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Environmental and toxicological concerns associated with nanomaterials used in the industries

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1. Introduction

In recent years, nanotechnology has emerged as a significant innovation for scientific and economic development. Nanotechnology refers to the discipline of science and engineering dedicated to developing, manufacturing, and utilizing systems devices and structures, by manipulating atoms and molecules at the nanoscale (1−100 nm) (Barhoum et al., 2022; Bayda et al., 2019). These nanomaterials (NMs) are of great interest because of their unique optical, magnetic, electrical, and other characteristics at such a small scale (Saleh, 2020a; Sudha et al., 2018; Madkour and Madkour, 2019). In modern worlds, NMs are used in almost every aspect of life such as electronics (De et al., 2020; Jariwala et al., 2013;

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Dresselhaus et al., 2004), automotive engineering (Virmani et al., 2021; Manu and Gupta, 2020), power generation (Kalyanasundaram and Grätzel, 2012; Chen et al., 2013; Xu et al., 2018; Valipour et al., 2016), batteries (Chen and David Lou, 2013; Long et al., 2021), sensors (Liyanage et al., 2021; Yin and Qin, 2013; ul Gani Mir et al., 2022), aviation and space (Abbasi et al., 2020; Bhat et al., 2021a; Dhinakaran et al., 2021), chemical industry (Generalov, 2007), thermoelectric devices (Gan, 2018; Uddin et al., 2016; Sharma and Hussain, 2020), and cosmetic industry (Fytianos et al., 2020; Mu and Sprando, 2010). One of the most essential applications of NMs is their potential use in environmental remediation (Tratnyek and Johnson, 2006). Due to their greater surface-to-volume ratio, NMs exhibit more reactivity and, thus, greater efficacy than their bulkier counterparts. Furthermore, compared to conventional techniques, NMs can exhibit unique surface chemistry, allowing them to be functionalized with functional groups that can target particular components of interest (pollutants) for effective remediation (Guerra et al., 2018). Additional advantages may be gained by manipulating the physical properties of NMs (such as shape, size, chemical composition, and porosity) to effectively improve their performance for pollutant remediation (Lu and Astruc, 2020; Wang et al., 2019). A brief overview of the NM-assisted remediation of the environment has been discussed in the latter part of this chapter.

The use of NMs has revolutionized the modern way of living. However, its widespread use and high-dose introduction have had a negative impact on the environment (Bernhardt et al., 2010). Furthermore, the uncontrolled discharge of these created NMs from industrial waste and sewage sludge is a diverse and mostly unexplored phenomenon, raising concerns about their ecological toxicity. As a result, there is a substantial public interest in comprehending the negative health impacts of NMs prevalent in the human environment (Brar et al., 2010; Musee, 2011). The current understanding of the negative health impacts of NM exposure on living organisms is limited. The increased usage of NMs would increase their prevalence in the environment and ultimately increase their potential for human exposure. These NMs can enter the human body through inhalation. ingestion or dermal absorption (De Matteis, 2017; Malakar et al., 2021). Consequently, there is a rising interest among the scientific community in understanding their possible toxicity. Over the past few years, efforts have been made to develop methodologies for assessing the toxicity and health impacts of NMs. These efforts have resulted in the formation of a new discipline of toxicology known as “nanotoxicology.” Nanotoxicology is an emerging field of modern toxicology and specifically deals with the toxicity of NMs.

The most important considerations for establishing the potential toxicity of NMs are the size, shape, surface charge, solubility, chemical composition, aggregation, and presence of functional group (Schrand et al., 2010; Sayes and Warheit, 2009). Because of the widespread use and disposal of ENMs in daily life, the ecosystem, especially the aquatic ecosystem, has been severely affected by environmental contamination. The most commonly used nanoparticles (NPs) are gold NPs, silver NPs, zinc NPs, titanium oxide NPs, and carbon nanotubes. The toxicity of these NMs is now being analyzed, with more efforts being made to explore the effects of these NMs on the ecosystem. So far, various studies have been conducted to study the ecological behavior of these NMs to encourage the sustainable usage of these innovative materials in the future. This study highlights the environmental and toxicological concerns associated with the different types of NMs. Additionally, microbe-assisted bioremediation of NMs has been briefly outlined in this chapter.

2. Nanoremediation

The rapid increase in population and industry, along with increasing populations and refinement of agronomic systems, has led to the contamination of water and soil with various toxic substances (Willner and Vikesland, 2018). This has led to an increase in the prevalence of diseases and other health problems. Nanoremediation has quickly emerged as one of the most promising emerging methods for the removal of contaminants from both soil and water (Mao et al., 2015). This is large because of the high reactivity of NPs. This achievement can be credited to the fact that NMs are of an exceptionally microscopic scale. To determine whether or not NMs are effective at removing pollutants, a number of studies have been carried out (Saleh, 2020b). The uses of these NMs in novel remedial procedures at attracting a significant number of researchers worldwide. Some examples of these remedial approaches include adsorbent, catalysis, photolysis, electro-nanoremediation, and nano-bioremediation. The significance of NMs can frequently be improved by altering them with polymer, clays, zeolites, activated charcoal, and biochar (Wu et al., 2018). Identifying materials that are not only inexpensive but also friendly to the environment is a pressing requirement to decontaminate polluted land and water (Lan et al., 2017). Nanotechnology offers solutions that are not only quick but also inexpensive, as well as safe for the environment (Liu et al., 2018). In addition, nanotechnology has a tremendous potential to reduce pollutant levels to “nearly zero.” Nanoremediation of the ecosystem is the practice of using suitable NPs to clean up ecological water and air contaminants (Abdi et al., 2008). Since the cleanup process typically takes place in its natural environment, the implementation of nanoremediation technology can eliminate the requirement of excavating or transporting pollutants. In addition, a wide range of approaches can be utilized in the context of applications pertaining to contamination treatment to regenerate and reuse NMs. The separation process of NPs and recovering metal from used nanosorbents are two examples of processes that fall under this category (Yuan, 2004). Based on the characteristics of NMs, researchers are able to classify NMs as either adsorbent materials (for the adsorption of heavy metals) or catalyst supports (for the degradation or transition of pollutants). Adsorbents are used to remove pollutants from the environment by capturing them (Sanchís et al., 2016). Catalysts are used to break down or transform pollutants. The impurities in the water can be removed using sorbents, while the pollutants themselves can be broken down or transformed using catalysts. On the other hand, the vast majority of the research that has been published focuses on the purification of aqueous environments, and the majority of these investigations are carried out at the bench scale (Das et al., 2018).

The widespread application of nanotechnology in environmental cleanup has been delayed by several hurdles in the technological, societal, and economic aspects. The application of NMs in the processes of decontaminating contaminated soils has received a surprisingly low amount of attention. Different types of NMs, including inorganic or metal-based NPs, carbon-containing NMs, polymer-based NMs, and composite NMs, are highly preferred by researchers for environmental cleanup studies (Kumar et al., 2021). Polymer NMs (e.g., chitosan and alginate) and composite NMs (e.g., clay-polymer NMs, zeolite, and charcoal-supported nanocomposites) have attracted a significant amount of attention from researchers, but their applicability in the real world is restricted. Metal-based NMs (e.g., iron-based NPs, copper-based NMs), in contrast to the few instances of BNPs, other oxide NPs (Such as TiO_2), and carbon nanofibers have also proven to be beneficial to the area of nanoremediation (Khurana et al., 2019). The key advantages of utilizing NMs for environmental clean-up are their excellent selectivity, high adsorption capacity (due to their high surface area and many adsorbents), and the simplicity with which the NMs may be rejuvenated after use. In recent years, metals and oxide NPs have received a growing amount of attention due to their high efficacy and low cost in removing environmental contaminants.

The use of NPs as magnetic adsorbents has also become more common in recent years (Thines et al., 2017). According to studies, nanosized metal alloys and metal oxides display favorable binding toward metallic pollutants such as arsenic, heavy metals, chromium, and uranium, as well as favorable sorption toward other common air pollutants such as phosphate as well as organics, in addition to high capacity and selectivity. Metals and metal oxides NMs exhibit favorable sorption toward organic pollutants such as carbon monoxide and nitrogen dioxide. These results can be explained by the fact that nano-sized metals and metal oxides can successfully eliminate metallic impurities (Ren et al., 2013). The use of nano-sized zinc ferrite and hematite for the absorption of inorganic arsenic, chromium, arsenic, copper, lead, or nickel from synthetic wastewater and natural water infrastructure has been the subject of several studies (Shen et al., 2021).

