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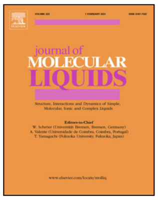

Nanomaterials: A comprehensive review of applications, toxicity, impact, and fate to environment

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ABSTRACT

The present era is considered the nanotech age. Nanomaterials have gained a great deal of importance in the field of technology, engineering, and medicine progression because of their tunable, physical, chemical, and biological properties rather than their bulk counterparts. Nanomaterials are classified based on their size, shape, composition, origin, and toxicity. Due to the increasing utility and industrial applications of nanomaterials, it has become important to investigate nanomaterials' toxicity and environmental risks. In the present review, we have critically discussed the applications, behavior, and toxic impact on humans, animals, and the environment. Its fate and challenges and future requirements for the development and design of safe nanotechnology for sustainable development have been discussed.

Contents

Abbreviations: ISO, International Organization for Standardization; ROS, Reactive oxygen species; SEM/TEM, Scanning/transmission electron microscopy; STM, Scanning tunneling microscope; MOFs, Metal organic framworks; ZVI NPs, Zero valent iron nano particles; MSNs, Mesoporous silica nanoparticles; GMs, Graphene materials; GO, Graphene oxide; rGO, Reduced graphene oxide; NNI, National Nanotechnology Initiative; LDE, Lactate dehydrogenase enzyme; MIP, Macrophage Inflammatory Proteins; IL, Interleukin; MCP, Monocyte Chemoattractant Protein; GM-CSF, Granulocyte-macrophage colony-stimulating factor; LOQ, Limit of quantification(; SOD, Superoxide-dismutase activity; RAPD, Random amplified polymorphic DNA; MWCNTs, Multi-walled carbon nanotubes; SRFA, Suwannee River Fulvic Acid; NOM, Natural organic matter; OECD, Organisation for Economic Co-operation and Development; WPMN, Working Party on Manufactured Nanomaterials.

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1. Introduction

Although the idiom of nanomaterials appeared at the end of the 19th century, as they have been used already in ancient civilizations. For example, in ancient Egypt, oil lamps smut was applied to make black dyes distinguished with stability and high opacity for writing on sedge papers. However, ancient Egyptians at that time did not know that smut contains carbon nanomaterials [1]. Moreover, they used synthetic chemistry to manufacture PdS_2 (Palladium disulfide) NPs with $\sim$ 5 nm diameter which was used as an ingredient in their hair dyes [2]. Moreover, for more than 4,500 old Cyprus years people reinforced ceramic matrix materials with natural nano-fibers of asbestos (50–200 nm in diameter) and used it for bleaching cloth and wool [3,4]. Around 2575 BCE ancient Egyptians invented the synthetic dye Egyptian blue which is composed of a nanosized mixture of glass and silicon dioxide (quartz) ($CaCuSi_4O_{10}$ and SiO_2). Likewise, in approximate time China produced blue dye by replacing Ca used in Egyptian blue with Ba ($BaCuSi_4O_{10}$) [5].

Nano term refers to a size that ranges between 1 and 100 nm according to International Organization for Standardization (ISO), (ISO 2008). Nanomaterials (NMs) are larger than a single atom or even small groups of atoms. The first-time word nanotechnology was used by Norio Taniguchi in 1974 during machining and finishing dimensional tolerances for semiconductor processes as a reference [6]. Meanwhile, the term nanotechnology was first coined by Richard Feynman in 1959 during his talk at the American Physical Society meeting [7]. Nanotechnology helps in the fabrication, processing, imaging, measuring, and application of materials that fall in the size range of up to 100 nm. So, nanomaterials possess particles and materials dispersed within the porous matrix with nanometer-sized pores in metallic clusters. It shows a remarkable change in physical and chemical properties like unique optical, thermal, electrical, magnetic, and catalytic properties when compared with non-nanomaterials due to their small size or nanoscale effect [8–12]. Nanomaterials have a large surface area, a high feature ratio, and a high surface-to-mass ratio [13]. These remarkable features of nanomaterials can drastically alter the physical, chemical, biological, electrical, and mechanical properties [14,15]. Nanotechnology provides a wide area of interdisciplinary research, innovation, development, and industrial activity which has been growing rapidly in recent years [12,16–18].

From the economical side, the worldwide market size of nanomaterials should dilate significantly during the period from 2021 to 2027 because nanotechnology is getting involved progressively in numerous industrial sectors [19] which include the food industry, cosmetics, healthcare, medicines, electronics, etc. [20]. During the COVID-19 epidemic, the worldwide market of nanomaterials was rated at US$7.1 billion in 2020 and will reach 2026 US$12.1 billion in, with annual growth of 9.7 %. In the United States (US) the nanomaterial market in 2021 was 2.1 billion US$, an ongoing increase in federal government grants for nanotechnology projects from $464 million in 2001 to about US$6.2 billion in 2019 reported by the US National Nanotechnology Initiative. Likewise, the investments by Japan and the European Union (EU) in nanotechnology increased during the period 2005–2010 from $1.8 billion and $1.5, respectively, to $3–4 billion in the 2019–2020 period [21,22]. South Korea, China, and Taiwan assigned $300, $250, and $110 million respectively, for nanotechnology projects in the 2010–2020 period [23,24].

Nanotechnology plays a vital role and has many applications in the fields of medicine [25], agriculture [26], food industries [27], biotechnology [28], environmental pollution detection and control [14,29,30], water treatment [13,31–35] and electronic [36], due to various physicochemical properties of nanomaterials in comparison to microscale and bulk materials. These unique properties are naturally due to elevated atoms fraction and surface energy of miniature particles in comparison to bulk materials [37]. During the 1980 s the first nanoceramics were developed. Since then there has been a huge excitement for its application in diverse technology. Nanoceramics are prepared from ultrafine particles<100 nm in diameter. Ceramic nanoparticles have confirmed themselves to be highly stable in comparison with metallic ones and their production tends to be economical [38,39]. Nanomaterial-based biosensors display attractive prospects over traditional biosensors [40]. It has many potential merits such as enhanced detection sensitivity/specificity in its applications in various fields such as environment and processing control, quality control of food, biodefence, agriculture along with agro-products, and particularly in the medical field [41].

To characterize the risk factors of nanomaterials and their fate in the environment, it is crucial to understand the various forms of nanomaterials and their potential route of exposure. The kind of nanomaterial may be uncertain via its production process (vapor deposition gas phase, attrition, colloidal, and so forth), which can potentially result in human exposure through various routes viz, inhalation, dermal absorption, or ingestion [42]. Studies by Ostiguy et al., reveal that engineered nanomaterials cause unanticipated toxicity in living organisms and harmful human health effects [43]. The properties of nanomaterials like reactivity, melting point, mechanical strength, fluorescence, and electrical conductivity which are altered at the nanoscale, make it more difficult to evaluate how nanomaterials will interact with living organisms as well as the environment [44]. Furthermore, some natural nanoparticles originated from a diversity of geological and biological processes and can be potentially toxic. It has been observed that both human beings and other species have more or less evolved, modified, and proliferated as a result of potentially detrimental exposure to natural nanomaterials [45,46]. The application of nanotechnology has been introduced to get better air, water, and soil in the field of environmental management. A remediation process based on nanomaterials has been developed to monitor and detect the pollutant released into the surrounding environment [47]. In the remediation process by nanomaterials, waste containing residues of nanoparticles is also obtained which ends up as wastewater that finally reaches other abiotic environmental sources such as soil, sediments, and surface water [42]. However, the application and release of nanomaterials that cause toxicity and potential impacts on the environment have drawn the attention of regulatory and environmental agencies and scientific researchers [48].

Numerous review articles that have already been published examine both naturally occurring and synthesized pathways. Additionally, they talked about the development and current uses of nanomaterials. However, there is a lack of information regarding the use of nanomaterials in the past as well as their negative consequences outside of their numerous applications [49–51]. Nearly all of these topics have been covered in the current review study with adequate reasoning. Contemporary biomedical advancements, the toxicology of nanomaterials, and other topics have also been discussed.

Moreover, the applications, toxicity, impact, and environmental fate of nanomaterials are also covered in the present review. Nanomaterials, their background in time, and their features are covered in the first section. The classification of NPs, which is based on a variety of characteristics including size, occurrence/origin, chemical compositions, natural and synthetic, nature of toxicity, and many more, is covered in the following sections. The classification's following section was mostly concerned with applications, including biogas production, drug delivery, vaccine research, disinfection, and other significant ones. The key topics covered in Section 5 include human exposure to nanomaterials, their toxicity, sources of exposure, and routes by which nanoparticles enter the body. The impact of NPs on ecology and animals as well as the effects of nanoparticles on plants are finally summarized at the end of the manuscript and are not previously mentioned [52,53].

Several studies have shown that during manufacture and applications, the negative effects of nanomaterials on human health and the environment occurs [44,54–58]. Some available evidence suggests that due to the small size of nanoparticles, these are generally more toxic than their larger counterparts (e.g., 41 mm) of the same substances [55,59]. There are several ways to produce toxic nanomaterials in the environment. Chemical activities which are considered primary mechanisms produce free radicals and finally produce toxic nanomaterials [60]. For example, iron nanoparticles produce highly oxidized OH radicals which contribute to their toxicity and damage biological systems via the Fenton reaction [61,62].

During various stages, industrial waste containing nanoparticles is directly released into lakes, rivers, and aquatic fields which are concerning sources of nanoparticle pollution [63,64]. In a very large geographical area, the depositions of nanoparticles can be observed in soil texture [65]. Sujatha et al. investigated the ecotoxicological consequences of TiO_2 nanoparticle (NPs) exposure on aquatic life. They have chosen zebrafish as a model system. During the study, a decreased activity of acetylcholine esterase, as well as enzymatic and non-enzymatic antioxidants, was observed. Vice-versa, there was an increase in protein content, reactive oxygen species (ROS), protein carbonyls, and lipid peroxidation products [66]. TiO_2 NPs induced oxidative stress which results in respiratory distress in zebrafish. In drug delivery processes, nanomaterials chemically react with cell surfaces and may change cell properties [67]. A study by Kocbek et al. revealed that during in vitro toxicity study of ZnO and TiO_2 nanoparticles on keratinocytes for short and long-term application, it results in decreased mitochondrial activity, loss of normal cell morphology, and arrest in the cell cycle when exposed to a long duration at 10 mg/mL^{-1} concentration of ZnO nanoparticles [68].

In the present review, an attempt has been carried out to access the toxic nature of nanomaterials, their exposure, impacts on humans, animals, and the environment along with their fate in the environment, and challenges faced for proper disposal to make a sustainable environment. Various applications of nanomaterials have also been discussed.

2. Classification of nanomaterials

Nanomaterials illustrate various classifications due to their unique characteristics. Classification is based on numerous properties such as dimensions, occurrence/origin, chemical compositions, natural and synthetic, toxicity nature, and many more. Nanomaterials can be broadly classified based on their origin (natural and artificial), chemical properties (organic, inorganic, and mixed), and homogeneity (single or hybrid composition) [69]. The natural and incidental origin of nanoparticles commonly referred to as ultrafine particles includes erupting volcanoes, soils, sand storms, forest fires, and breaking sea waves [70]. Certain forms of clay also comprise 1 nm thick nanoplates stacked to 70 to 150 nm in width. Natural sources of nanomaterials are also found in living organisms, for example, biogenic magnetite, a ferromagnetic crystalline composition coupled with magneto reception in some animals, ferritin, which acts as iron storage protein, and calcium hydroxyapatite, the hard nanocrystalline component of bones [71]. Recently, the presence of fullerenes has been detected in space [72]. NMs can be categorized into various groups based on different criteria. Usually, NMs can also be classified according to their dimensions, morphology, state, and chemical composition [73]. However, several authors have classified nanomaterials based on five factors: nanoparticle geometry, morphology, composition, uniformity, and agglomeration [74–76].

