Al-Rafidain J Med Sci. 2022;3:41-47.
DOI: https://doi.org/10.54133/ajms.v3i.80

AJMS
Online ISSN (2789-3219)

Review Article

Nanotoxicology: An Integrative Environmental Challenge

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Received: 29 August 2022; Revised: 29 September 2022; Accepted: 3 October 2022

Abstract

A contemporary and expanding area of toxicology research is nanotoxicology. It focuses on evaluating the toxicological characteristics of nanoparticles (NPs) in order to determine whether and how much of a risk to society or the environment they pose. Fundamental characteristics of nanoparticles (consisting of shape, size, surface charge, surface area, solubility/dissolution, coating and crystal structure), in addition to coincidental aspects (like climate, pH, salinity, ionic potency, and organic material), generally impact on NP attitude, circumstance, and movement, and basically toxicity. The processes underpinning nanomaterials' (NMs) toxicity have recently been intensively researched. One such mechanism is the toxicity of reactive oxygen species (ROS). Excessive production of ROS causes oxidative stress, which causes cells to lose their capacity to sustain normal redox-regulated processes. This review consists of details referring to physical and chemical characteristics of nanomaterials and properties for convenient toxicological assessment, disclosure, and coincidental transport, fate, and genotoxic effects.

Keywords: Nanomaterial, nanotoxicology, characterization techniques, nanoparticles

علم السموم النانوي: تحد بيئي تكاملي

الخلاصة

مجال معاصر ومتوسع لأبحاث السموم هو علم السموم النانوية. و يركز على تقييم الخصائص السمية للجسيمات النانوية من أجل تحديد ما إذا كانت تشكل خطرا على المجتمع أو البيئة ومقدار الخطر الذي تشكله. الخصائص الأساسية للجسيمات النانوية (التي تتكون من الشكل والحجم والشحنة السطحية ومساحة السطح والذوبان / الذوبان والطلاء والبنية البلورية)، بالإضافة إلى الجوانب المتزامنة (مثل المناخ ودرجة الحموضة والملوحة والفعالية الأيونية والمواد العضوية)، تؤثر بشكل عام على موقف الجسيمات النانوية والظروف والحركة ، والسمية بشكل أساسي. وقد تم مؤخرا إجراء بحوث مكثفة حول العمليات التي تقوم عليها سمية المواد النانوية. إحدى هذه الآليات هي سمية مركبات الأكسجين التفاعلية (ROS) حيث يؤدي الإنتاج المفرط لـ ROS إلى الإجهاد التأكسدي، مما يؤدي إلى فقدان الخلايا لقدرتها على الحفاظ على العمليات الطبيعية التي تنظمها تفاعلات الأكسدة والاختزال. تتكون هذه المراجعة من تفاصيل تشير إلى الخصائص الفيزيائية والكيميائية للمواد النانوية من أجل التقييم السمي المريح والكشف والنقل المتزامن، والمصير، والآثار السمية الجينية.

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Article citation: Hassan DS, Hasary HJM. Nanotoxicology: An integrative environmental challenge. *Al-Rafidain J Med Sci*. 2022;3:41-47. doi: 10.54133/ajms.v3i.80.

INTRODUCTION

Nanotoxicology is defined as the evaluation of the toxicological futures of nanoparticles in order to determine if the compounds pose a social or accidental risk. With tiny particles being employed in a variety of applications and professions, including industry, electronics, pharmacy, science, medical, and communication products, nanotechnology has gained promise during the past few years according to Vance *et al*. The market for nano-based materials increased by 30 times between 2011 and 2015 [1]. Furthermore, there was a wider reach than $8 billion by 2020, as presented in Figure 1.

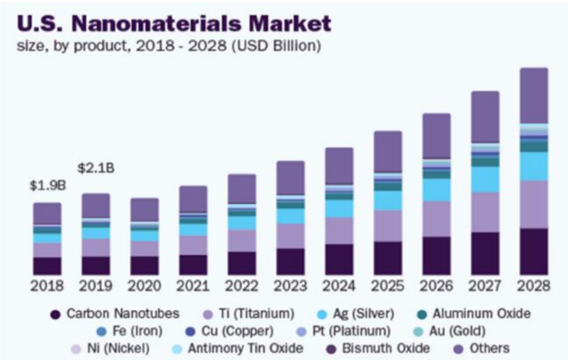

Figure 1: The cost of nanomaterials in the US market [2].

The most prevalent and rapidly expanding type of nanoparticle is a metal nanoparticle, specifically carbon and silver nanoparticles (NPs) [2]. As a result, both human and coincidental disclosure have previously occurred and are expected to increase dangerously. There are concerns about the potential negative environmental effects of this advancement in nanotechnology. Numerous publications have reported on the toxicity of certain NPs. But there are still many unknowns [3,4]. Nanomaterials (NMs) are substances that have molecules with 1–100 nanometers in length. Their distinct chemical and physical properties, which gave rise to them, are useful in a variety of applications. However, these properties have the potential to be toxic formerly announced into the environment [5] (Figure 2).

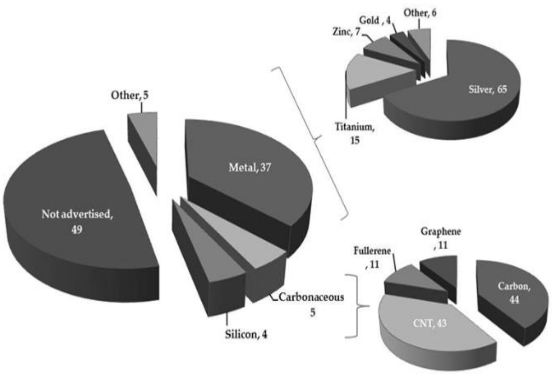

Figure 2: Constituent of nanomaterials [1].

The toxicity and fate of NPs, as well as their uptake by organisms, are all dependent on numerous conditions. The size, shape, and coatings of nanomaterials will have a significant impact on how long nanoparticles (NPs) will either accumulate or adsorb to suspended materials, partition to dissolved organic carbon in an aqueous column, or stay in suspension. Relevant methods must be accessible to solve the most pressing issues in nanotoxicology and learn more about the toxicity mechanisms of nanoparticles, such as genotoxicity, oxidative stress, inflammatory responses, and cytotoxicity. Adsorption to surface epithelia, such as the gills, and ingestion are the two main ways that NM is exposed to organisms [6].

METHODS

This review was concentrated on the nanotoxicology and its consequence on the environmental aspect. The facts regarding nanotoxicology were obtained through out searching PubMed databases, Google Scholar, Science Direct, ResearchGate in order to get an open access studies that published between 2004 to 2020. The applied keywords during the searching process were nanomaterial, nanotoxicology, characterization techniques, nanoparticles toxicity, oxidative stress, genotoxicity.

