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Review Article

Cutting-Edge Nanoparticle Innovations in Biomedical Science: Synthesis, Applications, Challenges, and Future Prospects

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Abstract

Nanoparticles (NPs), identified as particles measuring between 1 and 100 nanometers, exhibit distinct physical and chemical properties that set them apart from larger materials. These attributes, which encompass a substantial surface area relative to volume and quantum phenomena, render them highly across various sectors. With their ground-breaking approaches to medication distribution, therapeutic treatments, and diagnostics, nanoparticles play a crucial role in biomedical innovations. This paper presents the extensive use of nanoparticles in biomedical field, the techniques for nanoparticles, encompassing both top-down and bottom-up methodologies, and assesses their wide-ranging applications in healthcare, environmental studies, and the industrial realm. Despite the vast potential of nanoparticles, they also pose notable challenges like potential toxicity, ecological consequences, and regulatory obstacles. Tackling these hurdles is imperative for nanoparticle technology's responsible and sustainable advancement. But in recent years, there have been a number of attempts to develop eco-friendly technology that creates nanoparticles from natural materials rather than hazardous chemicals. Biological methods are used in green synthesis to create nanoparticles because they are easy to use, affordable, safe, clean, and very productive. The paper concludes by delving into future opportunities and ongoing studies dedicated to overcoming current restrictions, ensuring that nanoparticles can realize their revolutionary capabilities in various fields.

Keywords: Nanoparticles, Drug delivery, Imaging, Pollution control, Toxicity, Green synthesis

Introduction

Nanoparticles are at the center of nanotechnology's advances in biomedical research. Particles with diameters on the nanoscale (1-100 nm) are known as nanoparticles, and they have become a revolutionary force in a variety of scientific and technical fields [1]. Their tiny size, high surface area to volume ratio, and quantum effects are what give them these unique properties that distinguish them from bulk materials [2]. The unique characteristics (biomedical, electronic, optical, electrical, magnetic, chemical, and mechanical) of nanoparticles and nanostructured materials in comparison to the bulk material are caused by their tiny size, which also makes them appropriate for novel uses. The periodic boundary conditions of the crystalline particle are destroyed when a particle approaches the de Broglie wavelength, which is also the wavelength of light [3]. As a result, a great deal of the physical properties of nanoparticles are different from those of bulk materials, which opens up a variety of new applications for them. The utilization of nanoparticles - inorganic and natural [4] - in makeup is becoming very well-known these days. The capacity to control materials at the nanoscale has opened up unused conceivable outcomes over a wide run of areas, including pharmaceutical [5], natural science, and industry. Since the 10th-century advertisement, Au and Ag nanoparticles have been used as colored colors in recolored glass and ceramics [6] Parenthetical. For the past 20 years, features on computer chips have been formed using nanotechnologies. When an organizational structure is smaller than 50 nm, quantum effects become prominent, and if it is less than 10 nm, they appear even at ambient temperature. In any case, we have made great progress in understanding the nanoworld thanks to the development of imaging techniques like the Nuclear Drive Magnifying Instrument [7] and the Filtering Tunneling Magnifying Lens. The assembly of precursor particles and associated structures is the most common method of manufacturing nanostructured materials, making the synthesis of nanoparticles an essential component of nanotechnology, since the specific properties are obtained at the nanoparticle, nanocrystal, or nanolayer level. Because iron oxide nanoparticles lose their magnetization when the magnetic field is removed, researchers have studied them more than other forms of nanoparticles. Because iron oxide nanoparticles (Fe_3O_4 and Fe_2O_3) are simple to functionalize with polymers and other materials, they have really been used extensively for *in vitro* diagnostics and are still being used for additional purposes.

In biomedicine, nanoparticles are being developed for advanced drug delivery systems [8] of vaccines and genes, hyperthermia, photoablation therapy, bioimaging and biosensors diagnostic tools, operating equipment, regenerative medicine, medication delivery, therapeutic and imaging techniques that offer higher precision and efficacy. Nanoparticles have also been applied to the treatment of brain illnesses, including as brain cancer and abnormalities of the central nervous system, which are common but poorly managed diseases. Additionally, many therapies utilize nanoparticles for the treatment of cancer [9], diabetes [10], allergy [11], infection [12] and inflammation [13]. For use in biomedicine, nanoparticles are divided into three main types based on their chemical makeup. These nanoparticles include carbon-based nanoparticles, organic nanoparticles like polymers and liposomes, and inorganic nanoparticles including metals, metal oxides, ceramics, and quantum dots. Nanoparticles must be immuneogenic-inhibitory, water-dispersible, biocompatible, and stable in physiological fluids in order to be used in biomedical applications. The characteristics of inorganic and organic nanoparticles are changed as they go through the gastrointestinal tract, affecting their potential toxicity and biological consequences. Because of their small size, nanoparticles may readily enter the body through a variety of openings and may even get to the organs that are most vulnerable [14]. Ingestion, inhalation, skin absorption, and injection are the primary ways that nanoparticles can be exposed to an individual. Through systemic circulation, nanoparticles can travel throughout the body and eventually arrive to the organs. Furthermore, they can pass across the blood-brain barrier or travel by axonal transport via the olfactory nerve to the brain, depending on their properties including size, shape, and chemical reactivity. Environmental applications include pollution control technologies and enhancements in energy production, where nanoparticles contribute to more efficient solar cells and fuel cells. Since renewable energy doesn't emit harmful emissions, there is a strong desire to replace the current fossil fuels with new renewable energy sources and develop devices for effectively using them or storing the energy that isn't used [15]. In industrial settings, nanoparticles are used to create stronger, lighter materials, improve electronic devices, and even in consumer products such as cosmetics and coatings.

Despite the immense potential, the incorporation of nanoparticles into various applications is not without challenges. Issues such as potential toxicity [16], environmental impact [17], and regulatory hurdles [18] must be carefully considered and addressed. The creation of innovative nanoparticles with specialized functions that improve clinical applications' effectiveness, specificity, and safety has been the main focus of research in recent years.

This review attempts to give a thorough overview of the most recent developments in nanoparticle technologies in the biomedical field, addressing important topics such synthesis methods, creative uses, and obstacles to their wider acceptance. The assessment will also look at potential future directions and ongoing research efforts in (**Figure 1**), showing how to get over present constraints and discover new frontiers in nanomedicine.

Nanoparticle Innovations in Biomedical Science

This section provides a quick overview of the fundamental ideas behind each application as well as an analysis of how specific nanoparticles are used in them. One significant biomedical use is targeted drug delivery, which tries to deliver anticancer medications to the precise location of the tumor while protecting neighboring healthy cells. At the moment, the primary source of magnetic materials utilized to target certain locations with anticancer treatments is iron oxide nanoparticles [19]. Ag, TiO_2, and Fe–Pt nanoparticles are among the various nanosystems that may be used for targeted drug delivery [20]. Targeted medication delivery has also been studied with ZnO and Au nanoparticles. One significant biological use of nanoparticles is the treatment of magnetic hyperthermia. Using magnetic hyperthermia, tumors are heated to temperatures exceeding 42°C in order to kill malignant cells [21]. Compared to chemotherapy, this method has the advantage of directly targeting the tumor while sparing the surrounding healthy tissue. Iron oxide (Fe_3O_4) nanoparticles are, once more, the primary component now employed in this therapy [22]. Another significant biological application of magnetic nanoparticles is as contrast agents for bioimaging methods like computed tomography and magnetic resonance imaging. Utilizing light-sensitive materials, photoablation treatment eliminates malignant tumors and other damaged tissue [23]. Several nanoparticles have been studied for potential application in this treatment, including Au, Ag, Fe–Pt, ZnO, and TiO_2. Considering AgNPs' existing role in combating viruses, cancer cell lines, and microbes, Al-Radadi and Abu-Dief reported that they can be used to successfully manage the ongoing COVID-19 pandemic [24]. A significant biological application for sensing a range of biomolecules is the development of biosensors. Numerous nanoparticles have been studied for potential application in biosensors, including Au, Fe–Pt, CeO_2, and TiO_2.

Medicine

Figure 2 illustrates how nanoparticles have revolutionized the medical field, particularly in the areas of medication delivery, imaging, diagnostics, targeted treatment, gene delivery, and biomarker mapping.