Further based on nanoparticle geometry, nanomaterials are classified as 1D, 2D, or 3D [75]. According to electromagnetic properties and chemistry, NMs exist in discrete forms, suspensions, and colloids, or an agglomerated state, for example, magnetic NPs present in a bunch of an agglomerate state unless their surfaces are functionalized [77]. Further on the chemical composition, NMs have been classified as single constituent NPs and nanocomposites. In carbonaceous NMs carbon exist as fullerenes, graphenes, and carbon nanotubes (CNTs). Metallic NMs, are prepared from various forms of metals such as iron, copper, silver, zinc, alumina, silica, and titania. Branched dendrimers represent another kind of NMs having branch-like structures with nanoscale dimensions. Nanocomposite materials are organized by mixing of NPs into a matrix of standard materials to improve further properties like toughness, mechanical strength, and electrical or thermal conductivity [77]. The various kinds of nanomaterials and their classifications have been shown in Fig. 1 based on the above-mentioned criteria.

3. Characterization of nanomaterials

Nanomaterials are characterized by the presence of free nanoparticles in several nano dimensions i.e., 1D, 2D, or 3D, and are classified as nanosheets, 2D needles or filaments, and 3D particles, etc. Such geometries can be found in adjacent solids as dispersed or precipitated phases or adjacent nanocrystals forming nanograin solids. These nanomaterial structures are characterized by using principal imaging techniques like scanning/transmission electron microscopy (SEM/TEM), scanning tunneling microscope (STM) and atomic force microscope (AFM). SEM and TEM are the

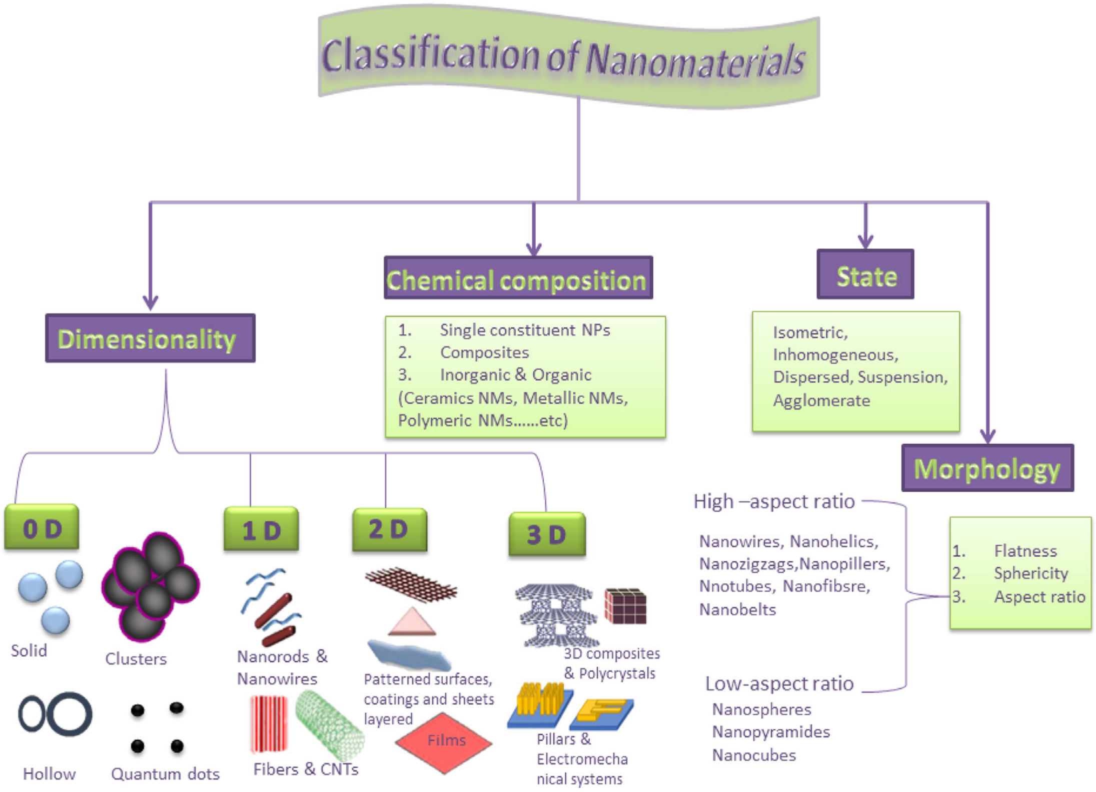

Fig. 1. Classification detail of various kinds of nanomaterials.

most commonly used tool in characterization because nanomaterials can be readily prepared and examined directly through SEM and TEM with resolutions nearly equal to 1–10 nm and < 1 nm, respectively. Whereas, atomic lattice structures can be characterized by either a single atom or crystal lattice plane levels at higher resolutions [78]. Microscopy, light scattering, and light spectroscopy are used for measuring the particle size of nanomaterials.

Hyphenated techniques based on chromatography or electrophoresis, and size-separation of colloidal suspensions, are also used [79]. Nanoscale materials have far larger surface areas than similar masses of bulk materials. As the surface area per mass of a material increases, a greater amount of the material can come into contact with surrounding materials, thus affecting reactivity. BET surface area analyzer is used to measure the surface area [33]. Functionalization and surface treatment of nanomaterials is an area of crucial importance in the emerging field of nanotechnology. Controlling the surface chemical composition and mastering its modification at the nanometer scale are critical issues for high-added value applications involving nanoparticles. The basic applications of surface functionalization range from altering the wetting or adhesion characteristics and improving the nanoparticles dispersion in matrices to enhancing the catalytic properties and ordering the interfacial region.

The creation of specific surface sites on nanoparticles for selective molecular attachment is a promising approach for their applications in nanofabrication, nanopatterning, self-assembly, nanosensors, bioprobes, drug delivery, pigments, photocatalysis, LEDs, etc. Novel and improved synthesis methods and approaches are being explored for controlling and functionalizing the nanoparticle surfaces to enhance the overall performance of the nanoparticles for targeted applications [31]. X-ray diffraction is a powerful nondestructive technique for characterizing the crystallinity of materials. It provides information on structures, phases, preferred crystal orientations (texture), and other structural parameters, such as average grain size, crystallinity, strain, and crystal defects [33]. Particle size distribution, shape, surface area, surface chemistry, solubility, etc. also play an important role in nanomaterial chemistry.

4. Applications of nanomaterials

Nanomaterials have various applications in the fields of medicine [25], agriculture [26], food industries [27], biotechnology [28], and electronics [36], as they differ in physicochemical properties as compared to their counterparts. The small size, large surface area, and elevated surface energy of miniature particles in comparison to bulk material are responsible for these properties [38]. A large number of applications in various fields have been explored in the development of the first nanoceramics during the 1980 s. Nanoceramics are stable and economic in comparison to their metallic counterparts [38]. Nanomaterials and their various forms have been widely and commonly used in household items such as sunscreens, socks, sports gear, garments, bedding items, detergents, mobile phones, and also in electronic gadgets. These vast applications of nanomaterials are due to the specific characteristics of materials. Mostly color, strength, conductivity, and reactivity of nanomaterials can be changed substantially according to desire, by manipulating their atoms.

Probably, nanomaterials are perfectly safe for general purposes mostly in the solid form [80]. Furthermore, nanomaterials possess some antimicrobial properties so they have been utilized in water disinfection [81]. Nanotechnology provides an opportunity for enhancement in the development of wastewater treatment technology for better sustainable water supply systems Ganesh et al., have utilized AlTiPbO Nanoparticles (ATPO-NPs), prepared from Eriochrome black-T as a potential adsorbent for the removal of toxic dye from the aqueous phase [82]. The isotherms and kinetic study reveal that ATPO-NPs have effectively been reused up to the 5th cycle of adsorption. It can remove up to 1000 mg/g of dye from the waste-containing industrial sample. Arora et al., and Soni et al., have explored nanoporous MOFs and modified MOFs for the removal of organic dyes from wastewater [31,33]. Nanomaterials have many folds of applications in various fields making life easier by adopting technology based on these applications. The detail of applications of nanomaterials has been described below.

4.1. Nanobioremediation

Nanobioremediation is an emerging technology for the removal of pollutants from the environment by using biologically synthesized nanoparticles which show a significant role in manipulating and detoxifying various pollutants. The nanobioremediation process is a nontoxic and economic method for providing a sustainable environment [83]. Nanomaterials are potential candidates for the bioremediation process, due to less toxicity towards microorganisms. Moreover, these exhibit better microbial activity against particulate waste and toxic material thus saving time along with cost reduction during the remediation process [84]. Carbon nanotubes, nano iron and its derivatives, nanosized dendrimers, engineered nanoparticles, and single enzyme nanoparticles are examples of nanomaterials used in nanobioremediation [84,85]. Some of the engineered polymeric nanoparticles have been utilized in the bioremediation process of hydrophobic contaminants [86] and soil remediation [87]. In uranium bioremediation, biogenic uranite-based nanoparticles have been utilized [88]. Moreover, some biologically synthesized nanomaterials obtained from organisms such as *Gundelia tournefortii, Centaurea virgata, Reseda lutea, Scariola orientalis, Eleagnum angustifolia, Bacillus* sp., and *Noaea mucronata* for the accumulation of heavy metals mostly focused on Cu, Zn, Pb and Ni [84,85,89]. Lincy et al., have demonstrated that nanoparticles increase the adsorption rate of dye and removal efficiency due to their smaller BV size and increased surface-to-volume (S/V) ratio. During their experiment, 82.4 % of azo blue dye was removed with an initial dye concentration of 25 ppm [90].

Silver nanoparticles have shown an admirable decoloration of more than 85.8 %, within 24 h when it is incubated with *Aspergillus niger* broth containing Congo red [91]. Nano-scale ZVI has shown up to 99.9 % remediation of lead (Pb) from contaminated water [92].

4.2. Biogas production

Anaerobic digestion is a multifaceted microbial process for the conversion of organic compounds such as animal manure, agricultural residues, industrial waste food, and sewage sludge into biogas/methane [93]. It consists of four microbial sequential stages namely hydrolysis, acidogenesis, acetogenesis, and methanogenesis which are carried out by a consortium of microorganisms [94]. The obtained final product i.e., biogas, which mostly consists of methane (CH_4) 60–70 %, Carbon dioxide (CO_2) 30–40 %, and some other gases like ammonia (NH_3), hydrogen sulfide (H_2S), hydrogen (H_2), nitrogen (N_2), oxygen(O_2) and little amount of water (H_2O) vapors [95–98]. Mona et al. reported the application of nanoparticles in anaerobic digestion and its mechanism which deals with the biogas production rate. Along with NPs studies, ZVI NPs is considered potent nanomaterials for enhancing biogas production via stabilizing the process of anaerobic digestion as well as stimulating the growth of beneficial microorganisms and enzymes evolved in the process [99]. In 2011, the impact of particle size of nano-metal oxides such as CuO, and ZnO was studied on methane and biogas production during anaerobic digestion [100].

Using NPs is beneficial due to its precise dosing of ions thus enabling enhancement of the anaerobic digestion process, which leads to higher biogas production. On the contrary, the large-scale application of NPs might have some concerns regarding toxicity and environmental issues [101]. Abdelsalam et al., have demonstrated the effect of 20 mg/L^{-1}Fe_3O_4 NPs on methane (CH_4) production from cattle dung slurry [102]. The investigations have shown an increase of 1.7 and 2.0 times, in the biogas and CH_4 production by the addition of 20 mg/L^{-1} Fe_3O_4 NPs. Similarly, CH_4 production was increased by 120 % with the addition of 100 mg/g^{-1} TSS Fe_2O_3 NPs [103]. Moreover, Rana et al., investigated the effects of different doses of α-Fe_2O_3-nanoparticles (IONPs) on the growth and biogas production potential of *Chlorella pyrenoidosa.* The highest growth (2.94 ± 0.01 g/L) of microalgae at 20 mg/L was observed in the study. A net augmentation in biomass, biogas, and methane production was achieved by 98.63 % at 30 mg/L IONPs supplementation [104].

