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Research Article

A REVIEW OF NANOPARTICLES FROM SYNTHESIS METHODS TO BIOMEDICAL APPLICATIONS

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Abstract

Nanoparticles are discrete entities identifiable by their sizes, which typically fall within the range of 1 to 100 nanometers, with at least one of their dimensions falling within this size range. These particles can be classified into three major categories, namely organic, inorganic, and carbon-based particles, displaying superior properties when compared to their larger materials. Due to their small size, nanoparticles exhibit enhanced characteristics, such as rapid chemical reactivity, robust mechanical strength, drastically increased surface area, remarkable sensitivity, and improved stability. The synthesis of nanoparticles has undergone remarkable advancements over time, employing diverse physical, chemical, and mechanical processes. These significant strides in methodologies have enabled precise control of nanoparticles, catering to both research and industrial needs, thereby expanding their potential applications. This review paper offers a comprehensive examination of nanoparticles, covering a wide array of nanoparticle types, their unique attributes, recent techniques for their synthesis, and their applications within the field of biomedical engineering.

Keywords: Nanoparticles, Drug Delivery, Genome Editing, Bioimaging, Biosensors, Tissue Engineering.

INTRODUCTION

Nanotechnology has garnered significant attention in recent decades, and nanoparticles have merged as its central focus. These particles, ranging in size from 1 and 100 nanometers, comprise various materials including carbon, metals, metal oxides, and organic matters [1]. Furthermore, alternative terms can be employed to describe more substantial particles with a diameter exceeding 100 nm. For instance, materials like nanowires, nanotubes, nanorods, nanofibers, and nanofilms are considered as nanomaterials, as they exhibit dimensions less than 100 nm, albeit having one dimension that extends beyond the customary nanoscale measurement[2]. Nanoparticles can exist in different dimensions, shapes, and sizes, running from zero-dimensional structures to three-dimensional forms. Their diverse shapes encompass spherical, polygonal, tubular, flat and various other structures. Furthermore, nanoparticles may have uniform or irregular surfaces with surface variations, and they can be either crystalline or amorphous, and can be found either as loosely dispersed entities or in agglomerated arrangements. They are commonly synthesized using either the top-down or bottom-up approach. In recent times, various methods for synthesizing nanomaterials have gained significance, including physical/chemical deposition, sputtering, pyrolysis, biological synthesis, and mores. These methods are often combined with one another to enhance the efficiency of nanomaterial synthesis [3]. At the nanoscale, nanoparticles exhibit unique physical, chemical, and biological properties distinct from their larger counterparts. These distinctive properties are attributed to the significantly increased surface area-to-volumeratio, superior mechanical strength, enhanced chemical reactivity, heightened sensitivity and greater stability [4]. As a result of these exceptional properties, nanoparticles have found applications across various fields including chemical sensors [1], biosensors [5], as well as medical treatments [6].

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Current research efforts are dedicated to developing and refining synthesis methods to improve nanoparticle properties while reducing production costs. Modified approaches aim to produce nanoparticles with tailored properties, thereby elevating their optical, mechanical, physical, and chemical characteristics. Advanced instrumentation has played a crucial role in improving nanoparticle characterization and enabling their diverse applications. Nanoparticles have found their way into numerous objects, from everyday cosmetics and electronics to critical and innovative industries like renewable energy and disease treatment. This review delves into the distinctive attributions of nanoparticles that find applications in various facets of biomedical engineering. It not only highlights the recent trends in leveraging nanoparticles for biomedical application but also places significant emphasis on the methodologies employed in their kinds and synthesis. The article discusses the evolving role of nanoparticles in advancing biomedical and healthcare domains, encompassing, drug delivery, bioimaging, tissue engineering, genome editing, and biosensors. Throughout the review, critical factors pertaining to nanoparticles, such as size, shape, concentration, and surface modification are discussed in relation to their relevance in live cell bioimaging. Additionally, it provides insights into diverse targeted drug delivery systems aimed at addressing chronic diseases.

