Environ Geochem Health (2020) 42:147–158
https://doi.org/10.1007/s10653-019-00317-3

ORIGINAL PAPER

ZnO and CuO nanoparticles: a threat to soil organisms, plants, and human health

Vishnu Rajput · Tatiana Minkina · Svetlana Sushkova · Arvind Behal · Alexey Maksimov · Eliza Blicharska · Karen Ghazaryan · Hasmik Movsesyan · Natalia Barsova

Received: 5 February 2019 / Accepted: 30 April 2019 / Published online: 20 May 2019

Abstract The progressive increase in nanoparticles (NPs) applications and their potential release into the environment because the majority of them end up in the soil without proper care have drawn considerable attention to the public health, which has become an increasingly important area of research. It is required to understand ecological threats of NPs before applications. Once NPs are released into the environment, they are subjected to translocation and go through several modifications, such as bio/geo-transformation which plays a significant role in determination of ultimate fate in the environment. The interaction between plants and NPs is an important aspect of the risk assessment. The plants growing in a contaminated medium may significantly pose a threat to human health via the food chain. Metal oxide NPs ZnO and CuO, the most important NPs, are highly toxic to a wide range of organisms. Exposure and effects of CuO and ZnO NPs on soil biota and human health are critically discussed in this study. The potential benefits and unintentional dangers of NPs to the environment and human health are essential to evaluate and expected to produce less toxic and more degradable NPs to minimize the environmental risk in the future.

Keywords Copper · Food chain · Human health · Nanoparticles · Toxicity · Zinc

Introduction

Nanoparticles (NPs) refer to materials that have at least one dimension in the nanoscale and do not exceed 100 nm. Due to specific characteristics, physical and chemical properties, and high surface–volume ratio, their applications in the industry, for instance, consumer products, agriculture, coatings, cosmetics, chemicals, electronics, optics, environmental remediation, food and packing, fuel additives, energy, textile and paints, next-generation medicine, and plastics, are increasing (Rajput et al. 2017a, b). It is expected that hundreds of types of products are available in the

---

V. Rajput (✉) · T. Minkina · S. Sushkova
Southern Federal University, Rostov-on-Don 344090, Russia
e-mail: rajput.vishnu@gmail.com

A. Behal
Xinjiang Institute of Ecology and Geography, Chinese Academy of Sciences, Urumqi 830011, China

A. Maksimov
Rostov Research Institute of Oncology, Rostov-on-Don 344037, Russia

E. Blicharska
Medical University of Lublin, Lublin-4A, Lublin 20–093, Poland

K. Ghazaryan · H. Movsesyan
Yerevan State University, Yerevan 0025, Armenia

N. Barsova
Moscow State University, Moscow 119192, Russia

market and many more could appear in the coming future with new characteristics and novel applications. Nano-era began in the late 1990s, and the application of nanomaterials to the environment reached \$23.4 billion in 2014. The global market for nanocomposites totaled \$2.0 billion in 2017 and is estimated to reach \$7.3 billion by 2022, growing at a compound annual growth rate of 29.5% for the period of 2017–2022 (BBC 2018). There are more than 1600 nanotechnology-based consumer products (Vance et al. 2015), and an online database (www.nanodb.dk) lists 3000 products in different categories that contain NPs or nanomaterial (Hansen et al. 2016). The actual figure of the global production of NPs is still unavailable. A recent estimation indicated that more than 200 metric tons of nano-sized Cu and CuO were produced in 2010 and yearly 5500 tons of Zn NPs are produced in the form of a wide range of products (Connolly et al. 2016; Zuverza-Mena et al. 2015). The literature on the basis of data and modeling analysis indicates that production, use, and disposal of various NPs lead to release of thousands of tons of most common NPs (Ag, Al, Ce, Cu, Fe, Si, Ti, Zn) into the environment each year with the majority of them ending up in the soil, directly or through landfills from sludge and other waste (Bundschuh et al. 2018; Gottschalk et al. 2009; Keller et al. 2017; Keller and Lazareva 2013; McGillicuddy et al. 2017). Water and air also get a significantly high amount of share (Keller et al. 2013). The widespread applications of NPs increased scientific attention and became a priority research area in recent years (Keller et al. 2017; Keller and Lazareva 2013; Rajput et al. 2018a; Servin et al. 2017).

The applications of NPs are increasing that also raise the number of issues such as ethical, health and safety, technological, policy and regulatory, and issues related to purposefully releases of NPs into the environment (Bundschuh et al. 2018; Tiede et al. 2016). Even in the absence of acute toxicity, bioaccumulation and long-term exposure of NPs to the plants may have an impact on the food chain, which is unanswered (Tiede et al. 2008).