Drug delivery: One common and established cancer treatment strategy is chemotherapy. Although chemotherapy has a variety of modes of action, its primary purpose is to destroy rapidly proliferating cells, including tumor and normal cells [25]. This can have substantial side effects, such as the suppression of bone marrow, hair loss, and gastrointestinal

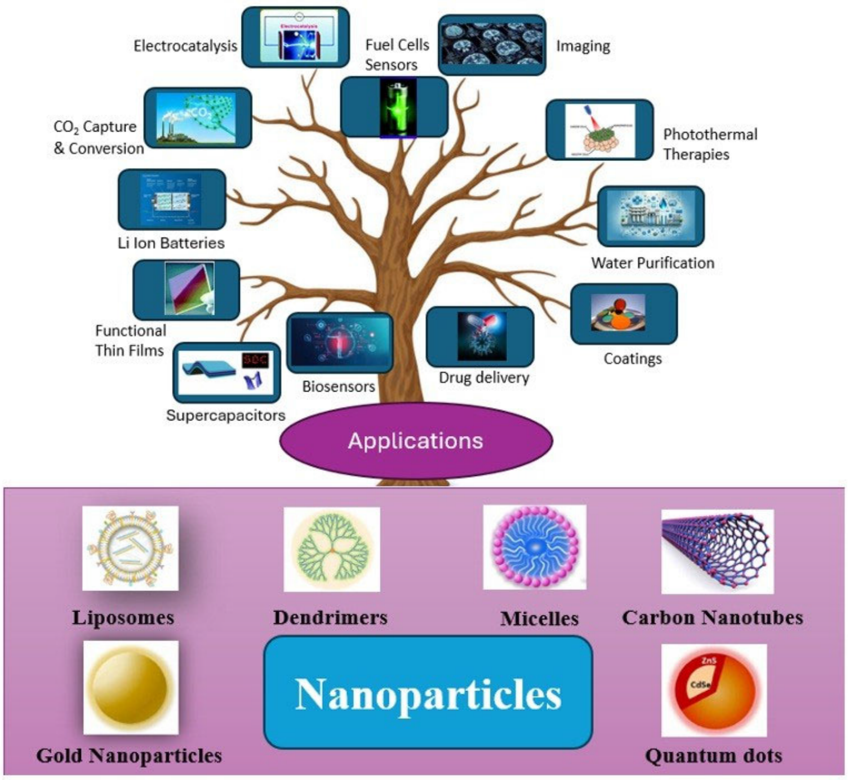


Figure 1. A schematic representation of nanoparticles and their applications.

Figure 2. Biomedical application of Nanoparticles.

problems [25]. Chemotherapy relies on the bloodstream to deliver anticancer medications to the tumor [26]. In this context, the one-pot hydrothermal method which is straightforward, inexpensive, and ecologically benign was used to create VSe_2 (Vanadium Diselenide), Cu_2Se (Dicopper Selenide), and VSe_2@Cu_2Se nanoparticles (Vanadium Diselenide–Copper(I) Selenide Core–Shell NPs) [27]. Thus, a major focus of cancer research over the past few decades has been on creating medications that more precisely target tumor cells rather than normal cells. Drug resistance has always been an issue, and even though targeted therapy has greatly advanced precision medicine, there are still a lot of inevitable side effects. Cancer is still the second most common cause of death today, and many malignancies still do not respond well to modern treatments. As a result, more research is being done to find precise cancer treatment and ways to overcome medication resistance. Many benefits of using drug delivery systems based on nanoparticles (NPs) in the treatment of cancer have been demonstrated, including improved pharmacokinetics, specific targeting of tumor cells, decreased side effects, and decreased drug resistance. The size and features of nanoparticles (NPs) utilized in drug delivery systems are often selected or created in accordance with the malignancies' pathophysiology [28]. Nano-carriers in cancer therapy mechanically target tumor cells by means of the NPs' carrier effect and the targeted substance's placement impact upon absorption. According to Abu-Dief et al.'s research, quantitative, histological, and immunohistochemical studies will be used to examine the impact of PEGylated nanomaterial dose concentration on ABC induction [29]. When administered intravenously to mice that had previously received the same dose, a higher dose concentration (2 mg/kg) of PEGylated gold nanoparticles (PEG-coated AuNPs) decreased the ABC phenomenon. On the other hand, the ABC phenomenon was strongly triggered by a lower dose concentration (¡ 1 mg/kg) due to the quick removal of the second dose of PEG-coated AuNPs from the bloodstream. The medications are then released onto the tumor cells to cause death. Traditional chemotherapeutic drugs and nucleic acids are among the medications found inside the nano-carriers, suggesting that they may be used in both gene therapy and cytotoxic treatments. Negative side effects of this treatment include the medicines' toxicity and non-specificity, which cause them to attack both malignant and healthy cells and organs [30]. As a result, one therapeutic option to chemotherapy is being developed: targeted medication delivery. By directing the medication to the precise location of the tumor, targeted drug delivery seeks to both decrease adverse effects and increase the amount of medication administered to the tumor site. Magnetic nanoparticles are employed in targeted medicine delivery to carry the medication to the desired site. In order to functionalize the magnetic nanoparticles and enable the anticancer medicine to be either conjugated to the surface or encapsulated in the nanoparticle, they are often coated with a biocompatible layer, such as polymers or gold. An external magnetic field is employed to direct the drug/nanoparticle combination to the precise location of the tumor once it has been delivered. Enzyme activity or variations in pH, temperature, or osmolality release the medication. They may be made to release pharmaceuticals that are entrapped in reaction to pH, temperature, light, or ultrasound. They are sized between 10 and 100 nm. Due to the NPs special physicochemical and biological characteristics, nanomaterial-based drug delivery systems (NBDDS) are widely employed to increase the safety and therapeutic efficacy of encapsulated medications [31]. The goal of nanoparticle drug delivery is to minimize cytotoxicity while optimizing medicine effectiveness. Diffusion over the polymeric membrane controls the drug's release if the nanoparticle is coated with polymer [32]. Medication solubility and diffusion inside or across the polymer membrane are crucial for drug release because the membrane coating serves as a barrier to drug release. Cancer is characterized by uncontrolled cell proliferation is a leading cause of concern. Traditional therapies including chemotherapy, radiation, and surgery can have negative side effects [25]. The systemic adverse effects associated with standard pharmacological treatment are reduced because nanoparticles may more efficiently transfer normally insoluble drugs to adjacent and distant tumor sites. Nanomedicines can successfully identify and treat cancers through targeted medication delivery [33]. Nanoparticles can improve medicine stability, solubility, and targeted delivery. Examples of controlled drug release include liposomes, dendrimers, and polymeric nanoparticles [34]. Peptides may selfassemble into nanostructures such vesicles, fibers, and rod-coils that can be exploited for wound healing, tissue engineering, atherosclerosis therapy, heavy metal detection from biological and environmental materials, and enhanced drug delivery [35]. Polymeric nanomicelles are commonly employed as medication delivery methods. These carriers have several remarkable advantages, including biocompatibility, biodegradability, simplicity of production, and high loading and delivery efficacy [36]. Amphiphilic polymers can readily self-assemble into nanomicelles. Antibiotic therapy is one application of drug delivery systems. Controlled drug delivery systems can be used to administer antibiotics for localized infections, such as in orthopedic implants, in order to limit bacterial colonization and biofilm formation [37]. Nowadays, it's been suggested that nanoparticle-based therapy may be able to defeat multi-drug resistance (MDR) in a number of cancer types, including prostate, ovarian, and breast cancer [38]. To assess the antibacterial efficacy against two strains of Gram-negative bacteria and one strain of Gram-positive bacteria, a comprehensive analysis was conducted. According to study by Khalil *et al.*, the combination Gd_2O_3/CS is more effective than CS alone as a bactericide [39]. Additionally, when exposed to the Gd_2O_3/CS nanocomposites, the MCF-7, HCT-116, and HepG-2 cell lines demonstrated anticancer activity. Furthermore, when compared to traditional vitamin C, nanocomposites show notable antioxidant activity. These results demonstrate the effectiveness of our nanocomposites in the fight against breast cancer.

Imaging: When it comes to the early diagnosis and evaluation of therapy response in a variety of illnesses, medical imaging technology frequently has the biggest impact. X-ray radiography, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US), positron emission tomography (PET), single photon emission computed tomography (SPECT), and fluorescence imaging are among the imaging modalities now in use [40]. In his chapter, Karpuz and Silindir-Gunay address imaging methods and contrast agents for inflammation and infection, talk about the benefits and drawbacks of lipid-based drug delivery systems, look at targeting tactics, and highlight research on lipid-based contrast agents for diagnosis. Certain non-invasive procedures have the ability to provide high-definition photographs of inside organs. In these bioimaging methods, contrast chemicals are often utilized to identify the target organ or tissue and distinguish healthy from sick tissue. The primary problems with the contrasting chemicals currently used for CT and MRI imaging are their limited imaging time, poor retention time, and toxicity. Different compounds, such as core-shell nanoparticles, have been researched as potential contrasting agents because they can offer an enhanced biocompatibility and imaging time, which can help to improve the imaging time and biocompatibility of contrast agents. Nanomaterials, including nanoparticles, nanorods, nanospheres, nanoshells, and nanostars, are widely utilized in biomedical imaging and cancer therapy [41]. Among their many uses are as efficient drug carriers, radiation dosage enhancers, photothermal, photoacoustic [42], and imaging contrast agents. NMR-based nanoscale medical imaging is made possible by nanotechnology. More detailed pictures may be obtained by assembling the atomic nuclei in a nanostructure that generates a magnetic field 10,000 times stronger than Earth's [43]. Nanoparticles' unique features allow for great resolution and sensitivity in molecular imaging applications. Nanoparticles outperform small molecule-based contrast agents in terms of biodistribution, circulation time, and other properties. Nanoparticles, such as fluorescent semiconductor nanocrystals (quantum dots) and magnetic nanoparticles, have demonstrated superior properties for *in vivo* imaging techniques [44] in a variety of modalities, including magnetic resonance and fluorescence imaging. The necessity of using natural resources for the "green" design of novel nanoformulations with therapeutic efficacy is covered in the work by Petrovic *et al*. Research on nanopharmaceuticals is still in its infancy, and great thought must be given to how to prepare nanomaterials. Therefore, it is important to consider the long-term impact and safety of pharmacological nanoformulations. Through the process of nano imaging, light is passed through a tiny aperture in the probe tip, enabling optical microscopes to surpass their diffraction-limited far-field resolution. The probe is positioned less than a wavelength of light away from the sample. Targeted cancer treatments, better MRI, CT, and PET diagnostics, regenerative medicine for tissue repair, improved vaccinations for antigen delivery, blood-brain barrier penetration for neurological disorders, wound healing for growth factors, organ transplantation for immunosuppression, medication combinations for synergy, theranostics for visualization and therapy, vascular health for atherosclerosis, neurological disorders for Parkinson's and Alzheimer's, and organ imaging for precision operations are just a few of the cutting-edge applications of nanoparticles in medicine [45].

Diagnostics: Over the past ten years, a range of targeted nanoparticles have been created for the detection and treatment of orthotopic and metastatic bone cancers [46]. Bone metastases are a common side effect of cancer that affect 65-80 percentage of patients with advanced prostate [47] and breast malignancies 35 to 45 percentage of individuals with thyroid, lung, and kidney carcinomas [48]. Because cancer patients are living longer, the frequency of bone metastases is continuously rising. Magnetic and gold nanoparticles can be employed in biosensors and early illness detection assays. Nanodiagnostics is a growing area that uses nanoscale characteristics to modify and analyze single-molecule systems for clinical diagnosis [49]. The potential biological uses of nanogold particles are greatly expanded by the ability to alter their surface with diverse targeting and functional chemicals, with a focus on cancer therapy [50]. **Figure 3** shows the characteristics of a normal and cancerous cell. Metallic nanoparticles have the ability to detect breast and colon cancer in blood or urine samples by conjugating with cancer-specific antibodies. Biomarkers are proteins that are found on the cell membrane, inside cells, or outside cells [51]. Although gold nanoparticles have lower toxicity than quantum dots [52], the optical characteristics of quantum dots appear to be far more superior in cell-based investigations [53]. By utilizing ligand-receptor interactions, active targeting allows nanocarriers to enter cells. Thus far, lymphoma, lung cancer, and liver cancer have all been treated and diagnosed using active targeting nanomaterials. Because of its high sensitivity, pathogen detection with nanotechnology is thought to be quick, easily accessible, and highly effective. Graphene-based materials, quantum dots (QDs), and gold or magnetic nanoparticles are among the nanomaterials that have demonstrated efficacy in the diagnosis of bacterial and viral diseases [54]. Numerous kinds of nanoparticles, such as metallic, magnetic, and fluorescent ones, have been successfully used to diagnose infectious diseases. As sensitive and photostable probes, fluorescent nanoparticles can be used to label a variety of biological targets [55].

Targeted therapy: Nanoparticle-based targeted therapy is a cutting-edge method of medical care, especially in cancer [56]. By delivering therapeutic chemicals directly to sick cells, nanoparticles provide a viable platform for reducing side effects and enhancing treatment success. Because of their special physicochemical characteristic and capacity to target tumor cells specifically, nanoparticles (NPs) hold great promise as

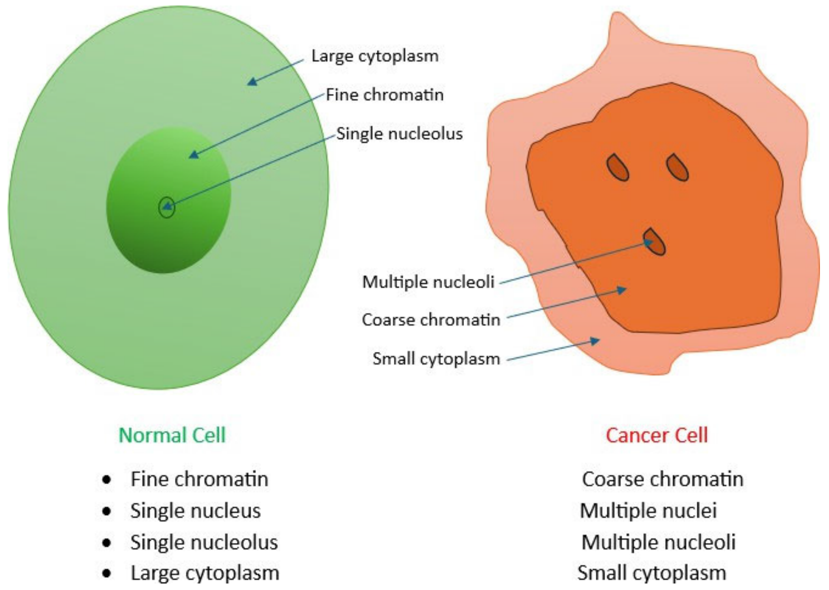


Figure 3. Characteristics of a normal and cancerous cell.

cancer therapeutic agents. NPs can be engineered to minimize harm to healthy organs while delivering medications, genes, or imaging agents to tumor cells specifically. A targeted therapy may be used as a stand-alone treatment or in conjunction with other medical interventions including radiation therapy [57], conventional chemotherapy [58], or surgery. Most targeted cancer therapy strategies function by interfering with specific proteins that help cancer grow and spread throughout the body. Conversely, chemotherapy typically causes all quickly growing cells to die. Targeted treatments mostly consist of two types: monoclonal antibodies and small molecule medications. Tiny molecule medications can penetrate cancer cells and kill them because of their small size [59]. About 25 percentage of breast tumors have overactive HER2 [60], a cell signaling molecule that is the target of trastuzumab. Lapatinib for breast cancer [61], crizotinib for lung cancer [62], bevacizumab for colon and lung cancer [63], and sorafenib for liver and kidney cancer [64] are a few other examples of targeted therapy. Compared to conventional chemotherapy, targeted treatments may have less adverse effects in certain people since they only target cancer cells. The following adverse effects might occur with the sort of targeted treatment you receive: diarrhea. Changes to the skin, such as rashes, itching, or pigmentation shifts. Targeted treatment is successful in up to 80 percentage of instances, whereas chemotherapy only delivers a success rate of about 30 percentage.

Gene delivery: The method of transferring foreign genetic material such as DNA or RNA into host cells is known as gene delivery [65]. For gene delivery to be successful, the foreign gene delivery must be stable inside the host cell and be able to either multiply on its own or integrate into the genome [66]. With recent developments showing promising results in inherited illnesses and some types of cancer, gene treatments hold great promise for repairing genetic defects [67]. The technique of delivering genes to bacteria or plants is known as transformation, while the process of delivering genes to animals is known as transfection. This is thus because, in the case of animals, metamorphosis denotes a shift toward a malignant condition. Exogenous nucleic acids, such as genes, gene segments, oligonucleotides, miRNAs, or siRNAs, are used in gene therapy [68]. Because of their low immunogenicity and toxicity, versatility in functionalization, and ability to target targets, nanoparticles have been widely used as carriers in gene therapy. Some nanomaterials have the ability to selectively attack cancer cells without damaging healthy cells, which makes them ideal for improving early diagnosis and treatment of neurodegenerative diseases or cancer. In gene therapy, lipid nanoparticles (LNPs) have been created and widely utilized as nonviral (or synthetic) vectors to treat inherited and acquired illnesses [69]. Because of their special magnetic characteristics, magnetic nanoparticles (MNPs) have become a hot topic in biological research and have been employed extensively in recent decades. Pure metals like Fe, Co, and Ni nanoparticles, magnetic nano-metal alloys like FePt and CoPt, nano-ferrites like Fe_3O_4 and -Fe_2O_3, and metal-doped iron oxides like $MnFe_2O_4$, $CoFe_2O_4$, and $NiFe_2O_4$ are the primary types of MNPs [70].

Biomarker mapping: A biological marker, or biomarker for short, is an objective metric that records the current state of an organism or a cell. Your health may benefit from biomarkers acting as early warning systems. Biomarkers are crucial to the rational development of medical treatments, however, there is still a lot of misinformation about the fundamental concepts and vocabulary that support their use in clinical settings and research, particularly in the fields of nutrition and chronic disease [71]. Identification of a person's risk of personal illness, prevention and diagnosis of disease, and disease monitoring are just a few of the numerous beneficial uses of biomarkers in healthcare. In addition, they can be utilized to assess the toxicity or safety of a treatment plan or specific environmental exposures. The identification of treatment targets, early diagnosis, disease prevention, response to treatment, and other uses are aided by biomarkers. Numerous disease indicators, including blood pressure, serum low-density lipoprotein (LDL) for cholesterol, and MMPs (matrix metalloproteinase) and the TP53 (tumor protein) gene as tumor markers for cancer, have been discovered [72]. According to Jime´nez-Avalos *et al.*, the goal is to characterize exomiRs found in biologic fluids that can be utilized as a diagnostic and prognostic tool for noncommunicable diseases such as cancer, heart disease, renal disease, and neurodegenerative disorders [73]. Most cancer biomarkers are proteins, which has the disadvantage of not being disease specific. Although not all types of cancer contain genetic alterations, genetic biomarkers are more accurate than many protein biomarkers [74].

Synthesis of Nanoparticles

Synthesis of nanoparticles is vital for their qualities and prospective applications, which are significantly influenced by aspects such as size, shape, composition, and surface features. Using extracts at varied quantities reduced silver nitrate and resulted in the quick production of AgNps at room temperature [75]. This approach has a faster reaction rate than severe chemical methods, resulting in lower energy usage during synthesis. There are two types of nanoparticle synthesis methodologies: top-down and bottom-up, each with its own set of benefits and drawbacks. Understanding these techniques is essential for designing nanoparticles for specific uses.

Top-down methods

Top-down methods in nanotechnology involve the reduction of bulk materials to nanoscale particles using physical or mechanical processes (**Figure 4**). While these methods are generally more straightforward, they may lack precision in controlling the size and shape of the particles. While breaking down larger particles is one benefit of top-down methods for creating nanomaterials, other drawbacks include the usage of hazardous chemicals and environmental damage. Although they need a lot of energy, top- down techniques for synthesizing nanomaterials can transform bulk materials into nanoscale particles.

Mechanical milling: One common top-down method is mechanical milling, where bulk materials are ground into nanoscale particles using high-energy ball mills. Mechanical milling is widely utilized for generating various types of nanoparticles and is often employed for milling and post-annealing processes in nanoparticle synthesis under an inert atmosphere. The latest advancements in synthesis methods and mechanisms for a range of metal–organic framework (MOF) derivatives, including metal oxides generated from MOFs, porous carbon, composites/hybrids, and sulfides, were compiled by Payam *et al.* [76]. The primary factors impacting

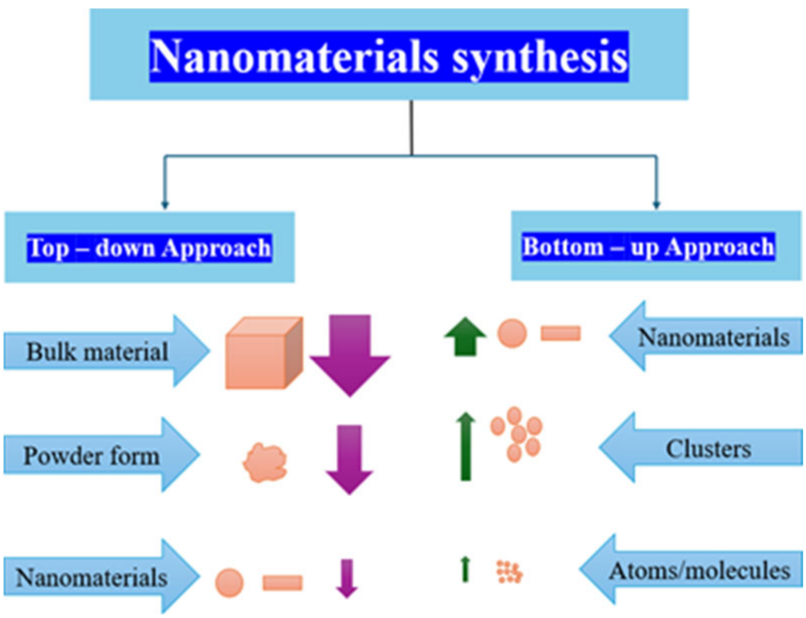


Figure 4. Difference between Top down and Bottom up approaches.

mechanical grinding are plastic deformation, which modifies the shape of the particle, fracture, which reduces the size of the particle, and cold grinding, which increases the size of the particle. Reactive milling, high-energy ball milling, mechanical alloying (MA), and mechanical grinding are a few mechanical processes. These techniques have the advantage of being simple, requiring little equipment, and processing any powder as long as it is possible to create a coarse feedstock powder. In mechanical alloying (MA), a solid-state powder processing technique, powder particles are repeatedly fractured and fused in a high-energy ball mill. Blended elemental or prealloyed powders can be the starting point for MA's ability to synthesize various alloy phases or ceramic powders. Blended elemental powder combinations can be processed into homogeneous products using a technique known as mechanical alloying (MA). The procedure was created about 1966 by John Benjamin and his associates at the International Nickel Company's (INCO) Paul D. Merica Research Laboratory [77]. The process was the result of a long-term endeavor to produce a nickel-base superalloy that would be suitable for gas turbines and have the high-temperature strength of oxide dispersion. Although initially designed for ODS (Oxide Dispersion-Strengthened) alloys, this approach permits the oxides and carbides to coat the metallic substrates directly. As a result, the metal's creep resistance and high temperature strength are significantly increased. Hammer mills, ball mills, pin mills, and roller mills are a few examples of mechanical mill types.

Nanolithography: Techniques like photolithography and electron-beam lithography are utilized to produce nanostructures by patterning bulk materials. A few types of mechanical mills are hammer mills, ball mills, pin mills, and roller mills. Making nanoscale structures with at least one dimension between 1 and 100 nm is known as nanolithography. Among the several nanolithographic methods are optical, electron-beam, multiphoton, nanoimprint, and scanning probe lithography [78]. Using lights, charged ions, or electron beams, a photoresist layerdeposited on a thin film material or most of the substrate receives a geometric pattern transferred from a prepared photomask in nanolithography. Nanolithography can be used to precisely define 2D metal arrays on substrates with finely controlled size, shape, and spacing through a series of steps. Lithography is basically the process of selectively removing material to imprint a particular shape or design on a light-sensitive material in order to achieve the desired structure. The capacity of nanolithography to produce particles or clusters of diverse sizes and shapes is a major advantage. However, the requirement for expensive and sophisticated equipment comes with a drawback [79].

Laser ablation: An intense continuous wave (CW) or pulsed laser beam can be used to thermally or nonthermally remove atoms from a solid. We call this procedure "laser ablation". It is applied to remove material layers in a selective manner. Although it can also be used for cutting, texturing, and marking, laser ablation is most commonly associated with laser cleaning. More precisely, it is used as follows: Contaminants, oxides, and coatings are removed by laser cleaning without removing any material from the substrate. These include core shell nanoparticles, semiconductor quantum dots, carbon nanotubes, and nanowires. Using this technique, species that have been laser-vaporized in a background gas condensation and grow to form nanoparticles. Laser Ablation Synthesis in Solution (LA-SiS) stands as a well-known technique for creating nanoparticles from various solvents. A metal in a liquid solution produces nanoparticles when it is subjected to a laser beam and generates a plasma plume [80]. This approach, renowned for its dependability, offers a substitute for the traditional chemical reduction method in the production of metal-based nanoparticles. By removing the need for additional chemicals or stabilizing agents and enabling the stable synthesis of nanoparticles in organic solvents and water, LA-SiS promotes an environmentally friendly method. The effective generation of homogeneous nanoparticles with superior oxygen vacancies is achieved by means of intense laser irradiation [81].