Classification of Nanomaterials

Nanomaterials are typically categorized into four groups based on their dimensionality [7]. First, there are 0D nanoparticles, which consist of a single point in space with fixed dimensions for length, height, and width. Nanospheres and clusters such as quantum dots, fullerenes and gold nanoparticles are examples of 0D nanomaterials. Second, 1D nanomaterials including nanotubes, nanowires, and nanorods possess only one dimension (length). Third, 2D nanomaterials such as nanofilm and nanoplates have dimensions in length and width. A typical example of a 2D nanostructure is the graphene nanosheet, which has a nanoscale thickness. Theoretically, a single-layer

graphene is approximately 0.345 nm thick (equivalent to one atom thickness). Finally, 3D nanomaterials have length, height, and width [8]. Among nanomaterials, nanoparticles fall into 3 main categories based on their chemical composition. These include organic nanoparticles such as micelles, liposomes, and dendrimers; inorganic nanoparticles such as metals and metal oxide; and carbon nanoparticles including fullerenes, carbon nanotubes, and graphene (Figure 1) [7,9]. Additionally, with respect to their porosity, nanoparticles can be classified into two principal categories: porous nanoparticles and non-porous nanoparticles [10]. Porous nanoparticles facilitate a medium fluid and absorb smaller molecules including atoms and ions. In contrast, non-porous materials have a denser structure, leading to poor absorption capabilities and limited medium exchange. However, recent research efforts have been dedicated to exploring the potential of mesoporous (or super-nanoporous) nanomaterials having pores ranging from 2 to 50 nm in diameter, minimizing drug leakage while delivering therapeutic agents to target cells [11].

Figure 1.Categories and examples of nanoparticles

Organic nanoparticles

In biological purposes, organic nanoparticles offer advantages in terms of biocompatibility and non-toxicity compared to alternative materials. Some of these nanoparticles even feature a hollow core referred to as nanocapsules. Additionally, they exhibit responsive to thermal and electromagnetic radiation, including heat and light, making them excellent choices for various biomedical applications such as drug delivery. Their suitability for drug delivery depends on several factors, including drug carrying capability, stability, and the delivery system employed, whether it involves entrapped or adsorbed drugs. Additionally, organic nanoparticles possess efficiency and the ability to target specific areas of the body, which is referred to as targeted drug delivery.

Inorganic nanoparticles

Inorganic nanoparticles do not contain carbon atoms, but typically made up of metals or metal oxides. Metal-based nanoparticles are commonly synthesized through the chemical reaction of metal ions or the breakdown of bulky metals, including but not limited to gold (Au), silver (Ag), iron (Fe), zinc (Zn), cadmium (Cd), and numerous other metals. These nanoparticles possess unique characteristics such as a high surface area-to-volume ratio and surface charge density. They can exhibit either crystalline or amorphous structure and specific colors, reactivity, and sensitivity to moisture, temperature, light and surrounding chemicals. Metal oxide nanoparticles are produced with the aim of altering the characteristics of their corresponding metal-based nanoparticles. The synthesis of metal oxide nanoparticles primarily centers on harnessing their improved reactivity and efficiency [12]. For instance, when Fe nanoparticles are exposed to oxygen at room temperature, they are oxidized to form iron oxide (Fe_2O_3), significantly enhancing their reactivity compared to pure iron. Commonly synthesized metal oxide nanoparticles include aluminium oxide (Al_2O_3), magnetite (Fe_3O_4), silicon dioxide (SiO_2), titanium oxide (TiO_2), zinc oxide (ZnO), and more.

Carbon-based nanoparticles

In contrast to organic nanoparticles, carbon-based nanomaterials consist entirely of carbon. They include fullerenes, carbon nanotubes, graphene, carbon black, and sometimes their derivatives such as activated carbon in nanoscale and graphene oxide. These materials have garnered substantial attention due to their distinctive structural properties, exceptional mechanical strength, and remarkable electrical conductivity and excellent chemical stability, which has expanded their applications to various fields, including biomedical applications. Recent efforts have centered on cell and tissue imaging, as well as, the delivery of therapeutic molecules and tissue regeneration. Regarding carbon-based nanoparticles, fullerene (C_{60}) has attracted considerable attention owing to its exceptional photophysical and photochemical characteristics ever since its discovery in 1985 [13]. The majority of fullerenes have a spherical shape, although there are also elongated variations resembling rugby balls, like C_{70}. One of the standout features of fullerenes is their capacity to serve as sensitizers for the photo production of oxygen reactive oxygen species (ROS), making them valuable in applications such as blood sterilization and photodynamic cancer therapy [13]. They have been developed for promising potential in serving as antimicrobial, antiviral, and antioxidant agents [14].