Metal oxide NPs ZnO and CuO, the most important NPs, possess a mixing characteristic of metal materials and NPs: essential elements with importance in metabolic and physiological processes in plant growth and human beings, wide use in antimicrobials, catalysis and skin products, semiconductors, plastic, glass, ceramics, cement, rubber materials, pigments, paints, food supplements, batteries, nonflammable material, agricultural industries, cosmetics, coatings, environmental remediation, fuel additives, textile industries, and wastewater treatments (Azizi et al. 2017; Rajput et al. 2017b, 2018c ; Sturikova et al. 2018). Applications of engineered NPs in agriculture and medical sectors are found to solve many problems as compared to the conventional approaches (Fernández-Luqueño et al. 2018; Rai et al. 2018; Raliya et al. 2017). Once NPs are released into the soil, they might impact soil physical and chemical properties, interact with other pollutants, form a new novel kind of toxic compounds, and disturb soil microbial functionality, plant growth, and performance (García-Gómez et al. 2018; Loureiro et al. 2018; Rajput et al. 2017b; Soni et al. 2015). Nanoparticles can exist for a long period of time in the soil and act as hazardous materials, which may impose a threat to human health (Assadian et al. 2018; Katsumiti et al. 2018; Mudunkotuwa et al. 2012).

Several studies suggest that CuO and ZnO NPs are highly toxic to a wide range of organisms, especially for plant growth (Adams et al. 2017; Assadian et al. 2018; Katsumiti et al. 2018; Rajput et al. 2018a, c; Servin et al. 2017), and the weathering of these NPs increases bioaccumulation within the terrestrial food chain (Rajput et al. 2018c; Servin et al. 2017). It is assumed that the CuO and ZnO NPs cause toxicity either by releasing ionic forms or by direct interactions with plant cells and tissues (Du et al. 2011; Perreault et al. 2014). However, the mechanism of NPs uptake is not well established. Like heavy metals, the varying impact of NPs on different plant species also depends upon the size, concentration, duration of exposure, plant genotypes, experimental conditions, and synthesis of NPs. CuO and ZnO NPs affected edible plants by inducing changes in seed germination, mineral uptake, modifications in cellular and subcellular organelles structure and ultrastructure, poor root and shoot growth, induce oxidative stress, cell death, increased activity of stress enzymes, photosynthesis, transpiration rate, and DNA damage (Adams et al. 2017; Rajput et al. 2018a, b, d; Zhang et al. 2018c). The accumulation of NPs in edible plant tissues is another concerning issue that could impact human health via the food chain. After interacting with plant roots, the NPs translocate to aerial parts and accumulate in cellular or subcellular organelles. Several microscopic studies exhibit the presence of NPs in different parts of plant tissues (Ahmed et al. 2018; Peng et al. 2015; Rajput et al. 2018a, d).

In the current overview, CuO and ZnO NPs toxicity on soil organism, plants, and human health is discussed, which could help to regulate the application of NPs in agriculture, food industry, and the medical sector. So the hazardous impacts on human health directly or via the food chain can be avoided.

Sources of soil contamination

The widespread use of NPs in a diverse range of products increases the chances to contaminate the environment. The NPs can be released accidentally or intentionally to the air, water, and soil system. Due to tiny size, nanoparticles can float into the air or get transported to another place through the water and ultimately accumulate for a long time in the soil. Tolaymat et al. (2017) suggested four main sources of NPs emission into the ecosystem, namely manufacturing of raw materials, nano-enabled products, product use, and waste management services. The modeling studies estimate NPs in sewage sludge in the range of 107 and 802 mg kg^{-1} and make up approximately 100 and 1000 t year^{-1} in Europe (Gottschalk et al. 2009; Piccinno et al. 2012). Anthropogenic and natural activities are the main sources of NPs in the environment (Fig. 1). Nanoparticles get into the cultivated soils due to their wide applications such as nano-fertilizers, pesticides, seed treatment, hydroponic solutions, and agro-films (Cornelis et al. 2014; Keller et al. 2013; Lowry et al. 2012; Mudunkotuwa et al. 2012; Nowack and Bucheli 2007; Strambeanu et al. 2015). Some applications in food ingredients and cosmetic products are the diffuse source of NPs in the soils. Nanoparticles usage in remediation technology can also lead to deliberate release into the environment. Waste treatment plants release NPs as concentrated sludge or water. Cu NPs are used as fungi- and bactericide in agriculture, which leads to toxic effects on aquatic life. It is predicted that more than 95% of Cu released into the environment will enter the soil and aquatic sediments and accumulate up to 500 μg L^{-1} (Keller et al. 2017). Similarly, Zn NPs are widely used in cosmetics industries, get released to aquatic system (Nowack and Bucheli 2007), and accumulate in sediments (1300 t a^{-1}), in natural and urban soil (300 t a^{-1}), as well as in landfills (200 t a^{-1}) (Bundschuh et al. 2018).

Data based on the modeling analysis indicate that the production, use, and disposal of various metal-based NPs lead to release of thousands of tons of most common metallic NPs into the environment each year with the majority of them ending up in the soil, directly or through landfills from sludge and other waste. Other components of the biosphere, water and air are also receiving the significantly high amount of NPs share (Keller et al. 2017; Keller and Lazareva 2013). Although the estimated concentration of NPs in the environment may not be entirely accurate as the values are indicated by predictive calculations (Sun et al. 2016). Thus, once entered into the environment, CuO and ZnO NPs are expected to undergo a series of bio/geo-transformation that ultimately decides their fates and toxicity. The predicted concentration of ZnO and CuO NPs in the soil and aquatic sediments is indicated in Table 1.

Bio/geo-transformation

Soil is a less dynamic component of the biosphere, has a relatively high capacity for pollutants accumulation than the water and air, and could be a depot for NPs. In soil, NPs pass through bio/geo-transformation. The process of bio/geo-transformation generally involves aggregation, dissolution, sulfidation, ad/absorption, and oxidation–reduction process (Gogos et al. 2017; Lowry et al. 2012; Ma et al. 2014). Aggregation and dissolution of CuO and ZnO NPs are generally influenced by a range of soil factors such as pH, organic matter, ionic species, and colloids (Feng et al. 2016; Peng et al. 2015, 2017). The process of aggregation largely impacts their colloidal stability that is one of the key factors controlling NPs fate and their toxic effects. However, the stability, mobility, and toxicity of ZnO NPs in soil depend on water chemistry, ionic strength, aggregation and sedimentation (Peng et al. 2017). The natural organic matter of soil influences the bioavailability of NPs in the soil through a diversity of mechanisms such as electrostatic interactions, ligand exchange, hydrophobic effect, hydrogen bonding, and complexation (Philippe and Schaumann 2014). Concentration, particle size, surface area, and surface coating are the properties of

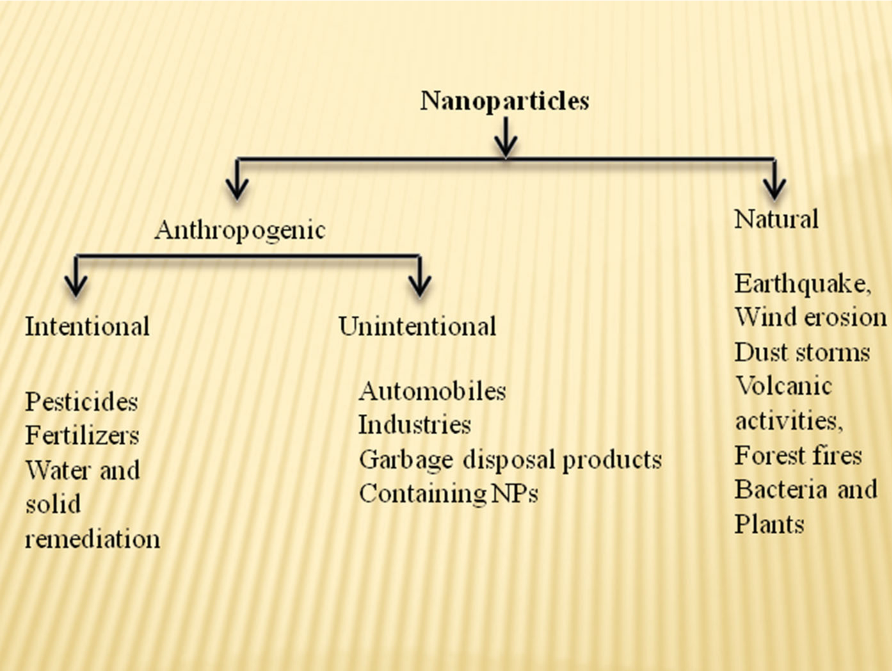


Fig. 1 Major sources of nanoparticles in the environment

Table 1 Predicted concentrations of ZnO and CuO nanoparticles in the soil and aquatic sediments

Nanoparticles	Source	References
ZnO		
3194 μg kg^{-1}	Soil	Boxall et al. (2007)
16–100 μg kg^{-1}	Soil	Feng et al. (2016)
0.5–1.5 μg L^{-1}	Wastewater treatment plant	Keller and Lazareva 2013
76–760 μg L^{-1}	Water	Boxall et al. (2007), Ghosh et al. (2016)
CuO		
0–540 μg L^{-1}		Adeleye et al. (2016)
50–500 μg L^{-1}	Aquatic sediment	Keller et al. (2017)

NPs which further affect dissolution (Peng et al. 2017).

CuO and ZnO NPs are often considered as insoluble, but the presence of organic acids such as citric acid and oxalic acid in soil enhances the dissolution of these NPs, which in turn increases their mobility and bioavailability to plants and soil organisms. These NPs have good solubility at low pH, whereas as the pH increases, its solubility decreases. In acidic/neutral medium, ZnO NPs showed ion-shedding ability which makes them more toxic (Liu et al. 2016). However, the presence of ligands including those with amine functional groups makes CuO NPs soluble at neutral pH also (Wang et al. 2013). The toxicity of these NPs greatly depends on soil pH (Ma et al. 2014; García-Gómez et al. 2018). The increases in toxicity of CuO NPs were observed at different pHs (4.8 and 5.8) of soils and affected root elongation of *Hordeum vulgare* (Qiu and Smolders 2017). In other study, a strong effect of ZnO NPs was observed in weak acidic (pH 6.0) soils on bacterial communities (Ge et al. 2011). Physicochemical properties such as size, surface area, and soil properties also affect ions dissolution from these NPs. The dissolution of CuO and ZnO NPs is often regarded as a passivation process which increases the solubility of Cu/CuO and Zn/ZnO NPs, resulting in enhanced bioavailability and toxicity (Ma et al. 2014). More dissolution of Cu NPs increases the likelihood that Cu is internalized as Cu^{2+} ions or in the form of organic complexes (Keller et al. 2017).

However, the stability, mobility and toxicity of ZnO NPs in soil depend on water chemistry, ionic strength, aggregation and sedimentation (Peng et al. 2017). Various experiments associate relationship between ions releases and toxicity of these NPs (Chen et al. 2019; Rajput et al. 2017b).

It is revealed that CuO NPs get accumulated in epidermis and exodermis regions of the plants and get precipitated with citrate or phosphate ligands or get bound to amino acids forming Cu–cysteine, Cu–citrate, and $Cu_3(PO_4)^2$ kind of products or get reduced to Cu(I) (Peng et al. 2015). Cu(I) is a highly redox active species capable of producing hydroxyl radical by Fenton-like reactions. The higher uptake of Zn by *Glycine max* was observed at 500 mg L^{-1} ZnO NPs due to lesser aggregation, and an increased aggregation was proposed at high concentrations (1000–4000 mg L^{-1}) due to difficult passage through cell wall pores which reduced the uptake and accumulation of Zn (Lopez-Moreno et al. 2010). The mechanism of bio/geo-transformation of CuO and ZnO NPs passes through several chemical and biochemical processes with soil biota. Thus, NPs present in even smaller quantities have significant biological importance.

Effects on edible plants

Uptake, translocation, and bioaccumulation of CuO and ZnO NPs in plants depend upon the size, chemical composition, shape, and plant anatomy because xylem serves as the most important vehicle in the distribution and translocation of NPs to leaves (Rajput et al. 2018a). The size of CuO and ZnO NPs affects their toxicity by differences in ions dissolution and forms inside the cell, internalization efficiency, and ROS production (Adams et al. 2017; Rajput et al. 2018c). The phytotoxicity threshold concentration in plant tissues is in the range of 200-500 mg kg^{-1} for Zn and 20-30 mg kg^{-1} for Cu (Broadley et al. 2007; Marschner 1995). The accumulations of Cu and Zn in crops reduce food and feed quality, and transference to the food chain can cause a serious threat to human health (Rajput et al. 2018; Wang et al. 2017b). The high accumulation of Cu and Zn dissolute by Cu- and Zn-based NPs in roots was found (Da Costa and Sharma 2015; Rajput et al. 2018a). Da Costa and Sharma (2015) observed an increase of 76-fold in Cu content (190.14 mg kg^{-1}) in the whole roots of rice treated with 1000 mg L^{-1} CuO NPs, whereas Rajput et al. (2018a) found 6.4-fold higher Cu content in leaves of barley than the control treatments. The recent studies on CuO and ZnO NPs accumulation and their toxic effects on plants are summarized in Table 2.

Seed germination is the beginning of a physiological process and is the first step toward the successful establishment of plants. The seed coat acts as a protector, and once it ruptures, the radicle is the first tissue to get direct contact with metals (Kranner and Colville 2011). CuO NPs significantly reduced seed germination in rice seedlings (78.6%), as compared to control (91.6%) (Shaw and Hossain 2013). CuO NPs affected seed germination and root elongation in *Lactuca sativa*, *Raphanus sativus*, and *Cucumis sativus* (Wu et al. 2012). Few studies were conducted to assess the effects of ZnO NPs on seed germination (Rajput et al. 2018c).

It is well understood that NPs enter plant tissues either via root tissues (root tips, rhizodermis, and lateral root junctions) or the aboveground organs and tissues (cuticles, trichomes, stomata, stigma, and hydathodes) as well as through the wounds and root junctions. Since the root is the first target tissue exposed to soil pollutants, it seems that the functional and structural disorders appear more often in root than in the aboveground tissues. The NPs are taken up by roots and could transport to the aboveground tissues through the vascular system, depending on the composition, shape, size of NPs, and anatomy of the plants (Rico et al. 2011). It has been suggested that the plants can accumulate NPs in their original form or as metal ions (Cota-Ruiz et al. 2018). In studies, CuO NPs showed 5% and 13% decrease in root and shoot lengths, respectively, of wheat and exhibited necrosis in roots, which as a result were thinner and more brittle compared to the control (Dimkpa et al. 2012). The lateral root growth of *Arabidopsis thaliana* a model plant was inhibited by CuO NPs (Xu 2018). The Cu NPs (15.6 mM) and Cu ions showed dose-dependent inhibitory effects on *Triticum aestivum* root growth decreasing by 60% and the formation of lateral roots was stimulated, possibly due to the enhancement of nitrogen uptake and accumulation of auxin in lateral roots (2018). Up to 80% of growth reduction was observed in *A. thaliana* treated with 300 mg L^{-1} ZnO NPs in soil pots (Wang et al. 2015). Similarly, 80% root and shoot biomasses of *Medicago sativa* were

Table 2 Effects of ZnO and CuO nanoparticles on edible crops

Crops	Nanoparticles	Concentrations mg $kg^{-1}*L^{-1}$	Specific effects	References
Raphanus sativus	ZnO, CuO	10–1000	Reduced root length, shoot length, decreased F1 seed weight with accumulated Cu and Zn	Singh and Kumar (2018)
Triticum aestivum	CuO	500	Reduced maximal root length, plant-induced changes in rhizosphere	Gao et al. (2018)
Arachis hypogaea	CuO	500	Decreased the 1000-grain weight by 10–31%	Rui et al. (2018)
Capsicum annum L.	CuO	500	Affected nutritional quality; reduced Zn by 55% in leaves and 47% in fruits	Rawat et al. (2018))
Solanum lycopersicon	CuO	0.2–2	The significant Cu accumulated in roots (341.6 µg g^{-1}) and in shoots (146.9 µg g^{-1})	Ahmed et al. (2018)
Cucumis sativus	CuO	800	Altered fruit nutritional supply especially metabolites	Zhao et al. (2017)
Glycine max	ZnO	0.05–0.5	Leaf chlorosis, necrosis	Priester et al. (2017)
Spinacia oleracea	ZnO, CuO	1000	Reduced root length and shoot length	Singh and Kumar (2016)
Zea mays/ Oryza sativa	CuO	2000	Inhibited root elongation, reduced shoot length	Yang et al. (2015)

reduced by ZnO NPs at concentration ranging from 0 to 750 mg kg^{-1} soil (Bandyopadhyay et al. 2015). The elevated concentration (10–2000 mg L^{-1}) of ZnO NPs revealed a biomass drop and damaged root surface cells of *Fagopyrum esculentum* at 2000 and 4000 mg L^{-1} (Lee et al. 2013). CuO NPs damaged the root tip and cap as well as the meristematic zone of *A. cepa* (Deng et al. 2016). Similarly, ZnO NPs also affected root tip and root morphology along with cortical cells, broke epidermis, vacuolated cortical cells, and shrank vascular cylinder of *Lolium perenne* (Lin and Xing 2008).

Nanoparticles affected ultrastructure of cellular and subcellular organelles: plastids, mitochondria, peroxisomes, plastoglobules, starch granules, protoplasm, vascular bundles, plasma membrane and cell wall (Rajput et al. 2018a, b). Decreased thylakoids number per granum, swollen intrathylakoidal space was observed in *Oryza sativa* treated with 1,000 mg L^{-1} CuO NPs (Da Costa and Sharma 2015). Increased periplasmic space of confluent parenchymal cells of *Solanum lycopersicon* was induced by CuO NPs (Ahmed et al. 2018). An increased number of plastoglobules, decreased size of starch grains, disrupted and irregular-shaped mitochondria, stroma displacing the grana, and dilation of the chloroplast membrane were observed in *Landoltia punctata* by CuO NPs (Lalau et al. 2015). Adams et al. (2017) found shorten zones of division and elongation and compressed epidermal cells in wheat by CuO NPs. ZnO NPs affected ultrastructure of chloroplasts of mesophyll cells, decreased the size, and increased the number of plastoglobules in *Brassica napus* L. (Mousavi et al. 2015). The highly collapsed cortical cells, broken epidermis and root cap, vacuolated cortical cells, and shrank vascular cylinder were observed in *Lolium perenne* treated with 1000 mg L^{-1} ZnO NPs.

These observations indicated a decline in seed germination, roots and shoots growth, and modifications in cell ultrastructure, especially in the photosynthetic apparatus, which could limit the surface area for water uptake and photosynthesis, respectively, and consequently affects the plant performance.

Effects on soil organisms

Nanoparticles are considered as a major cause of toxicity to both the pathogenic and beneficial microbes

(Lofts et al. 2013) and very toxic to the native soil bacteria (Concha-Guerrero et al. 2014). The effects of NPs could be observed by measuring the soil respiration and enzymatic activities of soil microbial community (Simonin and Richaume 2015). A review indicates the NPs significantly affected enzymatic activities (invertase, urease, catalase, phosphatase, dehydrogenase), microbial community structure, bacterial diversity nutrient cycling, changes in humic substances, and biological nitrogen fixation (Rajput et al. 2017a).

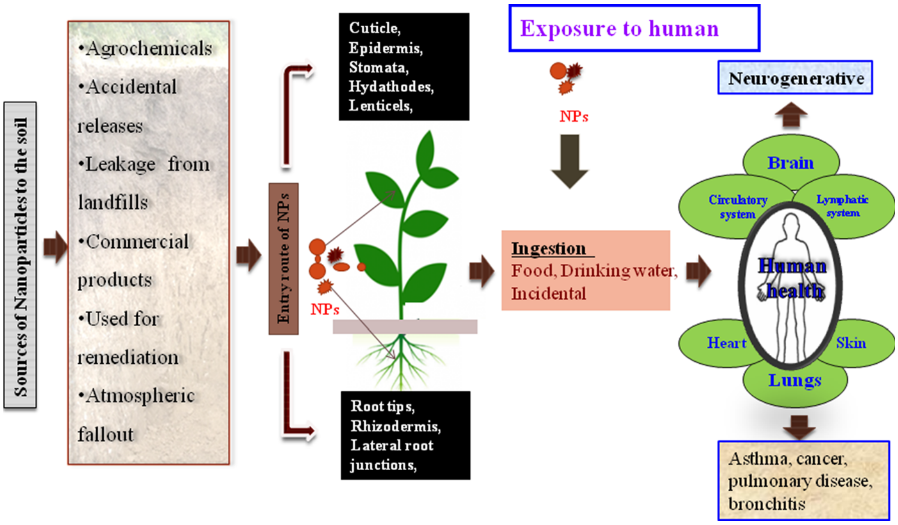
In flooded paddy soil, CuO NPs decreased microbial biomass, enzymatic activities, and disturbed community structures (Xu et al. 2015). Similarly, ZnO NPs affected enzymatic activities of bacterial communities in saline–alkali and black soils (You et al. 2017). Concha-Guerrero et al. (2014) have also shown that CuO NPs were toxic for native soil bacteria, as observed from the formation of cavities, holes, membrane degradation, blebs, cellular collapse, and lysis in the cell of soil bacterial isolates. At 30–60 mg L^{-1}, CuO NPs concentration affected the microbial enzymatic activity of activated sludge (Wang et al. 2017a). The study conducted on the effect of CuO on *Saccharomyces cerevisiae* shows increased toxicity over time due to increased dissolution of Cu ions from CuO (Kasemets et al. 2009). Bacterium *Sphingomonas* and *Rhizobiales* are well known for their importance in remediation and symbiosis with plant roots appeared susceptible to Cu NPs (Shah et al. 2016). CuO NPs were mostly bactericidal, while ZnO NPs had a bacteriostatic effect (Gajjar et al. 2009). ZnO NPs hindered the thermogenic metabolism, reduced the numbers of colonies of *Azotobacter*, *P-solubilizing* and *K-solubilizing* bacteria, and inhibited enzymatic activities such as urease, catalase, and fluorescein diacetate hydrolase activities (Chai et al. 2015). The effects of CuO and ZnO NPs on the soil microbial community are little explored. However, these results indicate the influence of CuO and ZnO NPs on soil microbial community structure and functionality which could impact biological nitrogen fixation.

Effects on human health

The CuO and ZnO NPs possibly enter the human cells via oral and skin exposure. Due to smaller size, NPs can easily penetrate through cell wall and membranes (Anreddy 2018). The schematic presentation of soil contamination by NPs and their possible impacts on human health is presented in Fig. 2. The studies on direct exposure of Cu NPs to human beings have not been reported; however, different human cell lines experiments demonstrate ill effects. CuO NPs treatment boosted the accumulation of mitochondrial superoxide anions and caused mitochondrial dysfunction in human umbilical vein endothelial cells (HUVECs) (Zhang et al. 2018b). It has also been observed in HUVECs that CuO NPs are deposited within the lysosomes and released Cu ions. Further, a caspase-independent cell death pathway is suggested in NPs-based cytotoxicity (Zhang et al. 2018a). CuO NPs damaged the mitochondria and lysosomes in human blood lymphocytes and increased ROS (reactive oxygen species) level (Assadian et al. 2018).

Increasing production and contamination of soil means higher chances of CuO and ZnO NPs to enter human body either accidently or by food chain; thereby, NPs can reach gastrointestinal tract. A concentration-dependent decrease in cell viability was observed in undifferentiated Caco-2 cells. Impacts including cell morphology, tight junction integrity, translocation, and IL-8 production were comparable to $CuSO_4$, suggesting NPs release ions inside the cells (Ude et al. 2017). Cytotoxicity of Cu-based NPs for breast cancer cells was more selected than for normal cells lines at a higher concentration. Nanoparticles were able to induce ROS leading to oxidative stress (Azizi et al. 2017). Intracellular ROS may proceed with epigenetic changes that alter DNA methylation patterns affecting genome (Lu et al. 2016). Membrane blebbing and reduced cell viability were observed in breast cancer cell lines by ZnO NPs in concentration-dependent manner and were suggested to be a result of ROS, metal ions (Zn^{+2}) (Umar et al. 2019). Cytotoxicity of ZnO NPs was induced by oxidative stress and inflammatory response, which depended on the size and concentration of NPs with the release of Zn^{2+} (Chen et al. 2019). Intracellular ROS was also associated with an increase in Zn ions in human aortic smooth muscle cells treated with ZnO NPs. An increase in endoplasmic reticulum stress biomarkers and occurrence of vacuolation of cells were related to NPs (Wang et al. 2018). The results highlighting damages to in vitro models signify the investigation of toxic effects of CuO and ZnO NPs.

Fig. 2 Overview of soil contamination and impacts on human health



Conclusion and future perspective

The CuO and ZnO NPs are the most extensively used nanoparticles.. These NPs are proven to pass through various chemical and biochemical reactions which could affect biological nitrogen fixation, damage a plant cell, and may cause a serious threat to human health. Therefore, the series of safety evaluation and toxicological risk assessment standards must be formulate, including exposure route and the safe exposure doses of ZnO and CuO NPs. Another way to reduce the release of NPs into the environment is to match their quantities with the stage of crop growth with the greatest response. An example, the appropriate application of small amounts of NPs had maximum benefits to crops when it applied to the seeds in a pre-germinative manner. Future studies should address some questions such as very less is known about the effects of NPs on food quality and threshold limits should be defined. Real-time data should be generated because most of the reported studies have been performed in hydroponics, potting soil, or synthetic soil and are little known about the interactions of NPs with plants in soils with different physicochemical properties. Based on these studies, the application of nanomaterials in field conditions will not be feasible until we reach a complete understanding of the phytotoxic effects and impacts on soil organisms and human health.

Acknowledgements This work was supported by the Ministry of Education and Science of Russia, Project No. 5.948.2017/PCh and joint projects: RFBR No. 18-55-05023 and SCS No. 18RF-077.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Adams, J., Wright, M., Wagner, H., Valiente, J., Britt, D., & Anderson, A. (2017). Cu from dissolution of CuO nanoparticles signals changes in root morphology. *Plant Physiology and Biochemistry, 110,* 108–117.

Adeleye, A. S., Oranu, E. A., Tao, M., & Keller, A. A. (2016). Release and detection of nanosized copper from a commercial antifouling paint. *Water Research, 102,* 374–382.

Ahmed, B., Khan, M. S., & Musarrat, J. (2018). Toxicity assessment of metal oxide nano-pollutants on tomato (*Solanum lycopersicon*): A study on growth dynamics and plant cell death. *Environmental Pollution, 240,* 802–816.

Anreddy, R. N. R. (2018). Copper oxide nanoparticles induces oxidative stress and liver toxicity in rats following oral exposure. *Toxicology Reports, 5,* 903–904.

Assadian, E., Zarei, M. H., Gilani, A. G., Farshin, M., Degampanah, H., & Pourahmad, J. (2018). Toxicity of copper oxide (CuO) nanoparticles on human blood lymphocytes. *Biological Trace Element Research, 184,* 350–357.

Azizi, M., Ghourchian, H., Yazdian, F., Dashtestani, F., & AlizadehZeinabad, H. (2017). Cytotoxic effect of albumin coated copper nanoparticle on human breast cancer cells of MDA-MB 231. *PLoS ONE, 12,* e0188639–e0188639.

Bandyopadhyay, S., Plascencia-Villa, G., Mukherjee, A., Rico, C. M., Jose-Yacaman, M., Peralta-Videa, J. R., et al. (2015). Comparative phytotoxicity of ZnO NPs, bulk ZnO, and ionic zinc onto the alfalfa plants symbiotically associated with *Sinorhizobium meliloti* in soil. *Science of the Total Environment, 515–516,* 60–69.

BBC (2018). Nanocomposites, Nanoparticles, Nanoclays and Nanotubes: *Global Markets to 2022*. *Accessed 20 December* 2018.

Boxall, A., Chaudhry, Q., Sinclair, C., Jones, A., Aitken, R., Jefferson, B., et al. (2007). *Current and future predicted environmental exposure to engineered nanoparticles*. York: Central Science Laboratory.

Broadley, M. R., White, P. J., Hammond, J. P., Zelko, I., & Lux, A. (2007). Zinc in plants. *New Phytologist, 173,* 677–702.

Bundschuh, M., Filser, J., Luderwald, S., McKee, M. S., Metreveli, G., Schaumann, G. E., et al. (2018). Nanoparticles in the environment: where do we come from, where do we go to? *Environmental Sciences Europe, 30,* 36.

Chai, H., Yao, J., Sun, J., Zhang, C., Liu, W., Zhu, M., et al. (2015). The effect of metal oxide nanoparticles on functional bacteria and metabolic profiles in agricultural soil. *Bulletin of Environmental Contamination and Toxicology, 94,* 490–495.

Chen, P., Wang, H., He, M., Chen, B., Yang, B., & Hu, B. (2019). Size-dependent cytotoxicity study of ZnO nanoparticles in HepG2 cells. *Ecotoxicology and Environmental Safety, 171,* 337–346.

Concha-Guerrero, S. I., Brito, E. M. S., Piñón-Castillo, H. A., Tarango-Rivero, S. H., Caretta, C. A., Luna-Velasco, A., et al. (2014). Effect of CuO nanoparticles over isolated bacterial strains from agricultural soil. *Journal of Nanomaterials*, *2014*, 1–13.

Connolly, M., Fernandez, M., Conde, E., Torrent, F., Navas, J. M., & Fernandez-Cruz, M. L. (2016). Tissue distribution of zinc and subtle oxidative stress effects after dietary administration of ZnO nanoparticles to rainbow trout. *Science of the Total Environment, 551–552,* 334–343.

Cornelis, G., Hund-Rinke, K., Kuhlbusch, T., van den Brink, N., & Nickel, C. (2014). Fate and bioavailability of engineered nanoparticles in soils: a review. *Critical Reviews in Environmental Science and Technology, 44,* 2720–2764.

Cota-Ruiz, K., Delgado-Rios, M., Martínez-Martínez, A., Núñez-Gastelum, J. A., Peralta-Videa, J. R., & Gardea-Torresdey, J. L. (2018). Current findings on terrestrial plants – Engineered nanomaterial interactions: Are plants capable of phytoremediating nanomaterials from soil? *Current Opinion in Environmental Science & Health, 6,* 9–15.

Da Costa, M. V. J., & Sharma, P. K. (2015). Effect of copper oxide nanoparticles on growth, morphology, photosynthesis, and antioxidant response in *Oryza sativa*. *Photosynthetica, 54,* 110–119.

Deng, F., Wang, S., & Xin, H. (2016). Toxicity of CuO nanoparticles to structure and metabolic activity of *Allium cepa* root tips. *Bulletin of Environmental Contamination and Toxicology, 97,* 702–708.

Dimkpa, C. O., McLean, J. E., Latta, D. E., Manangón, E., Britt, D. W., Johnson, W. P., et al. (2012). CuO and ZnO nanoparticles: phytotoxicity, metal speciation, and induction of oxidative stress in sand-grown wheat. *Journal of Nanoparticle Research*, *14*(9), 1125.

Du, W., Sun, Y., Ji, R., Zhu, J., Wu, J., & