



Engineered nanomaterials in the environment: bioaccumulation, biomagnification and biotransformation

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Abstract

Engineered nanomaterial manufacturing and usage have been increasing in commercial products. There were 1814 nanotechnological consumer products available in the market in March 2015. Nanomaterials can accumulate, transform and increase in concentrations in biological systems. Nanomaterials offer many benefits over traditional materials, yet their small size also increases their toxicity. Bioaccumulation of nanomaterials begins with nanoparticle accumulation in the organism, then biomagnification follows in the predatory organism. Biotransformation is the last stage, whereby the chemical concentration of toxins in the organism exceeds that in the environment. Here, we review the interaction of nanomaterials with biological substances. It has been observed that the effects of nanomaterials begin at the bottom of the food chain and move all the way through the human body. We have summarized the mechanisms of interaction between engineered nanomaterials and the environment.

Keywords Bioaccumulation · Biomagnification · Bioconcentration · Nanoparticles · Toxicity · Microorganisms · Silver · Gold · Quantum dots · Carbon nanotube · Titanium

Introduction

The rapid development and expansion of nanotechnology industries have ultimately led to the mass production of a wide variety of engineered nanomaterials. These novel engineered nanomaterials exhibit extraordinary performance in mechanical, electric, electronic, thermal, and optical applications due to their unique properties, which traditional or bulk counterpart materials cannot begin to match (Peng et al. 2017; Kumar et al. 2019; Uddin et al. 2018, 2019). The nanomaterials are used in consumer products, industries, and the remediation of pollutants, and these are the primary sources of their direct distribution into the environment. The nanomaterials can be released into different environments during their various life stages, including production, manufacturing, transportation, customer use, waste treatment plant, disposal, and landfilling. One of the main applications of engineered nanomaterials and nanotechnology is to diagnose and

treat diseases in humans, animals, and aquatic organisms. Engineered nanomaterials have proven their value and novel approaches, especially for biomedical applications (Seraz et al. 2017). However, the long-term effect of these nanomaterials is still unknown. That leads to inevitably increase the possibility of release into the environment and exposure to ecosystems or even humans. Their intensive commercial application and production raise concerns about their ecotoxicological effects. Therefore, engineered nanomaterials exposure assessment is crucial because the environmental effects of it are very little known. In recent years, several studies addressing the fate, toxicity, risk, and safety assessment of the nanomaterials in the environment and their effect on living organisms have been carried out. Various interactions of engineered nanomaterials include dissolution, agglomeration, sedimentation, or chemical transformations as well as uptake and transfer into the food chain (Núñez and de la Rosa-Álvarez 2018). To study the inherent properties of engineered nanomaterials and how they influence bioaccumulation, biomagnification, and biotransformation is a key issue in the current environment. Typically, bioaccumulation is defined as the increase in the concentration of contaminants or toxic chemicals in aquatic organisms following uptake from the

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ambient environmental medium (Wang 2016). Increased concentration of these toxic chemical in the food chain is known as biomagnification. Biotransformation is a bioactivation process which could produce reactive metabolites that are more toxic.

For aquatic organisms, the different sources of uptake are water (waterborne uptake) and/or food particles (foodborne uptake). However, in ecotoxicological studies, bioaccumulation and bioavailability are considered jointly. It would be impossible to study bioaccumulation without considering bioavailability, and vice versa. Thus, both are considered herein along with the use of bioaccumulation in biomonitoring. The rate of engineered nanomaterials uptake and adverse effects, especially, rely on the routes of exposure as well as internalization in the cell and organism (Gupta et al. 2017). As shown in Fig. 1, there are three main types of uptake, based on the exposure route: bioconcentration, bioaccumulation, and biomagnification. From all three, biomagnification is the most dangerous to the environment and human health.

This review aims to provide an overview of the principles and effects of various engineered nanomaterials due to bioaccumulation, magnification, and transformation to mammalian cells and a wide range of organisms from single-cell organisms, such as bacteria to more complex organisms, including plants, fishes, etc. This article is an abridged version of the chapter by Uddin MN., Desai F., and Asmatulu, E. (2019) [Bioaccumulation, Biomagnification, and Biotransformation of Nanomaterials, In V. Kumar, P. Guleria, S. Ranjan, N. Dasgupta, and E. Lichtfouse, *Nanotoxicology and Nanoecotoxicology*,] that will be published in the book series *Environmental Chemistry*

for a Sustainable World (<http://www.springer.com/series/11480>).

Exposure pathways and bioaccumulation of engineered nanomaterials

Information about how the engineered nanomaterials can affect nature and how they accumulate in the human body and the environment is relatively unknown. Various stakeholders are increasingly interested in the potential toxicity and other risks associated with nanomaterials throughout the different stages of a product's life cycle (e.g., development, production, use, and disposal). The uptake of nanomaterials by living organisms may have cumulative toxic effects, which organisms may counteract by either their storage or excretion in a benign form. The engineered nanomaterials could affect plant health and the food supply. Furthermore, environmental conditions may also impact toxicity, as was demonstrated with marine phytoplankton, the primary producers that support ocean food webs and are integral to the global carbon cycle. Persistent hydrophobic chemicals may accumulate in aquatic organisms through different mechanisms: via the direct uptake from water by gills or skin (bioconcentration), the uptake of suspended particles (ingestion), and the consumption of contaminated food (biomagnification). Even without detectable acute or chronic effects in standard ecotoxicity tests, bioaccumulation should be regarded as a hazard criterion. The implication of various nanomaterials with the environment, ecosystem, and human being is presented here.