Synthesis of nanoparticles

Nanoparticles are synthesized through diverse methods categorized as either top-down or bottom-up approaches. A simplified depiction of this process is illustrated in Figure 2.

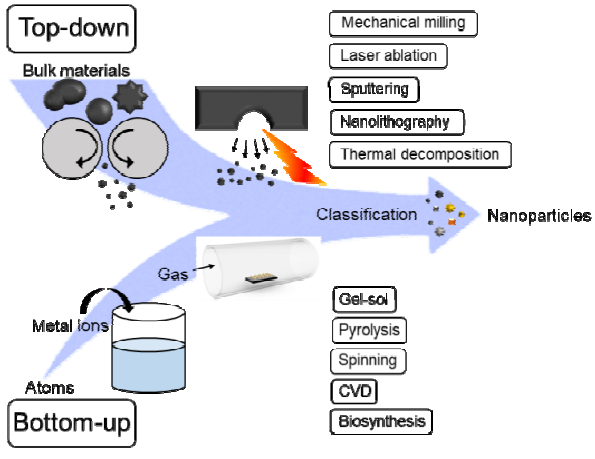

Figure 2.Schematic description of top-down and bottom-up methods for nanoparticle synthesis

Top-down method

Top-down or destructive method involves reducing a bulk materials into particles at the nanometer scale. Among the most commonly employed techniques for synthesizing nanoparticles are mechanical milling, laser ablation, thermal decomposition, sputtering, and nanolithography. Among them, mechanical milling stands out the most widely employed and simple method for manipulating diverse nanoparticles. In mechanical milling, nanoparticles are milled and subsequently subjected to annealing, wherein different elements are milled within an inert atmosphere [15]. During the process, plastic deformation influences particle shape, fracture, resulting in a reduction in particle size, and cold-welding increases the particle size.

Laser Ablation Synthesis in Solution (LASiS) is a frequently employed technique for producing nanoparticles in various solvent medium. This process involves irradiating a metal submerged in a liquid solution using a laser beam, resulting in the condensation of a plasma plume that yields nanoparticles [16]. It represents an environmentally friendly top-down approach, offering an alternative to the traditional chemical reduction of metals for synthesizing metal-based nanoparticles. The primary advantage of LASiS is the ability to produce stable nanoparticles in both organic and aqueous solvents without the need for stabilizing agents or chemicals. Metal nanoparticles are also synthesized by thermal decomposition, an endothermic chemical decomposition induced by heat. It involves the breaking of chemical bonds within a compound [17]. The temperature at which a substance undergoes this chemical decomposition is referred to its decomposition temperature, and the nanoparticles are manipulated through the decomposition of metals at precisely controlled temperatures, leading to a chemical reaction that results in the formation of secondary products. Sputtering is another destructive physical synthesis method, which involves the application of nanoparticles onto a surface through the expulsion of particles from the surface as a result of collisions with ions [18]. Typically, sputtering results in the deposition of a thin film of target materials, which is often followed by an additional annealing process to form nanoparticles. Therefore, the characteristics of the nanoparticles, such as their shape and size, are influenced by factors including the thickness of the film deposition, annealing temperature and duration, and substrate type [19]. Due to the recent advancements in nanotechnology, nanolithography technique has been also developed to create structures at the nanoscale, specifically involving at least one dimension within the range of 1 to 100 nm. Various nanolithographic techniques include photolithography, electron-beam lithography, laser interference lithography, multiphoton lithography, nanoimprinting, and scanning probe lithography [20]. In general, lithography is the process of transferring a predetermined shape or pattern onto a photosensitive material, selectively removing a certain area of the material to achieve the desired structure. The primary advantage of nanolithography is its ability to produce an individual nanoparticle as well as their clusters, all with precisely tailored shapes and sizes. However, such a state-of-art nanotechnology demands sophisticated equipment and is associated with significant costs [21].