Physiochemical Characteristics of NMs that Determine their Toxicity

The way NPs behave in varied environmental models is intricate and contains a variety of mechanisms. The characteristics of NPs are distinct from those of ordinary particles. Particle size, charge, surface area, solubility, shape/structure, and surface coatings are all known to have an impact on nanomaterial toxicity [6]. Due to its nano-sized, NMs have distinct physical and chemical properties like electrical, optical, magnetic, mechanical, and thermal capabilities, making them suitable for a range of applications in medical, electronics, and energy generation, as well as a range of consumer products. Nonetheless, these characteristics have the potential to harm people and the environment. NMs can readily infiltrate membranes of cells and other biological barriers, producing cell deterioration in creatures. Research shows particles have resulted in the widely held belief that NPs are more counterparts of destruction [7]. Despite the size of NPs being the most distinctive feature when correlated to traditional molecules, dimension and morphology are further key considerations when assessing whether NMs are poisonous. Nanomaterial dynamics and environmental mobility are influenced by morphology, which includes spheres, cubes, films, rods, wires, truncated triangles, and coatings. When NPs are eliminated, they are capable of ending up in aquatic organisms, which are highly toxic to aggregates and soluble ions found in the aquatic environment [8,9]. The key mechanisms that regulate NP toxicity and attitude in aquatic environments are aggregation and dissolution, which are greatly influenced by the surface and size characteristics of natural colloids, in addition to the stability aspects such as dissolved organic elements. Colloidal cohesion is influenced by a variety of circumstances, including environmental surroundings such as pH, temperature, and ionic stability. In their study of the stability of AgNPs, Romer *et al*. [10] discovered fast accumulation in high ionic solutions. Likewise, Walters *et al*. [11] described increased toxicity as a result of smaller aggregate formation at higher temperatures. These experiments noted changes in organism toxicity and disclosure levels as a result of aggregation levels. The process of NPs dissolving is important in assessing their impacts in aquatic circumstances. The majority of NPs do not solubilize in solutions; instead, they create colloid dispersions that will aggregate or remain dispersed. Consequently, interactions with other colloid components will affect how quickly particles aggregate in a given environment [12]. NPs do not exist in isolation in the natural environment. As a result, it's crucial to take other environmental stressors into account. As an example AgNPs were found to dissolve at higher temperatures by Liu and Hurt [13]. AgNPs have a propensity to aggregate and release ions in the presence of dissolved oxygen (DO), which in turn triggers aggregation and oxidation [12]. The properties of particle dispersion are significantly influenced by surface charge, which also affects ions and biomolecule adsorption [14]. FeO NPs were reported to have disaggregated by Baalousha due to increased surface charge [15]. Similar findings were made for AgNPs' surface charge-dependent toxicity by El Badawy *et al*. [16]. Surface coating is also thought to increase surface charge, which indirectly links it to aggregation and dissolution. These distinct chemical and physical properties of NPs are concerning because they call into question generalizations about chemical behavior and reactivity [16].

Characterization

The physical and chemical characteristics of nanomaterials have an impact on their behavior and toxicity. Therefore, determining how NMs' physical and chemical characteristics connect to various chemical, ecological, and biological responses is crucial. Finding the bulk (shape, size, phase, electronic structure, and crystallinity) and surface (surface area, arrangement of surface atoms, surface electronic structure, surface composition, and functionality) features of the NM is a necessary step in the complete characterization of NPs [6]. NP behavior and toxicity may also be impacted by environmental conditions such as temperature, pH, ionic strength, osmolality, and lipophilicity. Transmission electron microscopy (TEM) or scanning electron microscopy (SEM) is widely used to analyze the morphology of NMs. Elements of NMs are often characterized using energy-dispersive X-ray (EDX) spectroscopy in combination with scanning electron microscopy (SEM). Indirect methods for determining particle size in the aqueous phase include electrophoretic light scattering spectroscopy (ELS), which makes use of an oscillating electric field, and dynamic light scattering (DLS), which investigates the Brownian movement of the NPs. The Scherrer method is used with X-ray powder diffraction (XRD) to quantify particle size in the dry state [17]. Murdock *et al*. looked into the application of DLS to describe NM dispersion. The Brunauer-Emmet-Teller (BET) method is implied to calculate surface area. The zeta potential, which measures surface charge in aqueous particles, is a key variable that is known to influence stability. AFM and STM make it possible to image surfaces in three dimensions and quantify forces between surfaces at the piconewton level. Spectroscopic methods such as UV-vis and Fourier transform infrared (FTIR) spectroscopy are implied to characterize fullerenes in solution [18,19]. Surface enhanced Raman spectroscopy (SERS) is a surface-sensitive technique for detecting single molecules by enhancing Raman scattering by nanostructures. Chemical characterization methods used to investigate the elemental composition of NMs include inductively coupled plasma mass spectrometry (ICP-MS), inductively coupled plasma optical emission spectroscopy (ICP-OES), and energy-dispersive X-ray spectroscopy (EDS) [6].