4.3. Drug delivery

Mesoporous silica nanoparticles (MSNs) have fascinated and drawn attention due to their biomedical application. Due to mesoporous structures and high surface area, MSNs proved a potential candidate over conventional drug delivery systems [105]. In the year 2001, the first report of using MCM-41 type mesoporous silica particles (MSNs) as a drug delivery system has been introduced. An exponential increase in the applications of MSNs has been observed in biomedical research [106]. However, various applications of MSNs as nanocarriers, with unique mesoporous structures have been investigated as efficient drug delivery systems which act as therapeutic agents in fights against several kinds of diseases like diabetes [107,108] cancer [109] inflammation, [110] and in bone/-tendon tissue engineering [111–124].

An ocular drug delivery system needs efficient drug delivery to the eyes because of several anatomical barriers and the clearance mechanisms present in the eye. Since nanomaterial-based drug delivery will be more advantageous as compared to conventional methods. Scientists have been using liposomes, polymeric micelles, liposomes, cyclodextrins, hydrogels, and dendrimers, to enhance the bioavailability of ocular therapeutic agents in ocular drug delivery systems [115]. Recently nanocarrier-based ocular drug delivery systems are getting the most capable tool to fulfill the demands for an ideal ocular delivery system. Its small size makes it more appropriate for high diffusivity across the corneal epithelium membranes. Several studies have already demonstrated that the application of such nanomaterials through topical administration improved the corneal permeability of drugs [116–119]. Moreover, advancement in nanotechnology applications has been utilized in ocular drug delivery systems consisting of copious nanostructure carriers as probable ocular drug carriers [120]. Additionally, Ludwig has explained the employ of mucoadhesive polymer-based nanostructures in the ophthalmic delivery of drugs. It showed an enhancement of targeting and provided retention of the drugs at tissue sites such as the corneal surface [121].

4.4. Vaccine development

Vaccines are widely considered crucial immunological tools to fight against infectious diseases by providing long-lasting defensive immunity with good antibody response [122]. Nanoparticles have a wide range of biomedical applications due to their unique physicochemical properties as compared to other bulk chemicals [123]. NPs are capable to penetrate deeply into tissue and improve cellular uptake as well as escaping from lysosomal compartments [124–126]. At present time, the world is facing covid-19 pandemic and it has infected millions of people due to its high pervasiveness, long incubation period, and lack of well-supporting treatments or vaccines with no clear signs of abatement which make it even more terrible. Nanomaterials are potential candidates for antigen delivery, as adjuvants and as mimics of viral structures. Hence the first vaccine developed into clinical trials is an mRNA vaccine which was delivered with the help of lipid nanoparticles [127]. The prime role of the adjuvant is to enhance the specific response of the particular immune system to the least amount of the antigen supplied via the activation of antigen-representing cells [128]. Available vaccines like diphtheria, tetanus and influenza type b are making use of the adjuvanticity of Al NPs. These adjuvants are mostly used in vaccines to build strong antigen-specific immune responses [129].

Similarly, SiNPs and other antigen carriers, recently used are capable of controlled antigen release in vivo. This method has elevated the magnitude of both humoral and cell-mediated immune response against porcine circovirus type 2 in the rat [130]. Hyaluronic acid (HA) is another potential candidate for a nanoparticle vaccine being biodegradable, native to the human body, and has been successful in cancer therapy clinical trials [131]. HA consists of repeating units of D-glucuronic acid and *N*-acetyl-D-glucosamine, having a native biological role that depends on the length of the polysaccharide [132]. Dodi et al. investigated Au nanoclusters as carriers in the preparation of synthetic carbohydrate vaccines. Gold glyconanoparticles act as synthetic tetrasaccharide epitopes related to *Streptococcus pneumoniae* type 14 capsular polysaccharide (Pn14PS), the *T*-helper ovalbumin 323–339 peptide ($OVA_{323-339}$). The cytokine levels confirmed that glyconanoparticles help in *T*-helper cell activation. The antisaccharide antibodies promoted phagocytosis of type 14 bacteria by human leukocytes, indicating the functionality of the antibodies [133].

4.5. Water disinfection

Water disinfection methods have been developed to provide safe water. It works on the principle of inactivating and removing pathogens to provide safe drinking water without contamination by microbes [134]. Several methods have been developed for water disinfection such as the use of ozone, ultraviolet (UV) radiations, chlorine, heat sterilization, and filtration through the size exclusion technique [81]. The process of photocatalysis is gaining more attention over traditional water treatment technologies for waterborne biohazard inactivation. 2D nanomaterials-based novel photocatalysts have been used as building blocks for photocatalytic water disinfection viz. graphene, graphitic carbon nitride, 2D metal oxides, and metallates. Metaloxyhalides and transition metal dichalcogenides have been introduced for the photo-catalytic pathogen inactivation process [135]. Due to unique properties in structural features as compared to 0D and 1D nanomaterials, 2D nanostructures pose superiority in architecture modulation, light harvesting, charge separation, and tenability providing suitable sites for pollutant adsorption and surface reaction [136].

Nanoparticles have proved better disinfectants in comparison to chemical disinfectants viz. sodium hypochlorite (NaClO) and phenol (C_6H_5OH) [137]. The porous Ca-Si-based nanospheres can act as intracanal disinfectants-carrier and hence can serve in infected canal treatment [138]. Nano disinfectants developed into biofilm have shown excellent antimicrobial activity against some bacterial pathogens e.g., *Salmonella and Staphylococcus* sp. [139–142]. Consequently, an antimicrobial nanomaterial provides a substitute for energy-efficient methods for water disinfection [136 s]. Graphene-based nanomaterials and their derivatives have been introduced recently as potential antimicrobial disinfectants. Graphene materials (GMs) are broad-spectrum antimicrobial agents, capable to inactivate and control various kinds of living organisms. GMs consists of graphene, pristine, graphene oxide (GO), and reduced graphene oxide (rGO). They possess properties and superior structures capable to overcome pathogenic microorganisms and act as potent disinfectants due to specific structural and related properties [143].

4.6. Other applications

To examine the effectiveness of polymer-based nanoadsorbents for the adsorption of anionic and cationic dyes in the aqueous phase, nanostructured sulfonated polypyrrole adsorbents have indeed been developed by copolymerizing pyrrole and sulfophenylenediamine [144]. This increased number of functional groups, like $NH/NH_2/SO_3H$ present in the copolymers, may be the cause of the polymer-based (PPY-SPDA) adsorbents' high adsorption efficiency toward the anionic and cationic dyes in aqueous solution. In the batch adsorption method, the effects of temperature, pH, dye concentration, contact time, and adsorbent dosage have been researched. For the adsorption of Congo Red dye, a dosage of 0.15 g (PPY-SPDA) of adsorbent over a period of 3 h at pH 1 resulted in a 100 % adsorption efficiency.

Similarly, comprehensive review work offers a thorough analysis of the removal of pollutants from a multi-component system when there are other contaminants present (MCS). The many synergistic, antagonistic, and non-interactive interaction processes that could occur in MCS are reviewed. A detailed explanation of the MCS, which contains a combination of traditional toxins like heavy metals and colors and other emergent contaminants like antibiotics, organic contaminants, pesticides, and personal care items. Researchers interested in the simultaneous removal of pollutants from MCSs for wastewater cleanup will find the review paper useful [145].

The banana peel biochar (Ag-BBc) composite was successfully tailored using a green synthetic method. Ag nanoparticles were made using *Azadirachta indica* leaf extract as a reducing agent, while biochar was produced by pyrolyzing banana peels [146].

Through its use in energy storage and environmental restoration, the nanocomposite was examined for its multifunctionality. By using a variety of analytical techniques, the prepared composite was thoroughly characterized. Cyclic voltammetry and galvanostatic charge–discharge methods were used to examine the electrochemical aspects. Ag-BBc composite's enhanced specific capacitance was measured at 655 Fg-1 in 1 M.

By using a bimetallic composite made of silver (Ag) and copper (Cu) as well as ultrasonic technology, the study attempted to remove the dye rhodamine B (RhB) and the insecticide dichlorphenoxy acetic acid (2,4-D) from an aqueous matrix [147] When compared to Ag/CNF and Cu/CNF, Ag-Cu/CNF demonstrated superior adsorptive efficiency. Freundlich and Langmuir's isotherms were used to study the equilibrium of adsorption. Following analysis of the data, it was concluded that the Langmuir model best fit the equilibrium data, with maximum adsorption efficiencies of 201 mg/g for RhB and 112 mg/g for 2,4-D, respectively. Sonosorption is a successful choice for starting the adsorption phenomena due to convenient and easy diffusion, according to a comparison of adsorption assisted by ultrasound, magnetic stirrer, and vortex shaker-assisted methods.

The transport, fate, and distribution processes of PAHs in the environment with their influencing elements were detailed in a recent review study. Additionally, this research offered a summary of many conventional and cutting-edge prospective treatment methods utilized to clean up PAHs-contaminated locations, including nanoadsorption, chemical, thermal, electrokinetic, and biological treatments [148].

However, another study found that the most widely used adsorption method was superior because of its effectiveness, affordability, and simplicity of use. To assess the mass transfer mechanisms, the effectiveness of the nano-adsorbents was explained using adsorption kinetic models. However, several degrading techniques, such as catalytic reduction and photocatalysis, have also been developed. For the removal of pesticides from water, a variety of strong metals, metal oxide, and functionalized magnetic nanoparticles have been highlighted, organized, and compared. Additionally, the published work has suggested future directions as well as existing difficulties addressed by researchers [149].

5. Exposure and toxicology of nanomaterials

5.1. Effect on human beings

Nanotechnology is defined by The US National Nanotechnology Initiative (NNI) as "using and control of materials and structures with nanoscale dimensions, approximately between 1 and 100 nm, and that unique phenomenon enables new applications." Novel scientific reports expound on the potential benefits of nanotechnology. Based on these investigations more and more nanomaterials are expected to be used and offer a lot of benefits in numerous fields in industrial products and consumers including, cosmetics, medicine, food, and agriculture. This will result in the enhancement of exposure to nanomaterials by humans at their workplaces and daily lives [150]. People are exposed to a large range of natural and artificial nanoparticles via the environment, water supply, air, food chain, drugs, and medical applications [151]. To explain the modes of action of nanomaterial toxicity, it becomes necessary to underpin the processes of its environmental fate and behavior. Firstly, it is required to characterize the materials used in different studies as far as possible and compulsory.

5.2. Sources of exposure to nanomaterials

There are numerous examples of potential nanomaterials that may be exposed to humans during daily routines, for example, erosion from artificial materials such as ultrafine particles from car tires on roads. The particle diameter ranges from 15 to 50 nm [152]. Other ultrafine particles from vehicle exhausts, ranging from 18 to 300 nm, during the morning rush hours have the highest concentrations, especially of particle size < 50 nm. Exhaust concentration depends on vehicle type and speed [153]. Aerosol emissions from highway roads, where the particle size was < 50 nm increased generally with vehicle speed [154]. Volcanic eruption is a natural source of dust and ash containing ultrafine particles which are respirable affecting the respiratory system health [155]. Iron oxide nanoparticles (4–6 nm) utilized in ultrafiltration technology to improve disinfection of water supplies are left in drinking water in trace quantities [156]. Iron sulfide nanoparticles help in the removal of organochlorine pesticides from drinking water supplies to improve the quality of drinking water [157]. Silver nanoparticles coated with polyurethane foam have been used as low-cost and efficient agents in killing bacteria or providing an antibacterial filter for water treatment [158].

Radioactive nanoparticles are sparsest in the environment in small quantities but they could have access to groundwater and lungs through aerosol uptake [159]. Zerovalent metal nanoparticles containing iron used in soil treatment and removal of chlorinated hydrocarbons from contaminated soil can transfer to humans and animals through food chains [160]. Application of 1–2 kg of the active ingredients of nanoparticles containing fungicides to control fungal infection in soils may transfer kilos of the new nanomaterials in the soil to food chains through planted crops in the soil [161]. Another source is medical fluorescent nanoparticles used for imaging and detection of tumor cells in breast cancer along with potential application in chemotherapy (targeted drug delivery) [162]. Medical Chitosan nanoparticles are utilized in bone cement which is used to fix implants to combat bacterial contagion in bone surgically [163]. The utilization of medical nanocrystals has been reported for the delivery of anti-nausea and vomiting drugs used for the control of side effects of chemotherapy [164]. Various sources of the exposure of nanomaterials to the human body have been illustrated in Fig. 2.

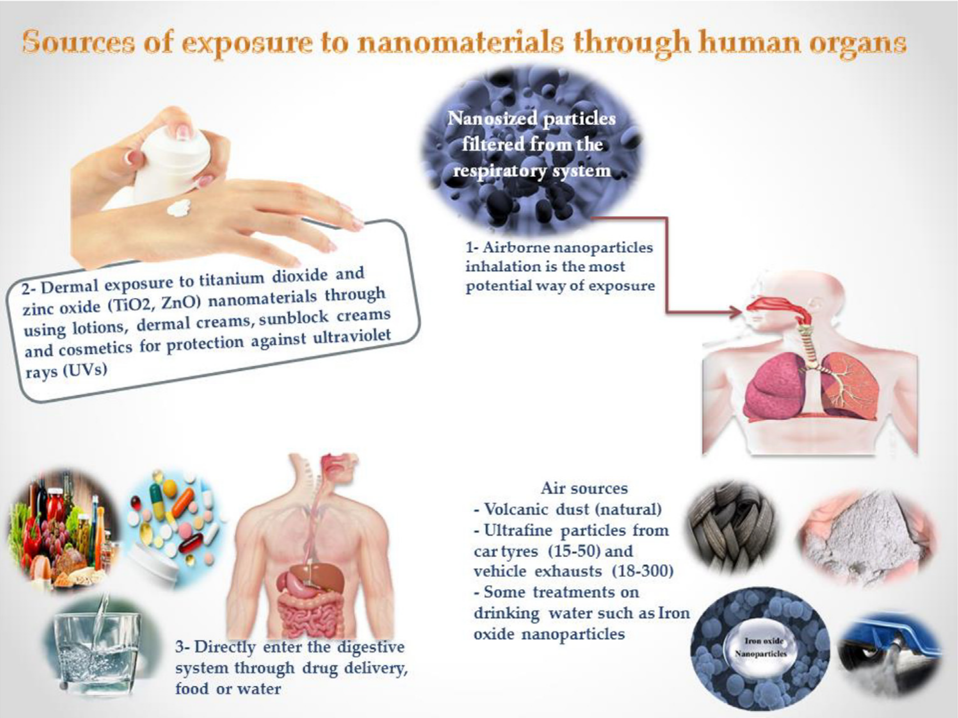

Fig. 2. Sources of exposure of nanomaterials to the human body.

5.3. Entryways of nanoparticles into the human body

Once nanoparticles enter the body, they may be translocated by blood circulation. Their plausible allocation in the body may be related to their surface characteristics and size such as lipophilicity, polarity, hydrophilicity, and catalytic activity [165,166]. As the particle size decreases, per unit surface area increases, and thus, the nanoparticles are expected to display increased biological and chemical activity in the human body [167,168]. As a result, it can be concluded that smaller size of nanoparticles might be more toxic and taken up faster than the larger ones by the cells. Nano-sized particles (NSPs) inhalation and entry through the respiratory system is the most potent way of exposure to nanoparticles. Exposure via other routes is less rational unless it is because of dermal contact of skin creams and oils, direct ingestion through drugs and food delivery, and nanoparticle-treated membranes in a water filtration system [169].

5.3.1. Respiratory system

Airborne nanoparticles inhalation is the most common way to enter the human body. Several researchers have reported that the inhaled nanoparticles are efficiently distributed by diffusion mechanisms in the lungs. The most common nanomaterials which easily enter the lungs are ball-shaped solid materials [170]. An exploratory study made about the pulmonary effects of single-walled carbon nanotubes (SWCNTs) by two separate groups concluded that carbon nanotubes (CNTs) can reach the lungs and cause more severe effects than carbon black or quartz [171,172]. A more in-depth study about the threshold length of nanofibers that prompt acute pleural inflammation was made by Schinwald et al., They utilized five defined length classes of silver nanofibers. Carbon nanotubes and nickel nanofibers were used to set the relationship between pleural inflammation and fiber length. The results showed a threshold effect which indicates that fibers pathogenic to the pleura are above 4 μm in length [173].

Moreover, the results can give a better understanding of the toxicity–structure relationship of asbestos-induced mesothelioma and eventual risk assessment for the aim of engineering non-pathogenic synthetic nanofibers. Likewise, toxicologic studies utilizing rodent models proved that some types of carbon nanotubes can have the ability to induce mesothelioma [174–176]. This later leads the World Health Organization (WHO) to evaluate rigid, long multi-walled carbon nanotubes as potentially carcinogenic to humans (International Agency for Research on Cancer, IARC Group[177]. Long, rigid CNTs can be more hazardous as compared to shorter ones [178].

A study made by Zhang et al. evaluated nanoparticle precipitation in the upper human airway system. The precipitation of nanoparticles with high concentrations appears around the carinal peaks as compared to the straight segments in the bronchial airways but, precipitation allocations are more regular along the branches of the airway[179]. Precipitation depends on particle size, bifurcation, and inhalation stream rate. The relatively massive regular distribution of nanoparticles leads to major toxicity as it possesses more area to interact with the cell membranes as well as transportation and absorption of toxic substances. Cell line A549 of human lung cancer has been utilized as a model for in vitro cell culture to study the toxicity of nanomaterials. Cell line A549 was used by Foldbjerg et al., to investigate the silver nanoparticle's genotoxic and cytotoxic effects. They used flow cytometry and atomic absorption spectroscopy to measure the cellular uptake of the nanoparticles. They studied the cytotoxicity dose-dependence of silver nanoparticles by the annexin V/propidium iodide assays and MTT. The silver nanoparticles' cytotoxicity was extremely reduced by pretreatment with the *N*-acetyl-cysteine antioxidant. They confirmed a strong linkage between reactive oxygen species (ROS) levels and mitochondrial damage along with early apoptosis [180]. The ROS-induced DNA damage has been measured after nanoparticle exposure by increased DNA adducts through^{32}P-post labeling. The cellular ROS levels were strongly linked with the DNA adducts level and were blocked by antioxidant pretreatment. The results suggested that silver nanomaterials act as the mediator of genotoxicity and ROS-induced cytotoxicity. Hazard damage might happen when exposed to nanomaterials through inhalation; NMs size allows endocytosis to perforate a cell and transcytosis to perforate several cells, one after another. Thus, when they are inhaled, NMs can reach the nervous ends of the olfactory epithelium and can travel upstream the axons towards the olfactory bulbs in the brain thus affecting neurons. NMs can reach the brain through the lungs, followed by blood, and finally the blood–brain barriers. They can also reach other organs via blood circulation such as the heart, bone marrow, spleen, and lymph nodes. They can cause inflammation, antioxidant and pro-oxidant activities, and oxidative stress. The effect depends on the dose and type of nanomaterial [150].

5.3.2. Skin layers

The skin is the largest organ of the human body and the fundamental route of exposure to the external environment. Skin structure consists of three layers: epidermis, dermis, and subcutaneous tissue. Dermal exposure is the second serious uptake source for nano-sized particles after the uptake from the respiratory system. There is augmented interest in investigations related to titanium dioxide and zinc oxide (TiO_2, ZnO) nanoparticles as these are utilized in various lotions, dermal creams, sun-block creams, and cosmetics for protection against ultraviolet rays (UVs) which can cause melanoma. Titanium dioxide (TiO_2) nanoparticles (5–20 nm) can infiltrate into the skin cells and intervene with the immune system function. Anatase TiO_2 nanoparticles (10 nm and 20 nm) can cause lipid peroxidation, oxidative DNA damage, and micronuclei origin. They also boost nitric oxide and hydrogen peroxide production in BEAS-2B cells which behave as human bronchial epithelial cell lines in the absence of photoactivation [181]. Consequently, it can be easily concluded that the smaller the nanoparticles, the easier skin perforation and damage induction. It was discovered that the photocatalytic activity of the anatase TiO_2 is higher than that of rutile. 200 nm rutile titania can induce oxidative DNA damage in the absence of light while the anatase of titanium dioxide remains inactive. The uptake of materials via the skin is a rather complicated process controlled by both external and internal factors [182].

The zinc oxide NP's toxic response was estimated in human epidermal keratinocyte cells by Lee et al. 2012. Results showed that ZnO NPs lessened the mitochondrial function and caused leakage of lactate dehydrogenase enzyme (LDH) which is a prediction tool for cutaneous lymphoma. Moreover, induction of both LPO and ROS was observed which indicates that ZnO nanoparticles motivated oxidative stress. These results clarified the significant cytotoxicity in human epidermal keratinocyte cells. Clinical side effects of nanoparticles following topical admonition, including skin inflammation, skin cancer, and genetic toxicity, etc. resulting from skin exposure have been summarized in Table 1[183].

5.3.3. Digestive system

Nanosized particles can enter the digestive system through filtration from the respiratory system or directly through drug delivery, food or water. Several reports are available in the literature which deal with the uptake of NMs in the intestines. Most of them showed that the nanosized particles pass through the intestinal tract and can rapidly be gotten rid of [169]. An important study was made by Bettini et al., to evaluate the uptake effects of food grades containing titanium dioxide nanoparticles (TiO_2-NPs) which

Table 1
Types of NPs, does, size, study at various medium and final findings of various nanomaterials.

Type of nanoparticle	Dose / size of nanoparticle	In vivo/ex vivo/in vitro study	Finding	Reference
TiO_2	400-µg TiO_2 per cm^2, 4–90 nm	In vivo porcine ear skin	Discovered in the SC, stratum granulosum, prickle cell layer and basal cell layer but not in dermis	Wu *et al., 2009*
TiO_2 and ZnO		Ex vivo porcine	skin Able to penetrate through porcine skin, but not to deeper layer	Gamer et al. 2006
TiO_2 and ZnO	ZnO: 3.0 µmol/g, TiO2: 0.41 mol/g	In vivo	skin obtained by biopsy with present at the skin surface and in the uppermost SC regions	Filipe et al. 2009
ZnO	Uncoated (65.5 ± 35.6 nm) and coated (74.3 ± 32.3 nm)	In vivo human	skin Penetration only into the superficial layers of the SC, with no penetration to the viable epidermis and no apparent toxicity in the viable epidermis	Leite-Silva *et al.*2016
ZnO	19 and 100 nm	In vivo human	^{68}Zn was not detected in blood and urine, and only trace was tracked after 5 days	Gulson *et al.*2010
Silver	20–80 nm, 34.0–0.34 µg/ml	In vivo porcine skin	On top of the SC and the superficial layers of SC	Samberg *et al.*2010
Silver	20–50 nm	*In vitro* the mouse skin samples from the Franz diffusion cell system. Investigation on dependence of the nanoparticle's shape on penetration was carried out.	TNP in the SC region whereas SNP in a viable epidermal layer was observed, indicating that both TNPs and SNPs could not penetrate through the dermal–epidermal junction into the underlying dermal layers. Rod-shaped nanoparticles were observed with high penetration ability through dermal–epidermal junction	Tak*et al.*2015
Silver	SNPs: 50 nm, length and diameter of RNPs: 50 and 20 nm, TNPs: 2 nm thick equilateral triangular length of 50 nm	*In vitro* Franz diffusion cell system In vivo mice skin	RNPs: most penetration, SNPs: moderate penetration, TNPs: lowestpenetration, presence of an SC and a collagen- and muscle-filleddermis. No major differences with differently shaped AgNPs	Tak*et al.*2015
Silver	10, 30, 50 µg/ml	*In vitro* human skinkeratinocytes (HaCaT)	Observation of apoptosis symptoms, decrease of cell viability and induce production of reactive oxygen species	Auffan*et al.*2009
Gold	15 and 6 nm, 90 µg/ml	Ex vivo excised human skin	Aggregation of AuNP (15 nm) in aq. solution on the surface SC but penetration of AuNP (6 nm) in toluene through SC and into epidermal layers of human skin	Labouta *et al.*2011
Gold nanorods	100 µl, 500 µg/ml	*In vitro* skin permeation using a Franz-type diffusion cell	Penetrated into the SC	Lee *et al.*2013
Gold	2 µl (5–10 nm)	in vitro human keratinocytes cell line	Penetration of NPs through the barrier of the SC, epidermis and the dermis. Nanoparticles were found over 500 µm deep into the skin	Goldstein*et al.*2014
Gold	22–186 nm	In vivo rat skin	In epidermal layers just below the SC	Raju *et al.*2018
Gold	90 mg/ml, 437 mg/ml	*In vitro* human skin permeation using a Franz-type diffusion cell	Penetration increases with increasing concentration and propertyof hydrophobicity, also by decreasing the size of NPs	Labouta *et al.*2011
Gold	109–1011 NPs/ml	*Ex vivo* rat hind-paw skin In vivo rat hind-paw skin	Epidermal penetration but in rats exposed to AuNPs demonstrated nanoparticles in blood, and histological analysis revealed	Raju *et al.*2018
Quantum dot	8.40 × 5.78 nm; 1, 2 and 10 µM for 24 h	In vivo porcine skin	Penetration of QD through the uppermost SC layers of the epidermis and near hair follicles. QD were found in the intercellular lipid bilayers of the SC	Zhang *et al.*2008