Bottom-up method

Bottom-up approach involves the construction of material starting from atom, progressing to clusters, and ultimately forming desired particles in nanoscale. The sol-gel method is widely favored among bottom-up approaches due to its simplicity and the broad range of nanoparticles that can be produced through this technique. The sol is a colloidal solution consisting of solid particles suspended within a liquid, while a gel involves a solid macromolecule immersed in a solvent. This wet-chemical process utilizes a chemical solution as a precursor to create an integrated system of distinct particles. Typically, metal oxides and chlorides serve as the primary precursors in the sol-gel process [22]. The precursor is subsequently dispersed in a liquid, achieved through simple processes such stirring or sonication, resulting in a system comprising both liquid and solid phases. To recover the resultant nanoparticles, a phase separation is performed, employing various techniques including centrifugation sedimentation, and filtration, followed by the removal of moisture through drying [23]. Nanoparticles can be synthesized using a spinning disc reactor, which comprises a chamber or reactor housing a rotating disc, allowing for control of physical parameters such as temperature. In this spinning method, to prevent any unwanted chemical reactions, oxygen is generally eliminated in the reactor by filling it with nitrogen or other inert gases [12]. The disc's rotation speed varies while the liquid consisting precursor and water is pumped into the reactor. The spinning action causes the atoms or molecules to merge and precipitate, after which they are collected and dried [24]. The properties of the nanoparticles produced via SDR are influenced by various operating factors, including the liquid flow rate, location of feed, rotation speed, liquid to precursor ratio, disc surface morphology, and more.

Unlike the sol-gel and spinning methods, chemical vapor deposition (CVD) is a dry process in which a thin layer of gaseous reactants is deposited onto a surface. This deposition process also takes place in a reaction chamber where gas molecules are combined. When a heated substrate comes into contact with the mixed gases, a chemical reaction occurs, resulting in the formation of a nanometer-thin film product on the substrate's surface, which can be harvested and utilized [25]. The temperature of the substrate plays a crucial role in CVD. CVD offers several advantages including the production of highly pure, uniform, durable and robust nanoparticles. However, it also has drawbacks such as the need for specialized equipment and the generation of highly toxic gaseous by-products [26]. For industrial purposes, pyrolysis stands out as the predominant method employed for the large-scale mass production of nanoparticle. This process entails the combustion of a precursor using a flame, where the precursor, which can be in liquid or vapor form, is introduced into a high-pressure furnace through a small aperture, igniting upon entry [27]. The resulting by-product gases are subsequently air classified to harvest the nanoparticles. Sometimes, laser or plasma is employed instead of flame to generate the high temperatures required for efficient evaporation [28]. Pyrolysis offers numerous advantages, including its simplicity, efficiency, cost-effectiveness, and continuous operation, yielding a high output.

On the other hand, biosynthesis represents an environmentally friendly and sustainable approach for nanoparticle synthesis, producing nontoxic and biodegradable nanoparticles [29]. It utilizes biological agents such as bacteria, fungi, plant extracts, and more, in conjunction with precursors, to synthesize nanoparticles. This innovative method replaces convention chemicals for bioreduction and capping purposes and produces

nanoparticles possessing unique and enhanced properties relevant in various biomedical applications.

Biomedical application of nanoparticles

Over the past few decades, there has been extensive exploration of the remarkable potential of nanoparticles in the realms of biomedical and healthcare applications [7]. Numerous case studies have illustrated that nanoparticles have the capacity to address prevailing challenges in biomedical and healthcare sectors related to raw materials. Depending on the distinct morphology of nanoparticles, they serve roles as performance enhancers, shape modifiers, moisturizers, nanofillers, and more in drug delivery, tissue engineering, bioimaging, and biosensors (Figure 3). The industrial breakthrough of nanoparticles relies on optimizing production and processing conditions, presenting both challenges and promising prospects.

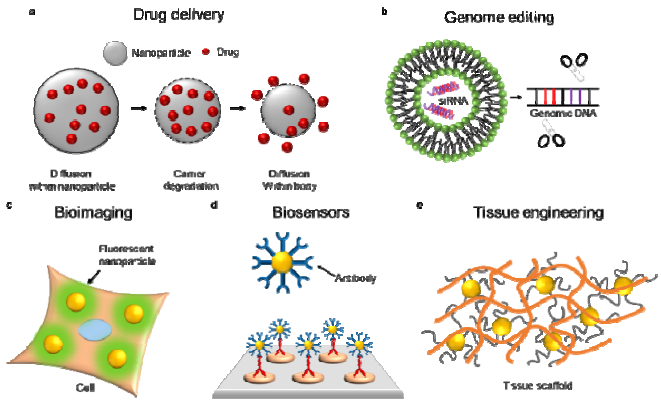

Figure 3. Schematic illustrations of examples for nanoparticles in biomedical application. a) Drug delivery using nanoparticle carrier. b) Genome editing using siRNA in liposome. c) Bioimaging of living cells using fluorescent nanoparticles. d) Sensing technology of biomolecules using nanoparticles attached with antibodies. e) Tissue engineering to form nanoparticle-assisted tissue scaffold