The production of nanocomposite materials is one possible technique that can be utilized in the effort to promote the application of nano-particulate materials (Hannon and Prina-Mello, 2021). These materials make use of the advantages provided by both the hosts and the NPs that are injected into them to maximize their overall usefulness. In addition, utilizing nanocomposites may lessen the emission of NPs into the surrounding environment and improve the compatibility of the nanoscale with the infrastructure already in place. In its most fundamental form, a nanocomposite has the appearance of a solid. A composite is a multiphase solid that can take on a range of various forms, such as porous materials, colloids, gels, and copolymers (Poynton et al., 2018). The selection of hosting for nanostructure is of utmost significance and has a dominant effect on the effectiveness of the NMs manufactured as a direct result of the process (Poynton et al., 2018). The performance and utility of nanocomposites experienced a notable improvement compared to the efficiency and usefulness of free NMs in nanoemulsion, stability, and recyclability (Khin et al., 2012). Nanocomposites were thought to be the most promising method to progress water technology from the level of lab studies to the stage of large-scale application up until fairly recently. The creation of nanocomposite materials is one method that offers a great lot of promise for advancing the use of NPs in various applications. These materials take advantage of the benefits offered by the hosts and the functional particles introduced into the hosts to achieve their intended purpose (Shakya et al., 2021). It is possible for hosts, which include polymers, phyto minerals, activated carbons, and membranes, to make it simpler for based NPs to dispersion while yet preserving the stability of the NPs.

3. Nanomaterial contaminants

NMs are beneficial in several aspects; however, the impact of their negative effects on the environment should also be concerned (Fig. 6.1). In many regions around the world, the continuous release of toxic compounds into the natural surroundings as a direct result of anthropogenic activities is evolving into an issue of progressively serious proportions (Zhu et al., 2019). Nanocontaminents are a group of chemical compounds or NMs that have been found to be a threat to the environment and toxic to humans. NMs may potentially disrupt the environment by facilitating chemical reactions that destroy plankton, beneficial bacteria, and small animals (Exbrayat et al., 2015). Several metal and metal oxide NPs are effective catalysts, and when discharged into the environment, they may trigger chemical reactions that produce toxic elements such as reactive oxygen species (ROS) or free radicals (Fu et al., 2014). Titanium dioxide (TiO_2) is one of such NMs with high photocatalyst and, when exposed to sunlight, may catalyze chemical reactions that raise the concentrations of ROS (such as hydroxide OH or superoxide O^{2-} radicals) in water (Čapek and Roušar, 2021; Song et al., 2012). These ROS are toxic to a wide range of aquatic species, such as small fishes and plankton (Morris et al., 2022).

NPs are released into the environment through several human activities such as burning fossil fuels, large-scale mining, and automobiles (Bundschuh et al., 2018; Saikia et al., 2018) (Fig. 6.2). Typically, automobiles and the combustion of fossil fuels generate

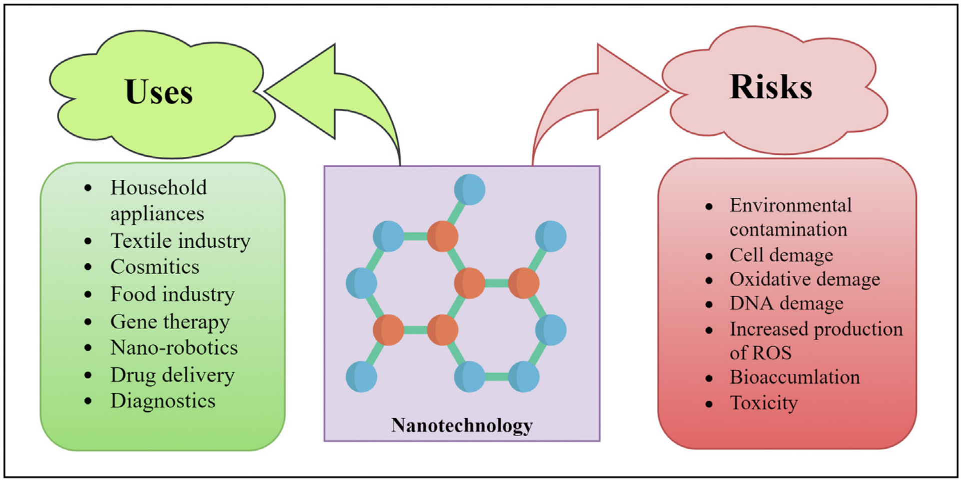

Figure 6.1 Potential used and risks associated with the use of nanomaterials.

Figure 6.2 Release of nanomaterial into the environment through several human activities.

NPs of soot or carbon black with dimensions of less than 100 nm. Carbon nanotubes and fullerenes have also been found to be produced as a result of fossil fuel combustion (Borm et al., 2006). NPs of metal and metal oxide have recently been shown to be produced during mining and metal refinery activities. The most harmful aspect of NPs released from the combustion of fossil fuels is that the NPs are often dispersed straight into the atmosphere. Such airborne NPs pose a potential environmental health issue (Borm et al., 2006; Sonwani et al., 2021). These airborne contaminants are difficult to manage and may spread easily to nearby ecosystems. Because of their small size, airborne particle pollutants are linked to a variety of pulmonary disorders, including chronic obstructive pulmonary disease, inflammation, and fibrosis (Manisalidis et al., 2020).

4. Environmental hazards of nanomaterial contaminants

Nanoparticles have always been a part of our ecosystem, and they can originate from either natural or artificial causes. When found in soil and water, NPs are classified as colloids and have a somewhat different size range than when found in the atmosphere, where they are considered to as ultrafine particles (Subbulakshmi, 2020; Ettadili et al., 2022). The release of manufactured NMs into the environment can be purposeful or inadvertent.

Examples of unintentional releases include emissions into the atmosphere and waste streams that are either solid or liquid that come from production units. The use of NMs for remediating polluted soils, such as the use of iron NPs to remediate groundwater, is considered an example of the deliberate release of NMs (Zhang and Elliott, 2006; Galdames et al., 2020). A new group of nanostructured sorbents is necessary for the efficient removal of NPs when they are being filtered out of stack emissions. In addition, the use of paints, textiles, and personalized care goods such as sunscreens and cosmetics releases NPs into the environment at a rate that is proportionate to the amount of usage of those products. The release of this particulate matter would ultimately accumulate on land and the surface of the water bodies (De Luca et al., 2017; Kabir et al., 2018).

NPs can contaminate the soil, travel into surfaces and underground water, and interact with many forms of life if they reach land (Fig. 6.3). Wind or rainstorm runoff can carry particles that are present in waste material, discharged effluent, direct emissions, or accidental leakages to aquatic systems. Spills that occur during the transit of manufactured NMs from production sites to other manufacturing units, purposeful emits for nanoremediation of the environment, and diffused discharges associated with durability and erosion from daily use pose the greatest risks for environmental release. As fugitive releases that occur during the manufacturing process are becoming increasingly under control, the main threats to environmental discharge come

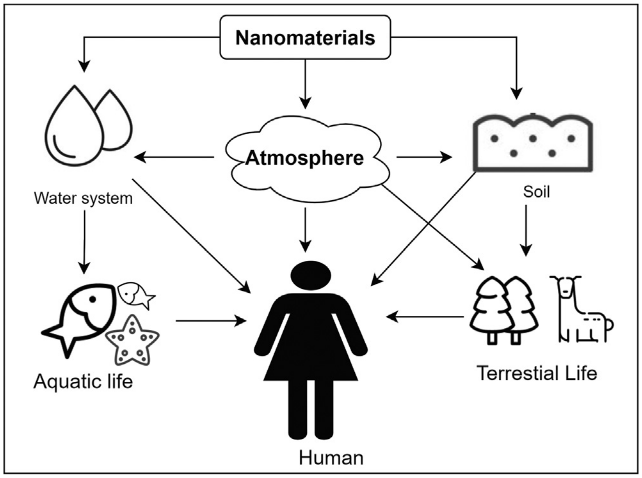

Figure 6.3 Possible pathway of nanomaterial to spread in an ecosystem.

from spillages (Zhang et al., 2019). NPs have seen an uptick in their use across a variety of industries, including medicine, consumer goods, and industrial uses, and this trend will probably continue in the years to come (Kessler, 2011; Stark et al., 2015). Studies have been conducted to estimate environmental contamination levels in the air, water, and soils, as well as to evaluate expected levels for their environmental and human health impact on the aquatic or land-based biota. This was done as a result of concerns associated with the environmental fate and consequences of these materials (Bouwmeester et al., 2015). Direct application of NPs to soils in the form of fertilizers or plant protection goods is one method, while indirect administration to land or treat wastewater products, such as slurries or biosolids, is another. Both of these methods are viable. Consequently, through industrial wastes or the disposal of treated wastewater effluents, or runoff water from soils, NPs may make their way into aquatic systems (Suppan, 2013; Rajendran et al., 2022). NPs, when exposed to the environment, have the capacity to go through a variety of different transformations, all of which are contingent not only on the characteristics of the NPs themselves but also on the medium in which they are found (Abbas et al., 2020). These transformations are mostly the result of physical and chemical processes, but they may also involve the biodegradation of coating materials that are employed by many NM formulations for the purpose of stabilization (Nowack et al., 2012). Adsorption of NPs onto cell surfaces and interruption of membrane transport are the two mechanisms that underlie the toxic effects of NMs on algae (Navarro et al., 2008).

