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Toxicological Implications of Emerging Nanomaterials on Human Health and Ecological Systems: A Comprehensive Review

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ABSTRACT

Nanotechnology has advanced at a very high rate leading to high rates of the production and application of many nanomaterials in medicine, industry, agriculture, and in the environmental systems. Their unique physicochemical characteristics have brought forth transformative benefits albeit with their own grave concerns as far as the unintended toxicological effects are involved. Nevertheless, despite the ever-growing body of information, there remains some limited knowledge that has been gathered concerning the risks of the newly emerging nanomaterials on human health and the ecological systems. This review will give a synthesis of what has been published on the toxicological pathways of nanomaterials with special attention to major sources of exposure such as inhalation, ingestion, dermal penetration, and systemic distribution. Of specific interest is the oxidative stress, genotoxicity, immunotoxicity, and bioaccumulation routes, and ecological effects like soil pollution, aquatic toxicity, and trophic transfer. In addition, the new systems of risk assessment and regulation are singled out in the article, yet it is observed that there are no standardized testing and monitoring, which should be done in long-term perspective. Providing biomedical and environmental toxicology, the review will provide an independent opinion on the effects of the nanomaterial exposures and the need of safer design programs, predictive programs of the toxicology and environment-friendly nanomaterial substitutes.

1. INTRODUCTION

Nanotechnology has emerged as one of the most radical aspects of the 21st century science that has affected the innovations in the medical sector, electronic devices, energy, farming as well as environmental design. The high surface-area-to-volume ratios, switchable reactivity, and enhanced mechanical and optical properties of nanomaterials have also added to their rapid development due to the exceptional physicochemical characteristics of the materials, such as metallic nanoparticles and carbon-based nanostructures in addition to novel two-dimensional materials. These attributes enable them to perform actions on bulk materials that could not be previously done and hence nanotechnology has become the front runners in science and industry. The toxicological considerations of the new nanomaterials in general cut across the systems of the human health and the ecology in itself, and this involves the route of exposure, the effects of the presence of the nanomaterial to the cells and the environment. This holistic has been provided in Figure 1 which is an overview of the two-fold effects of nanomaterials in two biological and ecological systems.

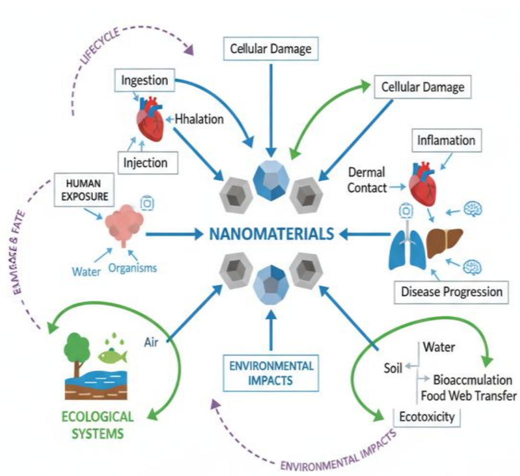

Fig. 1. Integrated toxicological implications of nanomaterials on human health and ecological systems.

Schematic showing how nanomaterials enter through multiple exposure routes, induce cellular and systemic effects in humans, and simultaneously impact ecological systems through soil, water, and air pathways, leading to bioaccumulation and food web transfer.

However, the same features that precondition the popularity of nanomaterials also raise serious concerns about the potential adverse effect of nano materials on the biological systems and ecosystems. Their nanoscale sizes allow them to penetrate biological barriers, also engage cellular components and exist in tissues and often provoke oxidative stress, genotoxicity or immune response. Similarly, nanomaterials remain in the environment once in the environment where they tend to be persistent, bioaccumulative, and disruptive to soil, aquatic and microbial ecosystems and eventually disrupt ecological balance and biodiversity. In this aspect, the toxicological analysis will play a very crucial role in ensuring that the benefits of nanotechnology are not to the detriment of human and environmental health. It necessitates the discursive understanding of exposure paths, affliction pathophysiology, and ecological effects in the long-term so as to establish effective safety actions and regulatory actions. The review is a synthesis of the available literature of the toxicological importance of novel nanomaterials, in which two distinct fields of interest of this material are involved, that is, the hazards to human health and the ecological impact. Combining the knowledge in the field of biomedical and environmental science, the review reveals the important processes of toxicity and notes gaps in existing risk assessment models and outlines new approaches to the safer design of nanomaterials and sustainable use.