Nanoparticle-assisted drug delivery systems

The utilization of nanoparticles in drug delivery systems is a relatively recent and rapidly advancing field of research. These approaches harness nanoparticles to transport drugs or imaging molecules to specific targets for diagnostic purposes [30]. The development of drug delivery often relies on nanostructures, encompassing organic, inorganic, and polymeric materials. Within these carrier systems, nanoparticles play pivotal roles in advancing personalized medicine, as they contribute to improved drug formulation, targeting, and controlled release [31]. These systems excel in their ability to precisely deliver drugs to designated sites at predetermined rates and in specific manners, ultimately enhancing drug bioavailability while mitigating side effects. Drugs can be introduced to nanoparticles either by physical or chemical adsorbing them onto the nanoparticle's surface or by loading them inside nanoparticles during the synthesis process [32]. The effectiveness of drug loading onto or into the carrier is determined by several factors including the carrier's size, the solubility of the drug and carrier, and the chemical interaction between the drug and the carrier [33]. The rate at which drugs are released from the nanoparticles primarily depends on the desorption behavior of the drug from the nanoparticle's surface, the diffusion of the drug within the nanoparticles, carrier degradation, and subsequent diffusion of the drug within the body. The timing and location of drug release can be adjusted through the thermo sensitivity or pH-sensitivity of the nanoparticles and their engineering techniques. Biodegradable polymeric nanoparticles have gained prominence in drug delivery systems due to their versatility and advantageous features. These characteristics encompass controllable drug release, stability within the bloodstream, non-immunogenicity, and non-toxicity [32]. Colloidal drug carriers such as micelles, liposomes, and emulsions serve as valuable tools for enhancing the transport of drugs across the blood–brain barrier. Utilizing nanoparticle system for drug delivery offers several advantages over conventional drug administration methods, notably exceptional precision, targeting delivery capabilities, stability, and sustainability at the intended site [34]. Delivery systems employing large-sized materials often suffer from significant drawbacks, including poor solubility, absorption, and stability, potentially compromising their effectiveness. Identifying suitable carriers entails addressing key challenges, such as (1) managing the timing of drug release, (2) ensuring the lifetime and reliability, (3) assessing the non-toxicity, (4) optimizing biodistribution and targeting, and (5) considering the possibility fornanoparticles to accumulate in the body with prolonged treatment.

Effective cancer therapy is an intricate challenge, primarily due to the complexity of the disease. Nonetheless, the concept of precision medicine has arisen as a promising approach, leading to the development of targeted chemotherapeutics designed to address specific biomarkers express by patients. A pioneering example of such targeted therapy is imatinib (Gleevec; Novartis), prescribed to individuals with chronic myeloid leukaemia who exhibit the BCR–ABL fusion protein as a result of the Philadelphia chromosome [35]. FDA approval of imatinib marked a significant milestone and pave the way for numerous other successful targeted chemotherapeutics. Moreover, imatinib has been successfully delivered using a nanoparticle system, resulting in enhanced tumor accumulation and regression. This innovative approach improved the survival rate of melanoma mouse to 40% after 60 days [36]. Enhanced delivery technique using nanoparticles hold potential to address limitations encountered by therapeutics that have struggled to progress to clinic use, including drugs with poor water solubility and unstable antibodies [37]. Additionally, various biological barriers are encountered with cancer, particularly at the tumor site. Nanoparticle delivery strategies have the potential to mitigate many of these challenges.

