, 923: 174934, (2022).

[58] Doane, T. L., and Burda, C., "The unique role of nanoparticles in nanomedicine: imaging, drug delivery and therapy", Chemical Society Reviews, 41(7): 2885–2911, (2012).

[59] Shao, H., and Varamini, P., "Breast Cancer bone metastasis: a narrative review of emerging targeted drug delivery systems", Cells, 11(3): 388, (2022).

[60] Verma, S., Goand, U. K., Husain, A., Katekar, R. A., Garg, R., and Gayen, J. R., "Challenges of peptide and protein drug delivery by oral route: current strategies to improve the bioavailability", Drug Development Research, 82: 927–944, (2021).

[61] Gunay, M. S., Ozer, A. Y., and Chalon, S., "Drug delivery systems for imaging and therapy of parkinson's disease", Current Neuropharmacology, 14: 376–391, (2016).

[62] Ahmad, A., "Pharmacological strategies and recent advancement in nano-drug delivery for targeting asthma", Life, 12(4): 596, (2022).

[63] Huang, Y., Yu, F., Park, Y. S., Wang, J., Shin, M. C., Chung, H. S., and Yang, V. C., "Co-administration of protein drugs with gold nanoparticles to enable percutaneous delivery", Biomaterials, 31(34): 9086–9091, (2010).

[64] Wadhwa, R., Aggarwal, T., Thapliyal, N., Chellappan, D. K., Gupta, G., Gulati, M., Collet, T., Oliver, B., Williams, K., Hansbro, P. M., Dua, K., and Maurya, P. K., "Nanoparticle-based drug delivery for chronic obstructive pulmonary disorder and asthma", Nanotechnology in Modern Animal Biotechnology, 2019: 59–73, (2019).

[65] Newman, S. P., "Delivering drugs to the lungs: the history of repurposing in the treatment of respiratory diseases", Advanced Drug Delivery Reviews, 133: 5–18, (2018).

[66] Nam, J., Won, N., Bang, J., Jin, H., Park, J., Jung, S., Jung, S., Park, Y., and Kim, S. "Surface engineering of inorganic nanoparticles for imaging and therapy", Advanced Drug Delivery Reviews, 65(5): 622–648, (2013).

[67] Wilson, B., and Geetha, K. M., "Lipid nanoparticles in the development of mRNA vaccines for COVID-19", Journal of Drug Delivery Science and Technology, 74: 103553, (2022).

[68] Oberhauser, W., Evangelisti, C., Tiozzo, C., Bartoli, M., Frediani, M., Passaglia, E., and Rosi, L., "Platinum nanoparticles onto pegylated poly(lactic acid) stereocomplex for highly selective hydrogenation of aromatic nitrocompounds to anilines", Applied Catalysis A: General, 537: 50–58, (2017).

[69] Vyas, K., Rathod, M., and Patel, M. M., "Insight on nano drug delivery systems with targeted therapy in treatment of oral cancer", Nanomedicine: Nanotechnology, Biology and Medicine, 49: 102662, (2023).

[70] Batty, C. J., Bachelder, E. M., and Ainslie, K. M., "Historical perspective of clinical nano and microparticle formulations for delivery of therapeutics", Trends in Molecular Medicine, 27(6): 516–519, (2021).

[71] Bhowmik, S., Bhowmick, S., Maiti, K., Chakra, A., Shahi, P., Jain, D., and Rajamannar, T., "Two multicenter phase I randomized trials to compare the bioequivalence and safety of a generic doxorubicin hydrochloride liposome injection with Doxil ® or Caelyx ® in advanced ovarian cancer", Cancer Chemotherapy and Pharmacology, 82: 521–532, (2018).

[72] Haba, M. Ş. C., Şerban, D. N., Şerban, L., Tudorancea, I., M., Haba, R. M., Mitu, O., Illiescu, R., and Tudorancea, I., "Nanomaterial-based drug targeted therapy for cardiovascular diseases: ischemic heart failure and atherosclerosis", Crystals, 11(10): 1172, (2021).

[73] Gaidai, O., Cao, Y., and Loginov, S., "Global cardiovascular diseases death rate prediction", Current Problems in Cardiology, 48(5): 101622, (2023).

[74] Wang, D. K., Rahimi, M., and Filgueira, C. S., "Nanotechnology applications for cardiovascular disease treatment: current and future perspectives", Nanomedicine: Nanotechnology, Biology, and Medicine, 34: 102387, (2021).