RNP: Rod-shaped nanoparticle; SC: Stratum corneum; SLN: Solid lipid nanoparticle; SNP: Spherical nanoparticle; TNP: Triangular nanoparticle.

were used as a white pigment in Europe(E171). This study was of utmost importance because daily oral intake of such TiO_2-NPs may be related to the increased risk of carcinogenesis and chronic intestinal inflammation [184]. After one week of oral exposure to E171 at human levels for rat models, regulatory T cells showed a decrease in inflammatory response inhibition. E171 use for one week did not launch intestinal inflammation, but a 100-day treatment confirmed micro-inflammation in the colon and initiated preneoplastic lesions, and also promoted the growth of aberrant crypt foci in chemically model-induced carcinogenesis. These results should be contemplated for risk estimation of exposure to NPs from dietary sources leading to Th17-driven autoimmune diseases and colorectal cancer in humans.

5.3.4. Immune system

A review dealing with the immunotoxicity testing for safety estimation of nanomaterials marked that nanoparticles can catalyze or suppress the immune responses [185]. Nanomaterials can alter the production of cytokine. They motivate pro-inflammatory effects in the lungs of experimental animals with increased expression of Macrophage Inflammatory Proteins (MIP), Interleukin (IL), Monocyte Chemoattractant Protein (MCP), keratinocyte chemoattractant, Granulocyte-macrophage colony-stimulating factor (GM-CSF), Chemokine (C—C motif) ligand 17 (TARC), activation of the stress-activated mitogen-activated protein kinases (MAPKs) p38 and Jun *N*-terminal kinase (JNKs). The results suggested that through the elicitation of an oxidative stress mechanism, nanomaterials may share pro-inflammatory disease operations in the lung, especially allergy diseases [186,187]. A positive role of nanomaterials in the immune system has been explained by Elechiguerra et al., in a study on the interaction of nanomaterials with microorganisms such as the HIV-1 virus. The silver nanomaterials under a size-dependent interaction with the HIV-1 virus showed that silver nanomaterials in the range of 1–10 nm exclusively united to the virus, because of this interaction, the silver nanomaterials prevent the virus from binding to the human host cells [188].

Oxidative stress is the main mechanism of toxicity in cellular organelles induced by engineered NPs due to some factors such as size, particle surface, presence of metals, and composition. Cellular oxidative stress causes damage to the mitochondrial membrane and immune cell activation acts as an early indicator of cellular stress. Mitochondrial membrane damage leads to mitochondrial abnormality function, a major step in cell death and cell injury [189,190]. Oxidative stress response which is caused by NP is a starter for numerous pathophysiological effects including; genotoxicity, fibrosis, and inflammation as investigated by activation of associated cell signaling pathways [191]. The cytotoxicity mechanism of SiO_2 nanomaterials in human embryonic kidney cultured cells (HEK293) has been investigated by Wang et al., They noticed a dose-dependent reduction in cell viability, a reduction in reduced glutathione content, and a rising level of intracellular ROS. These studies showed that the cytotoxicity of SiO_2 nanomaterials on kidney culture cells HEK293 was related to oxidative stress [192].

Besides the common paradigms of nanomaterial toxicity (inflammation and oxidative stress), there are other mechanisms of nanomaterial toxicity such as lysosomal and autophagy dysfunctions. Lysosomal cells are considered the most common NPs reservation and degradation intracellular sites. Lysosomal and autophagy dysfunction pathways have been attached to a variety of diseases. Autophagy dysfunction can be induced by some nanomaterials resulting in autophagic cell death or apoptosis [193]. Autophagy dysfunction has an important role in both cancer development and progression [194] as it might allow the damaged organelles such as mitochondria to pile up, which can further induce oxidative stress, DNA damage, and inflammation subsequently.

Vietti et al. highlighted the indirect and direct effects of CNT on fibroblasts. Both contribute to fibrogenic activity in the lung. Porter et al., carried out in vitro studies and revealed that a dose range of CNT between 1 and 100 µg/ml induces effects on the different cell types. The dose range used in in vivo experiments (10–100 µg/mouse, corresponding to 0.5–5 mg/kg) is relevant for the human exposure scenario [195].

5.3.5. Genotoxicity of nanomaterials

Several methods have been adopted for testing the genotoxicity of nanomaterials. They include mutations, chromosomal aberrations, micronucleus formation, oxidative DNA damage, DNA strand breaks, and DNA adducts [196,197]. Various studies reported that TiO_2 is genotoxic by its nature [165,198,199]. However, there are several studies [200–202] that reveal that TiO_2 is not genotoxic. Moreover, Sahu et al., utilized genotoxicity tests, the flow cytometric in vitro micronucleus test and the cytochalasin B-blocked micronucleus test, in vitro models (Caco2 cells from the colon and HepG2 cells from the liver) to compare the potential genotoxicity of two dissimilar sizes of nanosilver (20 and 50 nm) having similar surface charge, shape, composition and obtained from the similar commercial source. They observed that the smaller size of nanosilver (20 nm) was genotoxic by inducing micronuclei for both the cell types, but the larger size (50 nm) produced a weak response [203,204].

6. Impact of nanomaterials on ecosystem and animals

Since the introduction of nanomaterials (NMs), new technology has been developing day by day and extended to include most life aspects. However, the toxic effect of such materials must be deliberated to evaluate their impacts on the living organisms which live in terrestrial and aquatic environments [205]. NMs elements and their physicochemical properties may act as disturbing factors for organism development which interfere with their ordinary physiological functions, causing malformations that can be lethal for the embryos and growing animals. Not only does the chemical structure of NMs affect normal mechanisms, but the size of NMs itself has some properties which interfere with the chemical, physical, and biological activities of living organisms [45]. Cells have different reactions according to NMs sizes. Tiny nanomaterials can enter the cell easily by penetrating its membranes and reach to organelles. TiO_2 nanoparticles can target mitochondria and cause mitochondrial dynamic imbalance [206]. It might alter the cell metabolism causing cell death ultimately. If NMs are not in small sizes, they can't break through the cell and overlap with the cell membrane disrupting its functions (e.g., signal transduction and ion transport).

Furthermore, membrane lipid bilayers can be destroyed by positive electric charges of NMs, and surface coating of nanomaterials can also cause a disturbance effect on cell structure [207]. In a previous study, the ecotoxicity effects on some fish species, algae, bacteria, and mollusks as well as mammals had been studied by Handy et al.,[45] The data on biological effects revealed that nanomaterials can be toxic for these species. Diverse living models are used in more recent studies to measure the potential effects of NMs on living organisms. Using models from mammals (mice) or bony fishes (zebra fish) showed that nanomaterials (cadmium oxide NPs in mice and silica NPs in zebra fish) cause injurious effects on the embryonic and reproductive system [208,209]. Likewise, some more experiments with rat models showed the true hazardous effects of nanomaterials on the brain. During an experiment, an exhibition of Cu-NMs (40 and 60 nm diameter) encouraged an increase in brain capillaries endothelial cells when a low concentration of NM was applied (about1.5 µg/mL) in the rat. Furthermore, higher concentrations (about 50 µg/mL) encouraged the increase of prostaglandin E2. TNFα and ILβ Extracellular levels were significantly high and the toxicity affected the blood–brain barrier finally [210]. Similarly, another study on rat resulted that an exposition with24 hours to Ag-NMs (25, 40, and 80 nm diameter) affected the blood–brain barrier, causing a pro-inflammatory reaction that developed later into a brain inflammation joined with neurotoxic effects [211]. In the same direction, a comparable investigation carried out on pigs resulted in a pathogenic effect on the blood–brain barrier in presence of 40 and 60 nm Cu-NMs, 25, 40, and 80 nm Ag-NMs and 3 and 5 nm Au-NMs [212]. While Au-NMs exposed cells in mice showed a heavy chain degeneration of a cytoskeleton protein clatter in 72 h [213].

For the liver organ, Van der Zande et al., treated rats for 28 days orally with 15–20 nm nanosilver. They observed that nanosilver particles reached all examined organs with elevated levels in the liver and spleen [214]. The data collected from numerous rodent models indicate that liver cells play the main role in nanomaterials metabolism [215], and most nanomaterials often accumulate in the liver [216] when taken by the oral path and hold in cells, leading to tissue damage. For the potential disorders in the cardiovas-

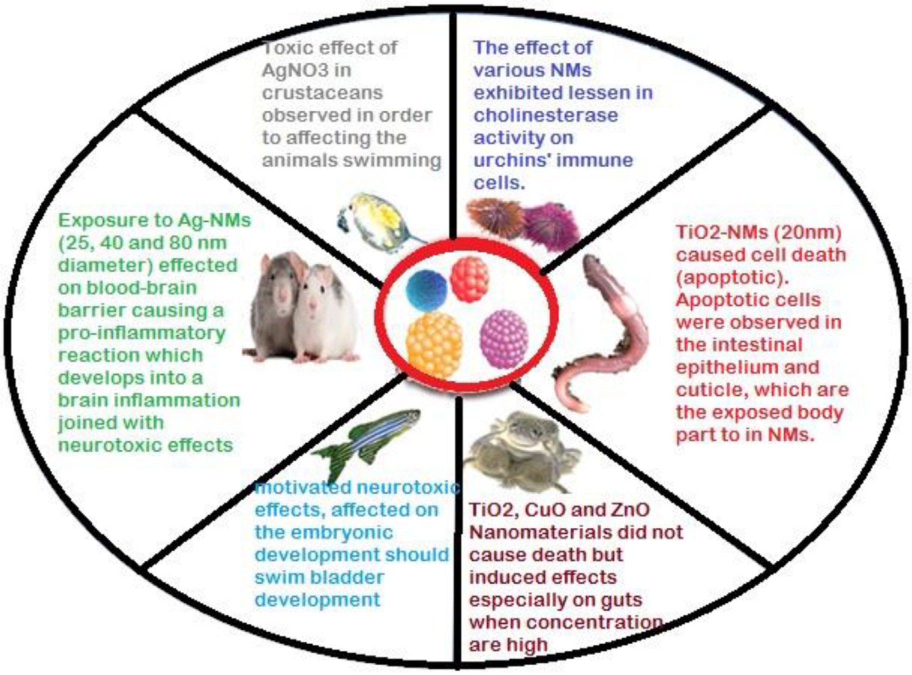

Fig. 3. Adverse impacts of nanomaterials on various animals and the environment.

cular system as a result of exposure to nanomaterials, Du et al., used rats' models to estimate the toxicity of silica nanomaterial. They used the hematologic parameters, oxidative stress, inflammatory reactions, myocardial enzymes in serum, and endothelial dysfunction [217]. Silica nanomaterials were detected passing into systemic circulation through the alveolar-capillary barrier. The results showed that the toxicity of silica nanomaterials in the cardiovascular system was dependent on dosage and particle size, the oxidative stress played a substantial role in endothelial dysfunction and inflammatory reaction. Persistent cardiac toxicity due to exposure to various sizes of gold nanoparticles by the tail vein in rats has been reported by Yang et al., They evaluated the cumulating Au NPs in the rat heart and the effects on cardiac function, structure, inflammation, and fibrosis. The left ventricular mass, the left ventricular end-diastolic inner dimension and body weight, heart weight were increased in rats receiving the smallest-sized gold nanomaterials (10 nm) after only 2-weeks of exposure. It has been concluded that cardiac hypertrophy is caused by gold nanoparticles [218].