Biomedical imaging

Biomedical imaging represents a diagnostic technology employed to monitor biological structure of living organisms without the need for invasive procedures. Recent advanced biomonitoring technologies allow the investigating of physiological phenomena without interfering body signals, including breathing and motion. Additionally, it facilitates the acquisition of data regarding the 3-dimensional nanostructure of samples [38] and enables the examination of tissues at both subcellular and multicellular scales [39]. Nanoparticles serve as ideal candidates for constructing nanoprobes due to their precise characterization through nuclear magnetic resonance and gel permeation chromatography, coupled with their easy elimination from the body. Recently, magnetic nanoparticles have garnered significant attention due to their advancement in image-guided therapy, such as fluorescence, X-ray CT,

magnetic resonance. They offer favorable properties, including adjustable size, the capacity to produce ROS, ability to transfer energy, and light absorption characteristics. Furthermore, it is imperative to conduct a thorough examination of their long-term toxicity and ability to remain stably dispersed. Fluorescent nanoparticles offers a versatile platform for tailoring their specificity, light-emission (particularly in the NIR-IR range), and biocompatibility with target tissues through alterations in their size, shape, and surface characteristics [40]. There are several key factors to be considered in the cellular uptake of nanoparticles employed in bioimaging [41]. For example, smaller nanoparticles exhibit superior cellular absorption compared to their larger counterparts with similar surface properties [42]. Also, nanoparticles with positive charge are preferred for cellular uptake, given the negatively charged nature of cell membrane [43]. Cell-specific targeting can be accomplished by attaching ligands to nanoparticles and protein or oligodexynucleotide conjugation can facilitate rapid absorption. These factors collectively contribute to the intricate dynamics of nanoparticle-cell interactions, influencing their effectiveness in various bioimaging applications. For instance, fluorescent metal quantum dots, such as those made from materials including Au, InP, InAs, ZnSe, CdTe, or CdS, and ranging in size from 1 to 10 nm, exhibit broad absorbance bands and narrow emission bands, making them suitable candidates for biological imaging within the near-infrared spectrum [44]. Such inorganic nanoparticles are widely employed in bioimaging due to their vivid coloration, diverse shapes and sizes, and high-intensity surface photoluminescence. They enable non-invasive disease detection and the tracking of disease progression or response to treatments in both human and animal subjects [45]. Metal oxide nanoparticles (e.g., Fe_3O_4 and WO_3) [46], lanthanide-doped nanoparticles [47], and ceramic nanomaterials like mesoporous TiO_2 and SiO_2 nanoparticles [48] have also been investigated for their potential in bioimaging and therapy.

Fluorescent carbon nanoparticles present a compelling option for bioimaging applications due to several advantageous characteristics, including their abundant source, simple synthesis, cost-effectiveness, and non-toxic nature [49]. Notably, conventional fluorescent quantum dots often contain heavy metals like cadmium, which can pose hazards to biological systems. In contrast, carbon-based fluorescent nanoparticles, such as carbon quantum dots and fullerenes, merge as promising substitutes and surpass conventional organic fluorophores based on their resistance to photo-bleaching and ease of surface modification [50]. Furthermore, their enhanced aqueous solubility, chemical stability, and fluorescence performance make them well-suited for biomedical purposes, particularly in vitro and in vivo bioimaging. It is crucial to functionalize the surface characteristics of nanoparticles in their utilization for bioimaging applications. Nevertheless, the task of identifying then a noparticles best suited for a particular bio imaging purpose is complex, requiring the evaluation of various factors including sensor size, brightness, photo stability, and biological safety. Once the optimal material is identified for a specific bioimaging application, all experiments must be fine-tuned to match the chosen material. To address these challenges effectively, a better understanding of the repercussions of nanoparticles on nature is essential. This knowledge will provide insights into their imaging capabilities and interaction with living cells. Consequently, there is a pressing need for further research endeavors to advance the utilization of nanoparticles in bioimaging applications.

Genome editing

The emergence of technologies like zinc finger nuclease (ZFN), meganuclease, transcription activator-like effector nuclease (TALEN), and clustered regularly interspaced short palindromic repeats (CRISPR) has significantly simplified genome engineering, opening up wide-ranging applications in biomedical engineering [51]. The latest advancements in genome editing hold the promise of linking human genes to many rare diseases without effective treatments. Nevertheless, efficient and safe delivery methods remain a critical requirement to specifically aim and penetrate the desired cells while keeping toxicity to a minimum [52]. The delivery of genome-modifying materials poses challenges due to their multifaceted nature, containing sensitive cargo, and the necessity to surmount various extra- and intra- cellular barriers to access the target genome. Both lipid- and polymer-based nanoparticles have been successful in delivering a spectrum of nucleic acids, and they are indifferent phases of clinical advancement [53,54]. For instance, patisiranis a medication for the treatment of amyloidosis using siRNA in lipid nanoparticles [55].

