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MINI REVIEW

Nanoparticles: A Risk for Humans and the Environment

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Abstract

Nanotechnology plays a major role in modern science and industry through the development of novel materials and advanced consumer products with unique physicochemical properties. Nanoparticles are increasingly utilized in medicine, electronics, agriculture, cosmetics, and industrial applications due to their enhanced functionality and efficiency. However, the widespread use of nanoparticles has also raised important concerns regarding their potential effects on human health and the environment. Because of their extremely small size, large surface area, and high reactivity, nanoparticles can interact with biological systems in ways that may lead to toxic effects in humans, animals, and ecosystems. This review summarizes the major characteristics of nanoparticles that contribute to their toxicity and discusses the primary routes of human exposure, including inhalation, ingestion, and dermal contact. In addition, the environmental impacts of nanoparticles on soil, water systems, plants, and microorganisms are highlighted. Since information regarding long-term exposure and safety remains limited, further toxicological investigations are necessary to better understand the short and long-term consequences of nanoparticle exposure. Finally, recent progress, existing limitations, and future challenges in nanoparticle safety research are briefly outlined.

Introduction

Interest in nanotechnology has been increasing over the last few decades, introducing materials belonging to unique classes ranging in size from 1 to 100 nm [1,2]. Nanoparticles (NPs) are distinguished by their three-dimensional size (NPs). Besides size, NPs can also be classified based on physical characteristics, including chemical composition and electrical charge [3]. At the nanoscale, materials often display distinctive physical, chemical, optical, electrical, and biological properties that differ substantially from their bulk counterparts [4]. These unique appearances arise predominantly from the increased surface area-to-volume ratio

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and quantum effects associated with nanosized materials. Scientists and researchers in the realm of biomedicine are using nanoparticles for numerous purposes, such as gene and drug delivery, diagnosis of unhealthy conditions, mapping of biomarkers, and targeted therapy for numerous cancer treatments [5]. Apart from the use of NPs in medicine, it is also being used in other areas such as agriculture, textile production, electronics, and some other industries. These days, we are struggling with the balance between the therapeutic use and toxicity of NPs, which is the core concern for researchers. Globally, the production and use of engineered NPs (ENPs) have increased over the last two decades due to their immense application in agriculture, medicine, cosmetics, and more in industrial products. In short, the nanomaterials required for use in these productions are increasing, and concerns are increasing in the scientific community due to persistence, bioavailability, and risk for both ecosystem and human health [6,7].

Nanoparticles (NPs) can be ranked into numerous categories, which include inorganic NPs (gold, silver, zinc oxide, titanium dioxide, and iron oxide NPs), carbon-based NPs (graphene, fullerenes, and carbon nanotubes), organic NPs (e.g., liposomes, dendrimers, and micelles), and composite NPs that combine multiple materials [8-10]. It is small and has a large reactive surface area. NPs have enriched catalytic activity, better mechanical strength, increased chemical reactivity, and distinctive optical and magnetic properties [11,12]. These features have led to their massive use in drug delivery systems, diagnostic imaging, antimicrobial coatings, cosmetics, food packaging, wastewater treatment, and advanced electronic devices [13,14]. The instant extension of nanotechnology has provided significant technological and economic benefits across numerous sectors [4].

Despite their various advantages, the increasing production and use of NPs have raised concerns regarding their possible impacts on human health and the environment [2,15]. Their small size enables them to penetrate biological membranes, enter cells and tissues, and interact with biomolecules such as proteins, DNA, and lipids [16]. Studies have exhibited that several NPs can induce oxidative stress, inflammation, DNA damage, apoptosis, and reduced cell viability, depending on their size, shape, chemical composition, surface charge, and exposure concentration [17]. Besides, NPs released into air, soil, and aquatic environments may accrue in ecosystems and affect microorganisms, plants, animals, and eventually human populations through different environmental exposure pathways [18,19]. Therefore, understanding the behavior, fate, and toxicity of NPs has become a critical area of research in nanotoxicology and environmental risk assessment [20].

Classification of Nanoparticles

Nanoparticles can be classified into several categories based on their chemical composition, structure, and physicochemical properties. Each class exhibits distinct characteristics that influence its applications, environmental behavior, and potential biological effects. The most important categories of engineered nanoparticles include metal NPs, metal oxide NPs, carbon nanotubes, quantum dots, and polymeric NPs, which are extensively utilized in industrial, environmental, and biomedical applications [4,21].

Metal NPs

Metal nanoparticles (MNPs) are nanoscale particles composed of pure metals such as silver (Ag), gold (Au), platinum (Pt), copper (Cu), and palladium (Pd) [22]. Heavy metals have a toxic impact on human health as well as on the environment [23-28]. These NPs hold exclusive optical, catalytic, electrical, and antimicrobial properties resulting from their

high surface-area-to-volume ratio and surface plasmon resonance effects [29]. Amongst them, silver NPs are widely used in medical devices, wound dressings, textiles, and food packaging because of their strong antimicrobial activity, whereas gold NPs have found applications in drug delivery, biosensing, diagnostic imaging, and cancer therapy [30]. Despite their beneficial applications, metal nanoparticles may induce oxidative stress, inflammation, and cytotoxicity when accumulated in biological systems, highlighting the importance of evaluating their safety for human and environmental health [3,31].