Several experiments have been carried out using *Eisenia fetida* (earthworms). It was observed that apoptosis (cell death) increased after exposure to Ag-NMs (20 nm). Apoptotic cells were observed in the intestinal epithelium and cuticle, which are the body parts exposed directly to NMs. They also influenced the nutrient intake and the immune protection presented by chloragogenous tissue [219]. The effects of TiO_2-NMs on earthworms have been investigated by several co-workers. TiO_2-NMs (10 to 20 nm) concentration, higher than 1 g/kg of soil have hazardous effects on *Eisenia fetida* including damage to mitochondria, affecting enzymatic activities, and inducing apoptosis [220]. Fullerene-NM sublethal concentrations decreased HSP gene expression and the worms exposed to these nanomaterials showed cuticle damage, and pathological signs on the epidermis, intestinal barrier, and muscles [221,222]. Recently, an experiment was carried out by Bourdineaud et al., to measure the toxic impact of exposure to gold and silver nanoparticles (Au and Ag NPs) on the earthworm *Eisenia fetida* in soil. The results showed that both Au and Ag NPs caused oxidative stress as clarified by decreasing catalase levels and increasing glutathione S-transferase and malondialdehyde concentrations [291]. Even at their lowest concentrations both Au and Ag NPs induced DNA modifications and they can suppress gene expression shared in the defense system and stress response. The negative impacts and exposure of nanomaterials on various forms of animals and the environment have been represented in Fig. 3.

Amphibians have destruction-reconstruction phases, but a lot of apoptotic cells were observed in tadpoles in that phase which make it fragile [223]. Transformation is under thyroid and pituitary control. Hence amphibians consider premium models to evaluate the toxic effects of substances such as NMs on the thyroid and pituitary. A study on *Xenopus laevis* tested Cu toxicity under three different forms. Cytotoxic effects depend on the compound formed and the cell cycle stage. Mitotic cells treated with the three forms of substances have a significant increase in the number of cell death and cells stopped division. Treatments after 48 h as well as 6 and 7 days, with 6 nm CuO-NM or Cu^{++}, respectively, induced a significant reduction of cell propagation and an increment in apoptosis (cell death) [224]. Another study on amphibian's embryonic development showed a weak fatal effect on embryos. TiO_2, CuO, and ZnO nanomaterials did not cause embryo death but induced teratogenic effects, especially on guts when concentrations are higher than 50 mg/L. ZnO-NMs caused the most damaging effects on the gut barrier which reached the connective tissue. TiO_2-NM showed weak teratogenic and hidden physiological effects [225]. An interesting study was dedicated to the transfer of NMs along the food chains by Unrine et al., when they exposed *Eisenia fetida* (earthworms) to 10–20 nm Au-NM which was later eaten by bullfrogs *Lithobatescates beianus* (Group I). The effect of NM exposure was compared with the bullfrogs, who directly consumed the same NMs (Group II). The presence of Au NM was detected in many organs viz. liver, intestine, spleen, muscle, kidney, and stomach of the frog. About 0.12 % and 0.09 % NM were detected in Group I and respectively. These results demonstrated the possibility of Au-NM transfer through food chains. Spence et al., studied the harmful effects of zinc oxide NPs on amphibian (*Taricha granulosa*) life stages. For the egg stage, the results showed that 10.0 and 100.0 mg of ZnO NPs caused higher mortalities. While larvae

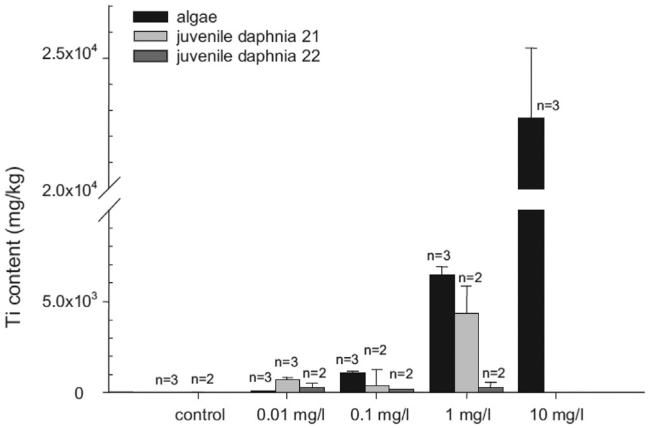

Fig. 4. Ti content measured by µ-XRF in contaminated algae and within individual daphnia juvenile [232].

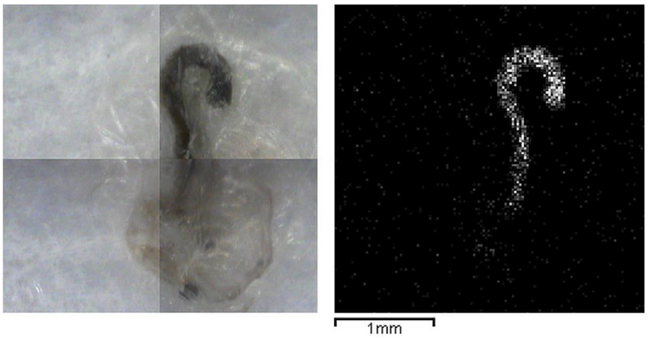

Fig. 5. Ti distribution within dried daphnia fed during 21 d with contaminated algae obtained by µ-XRF [232].

exposed to 10.0 mg concentration for 24 hr hatched earlier within 5 days with decreasing in development, and smaller size than the control. Both concentrations 10.0 and 100.0 mg exhibited larvae to sublethal effects, increased mortality in this stage by up to 75 %, and caused severe gill degradation. They concluded that NPs can have lethal and sublethal effects on all amphibians' life stages.

Considerable amounts of nanomaterials are found in both marine and rivers aquatic environments. Several investigations have been carried out to evaluate the effect of nanomaterials on aquatic living organisms. The novel studies consider nanomaterials as a new type of pollutant and their effects depend on their size. Zebrafish (*Danio rerio*) is considered an ideal model for studying the ecotoxicity effects of nanomaterials on marine life. *In vitro* studies by Myrzakhanova et al., on zebrafish showed that Ag-NMs cause neurotoxicity. Furthermore, Ag-NMs affected the embryonic development of zebrafish and the nervous system of adults leading to malformations and ultimately to mortality [226]. Similarly, Ni-NM was also found responsible for malformations, mortality, and thinning of the intestine. A large particle of Ni-NM (60 nm) clusters is toxic to skeletal muscles and the intestine [227]. The effect of TiO_2-NM consumption by *Danio rerio* embryos and larvae during the growth phase has been studied. In the first experiment, the nanomaterials were added to their commercial food while, in the second experiment, fishes were fed on algae exposed previously to TiO_2-NM. At low concentrations, premature hatching was observed while the impact on young animals was not significant. But, after 14 days of exposure to contaminated food, the digestive physiology was altered [228]. In the different trends of experiments, the zebrafish in vivo model was utilized to assess silica nanomaterial effects on the cardiovascular system. The effects were measured by using toxicological biomarkers, oxidative stress, cytotoxicity, and apoptosis. The results indicated that apoptosis and oxidative stress as prime factors for endothelial cell dysfunction, the exposure to silica nanomaterial is a potential hazard factor for cardiovascular system failure [229]. A recent study on the toxic impacts of exposure to high concentrations of silver nanoparticles was carried out on common carp fish (*Cyprinus carpio*). The findings revealed that silver nanoparticle bioaccumulation resulted in histopathological changes such as damaged gill tissues leading to necrosis and severe alterations in the intestine, which mostly occurred at the highest concentration of silver NPs of 0.09 mg/L [230].

Crustaceans are often used to evaluate the effects of toxic materials in polluted environments. The toxic effects of $AgNO_3$ and AgNM were investigated in *Daphnia magna*. Swimming apostasy and teratogenic effects were observed according to the Ag form and concentration. NM was aggregated under the carapace of crustaceans, affecting the animal swimming directly [231]. Persistent exposure of *Daphnia magna* to contaminated algae with TiO_2-NM, affect reproduction and growth [232]. X-ray fluorescence spectromicroscopy was used to study the Ti limit of detection (LOD) and limit of quantification (LOQ). LOD and LOQ were found to be 50 mg/kg for algae. Whereas, LOD and LOQ were 100and 150 mg/kg respectively for daphnia. Ti concentration increased in algae with nano residue concentrations exposed (Fig. 4). A significant amount of nano-residues was detected through µ-XRF in the gut of juvenile and adult daphnia which were fed with nanoparticle-exposed algae (Fig. 5).

Newly, a study aimed to evaluate the potential toxicological effects of silver nanoparticles (AgNPs) in the aquatic environment was made by utilizing micro-crustacean *Daphnia lumholtzi* as a model. Crustaceans in freshwater were exposed to two Ag NPs concentrations (0.2, 0.5 µg/l) for 21 days. The reproduction rate of *D. lumholtzi* was significantly lower than the control for both concentrations. This result indicates that a concentration higher than 0.2 of AgNPs can cause a toxic effect on *D. lumholtzi* reproduction rate during the exposure period of 21 days. The results concluded that Ag NPs have toxic effects on *D. lumholtzi* and it can be used as a potential ideal model for assessment of the toxicity of nanomaterials in freshwater [233].

Mollusk is another excellent animal model to evaluate the effects of toxic chemicals, pollutants, and nanomaterials in seas and oceans. The effects of SnO_2, CeO_2, and Fe_3O_4 nanomaterials were experienced on immune cells in the sea urchin *Paracentrotus lividus*. NMs were found in the sea urchins' immune cells. These cells have shown a decrease in cholinesterase activity, disturbances in stress protein regulation, and morphological alterations in ER lysosomes [234]. NP effects on *trans*-Golgi apparatus were studied through WGA-staining. Several strongly stained vesicles were seen in control cells. But, a lesser number of stained vesicles were seen in coelomocytes obtained from NP-fed sea urchins (Fig. 6A-7B). These vesicles were polarised on a single side of the cell, and this localization did not depend on the type of metal oxide nanoparticle (Fig. 6C–7H). In contrast, the DiOC6-stained endoplasmic reticulum showed a flat vesicle network in controls (Fig. 7I). Whereas, strictly packed non-resolvable membranes were seen in sea urchin cells fed with CeO_2 and Fe_3O_4 nanoparticles (Fig. 6L), sea urchin cells fed with SnO_2(Fig. 6J) showed structures like controls.