[75] Sabu, C., Henna, T. K., Raphey, V. R., Nivitha, K. P., and Pramod, K., "Advanced biosensors for glucose and insulin", Biosensors and Bioelectronics, 141: 111201, (2019).

[76] Liu, J., Liu, Z., Pang, Y., and Zhou, H., "The interaction between nanoparticles and immune system: application in the treatment of inflammatory diseases", Journal of Nanobiotechnology, 20: 1–25, (2022).

[77] Permana, A. D., Nainu, F., Moffatt, K., Larrañeta, E., and Donnelly, R. F., "Recent advances in combination of microneedles and nanomedicines for lymphatic targeted drug delivery", Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 13(3): 1–22, (2021).

[78] Ray, P., Haideri, N., Haque, I., Mohammed, O., Chakraborty, S., Banerjee, S., Quadir, M., Brinker, A., & Banerjee, S., "The impact of nanoparticles on the immune system: a gray zone of nanomedicine, Journal of Immunological Sciences, 5: 19–33, (2021).

[79] Ye, K., Li, F., Wang, R., Cen, T., Liu, S., Zhao, Z., Li, R., Xu, L., Zhang, G., Xu, Z., Deng, L., Li, L., Wang, W., Stepanov, A., Wan, Y., Guo, Y., Li, Y., Wang, Y., Tian, Y., Gabibov, A. G., Yan, Y., and Zhang, H., "An armed oncolytic virus enhances the efficacy of tumor-infiltrating lymphocyte therapy by converting tumors to artificial antigen-presenting cells in situ", Molecular Therapy, 30(12): 3658–3676, (2022).

[80] Rehman, H., Ali, W., Zaman Khan, N., Aasim, M., Khan, T., and Ali Khan, A., "Delphinium uncinatum mediated biosynthesis of zinc oxide nanoparticles and in-vitro evaluation of their antioxidant, cytotoxic, antimicrobial, anti-diabetic, anti-inflammatory, and anti-aging activities", Saudi Journal of Biological Sciences, 30(1): 103485, (2023).

[81] Song, F. X., Xu, X., Ding, H., Yu, L., Huang, H., Hao, J., Wu, C., Liang, R., and Zhang, S., "Recent Progress in nanomaterial-based biosensors and theranostic nanomedicine for bladder cancer", Biosensors, 13(1): 1–39, (2023).

[82] Lobatto, M. E., Fuster, V., Fayad, Z. A., and Mulder, W. J. M., "Perspectives and opportunities for nanomedicine in the management of atherosclerosis", Nature Reviews, 10: 835, (2011).

[83] Zhao, P., Li, B., Li, Y., Chen, L., Wang, H., and Ye, L., "DNA-templated ultrasmall bismuth sulfide nanoparticles for photoacoustic imaging of myocardial infarction", Journal of Colloid and Interface Science, 615: 475–484, (2022).

[84] Li, P., Wang, D., Hu, J., and Yang, X., "The role of imaging in targeted delivery of nanomedicine for cancer therapy", Advanced Drug Delivery Reviews, 189: 114447, (2022).

[85] Wangaryattawanich, P., Rutman, A. M., Petcharunpaisan, S., and Mossa-Basha, M., "Incidental findings on brain magnetic resonance imaging (MRI) in adults: a review of imaging spectrum, clinical significance, and management", British Journal of Radiology, 96(1142): 1–13, (2023).

[86] Quader, S., Kataoka, K., and Cabral, H., "Nanomedicine for brain cancer", Advanced Drug Delivery Reviews, 182: 114115, (2022).

[87] Mukhtar, M., Bilal, M., Rahdar, A., Barani, M., Arshad, R., Behl, T., Brisc, C., and Banica, F., Bungau, S., "Nanomaterials for diagnosis and treatment of brain cancer: recent updates", Chemosensors, 8(4): 1–31, (2020).

[88] Liao, C., Wu, Z., Lin, C., Chen, X., Zou, Y., Zhao, W., Li, X., Huang, G., Xu, B., Briganti, G. E., Qi, Y., Wang, X., Zeng, T., Wuethrich, A., and Zou, H., "Nurturing the marriages of urinary liquid biopsies and nano-diagnostics for precision urinalysis of prostate cancer", Smart Medicine, 2(1): e20220020, (2023).