Gold nanoparticles

Gold nanoparticles, due to their consistency and synthesis, firmness, and properties of integrating with molecules such as peptides and proteins, are especially useful for biomedical applications. Lasagna-Reeves et al. (2010) experimented with using gold nanoparticles in drug delivery, diagnosis, and treatment, and found that it is essential to characterize the bioaccumulation and toxicity associated with repeated administration of these molecules. Tissues were stained with hematoxylin/eosin as indicated in materials to assess for potential effects of gold nanoparticles treatment on the organ morphology and cellular damage. In all organs studied, there was a significant increase in gold levels after treatment, which was proportional to the dose administered. However, gold levels in the blood did not increase in proportion to the dose, indicating that gold nanoparticles are mostly taken up and accumulated by tissues. However, even assuming that no blood was removed from the organs, an estimation shows that from the quantity obtained in tissues, the contribution of blood was less

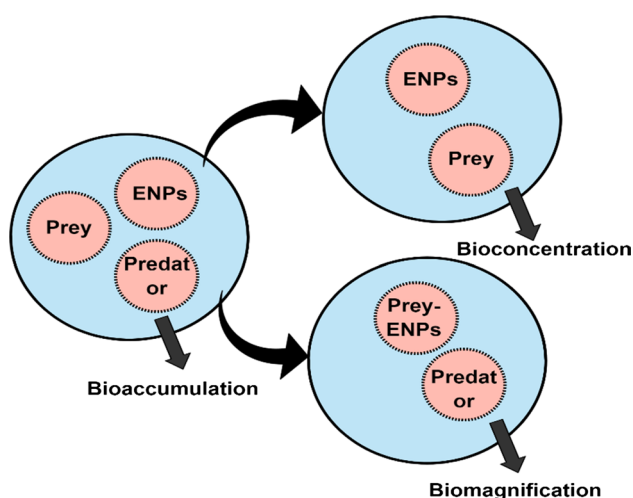


Fig. 1 Direct and indirect exposure paths of engineered nanomaterials in aquatic organisms to predator species from aqueous suspension and diet (prey) (Gupta et al. 2017). *ENP* engineered nanoparticles

than 6%, 2%, 3%, 1%, and 7.5%, for the values reported in brain, kidney, liver, spleen, and lung, respectively. Considering the relatively constant levels of gold in the blood after gold nanoparticles administration at different doses, the increased accumulation of gold in the brain suggests non-saturable uptake of gold nanoparticles across the blood–brain barrier. This is important for utilizing these nanoparticles for potential treatment and diagnosis of neurodegenerative disorders. Besides, gold nanoparticles of the size 12.5 nm could accumulate in the kidney, liver, and spleen. Also, it can pass through a filtration barrier because of its small size. In the context of a single trophic level, the localization of nanoparticles greatly affects their potential for bioaccumulation (Xing et al. 2016; Kahlon et al. 2018). The pharmacokinetic, bioavailability, bioaccumulation, clearance, and toxicity of nanoparticles are likely dependent on the particle composition, size, and surface characteristics. These properties may be altered to reach the most appropriate balance for different applications. One factor regulating the pharmacological properties of nanoparticles may be the electrostatic state of the particle (Judy et al. 2012).

Titanium dioxide nanoparticles

Titanium dioxide nanoparticles are mainly used in industrial and household applications, and their use is increasing rapidly. The uptake and accumulation of nanoparticles by living organisms may have cumulative toxic effects; however, organisms may counteract these effects either by storage or excretion of the nanoparticles in a benign form (Shi et al. 2013). Concentrations of titanium dioxide nanoparticles in organisms depend on their toxicokinetics, and organisms may be exposed to nanoparticles through multiple pathways. Nanoparticles with a polycationic or anionic surface may bind to mucoproteins because mucus can chelate cations. In fish, large materials can enter the tissues via endocytosis across the gut, and diffusion of lipophilic nanoparticles through the cell membrane cannot be ruled out. The epidermis is protected by mucous; thus, nanoparticles may not easily penetrate the skin of fish due to a lack of metal transporters in skin cells compared to gills (Hartmann et al. 2012; Schütz et al. 2012). In humans, titanium dioxide nanoparticles collaborate with plasma proteins, coagulation variables, and platelets. Furthermore, anatase-form titanium dioxide nanoparticles can penetrate red blood cells; this type of cellular uptake likely involves processes other than phagocytosis and endocytosis because erythrocytes do not have phagocytic receptors. Direct uptake via the skin is a possible route of exposure in soil organisms. The exposure routes and bioaccumulation patterns of titanium dioxide nanoparticles vary according

to the organism, and titanium dioxide nanoparticles may bioaccumulate through trophic transfer.

Silver nanoparticles

Silver nanoparticles are metal-based and mostly used in industrial applications. Investigation of the effects of silver nanoparticles on caudal fin regeneration in zebrafish (Yeo and Pak 2008) revealed that silver nanoparticles were able to penetrate fish organelles, including the mitochondria and nucleus, in addition to blood vessels. Total silver levels in intestinal tissues of the zebrafish increased during silver nanoparticle exposure. Levels of silver nanoparticles were highest in the gills and liver of perch and Japanese medaka and were primarily adsorbed and accumulated. Coating of silver nanoparticles can influence their behavior and transport at biological interfaces, such as fish gill epithelia; polyvinylpyrrolidone (PVP)-coated silver nanoparticles primarily passed over the multilayered gill multicellular epithelium, whereas citrate-coated Ag nanoparticles tended to be absorbed into individual cells (Thio et al. 2012). The extent to which the aquatic environment may alter the chemical properties of silver nanoparticles should also be taken into consideration when studying the bioaccumulation of nanoparticles.

Cerium oxide nanoparticles

Cerium oxide nanoparticles have become one of the most popular nanomaterials in the past several years and are currently being utilized in various fields as catalysts, cell electrolytes, semiconductors, antioxidants, coatings, and polishing chemicals (Khan et al. 2011). Cerium oxide nanoparticles are more toxic than bulk cerium oxide and may induce cell death, oxidative stress, and DNA damage (Arnold et al. 2013; Pulido-Reyes et al. 2015; Zhang et al. 2016). Zhao et al. (2017) constructed a freshwater ecosystem and studied the distribution, bioaccumulation, biomagnification, and impacts of cerium oxide nanoparticles via long-term exposure. Their results demonstrated that cerium was absorbed and accumulated by the tested biota and diluted in the constructed food web, as manifested by a negative relationship between trophic levels and lipid-normalized cerium concentrations. Cerium oxide nanoparticles induced obvious morphological abnormalities in aquatic hydrophytes due to their unique chemical or physical properties, potentially causing an irreversible disturbance in the sustainability of the aquatic system.

Carbon nanoparticles

Carbon nanomaterials, such as quantum dots, fullerene, carbon nanotubes, and graphene, have attracted great research

interest in the past decades (Uddin et al. 2014; Bhuyan et al. 2015, 2016; LeCroy et al. 2016; Yay et al. 2018). Their unique structures and fantastic properties make carbon nanomaterials suitable for biomedical applications. In particular, carbon nanomaterials have been found to have great potential in theranostics, including bioimaging, diagnosis, drug delivery, gene therapy, photothermal therapy, etc. (Luo et al. 2014; Son et al. 2016). The accumulation and toxicity of carbon nanoparticles in mice were investigated, where a carbon nanoparticle suspension injection was trapped in nature in many cases, and no apparent toxicity was observed. Carbon nanoparticle suspension injection accumulated dramatically in the liver and spleen after intravenous injection, but minor contamination was noticed in the lungs (Xie et al. 2017).

Zinc oxide nanoparticles

Zinc oxide nanoparticles are typical metal oxide nanoparticles broadly used in a range of products including sunscreens, cosmetics, paint, paper, plastics, ceramics, and building materials because of their high stability, anti-corrosion, and photocatalytic properties (Osmond and McCall 2010). The toxicity of nano-ZnO (96 h LC50, 4.9 mg L⁻¹) to zebrafish was much higher than that of titanium dioxide nanoparticles (96 h LC50, 124.5 mg L⁻¹) (Xiong et al. 2011). Hao et al. (2013) concluded that nano-ZnO exhibited much higher bioaccumulation and oxidative effects and more severe histopathological changes to the test fish than bulk-ZnO after a 30-day sub-acute exposure.

Biological magnification of engineered nanomaterials

Biological magnification begins with processes that include specific substances such as heavy metals and pesticides mixing with a body of water (e.g., river, lake, and ocean), moving into the food chain as water microorganisms that can be prey for fish, and traveling through the human body. Eventually, the substances are progressively gathered in tissues or inner organs as they progress through the food chain, for example, the use of the insecticide dichlorodiphenyltrichloroethane for insect control and it has a high toxicity level. The steadiness of dichlorodiphenyltrichloroethane in nature and its bioaccumulation and biomagnification have severely impacted numerous organisms. This insecticide has been associated with the occurrence of cancer, premature birth, infertility, and diabetes. It has more broadly been connected to the populace decay of bird species on the natural way of life; for example, the peregrine falcon and bald eagle may be linked to dichlorodiphenyltrichloroethane toxicity where the eggshell thickness has diminished (Olenick 2013). Besides, nanoproducts go into waste disposal areas where

release occurs and gets collected in water sources, such as wastewater treatment plants and aquatic environments. It has been assessed that 69,200 and 189,200 metric tons of nanoparticles are released every year universally into water sources and landfills, respectively. As nanomaterials are released into the natural environment, they go through various stages and cooperate with chemical, biological, physical, and ecological elements that may inhibit their performance and transport in ecological networks where the danger starts (Gupta et al. 2017). Herein, the biological magnification of different nanomaterials is described as follows:

Quantum dots

According to Stern et al. (2012), a wide range of metallic nanoparticles are associated with bacteria. For example, cerium oxide nanoparticles can be absorbed by *Escherichia coli* or can activate sludge, and CdSe quantum dots can get into a cell of *Pseudomonas aeruginosa* to affect the body function. Werlin et al. (2011) studied bare CdSe quantum dots that accumulated in specific bacteria called *Pseudomonas aeruginosa*, which were biomagnified in the *Tetrahymena thermophila* protozoa by consumption. The concentration of cadmium in protozoa as a predator is higher than in its bacterial prey. Because protozoa do not undergo lysis, they largely consume quantum dots to stay available at higher trophic levels. The detected biomagnification from bacterial prey is considerably high since they are at the center of the food chain.