The disintegration of NPs may result in the release of components that are potentially hazardous to the environment (Zhao et al., 2021). When NPs aggregate with one another, the process is called homo-aggregation. When NPs aggregate with natural organic and mineral colloids, the process is called hetero-aggregation (Ma et al., 2020). Both processes will significantly change the NPs' fate as well as potential toxic effects on the environment. Soluble organic material can interact with NPs, which could modify the surface charge and movement of the NPs and affect how they interact with biota. In the end, aquatic NMs end up accumulating in the sediments at the bottom of bodies of water, a process that is made easier in biological ecosystems by hetero-aggregation (Usman et al., 2020). The homo-aggregates of NPs settle more slowly than individual NPs. During the process of treating wastewater, NMs from urban, medicinal, and anthropogenic sources might undergo considerable modifications. Sulfidation of silver NPs, for instance, which occurs in wastewater treatment systems, transforms the majority of the NPs into silver sulfides (Ag_2S). Because the NMs tend to aggregate with the other organic and mineral constituents of the wastewater, most of the NM becomes associated with the other solids instead of continuing to exist as nanosized suspensions spread throughout the water (Kumar et al., 2022).

There is a growing amount of research that demonstrates NPs can pass the cellular membranes and thus become internalized after being taken up by a broad range of mammalian types of cells. These particles are also capable of being taken up by mammalian cells. The adsorption on NP is size-dependent. The primary factors determining uptake were aggregation, followed by size-dependent deposition onto the cells, or diffusion toward the cells. In specialized cells, the absorption might occur either through endocytosis or phagocytosis. One of the hypotheses suggests that perhaps the coating of the NP by protein in the growing medium causes conformational changes in the structure of the protein, which in turn triggers the uptake of the NP into the cell by specialized structures, thereby limiting uptake to NP with a size of less than about 120 nm (Nowack et al., 2012; Navarro et al., 2008).

5. Occurrence of nanomaterial contaminants in water

The widespread use of synthetic NPs is inextricably linked to the water cycle (Baumann et al., 2010). Water is required for several human activities, such as drinking, washing, and cleaning. It is incredibly difficult to track artificial NPs amid the changing and complex composition of water. Synthetic NPs can react with water components in several ways, including homo and hetero aggregation, biotransformation, flocculation, and sorption. NPs present in the atmosphere may make their way into water sources through precipitation, permeate groundwater, and finally through runoff make their way to surface water (Fig. 6.4). When treated wastewater is discharged, considerable amounts of NP residues are introduced into water sources. Similarly, municipal biosolids applied to soils and landfill leachate may penetrate the sources of surface water through a variety of routes. As a result, NPs pollute the environment throughout their manufacture, usage, and eventually after disposal when discharged (Bundschuh et al., 2018). NPs may be released directly or indirectly into the environment via wastewater treatment facilities and landfills. The characteristic properties of these NPs may alter throughout

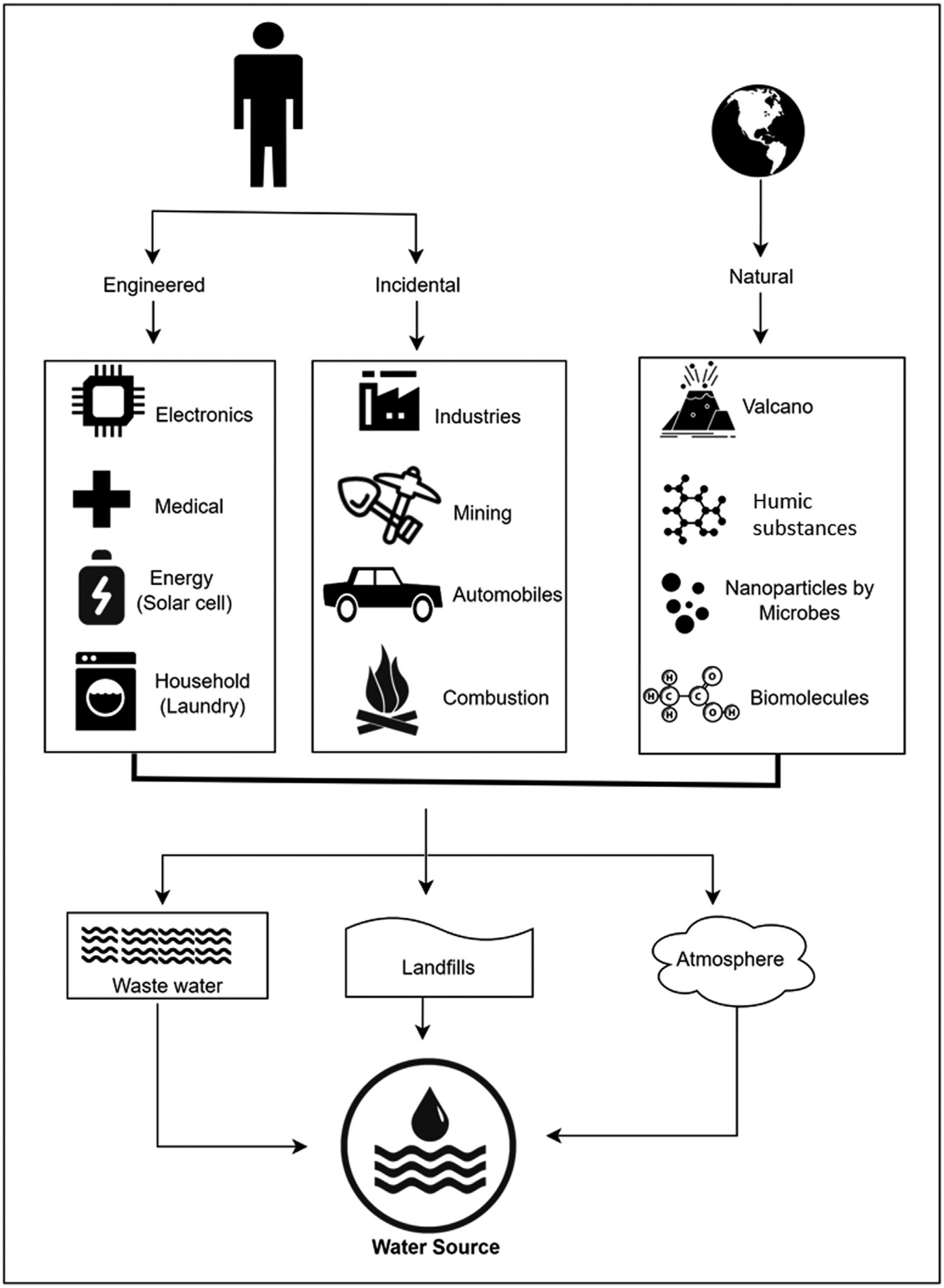

Figure 6.4 Scheme of the pathway for nanomaterial to contaminate water sources.

these release processes, particularly when they are released indirectly via a wastewater treatment plant or a landfill (Bundschuh et al., 2018; Malakar et al., 2020). Around 7% of total synthetic NP production is estimated to end up in water habitats globally (Keller et al., 2013). Other outdoor usages, like nano fertilizers and nano pesticides, would speed up the flow of matter into the water. NPs such as titanium-dioxide, which is often used to enhance brightness and opacity of paints, may enter water sources after getting peeled and decomposed. The majority of NPs are expected to be released during their usage and disposal (Keller et al., 2013; Kaegi et al., 1987).

The release of NP in NPs in water bodies requires a well-developed risk assessment model to address the presence of NM contaminants in waterbodies (Sun et al., 2016). TiO_2 NPs have been found to accumulate in biosolid-treated soils and sludge landfills. These NPs seem to be released mostly through wastewater and account for about 85% of total TiO_2 NP emissions (Keller et al., 2013). Zinc oxide NPs may also get accumulated in landfills and soil, as these NPs are mostly used in the production of cosmetics, electronics, and medicines. The dominant route is likewise wastewater discharge in this case (Mueller and Nowack, 2008). Carbon nanotubes, unlike metal oxides, are emitted mostly during manufacture and disposal in landfills, accounting for about 90% of the total emissions (Sun et al., 2016). Silver, Palladium, and platinum NPs are also discharged into the environment, mostly during manufacturing and usage, and finally accumulate in landfills and wastewater (Bundschuh et al., 2018). Synthetic NPs are eventually released into the environment, and the primary releasing pathway for these NPs seems to be industrial and municipal wastewater plus biosolids application (Lazareva and Keller, 2014; Westerhoff et al., 2013).

Repeated washing releases nanoparticulate silver imbedded in textiles, which accounts for 20% to 100% of total particle content and ends up in the wastewater stream (Choi et al., 2017). Titanium dioxide may be found in sunscreen, personal care products, and cosmetics and is discharged into the wastewater stream after use. About 26%–39% of NPs emitted into the wastewater stream end up in the aquatic ecosystem (Lazareva and Keller, 2014). A study on the quantification of TiO_2 concentration in a wastewater facility in Arizona revealed an average of 843 μg/L of total titanium in the inflow. In Germany, nine wastewater treatment facilities were sampled and analyzed for the presence of silver NPs. The results revealed a maximum daily load of 4.4 g of silver accumulation (Li et al., 2013).