7. Impact of nanomaterials on plants

Although using nano-fertilizers and nano-pesticides has many positive benefits for agriculture, it has some negative effects related to use in the long term which affects some physiological

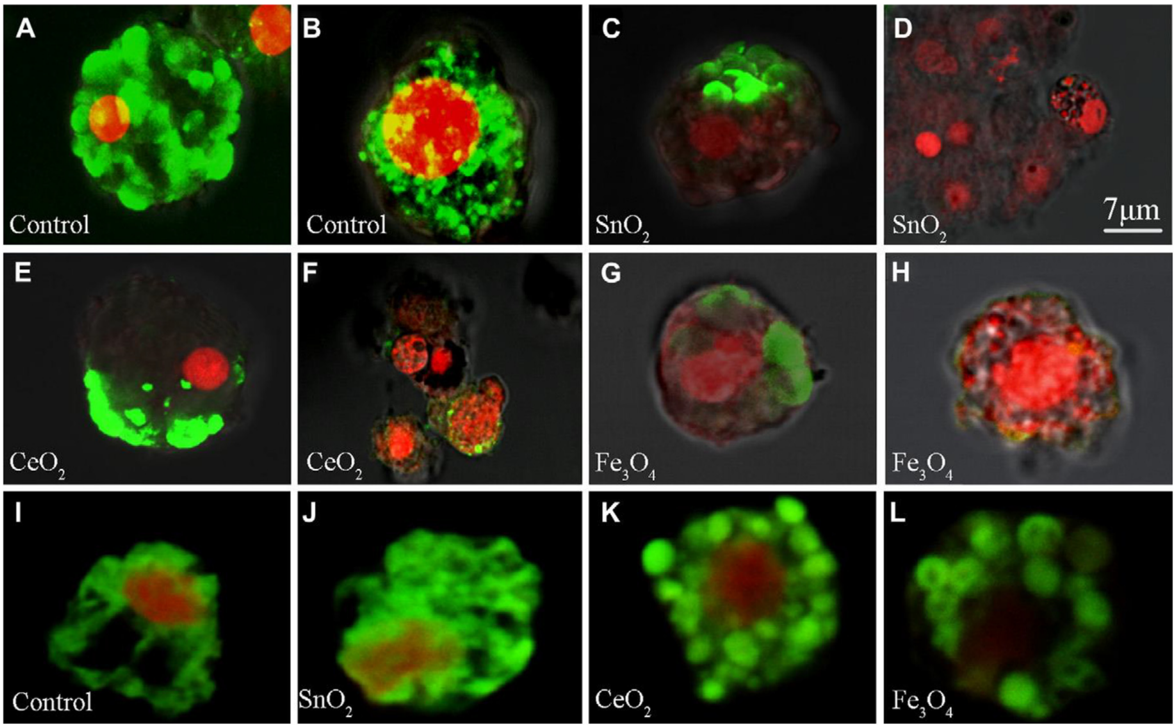

Fig. 6. Impact of different NPs on coelomocyte ER and lysosomes coelomocytes stained with: (A-H)WGA or (I-L) DiOC6 [234].

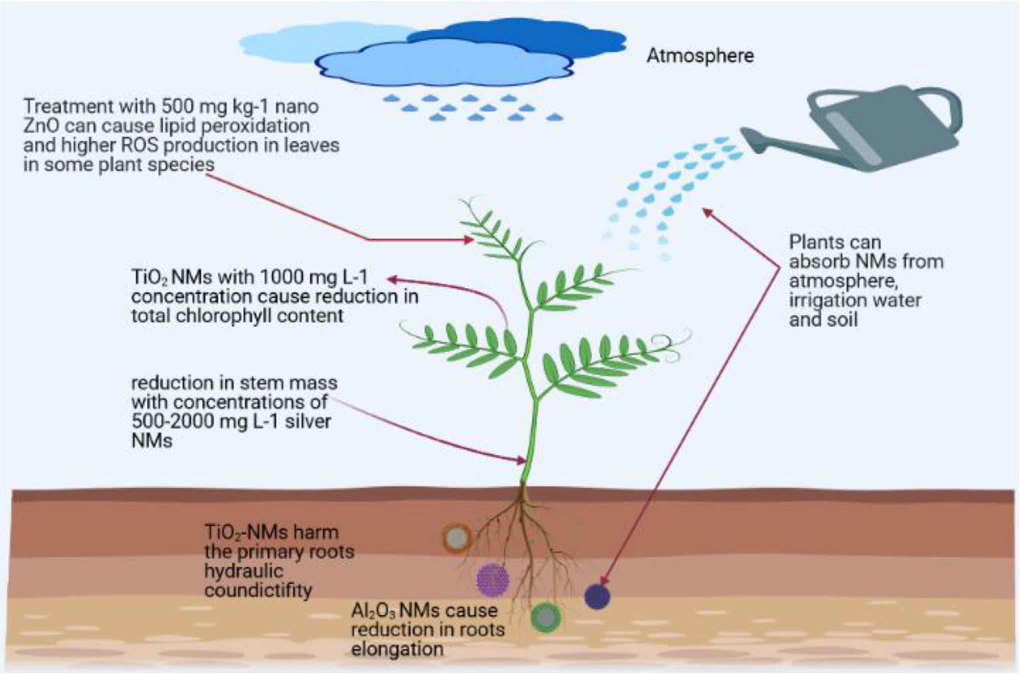

Fig. 7. Impact of nanomaterials toxicity to plants.

processes and causes deformations in plants causing reduced production. Moreover, these nanomaterials can enter plants and thus reach humans and animals through the food chains and food webs, causing hazardous diseases in the future. NMs can be absorbed by plants from water, soil, and the atmosphere. Relying upon the exposure mode and physical/chemical properties of the NMs, the uptake diverges to a wide range [235]. Carbon-based nanomaterials (CNMs) such as fullerene, carbon dots, and graphene utilized in numerous potential applications have been used for phytotoxic tests increasingly because of their ability to enter through the cell wall and plasma membrane [236]. Furthermore, metal NPs such as silver (Ag), iron (Fe), copper (Cu), aluminum (Al), silica (Si), gold (Au), and zinc (Zn) and their oxides such as titanium dioxide (TiO_2) and zinc oxide (ZnO) have been utilized for numerous applications in environmental remediation, agriculture and food processing research areas [237–242].

Studies on cultures of leaf cells treated with multi-walled carbon nanotubes (MWCNTs) produced in *Oryza sativa* leads to an increase of apoptotic processes (cell death) and reactive oxygen species (ROS) [243]. A decrease in superoxide-dismutase activity (SOD) in *Arabidopsis* related to the decay of chlorophyll production [244] was observed.

Numerous plant species can absorb NMs through roots and translocate them in stems and leaves [235], depending on the growth medium and the types of NMs and plants. Tests on hydroponic maize cultures referred to those slimy suspensions of TiO_2-NMs (1 g/L) with 30 nm size that harmed the primary roots' hydraulic conductivity by the physical action on the cell wall pores that influenced the perspiration and leaves growth. NMs can induce a cytotoxic effect on roots either after penetrating their organelles and cells or by making chemical changes in the surrounding medium or soil by obstructing the roots' absorbing function [245]. Treating maize seedlings with 1000 mgL^{-1} concentration of silicon dioxide (SiO_2) NPs reduced both shoot fresh weight and shoot length. While treating maize seedlings with titanium dioxide (TiO_2) NPs with the same concentration caused a reduction in pigments content (total chlorophyll content and chlorophyll/carotenoid ratio [246]. In addition, exposure of thale cress plants (*Arabidopsis thaliana*) to TiO_2-NMs with 100–1000 m g/Lconcentrations causes a reduction in Chlorophyll content, plant biomass, and antioxidant enzymes modifications [247]. Plants of *Zea mays*, *Daucus carota*, *Cucumis sativus*, *Glycine* max, and *Brassica oleracea* treated with Al_2O_3-NM haveshownd a reduction in root elongation because of the toxic action related to the particle's surface characteristics [248]. Hydroponic cultures of *Lolium perenne* treated with ZnO-NM and Zn^{2+} ions showed that ZnO-NM was able to penetrate the cells and cross root cell walls and reach vascular tissue via the endodermis. The uptakes damaged the cortical and epidermal cells and reduced the plant biomass [249].

Active mitotic tissues (root meristem) of different plant species were tested for cytogenetic aberrations induced by NMs. Roots of *Allium cepa*, *Nicotiana tabacum,* and *Glycine* max were vulnerable to Ag, ZnO, CeO_2, and TiO_2 NMs for cytological analyses [250], measured by random amplified polymorphic DNA (RAPD) and DNA laddering techniques. The root growth suppression in the treated plants was linked to cell division errors and chromosome behavior such as bridges, multiple breaks, micronuclei release, early chromosome separation, and DNA damage. The same results had been observed by De et al., after treating *Allium cepa* plants with Al_2O_3-NPs with different concentrations ranging from 1.25 to 5 μM and the impact include micronuclei and DNA damage with increased concentrations [251]. Some examples of nanomaterials' toxicity effects on plants have been illustrated in Fig. 7.

In tomatoes, the multi-walled carbon nanotubes (MWCNTs) can penetrate seedling roots and the seed coat through cell wall pores and enhance the ability of the plant to absorb water, with a good positive effect on germination and seedling growth. Concentrations of 50–200 μg/mL improved the reproductive and vegetative growth up to the double rate of flowering and fruiting [252–255]. Lu et al. observed that titanium and silicon dioxide NMs have increased soybean germination, and early growth as well as antioxidant defenses and nitrate reductase [256]. While Lei et al., concluded that titanium dioxide (TiO_2) NMs enhanced growth and photosynthesis rate in spinach through nominate ameliorations in photo-system activity II and electron transfer; likely these ameliorations were a function of reduced oxidative damage as a result of the maximal antioxidant response [257]. Zheng et al. showed that exposure to TiO_2 nanomaterial had increased spinach germination significantly at lower concentrations (250–4000 mg/L) but exposure to higher levels (6000–8000 mg/L) had shown phytotoxicity effects [258]. Although 20 and 200 mgL^{-1}concentrations of alumina NMs did not affect root elongation, when exposed to 2000 mgL^{-1} concentration it decreased the root growth of corn, broccoli, cucumber, and carrot crops by 13 % [248].

Nevertheless, the toxic nature of nanomaterial and bulk copper, silver, silicon, zinc oxide, and MWCNTs on root elongation and germination of zucchini has been investigated by Stampoulis et al., and they concluded that exposure regardless of particle size has no toxicity effect [259]. Similarly, exposure to copper NM in wheat and bean seedlings for 48 h has been studied by Lee et al., They noted that both species had a 40 % reduction in biomass at 200 mgL^{-1} and an 80 % reduction at 1000 mgL^{-1}[260] While, many other studies have reported no public effects on total plant mass, but noted a reduction in the mass of stem and increase in the root biomass with concentrations of 500 and 2000 mg/L silver NM when exposed [261]. Green peas plants (*Pisum sativum* L.) were treated with bulk and nano-ZnO for 25 days with concentrations (control, 125, 250, and 500 mg kg^{-1}) in the soil. Treatment with 500 mg kg^{-1} nano-ZnO has caused lipid peroxidation and higher ROS production in leaves, while the bulk-ZnO treatment does not affect lipid peroxidation [262]. Hence this result gives evidence of higher toxicity of ZnO NM as compared to the bulk form. Wang et al., cleared that iron oxide NM with 30, 100, and 500 mgL^{-1} concentrations induced greater stress/toxicity in pumpkin and ryegrass when measured by oxidative enzyme activity and compared with its bulk material [263].

8. Environmental fate and behavior of nanomaterials

Release of NMs in the environment may occur during transportation, and production and while disposing of the products at the end of their use. For instance; wastewater sewage, sludge, waste incineration residues, and landfill leachates all probably contain NMs. When these NMs are released into the environment the distribution and behavior are determined by the actual properties as well as the environmental conditions. To understand their environmental fate and behavior, the aquatic phase seems to be the starting or the main point of possible entry and dispersion in the environment, because the aquatic phase creates a link between the other environmental compounds such as sediment, soil, and air [264]. The transformation process occurs after the release of the NMs into the environment. Transformation occurrence depends on the environmental conditions and the nature of the nanomaterials. However, the variability and complexity of both factors predict their behavior as extremely challenging [265]. Transformations can be subdivided into physical, and chemical interactions with other substances and surfaces and biological processes. Physical processes include agglomeration, aggregation, and sedimentation, while chemical processes include dissolution, reduction, photocatalytic degradation, oxidation, and precipitation. Interactions with other substances and surfaces include adsorption and desorption processes, while biologically mediated processes include bio-modification and biodegradation, most probably by microbes [266,267]. These categories in some cases are overlapping because they are highly interlinked and influence each other.