Metal oxide NPs

Metal oxide NPs constitute one of the most extensively produced classes of engineered nanomaterials and include Titanium Dioxide (TiO_2), Zinc Oxide (ZnO), Iron Oxide (Fe_3O_4), Cerium Oxide (CeO_2), and Silicon Dioxide (SiO_2) NPs [32,33]. These materials are commonly utilized in sunscreens, cosmetics, paints, sensors, catalysts, environmental remediation technologies, and biomedical applications. Their unique physicochemical properties, including photocatalytic activity, magnetic behavior, and UV-light absorption, make them highly valuable in industrial and medical sectors [34]. However, studies have demonstrated that some metal oxide NPs can generate reactive oxygen species (ROS), leading to oxidative stress, DNA damage, and adverse effects on aquatic organisms, plants, and mammalian cells [35,36]. Therefore, knowing their environmental fate and toxicity remains an important aspect of nanotoxicology research [37,38].

Carbon nanotubes

Carbon nanotubes (CNTs) are cylindrical nanostructures composed of rolled graphene sheets and are categorized as single-walled carbon nanotubes (SWCNTs) or multi-walled carbon nanotubes (MWCNTs) [39]. CNTs exhibit exceptional mechanical strength, thermal conductivity, electrical conductivity, and chemical stability, making them attractive for applications in electronics, energy storage, sensors, environmental remediation, and biomedical engineering [40,41]. However, due to their high aspect ratio and fibrous structure, concerns have emerged regarding their potential toxicity. Research has shown that certain CNTs may induce pulmonary inflammation, oxidative stress, fibrosis, and genotoxic effects following inhalation exposure, drawing comparisons to asbestos-like pathogenicity under specific conditions [42,43]. Therefore, careful assessment of exposure risks is mandatory before extensive commercialization and biomedical use [37,44].

Quantum dots

Quantum dots (QDs) are semiconductor NPs generally ranging from 2 to 10 nm in diameter that possess unique optical and electronic properties due to quantum confinement effects [45]. Common quantum dots include Cadmium Selenide (CdSe), Cadmium Telluride (CdTe), and Indium Phosphide (InP) nanoparticles [46]. These materials displayed size-dependent fluorescence emission, making them valuable tools for biological imaging, biosensors, diagnostics, optoelectronics, and photovoltaic devices. Although they have technological advantages, concerns exist regarding the potential release of toxic heavy metals such as cadmium and selenium from quantum dots, which may cause oxidative stress, cellular damage, and environmental contamination [47]. Surface coatings and encapsulation approaches are therefore regularly employed to reduce toxicity and improve biocompatibility [3,48].

Polymeric NPs

Polymeric NPs are colloidal systems composed of natural or synthetic polymers such as chitosan, Polylactic Acid (PLA), Polylactic-Co-Glycolic Acid (PLGA), Polyethylene Glycol

(PEG), and Polycaprolactone (PCL) [49,50]. These NPs are broadly used in pharmaceutical and biomedical applications because they can encapsulate drugs, proteins, genes, and vaccines while enabling controlled release and targeted delivery [51]. Compared with many inorganic NPs, polymeric NPs largely demonstrate superior biocompatibility, biodegradability, and reduced toxicity [52]. However, factors such as particle size, surface charge, polymer composition, and degradation products can influence their biological interactions and safety profiles. As their use in nanomedicine continues to grow, complete evaluations of long-term toxicity and environmental impacts remain necessary [53,54].

Toxicity of NPs

The physicochemical properties of NPs are among the most important determinants of their biological activity and toxicity. NPs are composed of metals, and metals have huge toxicity on the environment [55-57]. Unlike bulk materials, NPs possess a substantially larger surface area-to-volume ratio, which enhances their chemical reactivity and interactions with biological systems [58]. Key properties persuading NPs' toxicity include particle size, shape, surface area, chemical composition, crystallinity, solubility, and surface charge [59,60]. Smaller NPs generally exhibit greater cellular uptake and tissue penetration, assisting them to cross biological barriers and accumulate in various organs. Besides, their increased surface reactivity may promote the generation of Reactive Oxygen Species (ROS), leading to oxidative stress, inflammation, and cellular damage [61]. Therefore, NPs with similar chemical compositions may show markedly different toxicological profiles depending on their physicochemical characteristics [3,44,62,63].

In addition to intrinsic properties, interactions between NPs and biological fluids can significantly alter their behavior and toxicity. Upon entering biological environments, NPs rapidly adsorb proteins, lipids, and other biomolecules, forming a "biomolecular corona" that determines their biological identity and cellular interactions [62,64]. Surface charge and surface functionalization strongly influence NPs stability, biodistribution, cellular uptake, and immune responses [65]. Positively charged NPs often present improved cellular internalization but may also induce greater membrane damage and cytotoxicity than neutral or negatively charged particles. Similarly, aggregation state, dissolution rate, and surface coatings can affect NPs persistence, bioavailability, and environmental fate [66,67]. Therefore, understanding how physicochemical properties manage NPs-biological interactions is essential for accurate risk assessment and the development of safer nanomaterials for industrial and biomedical applications [20,68].

NPs exposure routes in human

Human exposure to NPs can occur through multiple pathways depending on their source, application, and environmental distribution. As the use of engineered NPs continues to increase in medicine, consumer products, food packaging, cosmetics, and industrial processes, the likelihood of human exposure has also risen markedly. The primary routes of NPs exposure include inhalation, ingestion, dermal contact, and injection [69]. Each exposure pathway influences the absorption, biodistribution, accumulation, and toxicity of NPs in different organs and tissues, thereby affecting their potential health risks [70].

Inhalation

Inhalation is considered one of the most substantial routes of NPs exposure, particularly in occupational and industrial settings [71,72]. Airborne NPs can enter the respiratory tract and deposit in different regions of the lungs, depending on their size and physicochemical

properties [73]. Due to their small size, NPs can evade normal clearance mechanisms, penetrate deep into the alveolar region, and then translocate into the bloodstream [74]. Several studies have reported that inhaled NPs may induce oxidative stress, pulmonary inflammation, fibrosis, and respiratory dysfunction [75]. In some cases, NPs have also been shown to migrate from the lungs to secondary organs, including the liver, kidneys, and brain, potentially causing systemic toxic effects [76].

Ingestion

Ingestion represents another important route of NPs exposure and may occur through contaminated food, drinking water, pharmaceuticals, food additives, and the swallowing of inhaled particles cleared from the respiratory tract [70,76]. Following oral intake, NPs interact with the gastrointestinal environment, where they may be absorbed through intestinal epithelial cells and enter systemic circulation. Although an extensive fraction of ingested NPs may be excreted, some particles can accumulate in organs such as the liver, spleen, and kidneys [77,78]. Experimental studies have exhibited that prolonged exposure may disrupt gut microbiota, induce oxidative stress, and contribute to gastrointestinal and systemic toxicity, depending on the NPs composition and dose [79].

Dermal exposure

Dermal exposure normally occurs through the use of NPs-containing cosmetics, sunscreens, personal care products, textiles, and occupational handling of nanomaterials [80,81]. The skin acts as an effective barrier against many substances. However, NPs may penetrate through hair follicles, sweat glands, or damaged skin [82]. Factors such as particle size, surface charge, concentration, and exposure duration affect the degree of skin penetration [83]. While intact skin generally confines NPs' absorption, some studies have reported local inflammatory responses, oxidative stress, and cellular damage following prolonged exposure, stressing the need for continued evaluation of NPs safety in consumer products [83].

Injection

Injection is a deliberate route of NPs administration that is broadly used in nanomedicine for targeted drug delivery, diagnostic imaging, gene therapy, and vaccine development [84]. Unlike environmental exposure routes, injected NPs bypass many physiological barriers and directly enter systemic circulation. Subsequently, their biodistribution depends largely on particle size, surface properties, and interactions with plasma proteins. While NPs-based therapeutics offer significant clinical advantages, concerns remain regarding their accumulation in organs such as the liver, spleen, lungs, and kidneys, where they may induce inflammation, immune responses, or long-term toxicity [85]. Therefore, comprehensive toxicological evaluation remains essential for the safe development of NPs-based medical applications [86].

Mechanisms of NPs toxicity

There is a series of molecular and cellular mechanisms that have an adverse effect on biological systems due to NPs' toxicity. These NPs interact with cellular membranes, proteins, nucleic acids, and organelles due to their small size and surface-to-volume ratio, and as a result, it leads to physiological disturbances [76]. Oxidative stress, DNA damage, inflammation, and apoptosis are among the most widely recognized mechanisms induced by the toxicity of NPs [17,87]. Most of the time, these processes often happen concurrently and contribute to the development of tissue injury, organ dysfunction, and chronic diseases due to exposure to NPs. Sirtuin 1 (SIRT1), a NAD^+-dependent deacetylase, has emerged as an important regulator of cellular responses to oxidative stress and inflammation. SIRT1 exerts cytoprotective effects by activating

antioxidant pathways, including the Nrf2 signaling pathway, while suppressing NF-κB-mediated inflammatory responses and apoptosis. Increasing evidence suggests that exposure to certain engineered nanoparticles can downregulate SIRT1 expression or activity, thereby enhancing Reactive Oxygen Species (ROS) generation, inflammatory cytokine production, and DNA damage. Therefore, modulation of SIRT1 signaling may represent a promising therapeutic strategy for mitigating nanoparticle-induced toxicity [88,89]. All the toxicity mechanisms in cells by NPs are shown in figure 1.

Oxidative stress

The underlying central mechanism due to NPs' toxicity is oxidative stress [61]. Most types of NPs exacerbate the excessive production of ROS, including hydrogen peroxide, hydroxyl radicals, and superoxide. Cells have an antioxidant defense capacity for their own protection. When ROS production inside the cell increases due to NP toxicity, oxidative stress occurs. This oxidative stress inside cells causes mitochondrial dysfunction, lipid peroxidation, protein oxidation, and disruption of cellular signaling pathways [90,91]. It has been reported that metal (silver NPs) and metal oxide NPs (zinc oxide and titanium dioxide) induced ROS production due to the high activity of their surfaces [92]. Continuing oxidative stress can consequently initiate inflammation, DNA damage, and cell death, making it a key initiating event in nanotoxicity [17].

DNA damage

NPs may induce genotoxic effects either directly through interactions with DNA or indirectly through oxidative stress-mediated mechanisms [93]. Excessive ROS production can cause DNA strand breaks, base modifications, chromosomal abnormalities, and impaired DNA repair processes [94]. Numerous studies have reported that exposure to metal NPs, carbon nanotubes, and quantum dots can result in genomic instability and mutagenic effects [95,96]. DNA damage is of actual concern because constant genetic alterations may contribute to carcinogenesis, reproductive toxicity, and developmental abnormalities [97]. Recent investigations using genomics and omics-based approaches have further demonstrated that NPs exposure can alter the expression of genes

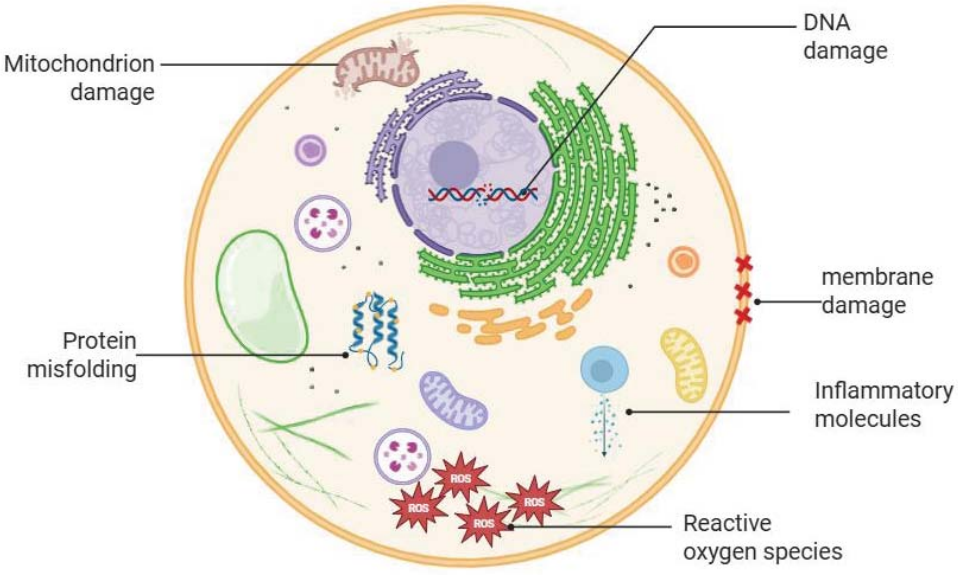

Figure 1 NPs induced toxicity mechanism in the cell.

involved in cell cycle regulation, DNA repair, and stress-response pathways [98].

2.15. Inflammation

Inflammatory responses are commonly observed following NPs exposure and are often initiated by oxidative stress and cellular injury. NPs can activate immune cells such as macrophages and neutrophils, leading to the release of pro-inflammatory cytokines, including tumor necrosis factor-alpha, interleukin-1β, and interleukin-6 [99]. Activation of signaling pathways such as NF-κB and MAPK further amplifies inflammatory responses. Chronic inflammation resulting from prolonged NPs exposure has been associated with respiratory disorders, cardiovascular diseases, neurotoxicity, and tissue fibrosis [100]. Consequently, inflammation is considered a critical mediator linking NPs exposure to long-term adverse health outcomes.

Apoptosis

Apoptosis is a programmed cell death, representing another major mechanism of NPs-induced toxicity [101]. Cellular stress caused by reactive oxygen species generation, mitochondrial dysfunction, DNA damage, and inflammatory signaling can activate intrinsic and extrinsic apoptotic pathways. This process is characterized by chromatin condensation, DNA fragmentation, activation of caspases, and eventual cell death. Numerous studies have exhibited that NPs can induce apoptosis in a variety of cell types, including epithelial cells, hepatocytes, neurons, and immune cells [102]. While apoptosis serves as a protective mechanism to eliminate damaged cells, excessive or uncontrolled apoptosis may contribute to tissue degeneration and organ dysfunction following chronic NPs exposure [103].

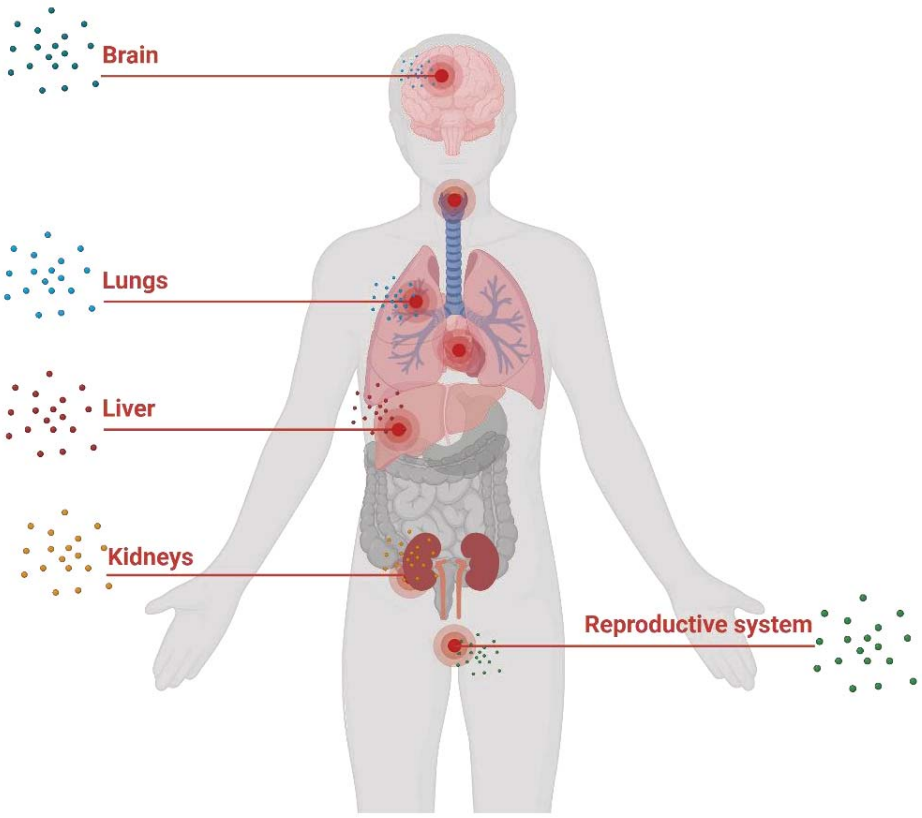

Figure 2 Different organs in humans affected by NPs' toxicity.

Organ-specific toxicity of NPs

Following exposure, NPs can enter systemic circulation and accumulate in various organs depending on their size, surface chemistry, charge, and biodistribution patterns [104]. Due to their nanoscale dimensions, these particles can cross biological barriers that are normally impermeable to larger materials, resulting in tissue-specific toxic effects. Accumulating evidence indicates that prolonged or high-dose exposure to certain NPs may adversely affect major organs, including the lungs, liver, kidneys, brain, and reproductive system [105]. The underlying mechanisms often involve oxidative stress, inflammation, mitochondrial dysfunction, DNA damage, and apoptosis, which collectively contribute to impaired organ function and disease development. Lungs, liver, kidneys, brain, and reproductive organs are mainly affected by NPs (Figure 2).

Lung toxicity

The lungs are the primary target organ for airborne NPs because inhalation is one of the most common routes of exposure. NPs deposited within the respiratory tract can penetrate deep into the alveolar region, where they interact with epithelial cells and alveolar macrophages [106]. Numerous studies have demonstrated that NPs exposure can induce oxidative stress, inflammatory responses, pulmonary fibrosis, and impaired respiratory function. Carbon nanotubes, titanium dioxide NPs, and metal oxide NPs have been particularly associated with lung inflammation and chronic respiratory disorders [107]. Persistent exposure may further contribute to tissue remodeling and fibrosis, increasing the risk of long-term pulmonary diseases [108].

Liver toxicity

The liver is one of the major organs involved in NPs accumulation because it plays a central role in metabolism, detoxification, and clearance of foreign substances. Following systemic absorption, NPs are frequently sequestered by Kupffer cells and hepatocytes, leading to their accumulation within hepatic tissues [109]. Studies have reported that exposure to silver, gold, zinc oxide, and silica NPs may result in oxidative stress, inflammatory responses, mitochondrial dysfunction, and hepatocellular injury [110]. Histopathological changes, including hepatocyte degeneration and altered liver enzyme activities, have also been observed in experimental models, suggesting potential impairment of liver function following prolonged exposure [111].