Mechanisms of NP Toxicity

Attempts have been made to clarify the modes of Np poisonous and differentiate between their bulk analogs. Nanomaterials differ greatly from their bulk counterparts in various aspects, such as surface/volume ratio. Np has many aspects that could affect the toxicity profiles of NP, like shape, size, surface coatings, dissolution, aggregation state, and solution chemistry [6]. Research has found that TiO2 NP [20], AgNP [21-23], CuONP [18,24], and Ni NP [25] have all been researched for their harmful effects on a variety of aquatic species, including Daphnia magna [23,24], fish [26], freshwater crabs [27], algae [28], and marine [29]. Titanium, silver, and carbon NMs are three of the most popular implied NM kinds that are used as additives in cosmetic and pharmaceutical preparations. Additionally, various NMs have different characteristics and hence differing degrees of toxicity. Heinlaan *et al*. [30], for instance, compared the toxicity of TiO2 NPs, ZnO NPs, and CuO NPs, three different nanometal oxides. according to Zhu *et al*., CuO NP was the most potent substance to demonstrate effects on cytotoxicity and genotoxicity, while ZnO NPs were shown to be the most toxic [31]. Most studies on the toxicity of NP have been conducted in vitro, with results showing that different types of deleterious effects can be induced at various levels of cellular structure. The most common end points studied are death and sublethal consequences include gene expression, oxidative stress, growth, malformation, and respiration. DNA damage, lipid peroxidation, and oxidative stress are all caused by the generation of reactive oxygen species (ROS), which can also activate or inhibit the antioxidant defense system. The following sections will go into greater detail regarding NP toxicity [6].

Oxidative stress

An imbalance between the production of reactive oxygen species (ROS) and a cell's ability to remove ROS is known as oxidative stress. This imbalance may be brought on by changes in the cell's defensive mechanisms, an increase in ROS production, or the development of both elements [32]. High generation of ROS can cause oxidative stress, which can lead to cell death and genotoxic impacts. Oxidative stress is caused when cells are unable to maintain their normal physiological redox-regulated functions. It also starts lipid peroxidation, causes DNA strand breaks and nucleic acid modification, and modifies proteins [33]. A sophisticated antioxidant system made up of enzymatic and non-enzymatic defensive pathways has been established by biological systems to reduce the negative impacts of ROS-oxidative on major cellular elements. provides a summary of the redox cycle, consisting of ROS production by NPs and the antioxidant defense scheme [6]. The generation and elimination of ROS must now be balanced thanks to the development of the antioxidant defense system. Several distinct enzymatic compounds, composed of Phase I and Phase II enzymes, catalyze these reactions. The detoxification process is started by phase I enzymes such as cytochrome P450, which add a polar moiety to increase the hydrophilicity properties of a hydrophobic pollutant. ROS generation normally rises while Phase I enzymes are active. The conjugation of metabolized xenobiotics to endogenous compounds is carried out by phase II enzymes. Phase III sees additional alterations and excretion. [34]

Genotoxicity

The tendency of NPs to destroy genetic material is a major concern when it comes to their toxicity in biological media, especially since they can cross cell membranes. DNA is a vital biological component that is extremely vulnerable to oxidative damage. As a result, there has been a surge in interest in studying the potential genotoxicity of nanoparticles in aquatic creatures [6]. In vitro studies have mostly been used to investigate the genotoxicity of various NPs. NPs have been shown to have the ability to cause chromosomal fragmentation, DNA strand breaks, point mutations, oxidative DNA adducts, and changes in gene expression profiles, which could exert carcinogenicity and mutagenicity effects. Predominant genotoxicity is accounted for as an outcome of the interaction of NP and DNA, which is processed after the internalization of NP [35]. Genotoxicity resulting from the formation of additional ROS, assigned to as "secondary genotoxicity," has been documented. Similar to NP toxification, comparing the compounds to their bulk equivalents, it is known that they produce more premature genotoxic effects. For instance, Park and Choi [23] investigated the genotoxicity of AgNPs on *Daphnia magna*. The obtained outcomes showed greater levels of DNA deterioration via DNA strand breaks when comparing AgNPs to Ag ions. Similarly, when compared to larger NPs, the size of the NP has a significant impact on genotoxicity, DNA degradation, and chromosomal instability. This criterion was approved when the researchers detected that smaller sized TiO_2 NPs (10 nm) have remarkable chromosomal negative impacts in comparison to the larger TiO_2NP (> 200 nm) [36]. Fundamentally, there is a popular agreement that NP with smaller sized forms has higher reactivity, and this produces higher genotoxicity effects [37,38]. On the other hand, particle size cannot be considered the sole element that influences particle (geno-)toxicity. For example, the surface coating of nanoparticles has also been linked to genotoxicity. Because surface coating changes the particle's surface, it could change the particle's genotoxicity. Hong *et al*. [39] found that iron oxide NPs with positive charged coatings lead to higher DNA strand breaks, whereas negatively charged coatings have no effect on genotoxicity. Likewise, Lui *et al*. [40] showed different genotoxic effects of iron oxide NPs with various coating materials. The implication of polyethylene glycol (PEG) coating was showed mutagenic impact, while no genotoxicity effect detected when of solid electrolyte interphase (SEI) coating was used.