Silver nanoparticles

Toxicity of the bioaccumulation and biomagnification of silver nanoparticles is another area of study that has been examined in the model food chain (Yoo-iam et al. 2014). In this study, the toxicity effect of silver nanoparticles (Ag⁺ and Ag⁰) on *Chlorella sp.*, *Chironomus spp.*, *Moina macrocopa*, and *Barbonymus gonionotus* was examined. Based on the test results, toxicity order on all four organisms was Ag⁺ > Ag nanoparticles. They found that the highest Ag⁺ bioaccumulation factor was 101.84 L g⁻¹ in *Chlorella sp.*, and the least bioaccumulation factor of Ag nanoparticles was 1.89 L g⁻¹ in *B. gonionotus*, because the food chain transfer of Ag nanoparticles happened only from *Chlorella sp.* to *M. macrocopa*, and there was no sign of biomagnification from food sources to consumers in a basic tropical food chain (Yoo-iam et al. 2014). The authors' findings indicate that the biomagnification of heavy metals did not occur at a higher trophic level. For biomagnification to be considered at the trophic level, trace metal concentration should appear in at least two trophic levels. A lower concentration of heavy metal in the animal body indicates a lower level of heavy metal in the water body/source.

Also, animals located in higher trophic levels might be more competent in removing heavy metals than organisms located in lower trophic levels. The antioxidant enzyme system in infected animals could also be in charge of the end of oxidative stress within the beginning time of the body's protective system (Thio et al., 2012; De La Torre-Roche et al. 2013).

Titanium dioxide nanoparticles

Kubo-Irie et al. (2016) studied biomagnification of titanium dioxide nanoparticles in the terrestrial food chain. The oviposited eggs of the swallowtail butterfly (*Atrophaneura alcinous*) were hatched on the leaves of the *Aristolochia debilis*, and the rootstock and hairs were dipped in a suspension prepared with the ratio of $10 \mu\text{g mL}^{-1}$ titanium dioxide nanoparticles in a 100 mL bottle. X-ray analytical microscopy was used to confirm the existence of titanium dioxide nanoparticles in the veins of the *Aristolochia debilis*. First instar hatchlings benefited from the leaves to shed into second instar hatchlings. Also, transmission electron microscopy results show that the little agglomerates of titanium dioxide nanoparticles under 150 nm in diameter were distinguished in the vascular tissue of the subjected plant, the midgut, and the excreta of the hatchlings. As a result of this study, titanium dioxide nanoparticles were transferred from the plant to the larvae and distributed throughout the environment by larval excreta (Kubo-Irie et al. 2016). The higher accumulation of titanium dioxide nanoparticles affects the ingestion rate and causes greater biomagnification. Zhu et al. (2010) conducted a toxicity assessment to understand the potential ecotoxicity of nanoscale titanium dioxide ($n\text{TiO}_2$) to the aquatic organism *Daphnia magna*. They performed a comprehensive study by modifying acute (72 h) and chronic (21 days) toxicity tests along with $n\text{TiO}_2$ accumulation analysis. As a result, $n\text{TiO}_2$ applied minimal toxicity to *Daphnia* within 48-h exposure time and caused high toxicity when the exposure time was longer, such as 72 h. From this perspective, exposure duration might be the contributing factor in NP-mediated toxicity. Furthermore, upon chronic exposure to $n\text{TiO}_2$ for 21 d, *Daphnia* exhibited critical growth delay as well as mortality, and reproductive defects. Captivatingly, an essential amount of $n\text{TiO}_2$ was observed in *Daphnia*. Conversely, *Daphnia* showed difficulty in eliminating $n\text{TiO}_2$ from its body with the increased bioconcentration factor values. A high level of bioaccumulation may interfere with food intake and eventually distress the growth and reproduction of individuals as well as the population, thereby posing risks to aquatic ecosystems (Zhu et al. 2010).

Gold nanoparticles

Most nanomaterial-containing consumer products complete their service life and end up in waste streams. Many classes of nanomaterials accumulate in the sludge obtained from wastewater treatment and finally in soil resulting in land applications as bio-solids. In order to evaluate the impact of nanoparticles on terrestrial ecosystems, model organisms *Nicotiana tabacum* L. cv *Xanthi* and *Manduca sexta* (tobacco hornworms) were chosen to examine plant uptake and the potential trophic movement for 5-, 10-, and 15-nm-diameter gold nanoparticles. The outcome indicated a trophic movement and biomagnification of gold nanoparticles from a first producer to a first user through mean factors of 6.2, 11.6, and 9.6 for the 5-, 10-, and 15-nm treatments, respectively. This outcome is essential for nanotechnology-related risks, involving the potential for human exposure (Judy et al. 2011).