Kidney toxicity

The kidneys are highly susceptible to NPs-induced toxicity because they serve as a major route for the filtration and excretion of circulating NPs. NPs can accumulate within renal tissues, particularly in the glomeruli and proximal tubules, where they may induce oxidative stress, inflammation, and cellular injury [112]. Experimental studies have shown that exposure to metal and metal oxide NPs can alter renal function, increase biomarkers of kidney damage, and cause structural abnormalities within kidney tissues [113]. The extent of nephrotoxicity is influenced by NPs size, dose, surface characteristics, and duration of exposure [114].

Brain toxicity

One of the most concerning aspects of NPs exposure is their ability to cross the blood-brain barrier and accumulate within neural tissues. NPs may reach the brain either through systemic circulation or directly via the olfactory nerve following inhalation [115]. Once inside the central nervous system, they can induce oxidative stress, neuroinflammation, mitochondrial dysfunction, and neuronal damage. Several studies have linked NPs exposure to alterations in neurotransmitter regulation, cognitive impairment, and neurodegenerative processes

[116,117]. Although the long-term neurological consequences remain incompletely understood, increasing evidence suggests that NPs-induced neurotoxicity may represent a significant public health concern.

Reproductive toxicity

Recent studies have highlighted the potential effects of NPs on reproductive health in both males and females [118]. Due to their small size, NPs can cross biological barriers such as the blood-testis barrier and placental barrier, thereby affecting reproductive tissues and fetal development [119]. Exposure to certain NPs has been associated with reduced sperm quality, altered hormone levels, ovarian dysfunction, embryotoxicity, and developmental abnormalities [118]. Oxidative stress and inflammation appear to be the primary mechanisms underlying reproductive toxicity [120]. Given the increasing use of NPs in consumer products and medical applications, further investigations are required to fully understand their long-term effects on fertility and reproductive outcomes.

Environmental fate and transport of NPs

The environmental fate and transport of NPs are governed by their physicochemical properties, including particle size, shape, surface charge, chemical composition, solubility, and surface coatings, as well as by environmental factors such as pH, ionic strength, temperature, and organic matter content. Following their release from industrial processes, consumer products, agricultural applications, wastewater treatment plants, and medical sources, NPs can enter air, soil, sediments, and aquatic environments [121]. Once released, NPs undergo various transformation processes, including aggregation, agglomeration, dissolution, sedimentation, oxidation, and adsorption onto natural organic matter. These transformations significantly influence their mobility, persistence, bioavailability, and toxicity in environmental systems. Consequently, the environmental behavior of NPs is dynamic and often differs substantially from that observed under laboratory conditions [122-124].

In aquatic environments, NPs may remain suspended in the water column, settle into

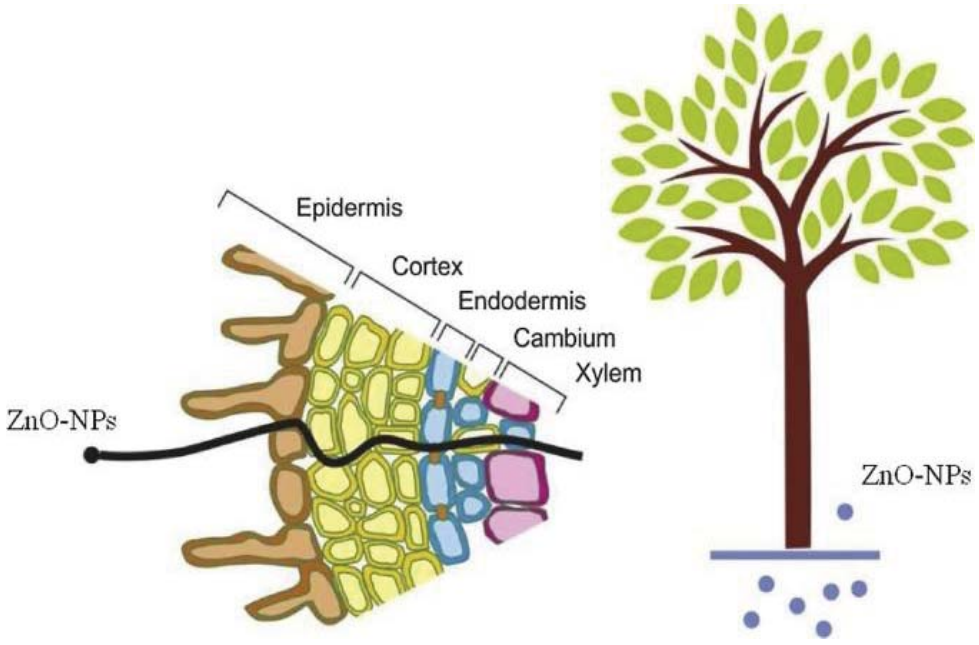

Figure 3 Translocation of metal NPs in plants through the root system [138].

sediments, or interact with microorganisms and aquatic organisms, depending on environmental conditions and particle characteristics [125]. Similarly, in soil systems, NPs can adsorb onto mineral surfaces, migrate through soil pores, accumulate within the rhizosphere, and potentially enter terrestrial food webs [126]. The interaction of NPs with natural organic matter often alters their stability and transport behavior, thereby affecting their environmental distribution and biological uptake. Increasing evidence suggests that engineered NPs can be transferred among environmental compartments through water flow, atmospheric deposition, and trophic interactions, raising concerns regarding their long-term ecological impacts [127]. However, substantial knowledge gaps remain regarding the environmental concentrations, transformation products, and long-term fate of NPs under realistic environmental conditions, emphasizing the need for further research and improved risk assessment frameworks.

Effects of NPs on Soil

The increasing release of engineered NPs into terrestrial ecosystems has raised concerns regarding their impact on soil quality and ecological functions [128]. Once introduced into soil through agricultural amendments, wastewater sludge, industrial emissions, or product degradation, NPs can interact with soil minerals, organic matter, and resident microorganisms [129]. These interactions may alter soil physicochemical properties, nutrient cycling, and enzyme activities that are essential for maintaining soil fertility. Several studies have reported that metal and metal oxide NPs, particularly silver, zinc oxide, and titanium dioxide NPs, can disrupt microbial-mediated processes such as nitrogen fixation, nitrification, and organic matter decomposition [130]. Long-

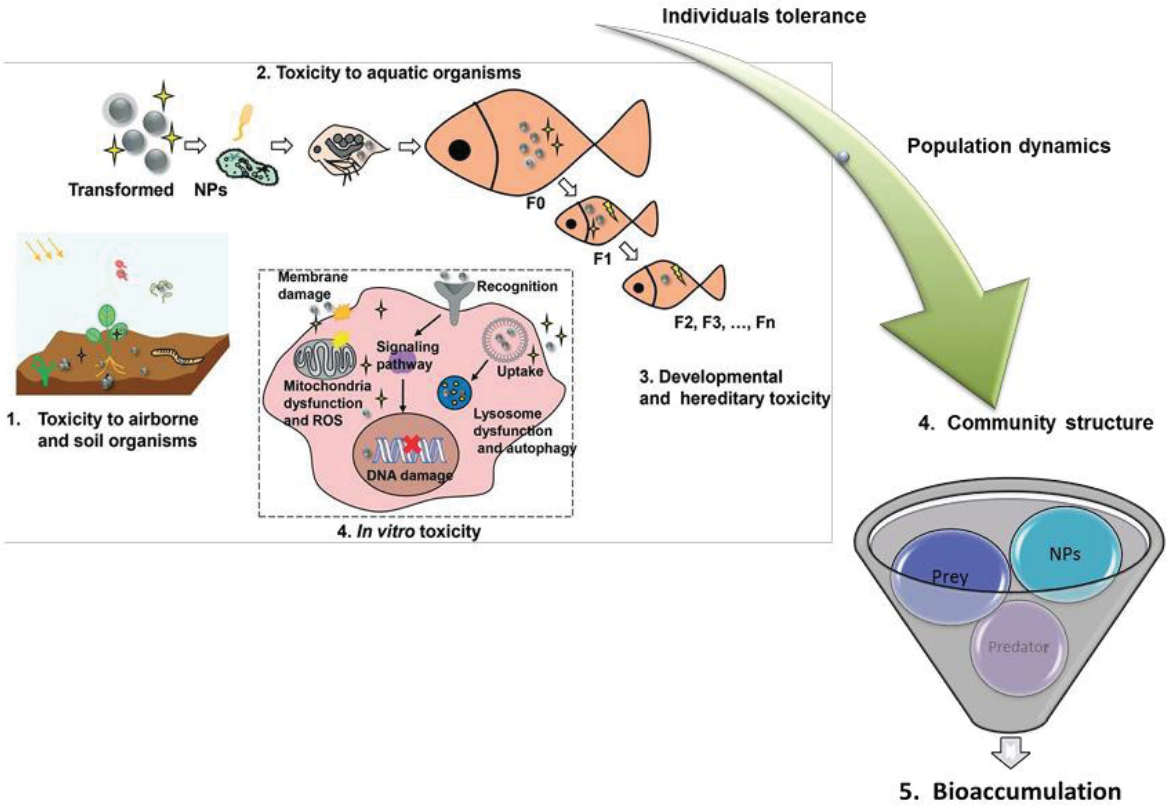

Figure 4 The adverse effects of NPs on aquatic community structure and bioaccumulation are summarized [142].

term accumulation may therefore influence soil productivity and ecosystem sustainability, although the extent of these effects depends on NPs type, concentration, and environmental conditions [131].

Effects of NPs on plants

Plants are continuously exposed to NPs present in soil, water, and air, making them important indicators of environmental NPs contamination. NPs can be absorbed by plant roots and translocated to stems, leaves, and reproductive tissues, where they may affect physiological and biochemical processes [132,133]. While certain NPs may enhance seed germination, nutrient uptake, and plant growth at low concentrations [134]. Excessive exposure can induce oxidative stress, inhibit photosynthesis, disrupt nutrient homeostasis, and impair growth and development [135]. Zinc oxide, silver, and titanium dioxide NPs have been shown to cause alterations in chlorophyll content, root morphology, and antioxidant enzyme activities [136] (Figure 3). Furthermore, NPs accumulation in edible plant tissues raises concerns regarding their transfer through food chains and potential risks to human health [137].

Effects of NPs on aquatic organisms

Aquatic ecosystems are considered major sinks for engineered NPs because many NPs eventually enter rivers, lakes, estuaries, and oceans through wastewater discharge, runoff, and industrial effluents. In aquatic environments, NPs can interact with algae, zooplankton, invertebrates, fish, and other organisms [139]. Numerous studies have demonstrated that NPs may induce oxidative stress, membrane damage, developmental abnormalities, behavioral alterations, and reduced reproductive success in aquatic species. Metal-based NPs, particularly silver and zinc oxide NPs, have been reported to impair photosynthesis in algae, disrupt gill function in fish, and alter energy metabolism in aquatic organisms [140]. Because NPs may accumulate and biomagnify through aquatic food webs, their ecological effects may extend beyond individual species and influence entire ecosystem functions [141]. The adverse effects of NPs on the aquatic system are shown in figure 4.

Effects of NPs on microorganisms

Microorganisms play fundamental roles in nutrient cycling, organic matter decomposition, pollutant degradation, and ecosystem stability; therefore, disturbances to microbial communities can have far-reaching ecological consequences. NPs possess strong antimicrobial properties, which are beneficial in medical and industrial applications but may adversely affect non-target environmental microorganisms [143]. Exposure to NPs can damage microbial cell membranes, generate reactive oxygen species, interfere with enzymatic activities, and disrupt DNA replication [144]. Silver NPs are particularly recognized for their potent antimicrobial activity and have been shown to reduce microbial diversity and alter community composition in both soil and aquatic environments [145]. Changes in microbial abundance and function may subsequently affect biogeochemical cycles, ecosystem productivity, and environmental resilience, highlighting the importance of evaluating NPs impacts on microbial ecosystems [146].

Regulations and risk assessment

The rapid expansion of nanotechnology has created an urgent need for effective regulatory frameworks and risk assessment strategies to ensure the safe production, use, and disposal of NPs [147]. Traditional chemical risk assessment approaches are often inadequate for nanomaterials because NPs possess unique physicochemical properties that influence their behavior, bioavailability, and toxicity in ways that differ from conventional bulk materials. Consequently, regulatory agencies such as the United States Environmental Protection

Agency, Food and Drug Administration, European Chemicals Agency, and Organization for Economic Co-operation and Development have developed guidance documents aimed at evaluating the safety of engineered nanomaterials [148]. Current risk assessment frameworks generally involve hazard identification, exposure assessment, dose-response evaluation, and risk characterization. However, challenges remain due to limited long-term toxicity data, difficulties in measuring environmental NPs concentrations, and the lack of standardized testing protocols. Recent advances in computational toxicology, predictive modeling, high-throughput screening, and omics-based approaches have improved the assessment of NPs risks and may facilitate the development of safer and more sustainable nanomaterials. Furthermore, the concept of "safe-by-design" nanotechnology has emerged as a promising strategy to minimize adverse effects while maintaining the desired functionality of nanomaterials [149,150].

Future challenges and research gaps

Significant progress is being made in nanotoxicology research, yet a knowledge gap remains in the comprehensive evaluation of NP safety. Current studies continue to be conducted under controlled laboratory conditions, using relatively high concentrations of NPs for exposure. These conditions do not accurately reflect real-world environmental and human exposure settings. Long-term and chronic exposure studies on bioaccumulation, persistence, and transgenerational effects of NPs in humans and ecosystems remain limited. Furthermore, the complex interactions between NPs and biological systems, including the formation of transformation products, biomolecular coronas, and interactions with co-existing pollutants, are not yet fully understood. Another major challenge is the lack of standardized methodologies for toxicity testing, environmental monitoring, and data interpretation, which complicates comparisons among studies. Future research should prioritize environmentally relevant exposure conditions, long-term ecological assessments, advanced omics technologies, artificial intelligence-based predictive models, and integrated risk assessment frameworks. In addition, greater efforts are needed to establish standardized and internationally accepted protocols for nanoparticle characterization and toxicity testing to improve the reproducibility, reliability, and comparability of results across laboratories. Future studies should also emphasize the development of safer-by-design nanoparticles by optimizing physicochemical properties, such as particle size, surface chemistry, coating, and composition, to minimize toxicity while maintaining their intended functionality. Furthermore, multidisciplinary collaborations among toxicologists, materials scientists, environmental researchers, and regulatory agencies will be essential for translating laboratory findings into safer and more sustainable nanotechnology applications. Strengthening international collaboration and harmonizing regulatory guidelines will also be essential to ensure the responsible development and sustainable application of nanotechnology while minimizing risks to human health and the environment.

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