2. Classes of Emerging Nanomaterials

Nanotechnology has currently experienced tremendous growth to produce a wide range of nanomaterials with different structural, chemical or functional characteristics. Such materials can be broadly described into metallic, carbon-based, polymeric/hybrid and emerging two-dimensional (2D) nanomaterials that have demonstrated promise in a large way yet present unique toxicological issues. Table 1 provides a comparative overview of the key classes of emerging nanomaterials, their common uses, most important advantages and their toxicological issues.

2.1 Metallic Nanoparticles

Metallic nanoparticles can be considered one of the most active studied because of the numerous applications in medicine, consumer products, and environmental technologies. Ag and Au are two types of nanoparticles that are commonly used in antimicrobial coatings, biosensing, and drug delivery systems because of their biocompatibility and surface plasmon resonance [1], [2]. The reason is that titanium dioxide (TiO2) and zinc oxide (ZnO) nanoparticles are used in sunscreens, food packaging, and photocatalytic application due to the absorption of UV radiation and oxidative reactivity [3], [4]. Their capacity to produce reactive oxygen species (ROS) however, is a cause of concern on cytotoxicity, DNA damage, and ecological persistence [5].

2.2 Carbon-Based Nanomaterials

Another essential category is carbon nanomaterials, i.e., graphene, carbon nanotubes (CNTs) and fullerenes. Graphene and its derivatives have been appreciated because of their high electrical conductivity, mechanical and surface properties, which include, among others, energy storage, biosensing, and biomedical engineering [6]. The high aspect ratios of CNTs are used in drug delivery, tissue engineering and electronic devices [7], whereas fullerenes have the antioxidant property that can be utilized in biomedical and environmental purposes [8]. In spite of these benefits, the use of carbon-based nanomaterial can cause pulmonary inflammation, fibrosis, or ecotoxicity because of their structural stability and bioaccumulation capabilities [9].

2.3 Polymeric and Hybrid Nanomaterials

The most promising biomedical application of polymeric nanomaterials such as dendrimers, nanogels and polymeric micelles is their tunable surface chemistry, control over release function and relatively low inherent toxicity [10]. Multifunctionality Hybrid nanomaterials, which can incorporate metallic, ceramic or polymeric materials, can be multifunctional as they incorporate complementary properties into one platform. An example is polymer-coated metal nanoparticles, which improve stability and biocompatibility whilst inorganic-organic hybrids can be used in the fields of catalysis, imaging and therapeutic delivery [11]. The degradation byproducts, surface functionalization, as well as long-term environmental accumulation of this class are toxicological issues of concern [12].

2.4 Novel Two-Dimensional (2D) Nanomaterials

In addition to graphene, a novel product of 2D nanomaterials is under development, including MXenes, molybdenum disulfide (MoS_2), and hexagonal boron nitride (h-BN). These stratified materials have extraordinary electronic, optical and catalytic characteristics and can be used in energy storage, optoelectronics as well as nextgeneration biomedical equipment [13]. Their extremely thin geometry and strong reactivity, nevertheless, pose the problem of cellular uptake, membrane perturbation, and longevity in the aquatic and terrestrial environment [14]. Since they are new, there is a lack of extensive toxicological information and a sense of urgency of systematic research [15], [16]. The combination of all these different categories of nanomaterials is the technological potential of nanotechnology, as well as complex toxicology challenges. Knowledge of their physicochemical diversity is fundamental to understanding much of their interactions with biological systems and ecosystems, and is the foundation of risk assessment and regulation approaches.

Table 1. Comparative overview of emerging nanomaterial classes, their applications, benefits, and toxicological concerns.

Nanomaterial Class	Typical Applications	Key Benefits	Reported Toxicological Concerns
Metallic nanoparticles (Ag, Au, TiO_2, ZnO, Fe_3O_4)	Antimicrobial coatings, biosensors, drug delivery, sunscreens, food packaging, catalysis	High surface reactivity, antimicrobial activity, optical/electrical tunability, cost-effective synthesis	ROS generation, cytotoxicity, DNA damage, organ accumulation, ecological persistence
Carbon-based nanomaterials (graphene, CNTs, fullerenes, carbon dots)	Energy storage, drug delivery, tissue engineering, imaging, sensors, electronics	Exceptional electrical conductivity, mechanical strength, surface functionalization, antioxidant properties (fullerenes)	Pulmonary inflammation, fibrosis, immune response activation, bioaccumulation, ecotoxicity
Polymeric & hybrid nanomaterials (dendrimers, nanogels, polymer–metal hybrids, micelles)	Drug delivery, gene therapy, imaging, catalysis, packaging	Biodegradability, controlled release, biocompatibility, multifunctionality, stability	Surface modification–induced toxicity, degradation byproducts, long-term environmental accumulation
Novel 2D nanomaterials (MXenes, MoS_2, h-BN, black phosphorus)	Energy storage, optoelectronics, photothermal therapy, biosensors, catalysis	High electronic/optical tunability, large surface area, novel catalytic and photonic properties	Membrane disruption, cellular uptake toxicity, oxidative stress, limited long-term toxicological data

3. Human Health Toxicological Implications

3.1 Exposure Routes

Nanomaterials are mainly exposed to humans in the form of inhalation, ingestion, dermal contact, and systemic circulation. The most important route is the inhalation one, because the airborne nanoparticles may reach deep into the alveolar areas of the lungs, be translocated to the bloodstream, and deposited in the secondary organs. Due to contaminated food, water or nanomaterial containing food additives, ingestion happens when particles come into contact with the gastrointestinal tract and microbiota. Exposure through dermal routes comes through cosmetics, textiles and medical devices and some nanomaterials have the potential to enter the systemic circulation through the stratum corneum. The systemic exposure in addition may occur due to medical applications like intravenous nanocarriers, which permits a direct interaction with the components of blood and organ systems. There are several ways in which nanoparticles may gain access into the human body, which are inhalation, ingestion, contacting with the skin, or spreading to the blood (Fig. 2). It is the exposure routes that dictate the biodistribution and the toxicological consequences that are ultimately experienced in the different organ systems.

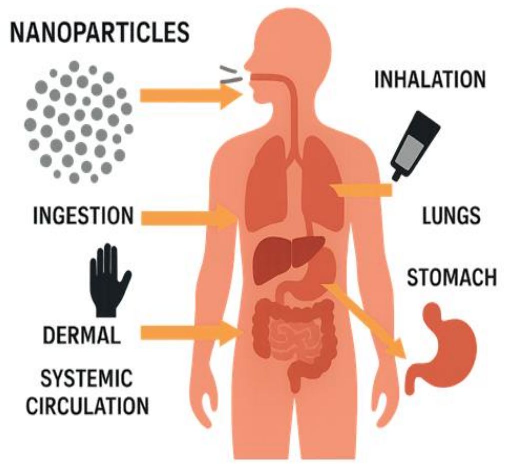

Fig. 2. Exposure routes of nanoparticles in the human body.

Schematic illustration showing the primary pathways of nanoparticle entry, including inhalation, ingestion, dermal penetration, and subsequent systemic circulation to target organs such as the lungs, stomach, liver, and intestines.
-Figure 1 was designed by the authors using original vector illustrations for academic and educational purposes.

3.2 Oxidative Stress and ROS Generation

One of the main ways of nanomaterial-induced toxicity is oxidative stress that is associated with excessive production of reactive oxygen species (ROS). The use of metallic nanoparticles like TiO_2 and ZnO is not new in catalyzing the generation of ROS in physiological environments and breaking the redox homeostasis. High concentration of ROS may result in the destruction of cellular membranes, proteins and organelles that cause apoptosis or necrosis. The production of ROS and antioxidants defense imbalance also causes the dysfunction of the mitochondrion, which is one of the major causes of cytotoxicity. Research has indicated that the toxicity of nanoparticles is dose and size-dependent, whereby smaller nanoparticles have a stronger toxic effect because of its increased surface reactivity. One of the most significant processes of nanomaterial-generated toxicity is oxidative stress which is mainly initiated by a big production of reactive oxygen species (ROS). This imbalance will cause damage to the DNA, immune dysregulation, and chronic inflammation (Fig. 3).

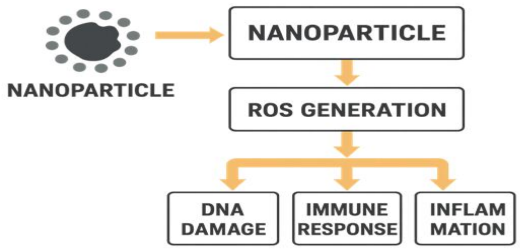

Fig. 3. Mechanistic pathways of nanomaterial-induced toxicity.

Schematic showing how nanoparticle exposure leads to reactive oxygen species (ROS) generation, resulting in oxidative stress and downstream effects such as DNA damage, immune responses, and inflammation.

3.3 DNA Damage and Genotoxicity

Nanomaterials may have a direct or indirect interaction with genetic material, leading to DNA strand breaks, chromosomal aberration, and mutations. An example of these is that silver nanoparticles have been shown to gain access to the nucleus leading to structural DNA damage whereas CNTs can physically contact chromosome structures during mitosis. Oxidative DNA lesions that occur due to the presence of ROS tend to have indirect genotoxic effects, and damage replication fidelity and repair. This type of damage is worrying regarding the carcinogenesis and hereditary mutation and genotoxicity is one of the most significant endpoints in nanotoxicology.

3.4 Immunotoxicity and Inflammation

Nanomaterials have the ability to affect immune responses in a great way by interacting with immune cells in macrophages, dendritic cells, and lymphocytes. Among the effects is the discharge of pro-inflammatory cytokines, which is often elicited by the identification of non-self nanoparticles. The outcome of chronic or excessive inflammation has the potential of being tissue damage, fibrosis, or autoimmune-like. Using the example of CNTs, the granuloma of the lungs was proven to be caused by this type of nanoparticles, and on the other hand, TiO_2 nanoparticles triggered macrophage and cytokine secretion. On the other hand, there are other nanomaterials that can suppress the immune system and this will paralyze the host defense. The immunotoxic effects and dose-response analysis of the duality in these effects demonstrates why caution should occur during role interactive processes.

3.5 Neurotoxicity and Endocrine Disruption

Certain nanomaterials can enter the bloodbrain barrier due to its size in nanoscale and that is the danger of neurotoxicity. A study done on metallic and carbon based nanoparticles has indicated neuronal oxidative stress, impaired neurotransmitter homeostasis, and impaired synaptic signaling. These effects are associated with neurodegenerative phenotypes such as the animal models of alterations of the Alzheimer/Parkinson-like pathology. Also, it is reported to cause endocrine disruption, where nanoparticles disrupt hormone synthesis, receptor binding, and signaling pathways. An example of such is the ZnO nanoparticles which have been reported to cause dysregulation of thyroid hormones whereas certain polymeric nanoparticles influence hormone balance of reproductive glands. These results show the long-term systemic risks of chronic exposure to nanomaterials.

3.6 Case Examples from Recent Studies

Recent studies have demonstrated strong evidence of the health hazards that are caused by nanomaterials. The occupational exposure to CNTs was studied showing that the markers of inflammation in the lungs were high in the exposed workers, which are correlated with the results of the animal inhalation models. Likewise, oral exposure to TiO_2 nanoparticles has been reported to cause intestinal dysbiosis and systemic oxidative stress, in vivo. In biomedical, intravenous injection of silver nanoparticles in animals has demonstrated the accumulation of the same in the kidney and nephrotoxicity. All of these case studies demonstrate that even though nanomaterials are incredibly promising in the context of therapeutic and technological use, their potential health risks cannot be ignored without careful safety consideration.

4. Ecotoxicological Implications

4.1 Soil and Microbial Diversity Impacts

Nanomaterials emitted to the ground surface have the capability of drastically changing the health and microbial diversity of the soil. Silver and Zinc oxide are some of the metallic nanosensors which are known to disrupt the microbial populations of soil by inhibiting the proliferation of beneficial bacteria and fungi, which are also involved in nutrient recycling. This kind of disturbance can disrupt such processes as fixation of nitrogen, degradation of organic matter and soils fertility. Besides, nanomaterials can be deposited on soil particles, altering the pH, redox, and so forth, thereby influencing the microbiological activity and stability of an ecosystem. The domino effect of development of plant life and food production can also take place due to microbial degradation.

4.2 Aquatic Ecosystems

Aquatic systems are among the greatest sources of nanomaterial contamination due to wastewater, runoffs and industrial effluents. Nanoparticles may have multiple interactions with aquatic organisms at different troic levels which result in bioaccumulation and toxicity. Research has also established that silver nanoparticles affect photosynthesis and growth in algae, as well as interfering with primary productivity. Equally, TiO_2 nano can settle in the gills and intestines of fish leading to oxidative stress, reproductive dysfunction, and behavioral changes. The continued presence of nanomaterials in the water streams is of concern regarding the effects in the long-term on biodiversity and ecosystems.

4.3 Trophic Transfer and Food Web Implications

A possibility of trophic transfers via food webs is one of the most worrying issues about environmental nanotoxicology. Ingested by lower organisms, e.g. plankton or the invertebrates, nanoparticles may bioaccumulate and be passed on to higher predators. The process of biomagnification leads to an increase in levels of exposure in the fish, birds and mammals including humans who consume contaminated sea food. Not only can such trophic transfer be dangerous to the stability of the ecosystem, but it also poses serious food safety issues, since the residues of nanomaterials can be present in the edible tissues. The movement of nanomaterials throughout the various ecosystems through the trophic process demonstrates how environmental exposure may eventually be harmful to the human population. The summary of this interconnected cycle is demonstrated in Fig. 4 that shows the development of environmental release to human exposure.

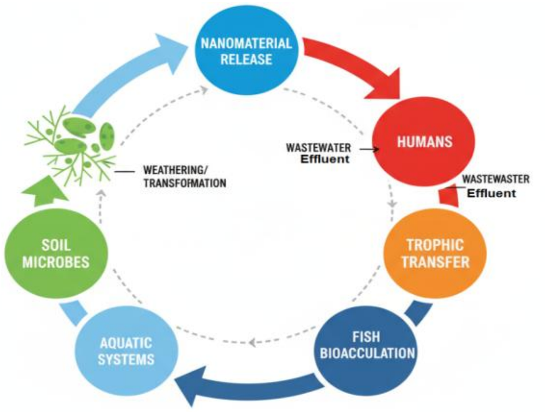

Fig. 4. Ecotoxicological pathways of nanomaterials.

Circular schematic showing the release of nanomaterials into the environment, their interactions with soil microbes and aquatic systems, bioaccumulation in fish, trophic transfer, and eventual human exposure.

4.4 Long-Term Persistence and Bioavailability

Certainly, in contrast to most traditional pollutants, nanomaterials have peculiar physicochemical characteristics that increase their environmental resistance. They are small, highly reactive to the surface, and agglomerative, which enables them to stay long in the soil and water as a bioavailable form. Their mobility and transformation is affected by environmental factors like pH, ionic strength, and natural organic matter, yet numerous nanomaterials still have toxic potential following the coating. These particles have long-lasting bioavailability that makes them highly likely to have chronic exposure to ecological effects necessitating the continuous surveillance and predictive models to assess the risks over the long-term.

5. Risk Assessment and Regulatory Perspectives

Several international bodies have initiated structures to manage the security of the nanomaterials. Other agencies such as OECD, EU REACH and US EPA have adapted the conventional methods of chemical risk evaluation to incorporate the consideration of nanomaterials which incorporate a physicochemical description, exposure route, and toxicological endpoint. Still, significant gaps remain, as the existing regulations currently are inclined to regard nanomaterials as bulk analogs, but they seemingly do not focus on the size-dependent qualities and biological peculiar interactions. Other difficulties of standardization of toxicity tests are due to the diversity of nanomaterials classes, the variation of the processes of their production and the lack of shared standards of investigation. Such limits make cross-studies not comparative and these make it tough to regulate through decision making. Improving nanomaterial-specific concepts, harmonizing testing standards and integrating innovative tooling devices such as omics technologies and predictive modeling are also highly significant in helping to obtain appropriate risk governance. Various international standards like OECD guidelines, EU REACH, and the US EPA have tried to control nanomaterials each having its own strengths and weaknesses (Table 2). Regional harmonization has been a significantly big problem to a uniform world governance.