Biotransformation of engineered nanomaterials

Understanding the biotransformation (biochemical modification by living organisms) of nanomaterials and their cytotoxicity and potential environmental health issues involving their applications is inevitable. Knowing the interactions of nanomaterials with their environment is essential to assess their exposure, hazards, and risks. The development and usage of nanomedicines in the medical sector validate the assessment of the fate of nanomaterials in vivo. Some acute effects of nanomaterials have been described, but their transformation by the biological environment is little investigated and therefore gaining a research interest these days. Nanoparticles can enter the human body through inhalation, ingestion, and dermal penetration from contaminated environments and food (Sanchez et al. 2012). The interaction of nanomaterials with the biological environment, such as biological fluids, membranes, cell components, proteins, and DNA, remodels their structure, surface properties, biotransformation, enzymatic attack, toxicity, degradation, particle distribution, fate, and bio-assimilation throughout the organism (Fig. 2) (Kolosnjaj-Tabi et al. 2016). This, in turn, leads to the transport of nanomaterials in physiological media, cellular internalization, and potential toxicity (Loefer et al. 2013). Although nanomaterials have a lengthy tenacity within the body, their transformation or transportation through kinetic processes is an ultimately slower processes, which can evoke chronic inflammatory reactions. Hence, the life cycle of nanomaterials within the body from initial exposure to complete elimination is a critical issue. Sometimes reactive, rapidly degradable nanomaterials are desired, whereas for persistence nanomaterials, remain inactive in the

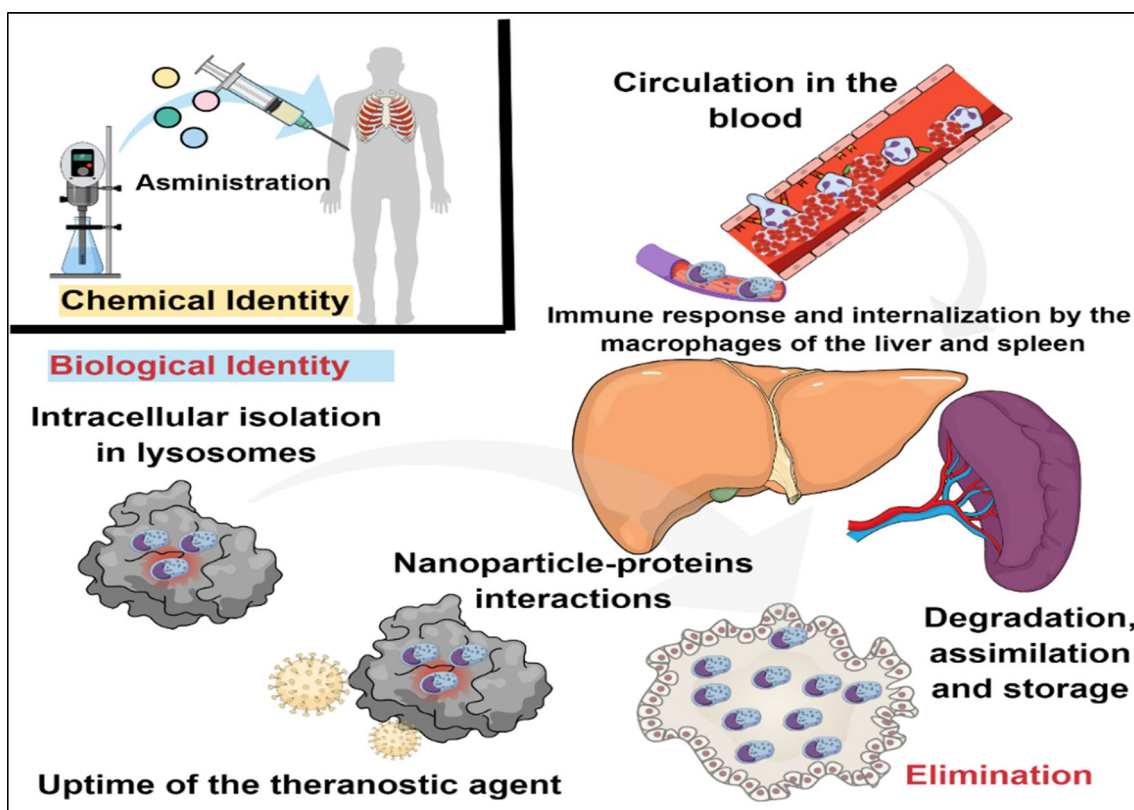


Fig. 2 Nanoparticle life cycle after administration into veins

organism. However, unexpected biological reactions with nanomaterials produce by-products that saturate lysosomal compartments and perturb degradative and autophagic pathways that are essential for cells to degrade proteins (Stern et al. 2012). Herein, the biotransformation of different nanomaterials and toxicity of pristine and bio-transformed nanomaterials and other health-related issues are discussed.