Sputtering: The process of sputtering involves ejecting particles from a surface through ion collisions, leaving behind nanoparticles [82]. Typically, sputtering is a tiny coating of nanoparticles is deposited and then heated. The kind of substrate, the annealing temperature and duration, the layer thickness, and other variables influence the size and shape of the nanoparticles [83]. Sputtering is just one of several methods used to create thin films. The gift of contemporary engineering technologies is thin films and nanotechnology. The sputtering mechanism has two theoretical models. First one is the thermal vaporization theory, which suggests heating the target's surface to produce vaporization following an energetic particle bombardment. Second one is the momentum-transfer theory, which postulates that surface atoms are released following the transfer of incident particle kinetic momentum to target surface atoms. Sputtering is the result of incident particles interacting with target surface atoms. The variables can affect the sputtering process' maximum yield are powerful and effective ions' or particles' energy, nature and magnitude of the target material, incident particle's angle of reflection and crystal structure of the target surface substance.

Thermal decomposition: The word "thermal" describes something that is heated. Breaking down is the process of decomposition. Thermolysis, also known as thermal decomposition, is the breakdown of chemicals caused by high temperatures. An endothermic chemical breakdown occurs when a substance's chemical bonds are broken by heat [84]. The precise temperature at which a material breaks down chemically is known as the decomposition temperature. The nanoparticles are produced by subjecting the metal to specific temperatures during a chemical process that yields secondary products. Since heat is needed to break chemical bonds in the compound that is decomposing, the reaction is typically endothermic. For instance, calcium oxide (CaO), commonly referred to as quicklime, is created when calcium carbonate is thermally broken down. An essential component in the creation of concrete is quicklime. Certain impure ores can also be roasted with the help of thermal decomposition. The process is not reversible.

Bottom-up methods

In the bottom-up approach, nanostructures are fabricated by building upon single atoms or molecules. Atomic or molecular precursors are formed into nanoparticles using bottom-up techniques (**Figure 4**). The bottom-up approach in nanofabrication is becoming a more significant supplement to top-down techniques as component sizes decrease. Among the important methods are:

Chemical vapor deposition (CVD): During chemical vapor deposition (CVD), a chemical process involving vapor-phase precursor produces a thin layer on the substrate surface. In order to produce carbon-based nanomaterials, chemical vapor deposition processes are crucial. Using chemical reactions that take place in the vapor phase, nanoparticles are formed on substrates. The phase, size, and morphology of the TiO_2 nanostructures can be controlled by adjusting the reaction conditions in a CVD procedure [85]. During the process of creating the finished product, chemical processes such as oxidation, hydrolysis, pyrolysis, reduction, and displacement may take place. As a result, several parameters must be controlled in CVD to produce a predefined material. The capacity of CVD to deposit uniform, superior films is one of its benefits. Chemical vapor deposition is a cost effective and scalable method for creating graphene films. Metal-organic CVD (MOCVD), aerosol-assisted CVD (AACVD), and direct-liquid-injection CVD (DLICVD) are other classifications for CVD based on the precursor phase. The electrical characteristics of CVD graphene show promise for several applications. For example, few-layer graphene produced on nickel may be used to create flexible, transparent, conductive electrodes for organic solar cells. Furthermore, because large-grain graphene can be produced on Cu foil, it possesses electrical characteristics that make it appropriate for use in field effect transistors [86]. Furthermore, CVD coatings offer excellent conformal coverage, fine regulation of film thickness, and the ability to coat complex shapes and interior surfaces. These coatings can provide improved features such as electrical conductivity, thermal stability, wear resistance, and corrosion resistance. With its advantages, CVD has drawbacks such expensive precursor gas and equipment, possible risks from precursor gases, and high working temperatures.

Sol-gel process: A sol (liquid) is chemically changed into a gel (solid) in the sol-gel process. In a gel matrix, metal alkoxides undergo hydrolysis and polymerization to create nanoparticles. A sol is a colloidal solution of particles suspended in a liquid phase. A gel is a solid macromolecule submerged in a liquid. Sol-gel is the most widely used bottom-up approach due to its simplicity of usage and capacity to synthesis most nanoparticles. This wet chemical technique uses a chemical solution as a precursor for an integrated system of discrete particles. In the sol-gel process, metal oxides and chlorides are commonly utilized as precursors [87]. In the system that results from the precursor being dispersed throughout the host liquid through sonication, shaking, or stirring, there are three phases: liquid, solid, and mixture. The nanoparticles are extracted using a range of methods, such as sedimentation, filtering, and centrifugation; the moisture is then removed further through drying [88]. The solgel process has been thoroughly studied and used to produce ceramic materials for a range of applications over the past 50 years. With a focus on biomedical research, the sol-gel synthesis method produces a wide range of biomaterials with diverse morphologies and has a high potential for creating novel biomaterials for novel tissue engineering therapies or drug delivery systems, as well as for enhancing the biocompatibility of a variety of materials commonly used in the biomedical field, such as metallic implants [89]. Solgel synthesis has several benefits, including as monodispersity, excellent control over particle size and microstructure, the ability to produce products with desired lengths and shapes, high purity, and good crystallinity. This method's drawbacks include the result becoming contaminated with the matrix component, its lengthy completion time, and the use of hazardous organic solvents [90].

Biological methods: Traditionally, nanoparticle synthesis was accomplished by physical and chemical methods. These methods have significant drawbacks, hence the biological manufacturing of nanoparticles has gained popularity. The number and quality of the generated nanoparticles, as well as their characterization and uses, are significantly influenced by a wide range of parameters. The synthesis process, pH, temperature, pressure, time, particle size, pore size, environment, and proximity are some of these variables. Small changes in surface functionalization, charge, size, and chemical makeup can produce a wide range of interactions with biological systems [91]. These interactions ultimately influence the nanomaterial's biocompatibility, stability, biological performance, and side effects. The rate of synthesis is slow and the biological nanoparticles are not monodispersed despite their stability. In order to solve these issues, a combination of strategies, including photobiological techniques, may be employed, including the optimization of microbial cultivation methods and extraction techniques [92]. By biological processes, microorganisms and extracts from plants can generate nanoparticles. It is an eco-friendly method for creating non-toxic, biodegradable nanoparticles that is favorable to the environment [93]. The biological approach creates nanoparticles by combining the precursors with bacteria, plant extracts, fungi, etc., in place of traditional chemicals for bioreduction and capping. When it comes to nanoparticles, biological sources are frequently better than metal-based ones because of their higher quality and stability; most metal-based nanoparticles are hazardous to human health [94]. The features of the biosynthesized nanoparticles are distinct and improved, and they are used in biomedical applications [95]. This biological approach has produced a system that is dependable, simple, safe, and environmentally beneficial. These days, magnetic nanoparticles (MNPs) synthesis may be accomplished using certain cultivated strains of magnetotactic bacteria.

Spinning: By spinning, a spinning disc reactor (SDR) creates nanoparticles. The device comprises of a rotating disk that may be used to change physical parameters like temperature inside a chamber or reactor. Reactors are frequently supplied with inert gases to stop chemical reactions and remove oxygen [96]. The disk rotates at varying speeds, allowing liquids such as precursors and water to be pushed inside. Spinning combines atoms or molecules, resulting in precipitation, collection, and drying [97]. Operational factors such as the liquid flow rate, the rotation speed of the disc, the liquid/precursor ratio, the feeding position and the surface of the disc affect the properties of the nanoparticles generated from SDR [98]. **Table 1** explains the comparisons between different nanoparticle synthesis methods and the results of clinical trials.

Table 1. Comparisons between different synthesis methods of nanoparticles and its clinical trial outcomes.

Synthesis Method	Key Features	Advantages	Disadvantages	Typical Applications	Clinical Trial Outcomes	References
Chemical vapor deposition (CVD)	Uses high temperature to vaporize a precursor, which reacts to form nanoparticles.	High purity, controlled size, and shape.	High energy consumption, complex equipment, potential environmental concerns.	Semiconductor manufacturing, sensors, catalysis	Used in drug delivery systems for targeted therapies; trials show controlled release in cancer treatments.	[99-102]
Sol-gel process	Involves transitioning from a liquid solution to a gel phase to create nanoparticles.	Low cost, relatively simple, can produce large quantities.	Long processing times, potential for high solvent use.	Coatings, catalysis, drug delivery	Trials show success in the delivery of anti-cancer agents, though stability can be a concern.	[87,104-107]
Green synthesis	Uses plant extracts, bacteria, or fungi to reduce metal salts into nanoparticles.	Environmentally friendly, low cost, less toxic byproducts, sustainability.	Slower process, sometimes inconsistent results.	Environmental cleanup, biosensors, drug delivery	Trials have shown promising results in using plant-based nanoparticles for improved bioavailability in oral drugs.	[108-112]
Laser ablation	Laser is used to break a bulk material into nanoparticles in liquid or vacuum.	High purity, no chemical reagents required, can produce nanoparticles with specific properties.	Expensive equipment, energy intensive.	Optical applications, medical imaging	Effective in the preparation of nanoparticles for MRI contrast agents, with reduced toxicity in trials.	[113-117]
Hydrothermal synthesis	Involves using water at high pressure and temperature to synthesize nanoparticles from precursor materials.	High quality, controlled size and morphology, scalable.	Energy and time consuming, requires precise temperature and pressure control.	Energy storage, catalysis, sensors	Clinical trials are ongoing for using hydrothermal nanoparticles in drug delivery, especially for gene therapies.	[118-122]
Microemulsion Method	Uses surfactants and co-surfactants to form a stable microemulsion that encapsulates the precursors for nanoparticle formation.	Precise control over particle size and shape, suitable for water-insoluble drugs.	Requires use of surfactants, which can lead to toxicity concerns.	Cosmetics, drug delivery, diagnostics	Trials for oral drug formulations have shown increased absorption rates and enhanced therapeutic effects.	[123-127]

Applications of Nanoparticles

Environmental science

The development of nanoscale materials with environmental applications has accelerated in the past several years. For instance, nanoscale materials have been used to restore polluted soil and groundwater in hazardous waste sites affected by oil spills or chlorinated solvents. **Table 2** displays metal-based nanoparticles and their uses in environmental contamination cleanup. Nanoparticles answer environmental concerns such as pollution management and energy generation shown in **Figure 5**.

Pollution control: Contaminated soil and water can also be cleaned with nanotechnology. For instance, heavy metals and other toxins can be eliminated from water sources and organic pollutants in soil can be broken down using nanoparticles. Titanium dioxide nanoparticles destroy organic contaminants in water through photocatalytic processes. TiO_2-based materials, as the most promising semiconductor photocatalyst, are projected to play a significant role in addressing environmental and pollution concerns, as well as alleviating the energy crisis through sustainable solar energy [138]. The degradation of dyes and other colorless pollutants in wastewater streams is another significant way that nanotechnology contributes to environmental remediation [139]. Numerous nanomaterials have been shown to absorb greenhouse gases, which may contribute to a decrease in global warming. There are various approaches to use nanotechnology to remedy air pollution. Using nano-catalysts with greater surface areas is one method for gaseous reactions. The way catalysts work is by quickening the chemical processes that change hazardous fumes from factories and cars into safe gases. Additionally, nanostructured membranes with tiny enough holes to separate different contaminants from exhaust can be used to regulate air pollution. In order to identify harmful gases including hydrogen sulfide, sulfur dioxide, and nitrogen dioxide, nano materialenabled sensors are also used [140].

Table 2. Metal-based nanomaterials and applications in environmental remediation of contaminants.

Material	Application	References
TiO_2 NPs	Water disinfectant, hepatitis B virus	[128]
Metal-doped TiO_2	Water contaminants—2-chlorophenol, Rhodamine B	[129]
Ag NPs/Ag ions	Therapeutic, Water disinfectant—*E. coli*	[130,131]
Bimetallic NPs	Drug delivery, soil—Chlorinated and brominated contaminants	[132,133]
Iron-based	Water—Heavy metals, chlorinated organic solvents	[134,135]
Binary mixed oxide	Water—Methylene blue dye	[136]
Titanate nanotubes	Gaseous—Nitric oxide	[137]

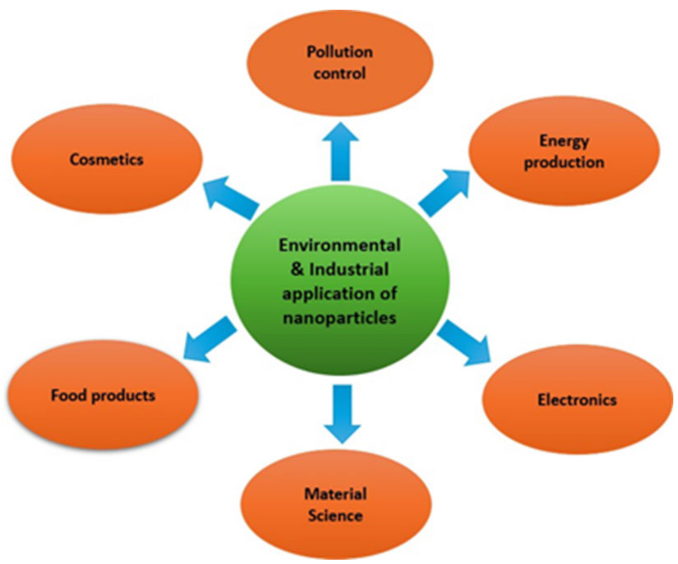


Figure 5. Environmental and Industrial application of nanoparticles.

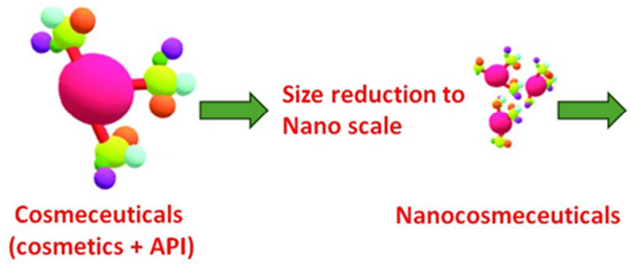
Energy production: Nanoparticles enhance the efficiency of solar and fuel cells. Because of their special physical and chemical properties, nanoparticles are great for cleaning up the environment and enhancing the efficiency of renewable energy sources [141]. Almost all renewable energy sources, including solar, hydrogen, biofuels, geothermal, wind, and others, have extensive uses for nanotechnology [142]. Renewable energy sources like solar and hydrogen energy may be effectively stored using nanomaterials. A crucial component of today's solar cells is engineered nanomaterials. In order to create robots at the nanoscale, the multidisciplinary area of nanorobotics integrates the concepts of material science, nanotechnology, and robotics [143]. Significant progress in industries like manufacturing, energy generation, medical, and environmental remediation might result from the application of nanorobots. Quantum dots improve light absorption in photovoltaic cells, and platinum nanoparticles act as catalysts in fuel cells.

Industry

In a variety of sectors, nanoparticles improve material characteristics and production processes **Figure 5**.

Electronics: There are several applications, including computing and electronic gadgets. Devices include antimicrobial and antibacterial coatings for mouse and keyboards. Additionally, mobile phone castings are excellent instances of nanoelectronics. The creation of batteries that are more durable and efficient is another way that nanotechnology may be applied to meet the needs of the growing electric car and renewable energy storage industries. For example, using nanomaterials in lithium-ion batteries can boost capacity while decreasing charging time. Nanoparticles such as carbon nanotubes and graphene are utilized in transistors, conductive inks, and flexible electronics [144]. Compared to typical silicon technologies, printed electronics research has gained favor since it is more affordable and can handle flexible panels and sensors. In the near future, it is anticipated that printed electronics, which employs various functional inks containing nanoparticles (NPs) such carbon nanotubes (CNTs), metallic and ceramic NPs, and organic electronic molecules, would become a largescale production technique for novel electronic devices. With their unique electrical, structural, and optical properties, one-dimensional metals and semiconductors play a significant systemic role in the development of a new class of photonic, electronic, and sensor materials [145]. Because they have a considerably higher energy storage capacity than conventional materials, nanocrystalline materials are perfect for separator plates in batteries. It is anticipated that nickel-metal hydride batteries, which are made of nanocrystalline nickel and metal hydrides, would last a great deal longer between charges. Semiconductor and superlattice nanowires can be used to fabricate basic electronic devices like transistors, junction diodes, field effect transistors (FETs), and logic gates. Nanowires are being developed not only for bioelectrical–mechanical applications but also for biomedical sensor applications. Nanoparticles, can be employed to make transistors that are both smaller and faster than standard ones. They can also be utilized to make sensors more sensitive than ordinary ones. There are numerous advantages of adopting nanotechnology in electrical and electronics engineering. Because the band gap energy of nanomaterials increases with decreasing particle size, especially in the case of semiconductor nanomaterials, their electrical conductivity is typically lower than that of bulk materials [146].

Cosmetics: Many cosmetic goods, such as toothpaste, skin care products, sun protection, and decorative cosmetics, use nanoparticles [151]. To improve UV protection, skin penetration, long-term effects, and color intensity, chemicals are used in nanoscale forms. Numerous research has shown that healthcare nanoparticles are widely employed in several dental applications, including prevention, diagnosis, treatment, and repair. The efficiency of toothpaste and mouthwash is increased when nanoparticles are used into dental cosmetics [152]. Sunscreen products already frequently contain nanoparticulate materials. They offer more effective protection from the sun's UV rays and better skin coverage. Cosmetic ingredients can be delivered by solid lipid nanoparticles [153]. These lipid carriers offer controlled occlusion, stability, improved hydration, and bioavailability to the skin. These are pure active material particles that have been ground or crystallized into nanoscale particles. Numerous nanomaterials are used in the cosmetic industry, such as liposomes, ethosomes, nanocapsules, dendrimers, solid lipid nanoparticles, nanocrystals, cubosomes, and nanoemulsions [154]. Because of their ability to filter UV rays, zinc oxide and titanium dioxide nanoparticles are found in sunscreens [155]. Sunscreens are made of mineral-based, insoluble ingredients whose effectiveness is dependent on how big their molecules are. The most effective wavelength range for mineral particles, such TiO_2, to reflect and disperse UV radiation is between 60 and 120 nm. Due to its ability to absorb and reflect UV rays, as well as their simplicity in absorbing noticeable light, titanium oxide and zinc oxide nanoparticles have found application as sun screens. Press oxide nanoparticles are used in certain lipsticks as a shade [156]. Numerous applications of nanoparticles in beauty care products are conspicuous in sunscreens, breast cream, hair care, make-up, moisturizers/anti-wrinkle creams, toothpaste, and fullerenes. An extremely potent antioxidant for skincare, fullerene may be used to address a wide range of issues, including redness, acne, skin texture, and hyperpigmentation [157]. Fullerene has more than 250 times the antioxidant activity of vitamin C. More importantly, though, is that it keeps this action going even after being exposed to UVB rays [158]. **Figure 6** illustrates how nanoparticles work generally in cosmeceuticals and cosmetics.



Advantages	Disadvantages
↑ Stability & effectiveness of the cosmetic formula	Because of the placenta's easy penetration, it is teratogenic.
↑ Appearance, covering power, aesthetic appeal & adherence over the skin	↑ Environmental concern
↑ Skin penetration & bioavailability	↑ Production expenses
↑ Texture & transparency of the cosmetic formulation	Require sophisticated equipment for manufacturing
Control & targeted delivery	Nanoparticle toxicity may lead to inflammation, oxidative stress, & consequent damage to membranes & proteins
Increased ability to hold drugs	May damage DNA & cause cancer

Figure 6. Advantages and disadvantages of nano cosmeceuticals.

Challenges of Nanoparticles

Toxicity

Nanoparticles' tiny size and strong reactivity can lead to unexpected recognized biological interactions and possible toxicity. Nanoparticle toxicity varies based on size, type, and surface functionalization etc [159] . Examples of nanomaterials that are often seen in daily life include zinc oxide nanoparticles (ZnONPs), titanium dioxide nanoparticles (TiO_2NPs), silica nanoparticles (SiO_2NPs), silver nanoparticles (Ag-NPs), gold nanoparticles (AuNPs), and polymeric nanoparticles. Studies suggest that some nanoparticles may induce cytotoxicity, inflammation, and oxidative stress in living things. The *in vitro* toxicity of magnetite MIL-53 (Fe) series NPs was examined on three distinct cell lines: the MCF-7 cell line (breast carcinoma), the Hep-G2 cell line (hepatocellular carcinoma), and the HCT-116 cell line (colon carcinoma), according to a paper by Abu-Dief *et al*. With IC_{50} values as high as 11.75 µg·mL^{-1}, these nano MOFs demonstrated a significant cytotoxic profile against breast cancer cells, guaranteeing sufficient cell growth after 24 hours [160]. There are several ways to expose the plant to NPs, including injecting NPs directly into plant tissue [161], NPs being sprayed onto leaves or any other plant portion [162,163], using NP suspensions to irrigate plants or introducing NPs into the soil [164], and infecting cellular pollen or seeds [165]. Nonetheless, it has been discovered that pesticides are poisonous to the environment, deadly, and many of them seriously endanger the health of people and animals. Identified a number of significant challenges, including the overuse and careless use of pesticides at high quantities that harm the ecosystem, encourage bioaccumulation, destroy soil fertility, and disrupt the microbiota of the soil [166]. Inhaled nanoparticles can cause heart issues and lung inflammation in the body problems [167]. A few of the drawbacks of nanoparticles is their potentially fatal impact on healthy cells in the body. As a result, treatment meant for tumor cells is deadly for healthy cells, resulting in neurotoxicity, bone marrow suppression, cardiomyopathy, and other problems.

Strategies to mitigate nanoparticle toxicity: The reactivity and toxicity of nanoparticles can be decreased by the use of surface coatings made of biocompatible or inert substances like polyethylene glycol (PEG), lipids, or polymers such as chitosan, Polylactic Acid (PLA), 3-phosphoglycerate phosphoglyceric acid (PGA), poly(lactic-co-glycolic acid) (PLGA), or polycaprolactone (PCL) [168]. Nanoparticles can be directed to particular cells or tissues by functionalizing them with particular ligands (such as peptides or antibodies), minimizing unwanted interactions with healthy cells and tissues [1]. Reducing aggregation of nanoparticles or minimizing toxicity through decreased protein adsorption can be achieved by altering their surface charge (neutralizing or changing to a slightly negative or positive charge) [169]. A charge that is neutral or slightly negative is frequently more biocompatible and less likely to cause cellular aggregation or harm. The toxicity of nanoparticles is also influenced by their form. Compared to rod or needle-shaped nanoparticles, which are more prone to mechanically harming cells, spherical nanoparticles are often less hazardous [170]. Before using nanoparticles in clinical or industrial applications, thorough toxicity evaluations (including cytotoxicity tests, genotoxicity studies, and long-term animal testing) can help discover and limit negative consequences. In contrast to conventional chemical synthesis techniques, certain nanoparticles may be produced using plant-based materials or other eco-friendly techniques (green synthesis methods), which may help lower the risk of harmful side effects. One of the main causes of nanoparticle toxicity is oxidative stress, which may be decreased and the likelihood of inflammatory reactions reduced by including antioxidants (such vitamins or enzymes) into the nanoparticle structure. *In vivo*, this can improve the nanoparticles' long-term biocompatibility. However, all biodegradable polymers are unsafe for human use. Ensuring that safety and toxicity are fully addressed in nanoparticle design, testing, and application requires adherence to recognized rules and regulations (such as those issued by the Food and Drug Administration (FDA) or Organization for Economic Cooperation and Development (OECD)). In certain cases, nanoparticles can cause tissues to become inflamed and experience oxidative stress. Keeping an eye on these indicators will help identify any toxicity early and enable prompt treatment [171]. Numerous current studies demonstrate that nanoparticles may build up in bodily cells, which might result in harmful responses unique to particular organs. Therefore, a detailed investigation of how nanoparticles affect biological cells is necessary and discussed prior to their use in therapy.

Environmental impact

Since nanoparticles are becoming more and more commonplace in consumer goods, studies have concentrated on finding out how these materials travel through the environment and affect higher creatures. Predictive models have been used in the US and Europe to estimate AgNP concentrationsace waters, wastewater treatment plant effluents, and sewage sludge; however, the available data do not support modelling [172]. To apply harmonized air and aquatic AgNP screening, additional experimental assay modeling is necessary. Although research on the effects of AgNP production and usage on the environment is still in its early stages, most experts agree that AgNPs can enter the environment through a variety of different routes and processes, including synthesis, product inclusion during manufacturing, recycling and disposal [173]. Several previous studies have concentrated on evaluations and quantifications of Ag release from consumer goods containing AgNP [174]. These studies help to assess risk by enabling researchers to comprehend how AgNPs behave in practical situations. Furthermore, these particles change the amount of radiation in the world by warming the planet (by absorbing solar energy) and cooling the planet (by dispersing solar radiation) [175]. Passive smokers are more likely to develop cancer, have a higher BMI, and have worse lung function compared to non-smokers [176]. To address unpredictable climate variability, farming systems must adapt to new crop types that can withstand drought, heat, and environmental stress. This requires a comprehensive approach to current farming methods globally.

Regulatory issues

Nanoparticles' various applications and features of nanoparticles make regulation complex. The healthcare industry is primarily concerned with the harmful effects of nanoparticles on brain illnesses and regulatory challenges. These particles are easily absorbed by the body when applied to the skin. In certain animals, these particles have the potential to cause death or significant brain damage. They may even have an impact on the immune system in humans and have been associated with liver damage. The challenge in regulating nanomedicines is developing sensitive tests that can detect nanomaterials at low concentrations while distinguishing them from metabolic forms or aggregates [177]. The widespread use of nanotechnology has detrimental effects on the environment, including the emission of nanoparticles, which can damage cells when they enter them. Additionally, the growing use of nanotechnology in industry leads to the continuous release of leftover nanoparticles into the environment, which can cause harm to living things and their habitats. Nanoparticles can cause DNA damage, mitochondrial damage, and cell death in sensitive tissues such as the kidneys, lungs, and liver [178]. Standardized testing techniques and safety rules ensure responsible development and use.