Table 2: Comparison of global risk assessment frameworks for nanomaterials.

Framework / Agency	Scope & Focus	Strengths	Gaps / Limitations
OECD (Organisation for Economic Co-operation and Development)	Safety testing guidelines for chemicals, including nanomaterials; focuses on physicochemical characterization, environmental fate, and toxicological testing	Internationally harmonized protocols; strong emphasis on standardization; facilitates cross-country collaboration	Slow adaptation to emerging nanomaterials; limited coverage of novel endpoints (neurotoxicity, endocrine disruption); mainly guidance, not binding
EU REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals)	Comprehensive regulatory framework for chemical safety in Europe; requires registration and safety data, including nanoforms of substances	Legally binding; requires industry data submission; specific guidance for nanomaterials introduced since 2020	Complexity of compliance; high cost for industry; uncertainties in long-term exposure and environmental impacts
US EPA (Environmental Protection Agency)	Regulates nanomaterials under TSCA (Toxic Substances Control Act); focuses on environmental release, workplace safety, and ecological exposure	Strong regulatory authority; can mandate data submission; targeted risk management for nanomaterials	Case-by-case assessment; limited standardized testing protocols; lacks a unified framework specific to nanomaterials

6. Emerging Trends and Mitigation Approaches

Recent studies on nanotoxicology research have focused on the ways to achieve a balance between innovation, safety, and sustainability. Safer-by-design nanomaterials are directed to the design of surfaces chemistry, the size of particles and their surfaces to reduce toxicity without loss of functional activity. Similarly, alternative biodegradable and environmental-friendly materials (e.g. polymeric or naturally-derived nanomaterials) are underway to minimize persistence and bioaccumulation into the environment. Predictive toxicology is becoming feasible thanks to AI-based models, high-throughput screening, and omics-based methods, which are improving the predictability of biological reactions and allow people to detect threats at an earlier stage of the design process. Moreover, green production systems using plant extracts, microorganisms, and sustainable precursors are low-impact production routes, and connecting to a system of circular economy will enable nanomaterials to be recycles, recovered, and safely managed through the lifecycle. All of these efforts are a move towards responsible innovation, a goal to balance the positive aspects of nanotechnology with human and environmental safety in the long run.

7. Future Directions

Future studies should be primarily centered on the concept of longitudinal human exposure studies in order to pick up the long-term health effects of nanomaterials, particularly in the case of occupational and consumer exposures where chronic exposure is likely to occur. There will be the need to come up with the models of integrated nano- bio-eco interaction to know the behaviors of nanomaterials under diverse systems and ecosystems of the biological systems to predict the aggregate risks in a better way. The other aspect that would be of much significance will be the standardization of toxicological testing among the laboratories and this would ensure reproducibility, comparability and acceptability of toxicity data by regulations. Both these programs will help in the sound scientific foundation of risk assessment and result in the development of safer and more sustainable nanomaterials.

8. CONCLUSION

Nanomaterials are a completely new frontier in science and technology that offers unprecedented potential in medicine, industry as well as in the environment. In the meantime, their special physicochemical characteristics represent a great threat to human health and the environmental setting in the form of the toxicological risk. These have to exist in a middle ground of opinion, even, however, a middle ground of opinion that recognizes the duality of nanomaterials as the realms of innovation and the realms of harm. Multi-disciplinary safety systems that involve the combination of toxicology with material science, environmental science, and regulatory policy are the conditions of the responsible development of this area of work. Nanotechnology can be used as an innovation and precaution can be applied which will reap the benefits and minimize the risks of using nanotechnology to human and environmental well-being.

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