Ecotoxicity

Due to discussions about the hazards and benefits of these materials, the potential ecotoxicity of NPs has recently sparked public and scientific discourse. As a result, research on the ecotoxicological fate and consequences of NMs has grown recently. Numerous recent reviews on the ecotoxicology of NPs [3,4] have reported on the results of considerable research on the toxicity of NPs to aquatic species. According to data on NPs' biological impacts, NPs can be hazardous to bacteria, algae, invertebrates, fish, and mammals. Nevertheless, due to the fact that the majority of research has generally been limited to a small number of test species, nano-ecotoxicology studies continue to be inadequately and unevenly dispersed. The majority of the most recent ecotoxicological research on NMs was conducted on Daphnia magna. These discoveries are especially pertinent because these crustaceans serve as the food and energy link between algae and fish [41]. AgNP ecotoxicity effects on D. magna were investigated by Park and Choi [23], who found increased mortality. In response to exposure to AgNPs, Asghari *et al*. noted aberrant swimming in D. magna, whereas Heinlaan *et al*. [24] noted ultrastructural alterations in the midgut of D. magna. Some aquatic species' semipermeable membranes can be penetrated by nanoparticles, which causes them to clump together around their exoskeletons [42]. Numerous NPs have been reported to be taken up by aquatic organisms, including the polychaete *Nereis diversicolor* [21], the freshwater algae *Ochromonas danica* [22], and the crab *Daphnia magna* [24,43].

Conclusions

Nowadays, NMs are widely used in various consumer products, and the possible risks they pose to the environment and public health are subjects of growing concern. Nano products will become more prevalent in the environment and water sources as nanotechnologies and their products proliferate, potentially posing a greater threat to species. This review provides information on nanotoxicology, a new, interdisciplinary topic of study, with a specific emphasis on the effects of metal-NMs. Oxidative stress can result in nano-level toxicity, genotoxicity and Eco toxicity as well, and it can be influenced by various elements such as size, shape, composition, and surface functional groups of NMs. The dangers posed by NMs, including their fate, behavior, and environmental toxicity, are mostly unknown and impossible to anticipate. Although our understanding of the environmental toxicity of many NMs has grown in recent years, we still know very little about exposure doses, tissue bioaccumulation, or environmental conditions that can influence toxicity or bioaccumulation. Since NPs are being used more frequently, exposure to them is inevitable, but there is still much to learn about the safety aspect. Despite existing safety assessment procedures may commonly be used to identify harmful effects linked to NPs, research on the control mechanisms of NMs' toxicity is still underway. To address the special traits of NMs, innovative analytical approaches need to be studied. Scientists will be able to foresee the harmful impacts of AgNPs as a result of the findings in order to guide their development, utilization, and regulation. When thinking about AgNP environmental cleanup and exposure control strategies, this will be crucial.

Conflict of interests

The authors declare no conflict of interests.

Source of fund

No specific fund received.

Data sharing statement

N/A

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