Future Prospects

Nanotechnology may one day enable items to gather energy from their environment. The goal of current research is to develop new nanomaterials and ideas that can produce energy from a range of sources, such as glucose, light, movement, and temperature changes, with a high conversion efficiency. One future prospect for nanoparticles is in the creation of scaffolds for tissue engineering and regenerative treatments, which might lead to the replacement of organs and tissues. The future of nanoparticles is bright, with current research concentrating on:

Safe and sustainable synthesis

Developing green chemistry approaches for nanoparticle synthesis to minimize environmental effect. Green synthesis, which reduces metal ions with plant extracts rather than industrial chemicals, has been established. Green synthesis has advantages over traditional chemical synthesis, including lower costs, reduced pollutants, and improved environmental and human health safety [179]. Green nanoparticle synthesis is examined through the integration of environmental sustainability concepts with nanotechnology. Physical and chemical methods are gradually being replaced by green synthesis methods [180] due to problems associated with excessive energy use, release of toxic and harmful chemicals [181], and use of complex equipment and synthesis conditions [182]. At present, green synthesis mainly uses microorganisms (fungal, bacteria, and algae) [183] or extracts from leaves [108], flowers [184,185], roots, peelings [186], fruits [187], and seeds [188], of various plants [46]. Green materials contain polyphenols and proteins [189] that can replace chemical reagents as reducing agents to reduce metal ions into lower valence state. Metal nanoparticles may be produced with green materials and under the right parameters (temperature, concentration, air quality, etc.). Green synthesised metal nanoparticles can even outperform chemically synthesized ones in some circumstances.

Advanced applications

Exploring new applications in fields like nanorobotics, personalized medicine, and quantum computing. With the continuous development of nanotechnology, more and more new materials and new technologies have emerged [190]. To optimize the usage of micro/nanorobots in biomedicine and other domains, novel approaches to their production should be investigated, and a greater selection of biocompatible nanomaterials should be made in order to lower costs and increase the range of applications [191]. There are now many developing biomarkers in biological fluids, and bionanomaterial-based electrochemical biosensor systems, as well as clinical and pharmacological settings, have garnered significant interest. Electrochemical systems have been used to biomaterials including proteins, nucleic acids, and biopolymers to quickly, sensitively, and selectively identify biomarkers [192]. Researchers are currently putting forth the idea that, in light of the development of personalized medicine, NP designs should be tailored to each particular patient [193]. A gold-silica hybrid nanoparticle system intended for targeted medication delivery might be used to treat a patient with a specific disease type (e.g., breast cancer) [194]. While the silica shell gives a biocompatible covering that may be further functionalized with particular targeting ligands, such antibodies that identify receptors overexpressed on breast cancer cells, the gold core of the nanoparticle provides stability and the capacity to absorb and release therapeutic medications. Because of their unique functionality, high sensitivity, and specificity, nanoscale electrode materials have led to substantial advancements in food safety and environmentally friendly monitoring applications [195]. Nowadays, physicians may more safely administer radiation, chemotherapy, and the newest gene and immunotherapies directly to the tumor. With the use of magnetic iron oxide nanoparticles coated with a polymer shell containing chemotherapeutic medications, a patient with liver cancer may receive a customized course of treatment [196]. In addition to carrying a contrast agent for magnetic resonance imaging (MRI), these nanoparticles can administer chemotherapy straight to the liver tumor. Clinicians can use the MRI capabilities to track the tumor's reaction to treatment in real time. Because faulttolerant quantum computers that are capable of doing such calculations are currently unavailable, experts currently feel that quantum simulations can provide near- or mid-term prospects relative to quantum computers [197]. Nanoparticles, which produce controlled release mechanisms that respond to pH, enzymes, light, and temperature changes, significantly increase AIs environmental resilience [198]. A hybrid nanoparticle made of polymeric nanoparticles and gold nanorods might be created for pH-sensitive medication release in customized cancer therapy [199]. The microenvironment of cancer cells is frequently more acidic than that of healthy tissues. When exposed to the acidic pH present in the tumor, the polymer shell of the nanoparticles can be designed to break down or release the therapeutic payload (such as doxorubicin), causing drug release to occur precisely where the tumor is located [200]. Through the process of hyperthermia [201], the heating and localized tissue destruction caused by an alternating magnetic field nanoparticles can be employed to eradicate tumors. Additionally, photothermal treatment and magnetic hyperthermia can be used in concert to treat cancer lesions more effectively by combining magnetic and light fields [202]. RNA-loaded hybrid nanoparticles, which send gene-editing tools (such as CRISPR-Cas9 or RNA interference) straight to the lungs, may help a patient with cystic fibrosis, which is brought on by mutations in the CFTR gene [203]. In order to be both biocompatible and capable of carrying genetic material, the nanoparticles may be made of a lipid-polymer hybrid structure. Lung epithelial cell-specific targeting peptides would be added to them. Nanoparticles can be engineered to improve ultrasound or positron emission tomography (PET) pictures, as well as fluorescence imaging [204].

Regulatory frameworks

Creating extensive laws to ensure the safe use of nanoparticles while encouraging innovation. Legislators often face obstacles when introducing new technology, especially when the advertised benefits raise concerns about human health and environmental threats. In certain cases, new legislation or adaptations to current laws may be necessary. Regulators must stay up-to-date on new materials, technologies, and advances to ensure present regulation covers all elements of human and environmental safety. One potential hurdle to implementing smart nanomaterials in agriculture is a lack of sufficient risk assessment and regulation to address safety issues. This is an emerging technology [205]. The utilization efficiency of nutrients and pesticide AIs may be greatly increased with the use of nano-enabled controlled-release fertilizers and pesticides [206]. Future research should concentrate on maximizing their performance under practical circumstances, cutting costs, and resolving public and regulatory concerns about environmental and safety issues in order to increase their practical uses. However, this involves the use of the Responsible Production (RP) principle [207]. High production and research expenses are only one of the major obstacles to ensuring fair access to medicines based on nanoparticles. They could thus be easier to obtain in wealthy nations or for people who have enough money, leading to inequalities in access. This could restrict the use of medicines based on nanoparticles worldwide. In some areas, patients' and healthcare professionals' ignorance of the availability and possible advantages of medicines based on nanoparticles may further restrict equitable access. Although research on nanoparticles' potential to be harmful to living things is ongoing, there are worries that long-term exposure might have detrimental impacts on the environment. Some kinds of nanoparticles can linger in the environment for a long time, particularly those composed of metals or other non-biodegradable compounds. Nanoparticles may persist in ecosystems, changing ecological dynamics and perhaps contributing to pollution, in contrast to some compounds that decompose naturally. Soil and water pollution may result from the inappropriate disposal of industrial byproducts or medical waste that contains nanoparticles. The danger of environmental contamination might be increased by inadequate regulation. To regulate smart nanomaterials, it is necessary to first examine the current regulatory framework and fix any deficiencies by legal action.

Conclusion

Nanoparticle is enhancing everyday objects' performance and efficiency, improving our daily lives. With their distinct properties and applications, nanoparticles have the capacity to transform environments. Nanoparticles' unique properties provide novel solutions in medicine, environmental science, and industry. Nanoscale engineering has resulted in significant advances in targeted medicine delivery, diagnostic imaging, pollution control, and stronger, more efficient materials. However, the transition from laboratory research to real-world applications presents numerous hurdles. Nanoparticle toxicity and environmental impact must be thoroughly investigated to ensure safe use. Furthermore, strong regulatory frameworks are required to address these problems and promote the responsible development of nanoparticle technology.

The future of nanoparticles is promising. Continued research and development are necessary to solve existing issues, with a focus on sustainable synthesis techniques and sophisticated applications. By overcoming these obstacles, nanoparticles may fully realize their transformative potential, resulting in huge scientific, medical, and environmental breakthroughs. As the field evolves, interdisciplinary collaboration and creative methodologies will be vital to unlocking nanoparticles' full potential and ensuring their safe and effective assimilation into numerous aspects of daily life. To summarize, while nanoparticles present amazing prospects, their development must be preceded by rigorous evaluation of safety and environmental impact. By overcoming these obstacles, the area of nanotechnology can continue to advance, propelling discoveries and applications that benefit human health, environmental sustainability, and technological advancement. Moreover, the investigation of cutting-edge developments such as AI-driven nanoparticle design, medical nanorobotics, and green nanotechnology for sustainable development highlights the revolutionary potential of nanoparticles and opens the door to ground-breaking breakthroughs in a variety of sectors.

Author Contributions

The sole author conceived the study and designed the structure of the paper. She was responsible for the conceptualization, methodology, investigation, writing - the original draft, and writing - review editing.

Conflicts of Interest

The author declares that there is no conflict of interest regarding the publication of this paper.

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