NPs may be purposely released into the environment for a number of objectives, including pollutant cleanup, water treatment, and agricultural application. For groundwater cleanup, synthetic metal NPs of iron, such as zero-valent iron particles, are commonly used (Zou et al., 2016). Groundwater is being treated in situ by injecting zero-valent iron NPs directly into aquifers (Stefaniuk et al., 2016). Injecting directly into groundwater might have unintended implications, such as unwanted microbial interaction (Goldberg et al., 2007). Biogeochemical processes in the subsurface may be affected by exposure to biologically active NPs. Because of its diverse use for the remediation of organic pollutants like pesticides, and other toxic elements removal such as lead and arsenic, the use of synthetic NPs in water remediation is expanding. The residues of NPs left after remediation methods are assumed to be harmless (Troester et al., 2016); however, their toxicity owing to drinking water intake should be assessed considering their mobility, reactivity, and relative stability in water. The destiny of the NPs utilized in the remediation operations must be closely monitored; their dissolution, degradation, and interactions with trace elements must be examined before developing new techniques for water treatment. The implications of using NPs in various water treatment procedures are unclear, and there are no effective analytical techniques for measuring NPs in complicated matrices. Because of these information gaps, studying NPs as a contaminant is difficult. Synthetic NPs, in contrast to natural NPs, have received significantly more attention, although accounting for just a small portion of total NMs in the environment. In contrast to natural NPs, which have been related to trace element mobilization and geogenic pollution of water sources, synthetic NPs are potential contaminants.

Naturally occurring NPs formed by biogeochemical processes are also often detected in groundwater in low mg/L concentrations (Baumann et al., 2006). Up to 5% of the mineral matrix in the water bodies is expected to be in the nanoscale range. However, the form and concentration of natural NPs stay in equilibrium with the surrounding physio-chemical circumstances. Natural NPs from volcanic eruptions are able to make their way into surface water sources such as oceans, rivers, lakes, and seas through wind and rain (Hochella et al., 2019), potentially contaminating them. Natural NPs in volcanic ash may serve as a potential nutrient source in the marine ecosystem, resulting in enhanced phytoplankton production and potentially influencing carbon dioxide balance (Ermolin et al., 2018; Lindenthal et al., 2013; Maters et al., 2016). Toxic substances may be present in volcanic ash NPs, which might be incorporated into water supplies (Ermolin et al., 2018). Because of their nano-size and mobility, volcanic ash NPs may easily be swallowed or absorbed via skin pores (Buzea et al., 2007) and may induce toxicity.

Humans and other living species may be exposed to NMs employed for adsorptive remediation of water pollutants, which may have various health consequences that are difficult to diagnose (Hristovski et al., 2008). Both AuNPs and TiO_2 NPs have been shown to accumulate in fish and cause clastogenic effects, oxidative DNA damage, genotoxicity, and inflammation in fish cells (Bouwmeester et al., 2011; Chen et al., 2014). In developing fish, titanium NPs may increase oxidative damage (Fang et al., 2015). Although the long-term consequences of NPs as a possible contaminant in water supplies are well understood, there are few studies on their general prevalence, implying that there will be an increasing need to monitor and regulate NPs in drinking water (Westerhoff et al., 2018). A study conducted in 2018 on the surface water of the Dutch rivers (Meuse and Ijssel) revealed the presence of NPs of silver and cerium oxide as well as microparticles of titanium oxide (Peters et al., 2018). The results of this study revealed that silver NPs had a concentration of 0.8 ng/L and an average particle size of 15 nm; cerium oxide had a concentration of 2.7 ng/L and an average particle size of 19 nm, and titanium oxide had a concentration of 3.1 g/L and an average particle size of 310 nm (Peters et al., 2018). The knowledge of the consequences of synthetic NPs contaminating water systems is limited. This ignorance is due to a lack of awareness about the toxicity of these substances. Furthermore, there is an insufficient understanding of NP fate and modification in the aquatic environment.

6. Toxicological aspects of nanomaterials

The increased production and application of NMs would lead to increased exposure of these particulate matters to living organisms and their habitat. NPs are often introduced into the human body by skin contact, ingestion (gastrointestinal tract), inhalation (respiratory tract), and injection (blood circulation) (Fu et al., 2014; Wu and Tang, 2018). NPs upon entering the human body crosses multiple cellular barriers to reach various sensitive body organs such as kidney, lungs liver and may cause DNA alterations, mitochondrial damage, and cell apoptosis/death (Shin et al., 2015; Bahadar et al., 2016; Ahamed et al., 2010). The production of Reactive Oxygen Species (ROS), which may induce inflammation and oxidative stress, and damage to cellular membranes, proteins, and DNA, is a major contributor to toxicity (Manke et al., 2013; Liu et al., 2013a; Fard et al., 2015). The level of ROS produced by NPs is determined by various parameters, including aggregation/agglomeration, particle shape, size, solubility, composition, and the presence of transition metals (Manke et al., 2013; Gatto et al., 2018; Jeevanandam et al., 2018; Shvedova et al., 2012). Gliga et al. (2014) discovered that silver NP cytotoxicity is size-dependent. They found silver NPs (10 nm) to cause cytotoxicity in human lung cells at dosages of 20 g/mL (Gliga et al., 2014). The 10 nm citrate and 10 nm polyvinylpyrrolidone-coated silver NPs, on the other hand, showed no coating-dependent cytotoxicity. A brief overview of the toxicity of different commonly used NP has been discussed in the following part-

6.1 Gold nanoparticles

Exposure to Gold NPs (AuNPs) may occur during their synthesis and development, during administration by direct ingestion or inhalation, via implants or adherence of airborne and surface contaminants, or dermal injection absorption (Yokel and MacPhail, 2011; Uboldi et al., 2009; Yah et al., 2012; Lewinski et al., 2008). Exposure may also happen when AuNP-composite is affixed to home items, marketplaces, and other outdoor locations (Weinberg et al., 2011). These exposures may cause them to remain and accumulate in the environment, giving them the capacity to enter the food chain, affecting both abiotic and biotic components (Renault et al., 2008). This increases AuNP absorption by other species (fishes and algae) in the environment, which may then be ingested by animals and humans. AuNPs have been found to accumulate at high levels in the liver and spleen, causing severe harm to the organism (Zhang et al., 2012a; Sani et al., 2021). According to one study, Mice models were injected subcutaneously with gold nanorods (AuNRs), and it was found that the release of Au ions can cause oxidative damage to tissue at the injection site (Meng et al., 2014). The physicochemical features of AuNPs, such as shape, size, and surface coating, have an essential influence on their toxicity. According to Fraga et al. the surface coating of AuNPs had a significant impact on their toxic nature rather than their bio-distribution (Fraga et al., 2014). In another study, HT-29 and HepG2 cells and Wistar rats were exposed to AuNPs in an attempt to determine their location and distribution in cells and tissues. The results indicated the presence of AuNPs in the gut, spleen, kidney, liver, urine, and feces. Lopez-Chaves et al. (2018) injected PEG-coated AuNPs into mice which resulted in little liver injury (Lopez-Chaves et al., 2018). In another study, after intraperitoneal administration of AuNPs into rats, significant changes in several liver enzymes were detected (Abdelhalim and Abdelmottaleb Moussa, 2013). The AuNPs capped with trisodium-citrate-dehydrate have been found to cause minor nephrotoxicity and hepatotoxicity (Das et al., 2012). Cytotoxicity, hepatotoxicity, and toxicity to the lung and spleen are some toxicological concerns caused by AuNPs used as biolabels, biosensors, and drug carriers (Daraee et al., 2016; Lin et al., 2016). The oral, tail vein, and intraperitoneal (IP) doses of citrate-coated AuNPs given to mice showed high toxicity and affected the organ index of the mics (Zhang et al., 2010).

The use of certain capping, stabilizing or conjugating agents for AuNPs, such as CTAB (Alkilany et al., 2009), polyelectrolyte poly (allylamine) hydrochloride (Bozich et al., 2014), and hydrazinium hydroxide, sodium borohydride (Vijayakumar and Ganesan, 2012), has shown varying degrees of toxicities. The dose AuNPs (15 ppm) in drinking water has been found to cause histopathological changes, up-regulation of IL-6, expression of the Nrf2 gene, oxidative damage to blood, DNA fragmentation, and a significant reduction in antibody titer against Newcastle disease (ND) and avian influenza (AI) among broiler chickens (Hassanen et al., 2020). Mice with a high concentration of AuNPs have been found to cause decreased body weight, spleen index, and RBC count after oral treatment (Zhang et al., 2010). After being exposed to naked colloidal AuNPs (8–37 nm) for 21 days resulted in the loss of weight and appetite in mice; moreover, a considerable percentage of the mice died (Chen et al., 2009). The cytotoxicity of various stabilizing agents such as Gum Arabic, starch, and citrate on the PC-3 and MCF-7 cell lines were compared by Vijayakumar and Ganesan (2012). Citrate-AuNPs were shown to be more cytotoxic at higher concentrations than Gum Arabic and starch NPs.