Transformation processes, chemical transformation, and photocatalytic degradation are the chemical change induced by the light, which includes photocatalytic NMs irritation (absorption of a photon causing generation of free radicals) and photolysis of the NM or components of the NM (e.g., the coating material degeneration). For NMs the focus is on the relationship between photochemical reactions and their potential phototoxic effects. For instance; some metal oxide of NMs can work as photocatalysts and when irradiated (absorption of photons) produce reactive oxygen species (ROS) causing toxic effects e.g.; TiO_2 NMs were found to be extra toxic (2–4 times higher) to the crustacean *D. magna* and the Japanese fish Medaka under artificial solar radiation compared to exposure under surrounding laboratory light [268] Oxidation is oxidizing nanoparticle surface molecules or atoms by loss of electrons, while reduction is reducing nanoparticle surface molecules or atoms by the uptake of electrons. Speciation or complexation of NMs (released molecules or ions) can be defined as linking with other molecular or ionic chemical substances dissolved in the environmental matrix (e.g., the NM surface chemisorption to form a surface coating). Oxidation-reduction reactions (redox reactions) have an important role in several natural phenomena ranging from cellular respiration to geological processes through complex or simple reactions including electron transfer between chemical species [269]. For instance, Auffan et al. suggested that the cytotoxicity of metallic (metal oxide or metal) nanomaterials is correlated with their potential to be reduced, dissolved, or oxidized in *in-vitro* biological conditions [270]. The transfer of electrons or ions during redox reactions is considered a major source of toxicity for metallic NMs. When a solid NM dissolve (release of individual molecules or ions) in water, the phenomenon is known as the dissolution process [271].

Nanomaterials are multi-molecule objects consisting of metals in their elemental state (Me^0) or crystal solids. NMs could be soluble to different extents ranging from non-soluble, poorly soluble, completely soluble, or partially soluble. The way they dissolve will affect their environmental behavior, effects, and fate [272], which may be controlled by their particulate shape or the existence of dissolved species. When nanomaterials are dissolved in the aqueous media, molecules or ions may react with media ingredients, e.g., anions such as sulphate, hydrogen carbonate, organic matter, and chloride to form for example; dissolved metal complexes or residues. Precipitation is the process when dissolved species form a solid phase when the metal ions are released from the NM and grouped into a solid material. The specific metal complex formation depends on media components (including the number of cations, anions, and organic matter such as humic and fulvic acids), pH and temperature. Approximately 200 various products containing nano-silver particles have been registered for consumer use [273] although Ag NMs have toxic effects on living organisms [274]. Hence, Ag NMs are under intensive environmental toxicological research with efforts to link observed harmful effects to dissolved Ag ions [275]. When nano-silver is released into the wastewater system, nano-Ag particles turn into silver sulfide (Ag_2S) nanoparticles [276,277]. Blaser et al. estimated that the biocidal use of silver (including ionic forms as well as silver nanoparticles) has reached up to 15 % of the total silver emissions into sewage [277].

When Ag nanoparticles are released into the environment, the reaction of sulphur and silver ions takes place. In a study, Lowry et al. explained that after 18 months of nano-Ag particles, in addition to freshwater, the speciation of Ag in residues was dominated by Ag complex and Ag_2S leading to a reduction of S in organic matter which is another example of speciation change. Nevertheless, Lowry et al., found that although Ag-NPs were transformed into S-containing species, some of the added Ag was taken by plants, insects, and fishes in the mesocosms showing that Ag produced from the NPs was bioavailable in the aquatic environment even after transformation. Physical transformations include agglomeration which is primary particle reversible coagulation from clusters [278]. Aggregation is primary particles' irreversible fusing to form larger particles from the same material. Agglomeration or aggregation can occur at all life-cycle stages of the nanoparticles such as in production, during handling, and storage. If the NMs are not stabilized or coated, these processes will occur inevitably, even whether the nanoparticles are in powder or solution form or hanging in the air [266,278]. Both agglomeration and aggregation in test media depend on the chemical composition, size, and surface charge of the nanoparticle as well as media composition, mixing rates, and the presence of natural organic matter such as humic acid [279]. The effects of different concentrations of the Suwannee River Fulvic Acid (SRFA), ionic strength, and pH on the aggregation of 5 nm TiO_2 bared particles were studied by Domingos et al., Aggregation was observed to increase at the pH values near the zero-point charge. Furthermore, adsorption of the SRFA was observed as a result of less aggregation rate of TiO_2 nanoparticles, perhaps due to steric repulsion increased [280]. Sedimentation is the process when NMs in suspension settle out of the water phase. There is a clear link between sedimentation and agglomeration as a result of the transfer of particle size distribution towards the higher side. During the agglomeration process of scattered particles, agglomerates or larger particles will diffuse more slowly but under gravity, it tends to settle more rapidly. Sedimentation may be affected by gravitational agglomeration. The smaller particles (slower sediment) are captured by larger particles. Quik et al. found that the sedimentation of CeO_2 NMs was sizeable in synthetic algae media (average particle diameter: 417 nm) compared to deionized water (average particle diameter: 301 nm) [281]. The addition of natural organic matter (NOM) is found to reduce agglomeration in algal media while sedimentation with NOM concentration increases. Interactions with other surfaces can take place in two ways (i) NM can act as sorbent: when the other substances are adsorbed onto the NM surface and (ii) NMs as sorbate: when NMs are adsorbed onto other surfaces. Desorption is the detachment of the NM into the water from the other surfaces. The studies showed that the presence of natural organic matter (NOM) as well as changes in pH affects NM adsorption [282–285].

The change in pH affects the colloidal stability as well as the dissolution of NMs. It happens due to the charge changes on the NM surface. A positively charged NM more easily binds to the soil since most soils are negatively charged due to electrostatic forces. The stabilizing effect of NOM on NM by sticking to the surface leads to the formation of a steric coating around the particles. It results in higher mobility of NMs in soil with high NOM content. Adsorption and desorption of NM on various solid surfaces have great importance to understand their fate and transport in the environment. For instance; NMs may get adsorbed at particles of suspended solids in water, soil, and sediments. It affects their transport and mobility. If the organic matter gets adsorbed onto the NM surface in the environment, the NM acts as a sorbent. The solubility and retention of CeO_2 NM in 16 various samples of soils with different chemical and physical characteristics were studied by Cornelis et al., [283] They carried out an investigation for Ce, ionic Ce, and bulk CeO_2 and CeO_2 NM (20 nm in powder form). After making suspension in the media the particles rapidly agglomerated and size increased from 20 nm to 130 nm at 5 pH. Bigger particles ($\geq 1\ \mu m$) were observed at pH < 4.5 with the addition of phosphate and citrate. They concluded that citrate and phosphate addition and pH changes affected the agglomeration type. Biological transformation is a biologically mediated process when the NM undergoes a transformation due to the presence of living organisms. This includes processes viz. degradation, biological oxidation, and interactions with bio-macromolecules excreted by micro-organisms. Biodegradation is the biological process that includes the decomposition occurring to the organic substance by microorganisms. This process is not related to inorganic NMs, even carbon-based NMs such as CB and CNTs, which tend to have non-organic nature and are generally considered flexible to biotic degradation. In a study about the biological mineralization of ^{14}C labeled MWCNT using a mixed bacterial culture, after 7 days incubation period at 39 °C, 2–7 % mineralization has been observed [286]. Saleemi et al., have discussed the mechanism of antimicrobial activity of CNT-based nanocomposite material including the individual and synergistic effects on the cell [287].

Bio-modification is a biological process-meditated transformation. Bio-modification occurs after uptake by organisms and processes that are mediated obliquely by an organism. For instance; by exudates releases that are linked to the NMs achangesnge their properties. A lot of studies investigated the modifications of NMs as a result of plant uptake. Zhang et al. observed that CeO_2, which is considered stable under normal environmental conditions, could be biotransformed in cucumber plants [288]. The researcher suggested that CeO_2 NMs are adsorbed first onto the surface of the root and then dissolve partly. It is suggested that substances like ascorbic acid, release from the roots take part in this process and the organic acids (e.g., citric acid) enhance CeO_2 dissolution. The transformation of NMs by aquatic animals such as *Daphnia magna* was studied by Roberts et al.,. They found that *Daphnia magna* was able to ingest and modify lysophosphatidylcholine-coated single-walled (CNTs). The CNTs ingested by normal feeding behavior and the coating of lysophosphatidylcholine are utilized as a food source. This changed the dispersibility of the CNTs which was probably caused by the removal of the lipid coating of the CNT [289].

9. Challenges and future prospects

Several challenges have been observed during the development of nanotechnology and methods based on nonmaterials. Detection and characterization of nanomaterials create many big challenges due to their ultra-small size. It became very difficult to differentiate the manufactured nanomaterials from particular similar natural materials. The lack of proper sensitive and selective techniques required for measuring the size, number, and surface area precisely was another limitation. The diversified form of nanomaterials in nature and their properties makes it more difficult its identification and proper characterization. During its exposure to the natural environment or biological components further, it became more complex to track the nanomaterials in the system and to investigate its effects on different systems of organisms exposed to nanomaterials. Since 2006, the Organisation for Economic Co-operation and Development (OECD) has co-ordinated, via its Working Party on Manufactured Nanomaterials (WPMN), an extensive programme (Testing Programme) on the testing of manufactured nanomaterials. One planned outcome of the Testing Programme was information for evaluating the need for OECD Test Guidelines (TGs) addressing additional Physico-chemical endpoints for nanomaterials. This programme included the testing of 11 types of nanomaterials, some covering several nanoforms, for 59 endpoints using OECD TGs and other methods. The OECD TGs are developed for regulatory purposes and are agreed upon under the OECD Mutual Acceptance of Data (OECD, 1981a), which is a legally binding instrument to facilitate the international acceptance of information for the regulatory safety assessment of chemicals. The Testing Programme is aimed to explore the usefulness of OECD TGs and assess the need for updated or new OECD TGs. The materials tested are Au, Ag (both colloidal solutions), TiO_2, SiO_2, CeO_2, ZnO, fullerenes (C_{60}), SWCNTs, MWCNTs, nanoclays (all in powder form) and dendrimers (liquid). It is useful to cover and address Physico-chemical properties, environmental fate, and human and environmental hazard properties [290]. The International Organization for Standardization (ISO) is also undertaking standardization in the field of nanotechnologies that includes understanding and control of matter and processes at the nanoscale. ISO establishes methods for characterizing the morphology of several nonmaterials using transmission electron microscopy, X-ray spectrometry, SEM, EDX, GC MS, photoluminescence spectroscopy, and chemical analysis by energy dispersive X-ray spectrometry.

It is required to carry out detailed investigations on the adverse effect of nanomaterials before launching the nanomaterial-based technology and products commercially. It is also required to find the hazard, evaluate the risks and formulate the precautions. It is needed to develop safe technology and products. Evaluation of long-term exposure to nanomaterials, complete investigations on toxicological studies, and accurate dose–response database including occupational exposure limits, threshold limit values, and occupational safety and health administration-permissible exposure limits should be carried out while developing new technology. Proper risk assessment and analysis tools could alleviate nanomaterial exposure-related risks and reduce exposure within safe limits.

10. Conclusion

The field of nanotechnology has been growing rapidly for the last two decades tremendously. It has grown business from the very quick obsolescence of present technologies to novel technologies. The applications of nanotechnology have been broadly involved in electronics, medicines, energy, defense, food, agriculture sector, disinfection, wastewater treatment, drug delivery, vaccine development, etc. However, extensive and non-judicious use of nanomaterials leads to some environmental, health, and safety concerns for the public. Therefore, in order to reduce the harmful effects of nanotechnology, researchers, scientists, engineers, and policymakers should work jointly to develop improved and safer nanomaterials for sustainable use.

Data availability

No data was used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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