Graphene-related materials

Through inhalation, skin contact, or ingestion, graphene-related materials can enter the human body; consequently, many *in vitro* and *in vivo* research studies have been carried out to assess their potential risk to humans (Ema et al. 2017). Once these materials enter the biological system, their physical–chemical properties may alter depending on the biological environment, such as temperature, pH, concentration, salts, and many other factors. Recent studies have shown that graphene-related materials may be degraded by oxidase enzymes, such as horseradish peroxidase and human myeloperoxidase, both of which usually exist in physiological fluids (Gebel et al. 2014). One recent study was carried out to investigate the biotransformation, cytotoxicity, and inflammatory response of graphene oxide/few-layer graphene in the gastrointestinal tract (salivary, gastric, and

intestinal) upon their *in vitro* digestion (Guarnieri et al. 2018). It is observed that graphene oxide and few-layer graphene exhibit typical D and G bands, and few-layer graphene also exhibits D' and 2D bands. However, physiological juices exhibit two bands at 1450 and 2900 cm^{-1} , which are attributed to the bending and stretching vibrational modes of $-\text{CH}_2$ or $-\text{CH}_3$, respectively. Apparently, a change in defects was observed as the graphene oxide/few-layer graphene passes through the simulated digestive tract. Another study was carried out to investigate *in vivo* biotransformation of graphene oxide in two simulated lung fluids: Gamble's solution and artificial lysosomal fluid (Qi et al. 2018). The results show that graphene oxide significantly alters its physicochemical properties, morphology, and functionality in two simulated lung fluids. The sheet-like graphene oxide was reduced to randomly wrinkled and stacked sheets, in comparison with Gamble's graphene oxide and artificial lysosomal fluid–graphene oxide. Also, after biotransformation, Gamble's graphene oxide and artificial lysosomal fluid–graphene oxide had increased functionalities compared to pristine graphene oxide. The physicochemical properties of the bio-transformed graphene oxide are depicted in Table 1. In addition, graphene oxide sheets are transformed by the blood plasma. However, little information is known about the effect of nanomaterial biotransformation in blood

Table 1 Physicochemical properties of pristine and bio-transformed graphene oxide materials (Liu et al. 2018)

	Graphene oxide	Gamble’s graphene oxide	Artificial lysosomal fluid–graphene oxide
C (wt%)			
Aromatic rings	24.62	29.04	22.88
Epoxy/hydroxyl	33.38	28.61	26.19
Carbonyl	6.02	1.92	–
Carboxyl	5.69	8.7	25.19
Total C (wt%)	70.23	68.27	74.98
Total O (wt%)	29.03	28.27	23.58
C/O ratio	2.41	2.43	3.18
pH	5.71	6.45	6.51
I_D/I_G	0.61	0.82	0.84
Hydrodynamic diameter D_h (nm)	144.3 ± 6.1	345.7 ± 22.9	323.6 ± 15.2
Polydispersity index	0.27	0.5	0.45

plasma. After 14 days of graphene oxide sheet exposure to human blood plasma, the graphene oxide sheets degraded and formed biological corona on them (Wen et al. 2016). Notably, the biotransformation influenced the cytotoxicity induced by graphene oxide.

Magnetic iron oxide nanoparticles

Magnetic iron oxide nanoparticles are favorable inorganic nanoparticles for diagnostic and therapeutic applications such as magnetic resonance imaging diagnosis. Iron oxide nanoparticles can reach the liver and the spleen because of their coating. Also, electron paramagnetic resonance discloses the coating-dependent elimination of superparamagnetic iron from these organs, which occurs a long while after injection. Correspondingly, with the desertion of superparamagnetic iron, magnetic iron oxide nanoparticles dissipated in the liver and spleen, and transformed into nonmagnetic iron (Lartigue et al. 2013). Figure 3 illustrates the in vivo time-dependent biodistribution and transformation of magnetic iron oxide nanoparticles. It is expected that