The in vitro study on HepG2 cells subjected AuNPs (10 nm) showed tails moments comparable to those seen in hydrogen-peroxide-treated positive control cells (Lopez-Chaves et al., 2018). In C17.2 and PC12 cells, high concentrations of AuNPs generated oxidative stress due to cell viability and actin and tubulin deformations (Soenen et al., 2012). On MG63 cells, AuNPs had a modest long-term cytotoxic impact (Schneider et al., 2017). AuNPs have been shown in many studies to induce DNA damage, which is a source of genotoxicity (Paino et al., 2012). The in vitro toxicity of AuNPs was investigated in airway epithelial cells and revealed an increase in lipid peroxidase, DNA damage, and cytotoxicity in cells (Ng et al., 2013). In the treatment of coated and uncoated hyaluronic acid AuNPs, DNA damage was seen in Balb/3T3 cells, indicating oxidative stress. Their cell internalization and cytotoxicity, on the other hand, were decreased (Di Guglielmo et al., 2012). In MRC-5 cells treated with AuNPs (20 nm), autophagy and oxidative stress have been observed (Li et al., 2010a,b). The genotoxicity and cytotoxicity of polyamidoamine dendrimers or sodium citrate-capped AuNPs in HepG2 and PBMC cells have been found at extremely low doses (Paino et al., 2012). Citrate-capped AuNPs have been found cytotoxic to HeLa and U937 cells (Maiorano et al., 2010). Some studies on the toxic effects of AuNPs are given in Table 6.1.

6.2 Silver nanoparticles

Various studies have been conducted to demonstrate the in vivo and in vitro toxicity of silver nanoparticles (AgNPs), and it has been found that the size and exposure of AgNPs are the main factors that induce toxicity among experimental models. Humans are exposed to AgNPs by means of dermal contact, inhalation, blood circulation, and oral ingestion (Wei et al., 2015; Akter et al., 2018; Jaswal and Gupta, 2021). AgNPs in sizes 10–100 nm and concentration range of 5–10 mg/L are very toxic in vivo experiments (Ahamed et al., 2008). The in vitro studies of AgNPs produce toxicological effects among nonmammals and may induce morphological deformities in reproduction (Zhang et al., 2015). AgNPs can pass the blood–brain barrier to enter the testicles and impact sperm cells (Panyala et al., 2008). AgNPs may also reach body organs such as the kidneys, liver, lungs, heart, and brain by crossing the blood–brain (Daniel et al., 2010). An investigation into whether or not silver NPs are hazardous to algae's ability to produce food has shown that they do not induce toxicity, but their consumption and release of $Ag+$ ions cause a decrease in photosynthesis (Salas et al., 2019).

Most characterizations of the cytotoxic effects of AgNPs have focused on DNA damage, oxidative stress, and regulation of cytokine production. The absorption of AgNPs by cells can potentially induce the production of ROS, which may lead to oxidative stress and genotoxic consequences. Disruption of ions and electrons across the mitochondrial membrane causes the production of ROS, which may lead to cell death through apoptosis or necrosis (AshaRani et al., 2009; Hwang et al., 2007; Almofti et al., 2003). Ag NPs could damage DNA by increasing ROS generation or lowering ATP synthesis through mitochondrial damage, thus inhibiting energy-dependent DNA repair pathways (Cha et al., 2008). AgNPs enter the circulatory system when ingested or inhaled (Sung et al., 2009). Studies have shown that when AgNPs are injected into Mice, the NPs show their response by reducing the Platelet

Table 6.1 - Toxicological effects of gold nanoparticles.

Nanoparticle	Animal model/cell line	Toxic effects	References
AuNPs	Human leukemia (HL-60) and hepatoma (HepG2) cell lines	Increase in production of ROS and reduction of glutathione (GSH)	Mateo et al. (2014)
AuNPs	C17.2 and PC12 cells	Cell viability and deformations of actin and tubulin resulted in oxidative stress	Soenen et al. (2012)
Citrate-stabilized AuNPs	Balb/3T3 cells	Disruption of the actin cytoskeleton	Coradeghini et al. (2013)
AuNPs	MRC-5 cells	Oxidative stress and autophagy	Li et al. (2010a,b)
AuNPs	Human liver cell lines (HL7702 cells)	Apoptosis, cytosolic GSH reduction, depolarization of mitochondrial transmembrane potential	Gao et al. (2011)
AuNPs	MG63 osteoblast-like cells	Cell death	Tsai et al. (2013)
AuNPs	A549 cells	Alterations in nuclear morphology and condensation caused cytotoxicity	Patra et al. (2007)
AuNPs	MRC-5 cells	DNA damage	Chueh et al. (2014)
AuNPs	Wistar rats	Small-sized NPS induced high DNA damage. Traces of AuNPs were found in the spleen, liver, urine, intestine, kidney, urine, and feces	Lopez-Chaves et al. (2018)
AuNPs	Male and female mice	Damage to kidney and liver	Chen et al. (2012)
PEG-coated AuNPS	Mice	Liver damage	Zhang et al. (2011)
AuNPs	Female mice	Accumulation of AuNPs in liver and macrophages	Sadauskas et al. (2009)
Citrate coated-AuNPs	Wistar rats	Accumulation of NPS in spleen, liver, kidney, and neurons. NPs crossed the blood—brain barrier	Lasagna-Reeves et al. (2010)
PEG-coated AuNPs	Rats	Accumulation of NPs on liver and spleen.	Lipka et al. (2010)
AuNPs	Broiler chicken	Oxidative damage to blood, reduction of antibodies against newcastle disease and avian influenza, expression of Nrf2 gene, and DNA fragmentation	Hassanen et al. (2020)

aggregation in the mice model (Shrivastava et al., 2009). Ag+ has also been reported to accumulate in the liver after exposure to AgNPs, suggesting that the liver and bile ducts are toxic targets for AgNPs (Kim et al., 2008; Ji et al., 2007). Hepatic vacuolization and localized necrosis, hyperplasia of bile ducts, enhanced infiltration of inflammatory cells, and dilatation of central veins have been observed in the mice exposed to AgNP. Apoptotic and inflammatory genes have also been shown to increase in the livers of mice exposed to AgNPs (Chi et al., 2009). Some other toxicological effects of AgNPs are mentioned in Table 6.2.

Table 6.2 Toxicological effects of some silver nanoparticles.

Nanoparticles	Animal/ cell line	Toxic effects	References
AgNPs (20 nm)	Male Sprague Dawley rats	Cardiac and liver oxidative stress with a mild inflammatory response in the liver.	Ebabe Elle et al. (2013)
PVP-coated AgNPs (20—30 nm)	Male Sprague Dawley rats	Abnormalities in sperm morphology with increased abnormalities at higher doses	Lafuente et al. (2016)
PVP-coated AgNPs (20—30 nm)	Male Sprague Dawley rats	Hepatocellular damage due to increased production of ROS, along with depletion of insulin signaling pathway and higher autophagy	Blanco et al. (2018)
CT-capped AgNPs	Male wistar rats	Oxidative stress in the brain at low doses for a longer period of time.	Skalska et al. (2016)
PVP and CT-coated AgNPs (20 nm; 110 nm)	Male Sprague—Dawley rats	Inflammatory and cytotoxic responses were greater when AgNPs were smaller in size. After 21 days of installation, larger particles produced a long-lasting impact	Silva et al. (2015)
CT-AgNPs (20 nm)	Male Sprague—Dawley rats	Resulting in cardiac ischemic-reperfusion injury.	Holland et al. (2015)
PVP-coated AgNPs0 (50 nm; 200 nm)	Female wistar rats	Ag accumulation in the peripheral organs, as well as a transient inflammation of the lungs	Wiemann et al. (2017)
PVP and CT coated AgNPs (50 nm; 200 nm)	Female BALB/C mice	Inflammatory responses in healthy and sensitized lungs after pulmonary exposure to AgNPs. The responses were size, dosage, and coating dependent.	Alessandrini et al. (2017)

6.3 Zinc oxide nanoparticles

One of the most widely used NPs, zinc oxide nanoparticles (ZnO NPs), can be found in a wide range of fields, including electronics, textiles, rubber, medicine, cosmetics, bio imaging, and drug delivery (Zhang et al., 2014; Ji and Ye, 2008). Humans are exposed to these NPs at a high rate because they come into contact with them on a regular basis. Their ability to enter the body via various routes, including the respiratory and digestive systems as well as dermis and parenteral routes (Vandebriel and Jong, 2012). Because of their ability to reach any tissue or body organ, they may pose a threat to the human body. The in vitro and in vivo studies have shown that ZnONPs have possible molecular consequences, such as a loss of membrane integrity, reduction in cellular viability, or trigger cell death (Table 6.3). The cytotoxicity of ZnO NP has been found to be shape and size-dependent. It has been found that spherical NPs about 40 nm in size are more toxic than larger nanospheres and nanorods (Hsiao and Huang, 2011). The surface composition is a second characteristic that influences the potential toxic effect (Guo et al., 2008). Zn^{2+} ion concentrations have been found to be significantly higher in media containing ZnONPs than in those containing Zn powder (Hackenberg et al., 2011). In humans, a severe inflammatory response in the lung tissue is one of the most toxic effects of ZnO NPs, where NPs can enter through alveolar epithelial cells (Kim et al., 2010a,b). The exposure of tissue to a solution containing ZnO NPs with a concentration of 5 g/mL or more increases the secretion of IL-8. Angiotensin-converting enzyme 8 (IL-8) has been shown to play an important role in the pathology of the lungs (Hadrup et al., 2019).