The majority of genome-editing systems involving nanoparticles are created by combining nucleic acids with cationic materials. These complexes are then introduced into cells through mechanisms such as receptor-mediated endocytosis and phagocytosis [56]. Cationic materials serve a dual purpose: they facilitate the complexation with DNA or RNA and provide nanoparticles with responsive characteristics that helpin escaping endosomes. Lipids and polymer slike polyethylene imine (PEI), poly(amido amine) (PAA), polylysine (PLL), and poly(β-amino esters) show promise for delivering genome-editing systems[57,58]. Since these systems are sensitive to the intracellular conditions, efficient endocytic uptake can be ensured through optimization of both passive and active targeting components.

Cystic fibrosis arises from genetic mutations affecting the gene responsible for encoding the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Despite being a life-threatening condition with no current cure, cystic fibrosis is considered a monogenic disorder, making it suitable for potential gene therapy interventions. Although it has been demonstrated that the CFTR gene is successfully treated in vitro, significant challenges related to gene expression and delivery have hindered progress when attempting gene therapy for cystic fibrosis in vivo [59]. As cystic fibrosis primarily affects cells responsible for producing mucus, they can produce abnormally thick mucus, which is the main symptom and a significant hurdle for effective drug delivery. To address this challenge, nanoparticles with enhanced muco-penetrating properties have been developed for use in delivering treatments to the lungs of individuals with cystic fibrosis, as well as for oral delivery. Nanoparticles that are smaller in size than the pores in the mucus meshwork and inert hydrophilic coatings demonstrate improved penetration [60,61]. While the utilization of nanoparticles for fetal delivery remains relatively limited, initial successes have been achieved in the delivery of peptide nucleic acids using nanoparticles in utero [62]. These achievements have yielded a level of gene editing that is substantial enough to mitigate the disease to manageable

levels. Several companies are actively engaged in the development of gene therapeutics. For instance, Intellia Therapeutics is currently at the forefront of using lipid nanoparticles to address various liver diseases such as amyloidosis and hepatitis B virus infection. By meticulously designing nanoparticles with precision gene editing holds the promise of not only curing genetic diseases but also significantly improving the lives of patient.

Biological sensors

Biological sensors (biosensors) typically consist of organic and electronic components to generate and measure discernible signals from biological features[63]. These electronic elements are adept at detecting the physiological variations triggered by surrounding conditions of the sensor [64]. Specifically, biosensors comprise five fundamental elements: the analyte, receptor, transducer, electronic component and display. The term 'analyte'denotes a substance that is being investigated forits presence and quantity are requires detection [65]. It is recognized and identified by an organic molecule called the receptor. The transducer is a specialized device with the role of converting the physiological changes resulting from the interaction between the analyte and receptor into a measurable optical or electrical signal [66]. The electronic component plays the pivotal role of receiving and quantifying the transduced signal. Finally, the displaying component present the response output in a comprehensible manner for the user's understanding [67].

Efficient signal collection poses a primary challenge in the development of biosensors, and the process is known as transduction. To address this challenge, measurable physiological variations are translated into various forms of signals, including optical, electrochemical, magnetic, or gravimetric signals through the use of a transducer. Engineered nanoparticles offer several advantages, such as enhanced electrical conductivity, signal amplification capabilities and biocompatibility. These nanoparticles have the potential to capture significant quantities of specific binding units and serve conductive mediums, making them promising candidates for enhancing the detection sensitivity of biosensors. For instance, carbon-based nanoparticles can be utilized for extensively improved sensing performance and lower detection limits. The exceptional intrinsic characteristics of nanoparticles can significantly enhance the effectiveness of biosensors especially when developing for monitoring biomolecules [68]. For instance, the detection of biomarkers using advanced biosensors is a promising diagnostic application. Magnetic nanoparticles were employed to facilitate amperometric biosensing for prostate cancer biomarkers [69].