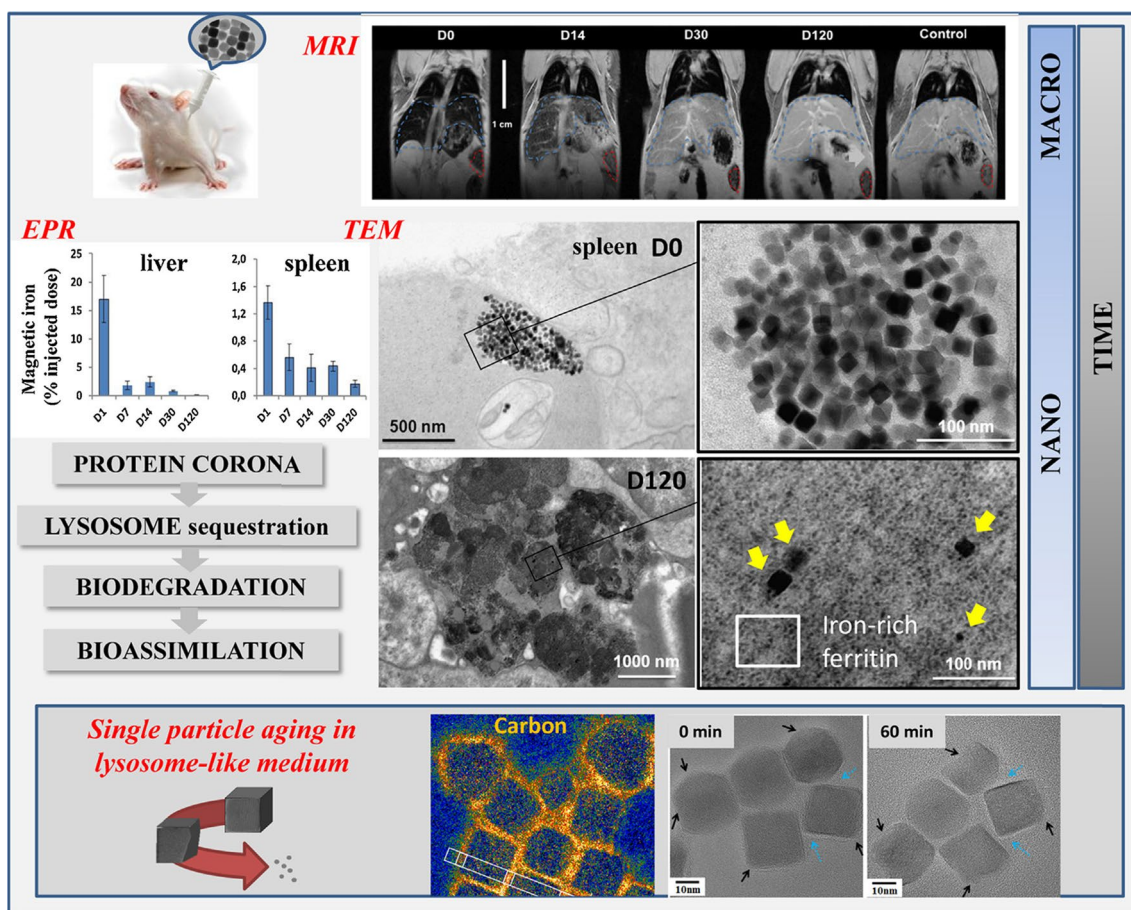


Fig. 3 In vivo biotransformation of magnetic iron oxide nanoparticles in mice using magnetic resonance imaging, ex vivo electron paramagnetic resonance quantification in organs, and associated transmission electron microscopy observations (Lartigue et al. 2013)

the metabolism that controls iron in the living being can likewise deal with magnetic iron oxide nanoparticles. The morphology and subcellular distribution of magnetic iron oxide nanoparticles have been studied by transmission electron microscopy (Fig. 3). After 1 day of injection and later period, the clusters of magnetic iron oxide nanoparticles within the lysosomes of splenic and hepatic macrophages shortened in the periphery and local degradation of magnetic iron oxide nanoparticles within the lysosomes. Another study by Levy et al. (2011) reported the biotransformation of magnetic iron oxide nanoparticles in vivo over a long period of time. They used ferromagnetic resonance and inductively coupled plasma to observe magnetic iron oxide nanoparticles in mice tissue. Results show a reduction in the magnetization of the liver or spleen over time after magnetic iron oxide nanoparticles are injected. The low-field magnetization for field-cooled and zero-field-cooled specimens of liver and spleen after injection exhibits similar results, revealing that superparamagnetic nanoparticles transformed to poorly magnetic iron species over a three-month time period.

Carbon nanotubes

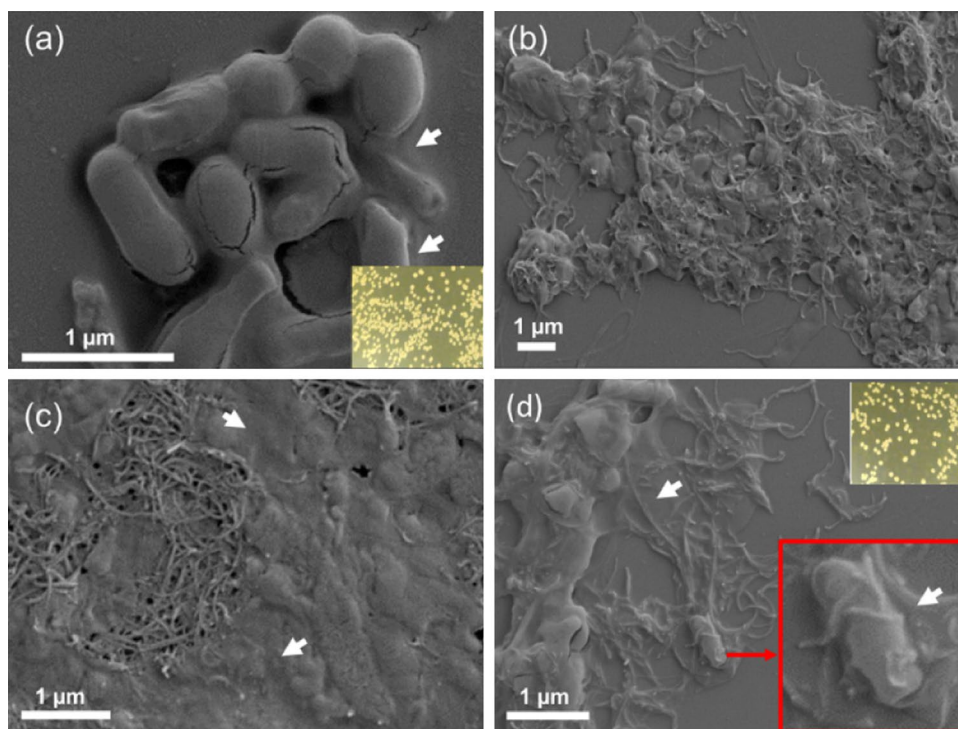
Carbon nanotubes are extensively used in biomedical applications such as targeted drug delivery and remediation agents. As a result, public awareness of carbon nanotubes in the environment and related issues has gained much attention in the research community. Chouhan et al. (2016) investigated the biotransformation of multi-walled carbon

nanotubes by bacteria identified as *Trabusiella guamensis*. The multi-walled carbon nanotubes and bacteria could interact in order to obtain insight into the biotransformation of their structure. Redox-enzyme activity and cell viability testing revealed that multi-walled carbon nanotubes are oxidized and bio-transformed through the formation of C=O and –COOH groups on the outer walls of nanotubes. Also, oxygen-containing functional groups on the surface of multi-walled carbon nanotubes increased. The morphological study showed that surface roughness and the number of concentric walls of the multi-walled carbon nanotubes were also reduced. The biotransformation process is oxidation and partial catalytic degradation process. The interaction between bacteria and multi-walled carbon nanotubes is presented in Fig. 4.

Silver nanoparticles

The potential routes of exposure of silver nanoparticles in humans are inhalation, dermal contact, and oral administration. In addition, they can gain access to the human body through coated contact lenses, bone cement, and other implants, eye drops, nanosilver-coated medical catheters, cardiovascular implants, etc. (Ge et al. 2014). These particles can enter and gather in different tissues and organs such as the lung, spleen, heart, kidney, ovary, and brain. Van der Zande et al. (2012) studied the biotransformation of silver nanoparticles in vivo. Experimenting with rats, they found that the amount of free silver ions released in a silver

Fig. 4 Scanning electron microscopy images: **a** bacteria; **b, c** bacteria and multi-walled carbon nanotube bundles; and **d** bacteria wrapped by multi-walled carbon nanotubes (Chouhan et al. 2016)



nanoparticles suspension is directly related to the silver content in the main organs of the rat. Even after 28 days, the rat blood treated with silver nanoparticles exhibited approximately 7–10 times lower silver content than in the silver nitrate group. Another study on silver nanoparticle-containing paint additive reported that silver nanoparticles release ions and dissolve, crossing the air–blood barrier (Smulders et al. 2015). These particles can enter the blood circulation system and be transformed into an ion or precipitate into other silver-containing matter, thereby being distributed in the organs and parts of animal bodies. The possible biotransformation of silver nanoparticles includes silver sulfide and silver chloride by reactions with sulfur and chloride species, respectively.

Cerium oxide nanoparticles

Cerium oxide nanoparticles have the potential to be used in a therapeutic strategy for cerium neurodegenerative diseases in humans (Kyosseva et al. 2013). The cerium oxide nanoparticles retained in the hepatic phagolysosomes and release secondary plum while in the biotransformation of the mammalian system. Zhang et al. (2012) studied the biotransformation of cerium oxide nanoparticles in cucumber plants. They treated cucumber roots with 2000 mg L⁻¹ cerium oxide nanoparticles. After 21 days of treatment, CePO₄ was observed on the epidermis and intercellular spaces of cucumber roots. It was also observed that in the biotransformation and particle dissolution process, the reducing substances (ascorbic acids) and organic acids played a vital role. The biotransformation process includes cerium oxide nanoparticles being absorbed on the root surfaces and dissolved and released Ce(III) ions being precipitated on the root surfaces and in intercellular spaces with phosphate.

Copper oxide nanoparticles

Copper oxide nanoparticles have extensive applications in surfactants, sensors, antimicrobials, and catalysts, and an impact on the agricultural industry. Up until now, very limited knowledge has been available on the possible translocation and biotransformation of copper oxide nanoparticles at tissue, organ, and cellular levels. One study was carried out to investigate the biotransformation of copper oxide nanoparticles in rice plants exposed to 100 mg L⁻¹ copper oxide nanoparticles for 14 days (Peng et al. 2015). The experimental results revealed that copper oxide nanoparticles moved into the root exodermis, epidermis, and cortex, and ultimately reached the endodermis but could not easily pass the Casparian strip. In addition, copper oxide nanoparticles were transported from the roots to the leaves, and Cu (II) combined with cysteine, citrate, and phosphate ligands and was even reduced to Cu (I).

Conclusion and recommendations

The manufacture and use of engineered nanomaterials have been increasing in both commercial and consumer products. Engineered nanomaterials have one-of-a-kind physical and chemical properties, which make them attractive materials for a wide range of applications but also contribute to their adverse behavior in biological systems including the environment and public health. Understanding the nanomaterial's accumulation and magnification for each species is still in its infancy. Nanoparticles are potential transfer mechanisms for human health as humans sit at the highest point of the food chain, so they could be risky if biomagnification proceeded as far up the food chain possible. Considering all three stages of nanoparticle movement in the food chain (bioaccumulation, biomagnification, and bioconcentration), manufacturers are playing a significant role in balancing the nanomaterial concentration. It is very important to develop safe engineered nanoparticles and nano-enabled products so that they can benefit human health (e.g., targeted drug delivery and imaging), mitigate climate change (e.g., fuel-saving vehicles), purify water (e.g., nanosized membrane filters and selective sorbents), produce energy (e.g., carbon capturing and solar cells), and be distributed and stored (e.g., long-life batteries, fuel cells, and catalysts for water splitting). The characteristic of nanomaterials can be tailored to be safer if manufacturers design them carefully. Finding the balance point between safety and application is essential.

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