6.4 Titanium oxide nanoparticles

The toxic effects of TiO_2 NPs seem to be species-specific (Hou et al., 2019). The exposure of TiO_2 NPs for 24 h has been found more toxic to *E. coli* than *B. subtilis*, with an LC50 of 68 mg/L for *E. coli* and 96 mg/L for *B. subtilis* in a 24-h period (Erdem et al., 2015). The ability of TiO_2 NPs at 200 mg/L to inhibit cell growth in *Pseudomonas aeruginosa* has been found to be greater than *Proteus vulgaris* (Priyanka et al., 2016). Toxicology studies on TiO_2 NPs indicated that the MIC varied in the increasing order of *E. coli, Staphylococcus aureus, B. subtilis, Klebsiella pneumonia,* and *P. aureus,* indicating that *P. aureus* was the most antitoxic among five bacteria species (Rajakumar et al., 2012). The toxicities of TiO_2 NPs are also dependent on their size. The majority of

Table 6.3 Toxicological effects of some zinc oxide nanoparticles.

Nanoparticles	Animal/cell line	Toxic effects	References
ZnO	*Drosophila melanogaster*	Oxidative stress induction caused damage to DNA	Carmona et al. (2016)
ZnO	Human nasal mucosa cell culture	Genotoxicity induced by the dissolution of ZnO-NPs in Zn^{2+}	Hackenberg et al. (2017)
ZnO	Male wistar rats	Neuroinflammation via Ca^{2+}-dependent mNF-κB, ERK, and p38 activation pathways	Liang et al. (2018)
ZnO	Rat hippocampal CA3 pyramidal neurons	Disruption of ionic homeostasis, enhanced neuron excitability, and disturbance of physiological functions	Zhao et al. (2009)
ZnO	Human fibroblasts and astrocytoma U87 cells	Induce cell death through apoptosis and necrosis	Lai et al. (2008)
ZnO	Rats	Effects on gestation, pregnancy, and lactation as well as induce developmental toxicity among offspring	Jo et al. (2013)
ZnO	Spermatocyte cell line (GC2-spd) and mouse sertoli cell line (TM-4)	An increase in MDA level, enhances ROS production, decrease in glutathione level	Liu et al. (2016)
ZnO	Human epidermal cell line (A431)	Genotoxicity due to lipid peroxidation and oxidative stress	Sharma et al. (2009)
ZnO	Human (HepG2) liver cells	DNA damage by the production of ROS	Sharma et al. (2011)
ZnO	Mice	Resulted in pulmonary toxicity through oxidative stress	Jacobsen et al. (2015)
ZnO	Male wistar rats	Increase in lactate dehydrogenase (LDH) with lung and liver tissue damage	Wang et al. (2010)

research found that as particle size decreased, so did the toxicity. Under the same circumstances, the LC50 values for *B. subtilis* have been found to be 96 mg/L for 16.2 nm NPs and 401 mg/L for 45.8 nm NPs (Erdem et al., 2015).

TiO_2 NPs have been found to accumulate and become harmful in several body organs after being ingested through various routes, including the gastrointestinal tract or inhalation (Cui et al., 2010; Jia et al., 2017; Hu et al., 2010). Nano-TiO_2 has been shown to be toxic to a variety of cell types, including human lymphoblastoid cells and hepatoma cells (Wang et al., 2007). TiO_2 may cause an acute stress response in glial cells of the mice brain, resulting in neuronal dysfunction and damage (Pogue et al., 2012). Neuron cell lines exposed to TiO_2 NPs particles had considerably lower survival rates in a time- and dose-dependent manner (Wu et al., 2010).

Several studies have shown that TiO_2 NPs may harm the human body by altering cell cycles, causing nuclear stenosis, and leading to apoptosis (Jia et al., 2017; Zhang et al., 2009; Rahman et al., 2002; Yang et al., 2010) (Table 6.4). In addition, TiO_2 NPs have been demonstrated to induce damage to DNA and the small intestinal epithelium (Gretzer et al., 2003). Shortness of breath and rashes on the forearms, hands, and face are some of the common symptoms of patients exposed to TiO_2 toxicity (Larsson et al., 2004). TiO_2 NPs, when inhaled or ingested, can accumulate in

Table 6.4 Toxicological effects of some titanium oxide nanoparticles.

Nanoparticles	Animal/ cell line	Toxic effects	References
Anatase TiO_2	Male BALB/c mice	TiO_2 caused an increase in the number of neutrophils and alveolar macrophages in the bronchoalveolar lavage of mice	Hussain et al. (2011)
Anatase + Brookite TiO_2	Male Crl: OF1 mice	Expiratory flow reduced	Leppänen et al. (2011)
TiO_2	Pregnant mice	TiO_2 found in fetal brain	Yamashita et al. (2011)
Rutile Fe-doped TiO_2	Male wistar rats	Increase in systolic blood pressure and heart rate	Nemmar et al. (2011)
Anatase TiO_2	ICR mice	Production of ROS, hepatocytes apoptosis, mitochondrial damage, titanium accumulation in the heart, brain, lung, and spleen, spleen, lung, brain, and heart	Jia et al. (2017)
Anatase TiO_2	Sprague–Dawley rats	Increase in glutathione peroxidase, superoxide dismutase, malondialdehyde, and oxidized glutathione	Wang et al. (2009)
Anatase TiO_2	Pregnant Slc:ICR mice	Disrupted and disorganized seminiferous tubules; reduced production of sperm, Sertoli cells, and decreased epididymal movement of sperm.	Takeda et al. (2009)

several organs, including the alimentary canal, kidney, heart, spleen, liver, and cardiac muscle (Shimizu et al., 2009; Yamashita et al., 2011). TiO_2 NPs may also lead to brain damage due to their high sensitivity to oxidative stress (Kreyling et al., 2017). TiO_2 NPs may potentially reduce particular recognition memory by altering the homeostasis of neurotransmitters (Zhang et al., 2012b). There have been a number of studies that have shown that exposure to NPs over a long period of time and degree of doses may produce toxic effects (Valentini et al., 2018; Czajka et al., 2015; Shabbir et al., 2021).

TiO_2 acts as a mediator of oxidative stress, causing different amounts of hydroxyl radicals to be produced irrespective of exposure to UV light (Uchino et al., 2002). These hydroxyl radicals can potentially increase DNA damage (Reeves et al., 2008). Anatase-TiO_2 NPs reduce cell viability in rats after the first UV light exposure, resulting in breakage in DNA strands and oxidative damage to DNA. Therefore, photo-activated TiO_2 particles have increased cytotoxic and genotoxic potential after UV irradiation is stopped, irrespective of particle size (Petković et al., 2011). TiO_2 NPs exposed to cells may affect the cellular signaling pathway, which governs activities such as inflammation, cell proliferation, and cell death by boosting ROS production (Barthel and Klotz, 2005). High levels of TiO_2 NP stress cause cell damage by lowering oxidative stress and inflammatory signaling pathways (Barthel and Klotz, 2005; Kang et al., 2008). Some other toxicological effects of TiO_2 are given in Table 6.4.

6.5 Carbon nanotubes

Since the discovery of carbon nanotubes (CNTs) by Iijima (1991), they have been intensively studied because of their large surface area, conductivity, thermal stability, and tensile strength (Schnorr and Swager, 2011). CNTs are allotropes of carbon made of either a single graphite sheet (SWCNTs) or multilayered graphene sheets (MWCNTs) (Schnorr and Swager, 2011; Sakhaee-Pour et al., 2008; Pumera, 2009). CNTs are now among the most widely available industrial NMs. These NMs are widely employed in electronics and materials science including radiation sources, probes, sensors, nanometer-sized semiconductor devices, field emission displays, conductive and high-strength composites, and interconnects (Dresselhaus et al., 2004). Orthopedic implants, biosensors for the detection of enzymes and proteins, cancer treatment, tissue engineering, and bone growth support materials for fracture healing are just some of the numerous applications for these NMs (Fiorito, 2007). Although CNTs have many appealing advantages, their toxicity is one of the major concerns. In vitro and In vivo studies have shown that the toxicity of CNTs is attributed to a number of factors, such as dosage, exposure duration, and exposure methods (Francis et al., 2015) (Table 6.5). Commercially available SWCNTs and MWCNTs (rich in Fe, Co, Mo, and Ni content) and acid-treated SWCNTs with decreased metal impurities have been found in the cell membrane (Pulskamp et al., 2007). Commercial CNTs enhance intracellular ROS production and decrease the potential of

Table 6.5 Toxicological effects of carbon nanotubes.

Nanoparticles	Animal/cell line	Toxic effects	References
MWCNTs	Wistar rat	Increase in BALF total cell counts, protein content, enzyme activities	Ma-Hock et al. (2009)
MWCNT	Wistar rat male, female	Inflammation at 0.4 mg/m^3	Pauluhn (2010)
Carbon nanofiber	SD rat male, female	Inflammation at 25 mg/m^3	Delorme et al. (2012)
MWCNTs	Male and female F344 rat	Increase in lung weights, BALF inflammatory parameters.	Kasai et al. (2015)
SWCNT	CD rat male	Transient inflammation	Warheit et al. (2004)
MWCNT	SD rat female	Inflammation and granuloma	Muller et al. (2005)
SWCNTs	Male ICR mice	Release of cytokines (NF-κB)	Chou et al. (2008)
MWCNT	F344 rat male	Persistent inflammation and fibrosis	Aiso et al. (2010)
MWCNTs	Male sprague—dawley rat	Increase in BALF neutrophils, eosinophils and LDH	Kobayashi et al. (2010)
SWCNTs	Male sprague—dawley rat	Increase in BALF neutrophils, eosinophils, macrophages, lymphocytes, LDH, and IL-1β, IL-6.	Kobayashi et al. (2011)
Purified SWCNTs	Female C57 BL/6 mouse	Inflammation, TNF-α and IL-1β increased	Shvedova et al. (2005)
Purified SWCNTs	Female C57 BL/6 mouse	Robust, acute inflammation (PMNs, TNF-α, IL-6, LDH increased).	Shvedova et al. (2007)
SWCNTs	Female C57 BL/6 mouse	Inflammation (TNF-α , IL-6, and TGF-β increased), lipid peroxidation, oxidized proteins, GSH depletion	Shvedova et al. (2008)

mitochondrial L-glutathione (mGSH). mGSH is an effective antioxidant peptide and protects cells from oxidative stress. SWCNTs with the presence of nickel oxide have been found to affect the redox properties of L-Glutathione (Fubini et al., 2010).

The toxicity of CNTs varies according to their length (Yamashita et al., 2010; Sato et al., 2005; Liu et al., 2013b). In vivo, 825 nm-long CNTs generated higher inflammation than 220 nm-long CNTs because macrophages were able to engulf 220 nm-long CNTs more easily (Sato et al., 2005). Long MWCNTs, as compared to short MWCNTs, have been found to induce high damage to DNA and increase the number of cells in abdominal lavage fluid (Yamashita et al., 2010). Different lengths of MWCNTs caused different amounts of granuloma to form. Injecting MWCNTs longer than 20 m is more toxic as compared to MWCNTs with low-aspect-ratio, tangled nanotube aggregates as macrophages are not able to engulf longer tubes (Sato et al., 2005; Poland et al., 2008). The aggregation state is one of the critical elements in determining the toxic potential of CNTs since it is one of the aspects that may influence the shape and surface area of CNTs. Highly agglomerated SWCNTs have been found to influence the reduction in total DNA content (Belyanskaya et al., 2009). It has been found that suspended CNT bundles are less toxic than asbestos; however, ropelike agglomerates of CNTs are more toxic than asbestos fiber at the same concentration (Wick et al., 2007). In animal studies, CNTs produced pulmonary inflammation at a lower dosage than micron-sized carbon particles (Kobayashi et al., 2017; Morimoto et al., 2010, 2013). Also, the inhalation of CNTs leads to the development of malignant mesothelioma (Takagi et al., 2008), indicating that CNTs may represent dangers comparable to asbestos. Animal studies have shown that CNTs inhaled via the lungs may harm other organs as well (Zheng et al., 2016; Lin et al., 2013). In some studies, maternal exposure to CNTs has been linked to developmental toxicity, such as teratogenicity (Ema et al., 2016). Various in vivo and in vitro studies have found that acute and chronic inflammatory reactions and granuloma may be induced by exposure to SWCNTs and MWCNTs (Narei et al., 2018). A study on the toxicity of SWCNTs in mice showed that high dosages of CNTs cause immediate and chronic granulomas and inflammation in the lungs.

CNTs have been shown to penetrate the cellular membrane of rat macrophages (NR8383) and modify their physiology and cellular functions (Pulskamp et al., 2007). Both rat macrophages (NR8383) and human A549 lung cells showed a dose-dependent increase in intracellular ROS and a reduction in the potential of the mitochondrial membrane when exposed to commercial

CNTs. Human MSTO-211H cells have been exposed to study the toxic effects of CNTs with varied agglomeration degrees. CNTs dispersed in surfactants were shown to be less toxic than CNTs that had been agglomerated (Wick et al., 2007). Several studies have found that carbon nanotubes have the ability to pass cell membranes (Pantarotto et al., 2004; Simon-Deckers et al., 2008; Francis and Devasena, 2018). A study was carried out to investigate the distribution of functionalized SWCNT on human fibroblast 3T6 and murine 3T3 cells. It was found that CNTs were able to pass the cellular membrane and accumulate in the cytoplasm or reach all the way to the nucleus. The study also revealed that functionalized SWCNTs were found to be nontoxic to cells at doses of 10 mM (Pantarotto et al., 2004).

In vivo and in vitro studies on the genotoxic ability of CNTs have shown that they may cause a variety of genotoxic effects (Narei et al., 2018). Carbon nanostructures, notably SWCNTs and MWCNTs, have been shown to be capable of causing single-strand breaks. This effect has been seen in a variety of cell types, including macrophages (Di Giorgio et al., 2011), lung epithelial cells (Jacobsen et al., 2008), fibroblasts (Patlolla et al., 2010), and stem cells (Akhavan et al., 2013). Pacurari et al. found that SWCNTs might cause DNA damage in both normal and cancer human mesothelial cells (Pacurari et al., 2008). DNA double-strand breaks have also been shown to be caused by CNTs (and CNT-like forms) (Akhavan et al., 2012).

So far, CNTs have been used in a broad range of applications because of their unique structural, physicochemical, and chemical features. However, because of their physical resemblance to pathogenic fibers and biopersistence, there has been substantial worry that CNT exposure may induce toxic reactions. Acute and chronic inflammation, oxidative stress, granuloma formation, fibrosis, lung tumor and mesothelioma, genotoxic effects, and several other systemic toxicities have been found caused by CNTs. Various other toxicological concerns of CNTs are given in Table 6.5.

6.6 Copper oxide nanoparticles

Copper oxide nanoparticles (CuO NPs) are being used in a wide range of applications, including heat transfer fluids, antimicrobial reagents, semiconductors, and intrauterine contraceptive devices (Bahadar et al., 2016; Aruoja et al., 2009; Naz et al., 2020; Bhat et al., 2021b). Studies have shown that copper NMs are toxic to the liver and kidney (Lei et al., 2008). Animal experiments have shown that nanocopper causes serious damage to the liver, kidneys, and spleens. Also, in vitro studies of copper oxide NPs (50 nm) have been found to cause cell membrane disruption and oxidative stress (Ahamed et al., 2010). Human cell lines such as lung epithelial A549, cardiac microvascular endothelial, neuronal, and kidney cells exhibit cytotoxicity to CuO NPs (Ahamed et al., 2010; Coble et al., 2009; Sun et al., 2011; Xu et al., 2013). Using A549 and HepG2 cells, the cytotoxicity and oxidative stress of CuO NPs have been studied, which resulted in a high amount of lipid peroxidation and ROS production, as well as a decreased level of antioxidant (GSH human hepatocellular carcinoma) cells (HepG2). Lipid peroxidation markers such as MDA and antioxidant enzymes like SOD and CAT were found to have risen, whereas GSH levels decreased. These results indicate that oxidative stress may be the primary mechanism causing toxicity by CuO NPs (Akhtar et al., 2016).

Increased concentrations of 8-isoprostane in the HEp-2 cell supernatant after treatment with CuO NPs show that the cells have suffered oxidative damage (Naz et al., 2019). CuO NPs were used in an experiment by Jing et al. on HBEC and A549 cells. Results showed that HBEC and A549 cells had increased ROS levels after 4 h of exposure (Fatahian-Dehkordi et al., 2017). Various studies have found that oxidative stress is also responsible for CuO-NP-induced cytotoxicity (Sun et al., 2011; Xu et al., 2013; Akhtar et al., 2016; Müller et al., 2010). Antioxidant enzymes, including SOD, CAT, and glutathione, are also affected by engineered NPs such as CuO NPs (Lanone et al., 2009). CuO NPs have been found to reduce GSH levels and inhibit SOD and CAT activities, resulting in oxidative damage in the embryo. These NPs also have been found to cause alterations in the physiology of zebrafish, such as inability to hatch, short body length, and reduced reproductive capacity (Ding et al., 2014).

6.7 Iron oxide NPs

The use of iron oxide nanoparticles (Fe_2O_3 NPs) is common in the drug delivery, biomedical and diagnostic domains. These NPs accumulate in the liver and other organs of the reticuloendothelial system (Bahadar et al., 2016; Naqvi et al., 2010; Albukhaty et al., 2013). Cell lysis, inflammation, reduced cell viability, and disruption of the blood coagulation system are some of the toxic effects of these NPs (Liu et al., 2013a; Zhu et al., 2008). Reduced cell viability is one of the common toxic effects of Fe_2O_3 NPs. The coating of Fe_2O_3 NPs shows different toxicity levels and different cell viability results. Dextran-coated iron oxide NPs (100–150 nm, 0.1 mg/mL) has decreased human macrophage viability by 20% after 7 days of incubation (Pawelczyk et al., 2008). According to Naqvi et al. super magnetic iron oxide NPs (30 nm) coated with Tween may cause toxicity in murine macrophage cells (Naqvi et al., 2010). Low concentrations of Fe_2O_3 NPs (25—200 g/mL, 02 h exposure) exhibit higher cell toxicity than high concentrations (300—500 g/mL, 06 h exposure). Fe_2O_3 NPs (25 nm) have also been shown to have less of a toxic effect on the morphology, permeability, apoptosis, and mitochondrial activity of the mouse neuroblastoma (Neuro-2A) cell line (Jeng and Swanson, 2006). Fe_2O_3 NPs (13.8 nm, 123.52 g/mL) coated with chitosan exposed to human hepatocellular carcinoma cells for 12 h showed 10% cell viability (Ge et al., 2009). The toxic effects of Fe_2O_3 NPs are attributed to the excessive production of ROS. DNA damage and lipid peroxidation are both enhanced as a result of the increased production of ROS (Liu et al., 2013a).

7. Microbes-assisted bioremediation of nanomaterials contaminants

Microbes are present everywhere and they are highly adaptable to fluctuating environmental conditions (Wani et al., 2022a). The usage of nanotechnology can be made more sustainable and less harmful to the environment through the process of biofabrication, which involves the creation of NMs through the action of bacteria. The usage of chemicals and the tendency of the chemically created NPs to self-agglomerate in an aqueous solution are two potential drawbacks associated with the chemical production of NPs. Therefore, one option that may be available is the environmentally friendly production of NPs using plant extract, fungal enzymes, and bacterial enzymes. They produce metallic NPs and function as reducing agents for the metal complex salt. These NPs achieve superior firmness in an aqueous environment as a result of coprecipitation or by attaching proteinaceous and bioactive components onto the exterior face of the NPs (Basnet et al., 2018). The production of NPs with the assistance of microbes has proven to be an approach that is both economical and kind to the environment. The generation of hazardous gases, as well as metal complexes, was stifled by the endogenous creation of NPs, which acted as an inhibitor. In the process of cleaning up industrial effluents, the application of biogenic particulates is a very effective method of remediation technology. But the manufacturing of NPs straight from the microorganisms is not the only way that microorganisms can aid increase nanotechnology. There are various ways that microorganisms might contribute. For example, the microorganisms may produce catalytic enzymes, which, when combined with NPs, are beneficial to the process of wastewater remediation (Li et al., 2011). In the process of biosynthesis, NPs are produced when microorganisms take target ions from their surrounding environment and then convert the metal ions into element metal using enzymes released by the activities of the cell. Based on the site where the NPs are created, one can divide them into two categories: intracellular synthesis and extracellular synthesis. In the intracellular technique, ions are transported into the microbial cell to produce NPs when enzymes are present (Abada et al., 2017). This process takes place inside the cell. The extracellular creation of NPs requires reducing ions in the context of enzymes and capturing metal ions on the surface of cells, where they are then trapped. The biosynthesized NPs have indeed been put to use in a wide variety of applications, such as drug delivery carriers for targeted therapy, treatment for cancer, genetic manipulation and DNA analysis, antimicrobial agents, biosensors, improving reaction rates, separation research, and imaging (MRI) (Patra et al., 2018; Bilal Ahmad et al., 2020). The majority of the processes that take place in the bottom-up process that microbes use to make NPs are reduction and oxidation reactions. The fundamental idea underlying bioremediation is the conversion of potentially harmful pollutants into substances that provide a lower risk (Wani et al., 2022b). NPs are able to transform pollutants into molecules that have lower toxicity, solubility, and mobility. Metallic NPs formed through biological processes have greater thermal stability over a longer time than those created through chemical processes. The application of a coating made of microbial proteins on the metallic surface of NPs provides a stable environment for biosynthetic processes. It is possible to cut the cost of creating NPs to one-tenth of what it would be using chemical synthesis procedures if the appropriate methodologies are used. Eliminating significant quantities of contaminants is possible with only a modest reduction in the number of biogenic NPs. Despite having a large surface area and a high level of catalytic reactivity, the biogenic NPs do not assemble due to the widespread presence of capping agents that are released by bacteria. NPs can be produced in microbes in two different ways: internally and extrinsically (Balakrishnan et al., 2017). Nanotechnology has piqued the interest of researchers due to its advantageous effects, which include a large supplied surface area, the capacity for many applications, its stability under difficult conditions, simple and effective manipulations of materials, and greater interaction, among others. Incorporating microbes with nanotechnology has resulted in a more environmentally friendly method for managing industrial effluents. Microorganisms can be used to reduce the risk related to NPs that have been chemically produced. Either the remaining residues are biocompatible or can be removed easily using filtration/precipitation procedures (Zhang et al., 2020). NP production by microbes is possible without the use of elevated temp, pressure, energy, stabilizers, or harmful compounds. It is essential to produce NPs with a variety of organic compounds by controlling microbial enzymes for targeted and multi-pollutant wastewater treatment. Synthesis of NPs by microorganisms like bacteria, yeast, fungi, actinomycetes, and algae has several advantages, including simple production, low cost, high efficiency, safety, and environmental friendliness (Kalaba et al., 2021). At polluted sites, the microbial NPs can be utilized to eliminate pollutants. The biocompatible residues remaining after the breakdown of pollutants by microbial NPs are easily separable via filtration or precipitation. By adding biochar into the production of value-added items, such as construction materials, there will be no waste in the end. Therefore, a green and eco-friendly method of NP manufacturing paves the way for numerous biotechnology applications (Bhatt et al., 2021). The biological production of metallic NPs has just been accomplished on a laboratory scale, but their bulk production requires scaling up to an industrial level. Unfortunately, only 1% of nanotechnology substances have been commercialized as of yet, despite the fact that the deployment of microbes-assisted nanotechnology can stimulate the industrial sector (Kapoor et al., 2021). The cost-effective manufacturing of microbial NPs is necessary to make this approach economically viable and sustainable for industry needs. The greater difficulty arises in commercializing these nanotechnological characteristics. Currently, just 1% of these nanotechnology-based aspects have been commercialized. Therefore, the deployment of these simple and effective nanotechnologies approaches helped by microorganisms on a broad scale will be a necessary step for companies (Shukla, 2020).

8. Conclusion and future considerations

The use of NPs is expanding across a wide range of industries. Human exposure to NPs, intentionally or accidently, is unavoidable due to their extensive use in several fields. NPs are constantly exposed to people, and it is crucial to understand the possible acute and long-term detrimental impacts they may have. NMs can pass biological barriers and reach cells, tissues, and organs. Inhalation or ingestion of NMs may allow them to enter the bloodstream. The nanomaterials may then be carried throughout the body and make their way into the organs and tissues, such as the heart, kidney, liver, spleen, nervous system, and bone marrow and induce toxicological effects. Therefore, all NMs must undergo toxicological screening before being used practically. To safeguard both humans and the environment, toxicological studies of NMs are essential. To fill up the knowledge gap and take advantage of the various possible uses for NPs, the relevant harmful effects of NPs must be evaluated using globally approved bias-free in vivo toxicological models.

The materials used for pollution remediation must not become another pollutant themselves once utilized. For this reason, using biodegradable materials is a particularly intriguing avenue of research and development. Using biodegradable materials would not only increase consumer confidence and acceptance of a particular technology but could also provide an environmentally friendly and safer alternative for the remediation of pollutants. Also, new technologies that can use target-specific capture of contaminants are very appealing for safe and effective environmental nanoremediation. There is a need for nanotechnological studies combined with the chemical and physical surface modifications of NMs to create tailored materials that can overcome many of the problems of contamination cleanup. Target-specific capture, toxicity, recyclability, easy synthesis, noncost-effectiveness, biodegradability, and the possibility of recovery after use (regeneration) are some of the most important things to consider while synthesizing new nanomaterials for environmental remediation. Methods should be developed in the future to avoid agglomeration, improve monodispersity, and boost stability. While beyond this, there needs to be a heightened awareness regarding the risks and repercussions of environmental NMs. In addition, efforts must be made to produce new materials using methodologies that are less detrimental to the environment that has somewhat of an influence on the natural world. Furthermore, certain rules and standards need to be developed to regulate the use of NMs and minimize the negative effects that they have on public health as well as the aquatic environment.

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