Tissue engineering

Tissue engineering aims to build constructs made of biological elements, combined with biomaterials, in order to replicate the attributes of natural organs or tissues. They have the potential to replace traditional organ and tissue transplantation procedures, thereby reducing the associated cost burden [70]. Advances in nanotechnology and fabrication techniques rapidly expanded the possibilities for incorporating various nanomaterials into tissue engineering fields, including skin, neural, and bone engineering [71]. Their role is pivotal in finely adjusting scaffold properties, mainly increasing their mechanical durability and biocompatibility [72].

In the field of dental tissue engineering, there is a pressing need for innovative approach to effective address periodontal disease, particularly considering the tissue decay with loosing healing ability, and nanoparticles hold significant relevance in dental tissue engineering for several reasons [73]. They can be employed as coating and filling materials to enhance the mechanical robustness of dental tissues, antimicrobial agents effectively preventing oral infections, and ingredients in the development of innovative personal care products and toothpaste formulations [73]. For instance, Xi et al. conducted research involving the creation of multifunctional nano-vesicles by co-assembling poly(ethylene oxide)-blockpoly (ε-caprolactone) and poly(ε-caprolactone)-block-poly(lysine-stat-phenylalanine). These vesicles were loaded with an antibiotic, ciprofloxacin hydrochloride, to demonstrate their ability to eliminate biofilms formed by Staphylococcus aureus and Escherichia coli [74]. Additionally, recent developments have introduced nanoparticles for designing nanostructured scaffold architectures to address significant skin wounds effectively. In the realm of skin tissue engineering, nanoparticles also find application as carriers for therapeutic molecules [75]. For example, Randeria et al. utilized Au nanoparticles that were functionalized with RNAs targeting ganglioside-mono sialic acid 3 synthase (GM3S), an enzyme contributing to insulin resistance and subsequently impeding would healing. These nanoparticles were further modified with thiolated ethylene glycol and dispersed in Aquaphor. As a result, the skin wounds in mice treated with these nanoparticles fully healed within 12 days, a significantly faster rate compared to untreated mice [76].

Conclusion

This review comprehensively explores a wide range of nanoparticles, encompassing their various types, synthesis methods, and specially engineered designs for biomedical applications. Nanoparticles exhibit remarkable and adjustable physical, chemical, and biological attributes, positioning them as promising candidates for innovative materials in a wide range of biomedical engineering studies. Particularly, the exceptional progress in utilizing nanoparticles for targeted drug delivery has significantly addressed the limitations associated with conventional drug delivery systems. They also play an important role in tissue engineering for mending various types of tissues. Furthermore, carbon and metal-based nanoparticles utilized in biosensor development hold promise for a multitude of applications in both biomedical and agricultural fields. A broad spectrum of demands and complexities involved in advancing biomedical systems can be effectively tackled by well-designed nanoparticle platforms. These platforms provide an array of adjustable characteristics, including size, charge, shape, and surface properties, which can be precisely tailored to enhance their efficiency, sensitivity, and selectivity. This tailored approach can be synergistically employed alongside precision medicine treatments to refine patient stratification methods. Hence, it is essential to conduct more in-depth analyses of nanoparticle design and their interactions within the human body. By consistently exploring nanoparticle technologies in laboratory environments, researchers keep collecting data and evaluate outcomes, thus contributing to the growing library of established relationship between nanoparticle design and functionality. Nevertheless, it is crucial to place the observed relationship trends from the research settings into context before attempting to apply them broadly. This is because

seemingly minor disparities in nanoparticle composition, the choice of animal models, and underlying pathologies can significantly influence nanoparticle performance. All these factors must be taken into account when progressing nanoparticle technology towards practical applications. As we venture further into the exploration of advanced nanoparticle-based biomedical platforms, this research has the potential to shape the future of rational biomedical systems, catering to both personalized and general therapeutic applications. Furthermore, the approval of additional nanoparticle systems can facilitate their integration into everyday life for novel applications. By actively developing more nanoparticle platforms for biomedical use, we take significant steps towards more effective and environmentally sustainable approach to treating diseases. The expansion of advanced nanoparticle-based systems will play a role inadvancing personalized disease treatment, fostering the growth of seemingly specialized markets.

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Statement of Competing Interests

The author has no competing interests.

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