[89] Gomez-Marquez, J., and Hamad-Schifferli, K., "Local development of nanotechnology-based diagnostics", Nature Nanotechnology, 16: 484–486, (2021).

[90] Khademi, R., Mohammadi, Z., Khademi, R., Saghazadeh, A., and Rezaei, N., "Nanotechnology-based diagnostics and therapeutics in acute lymphoblastic leukemia: a systematic review of preclinical studies", Nanoscale Advances, 5: 571–595, (2023).

[91] Zhao, X., Xu, S., Jiang, Y., Wang, C., ur Rehman, S., Ji, S., Wang, J., Tao, T., Xu, H., Chen, R., Cai, Y., Jiang, Y., Wang, H., Ma, K., and Wang, J., "BSA-magnetite nanotorpedo for safe and efficient delivery of chemotherapy drugs", Chemical Engineering Journal, 454(3): 140440, (2023).

[92] Wu, R., Wang, K., Gai, Y., Li, M., Wang, J., Wang, C., Zhang, Y., Xiao, Z., Jiang, D., Gao, Z., and Xia, X., "Nanomedicine for renal cell carcinoma: imaging, treatment and beyond", Journal of Nanobiotechnology, 21: 1–24, (2023).

[93] Chedea, V. S., Palade, L. M., Pelmus, R. S., Dragomir, C., and Taranu, I., "Red grape pomace rich in polyphenols diet increases the antioxidant status in key organs— kidneys, liver, and spleen of piglets", Animals, 9(4): 149, (2019).

[94] Wang, Z., Liu, A., Li, X., Guan, L., Xing, H., He, L., Fang, L., Zvyagin, A. V., Yang, X., Yang, B., and Lin, Q., "Multifunctional nanoprobe for multi-mode imaging and diagnosis of metastatic prostate cancer", Talanta, 256: 124255, (2023).

[95] Çifci, S. A., Yalçın, N., Aksu, T., and Demirkan, K., "Liposomal amphotericin B related late-onset hyperphosphatemia in a pediatric patient with acute myeloid leukemia", Journal of Oncology Pharmacy Practice, 28(6): 1478–1482, (2022).

[96] Dellapasqua, S., Aliaga, P. T., Munzone, E., Bagnardi, V., Pagan, E., Montagna, E., Cancello, G., Ghisini, R., Sangalli, C., Negri, M., Mazza, M., Iorfida, M., Cardillo, A., Sciandivasci, A., Bianco, N., De Maio, A. P., Milano, M., Campennì, G. M., Sansonno, L., Viale, G., Morra, A., Leonardi, M. C., Galimberti, V., Veronesi, P., and Colleoni, M., "Pegylated liposomal doxorubicin (Caelyx®) as adjuvant treatment in early-stage luminal b-like breast cancer: a feasibility phase II trial", Current Oncology, 28(6): 5167–5178, (2021).

[97] Mukai, H., Ogawa, K., Kato, N., and Kawakami, S., "Recent advances in lipid nanoparticles for delivery of nucleic acid, mRNA, and gene editing-based therapeutics", Drug Metabolism and Pharmacokinetics, 44: 100450, (2022).

[98] Han, Y., Pan, J., Ma, Y., Zhou, D., and Xu, W., "Protein-based biomaterials for combating viral infections: Current status and future prospects for development", Biosafety and Health, 4: 87–94, (2022).

[99] Peng, C., Kuang, L., Zhao, J., Ross, A. E., Wang, Z., and Ciolino, J. B., "Bibliometric and visualized analysis of ocular drug delivery from 2001 to 2020", Journal of Controlled Release, 345: 625–645, (2022).

[100] Vittala Murthy, N. T., Paul, S. K., Chauhan, H, and Singh, S., "Polymeric nanoparticles for transdermal delivery of polyphenols", Current Drug Delivery, 19(2): 182–191, (2022).

[101] Uddin, S., Rafiqul Islam, M., Md Moshikur, R., Wakabayashi, R., Kamiya, N., Moniruzzaman, M., and Goto, M., "Transdermal delivery of antigenic protein using ionic liquid-based nanocarriers for tumor immunotherapy", ACS Applied Bio Materials, 5: 2586–2597, (2022).

[102] Yaqoob, S. B., Adnan, R., Rameez Khan, R. M., and Rashid, M., "Gold, silver, and palladium nanoparticles: A chemical tool for biomedical applications", Frontiers in Chemistry, 8: 376, (2020).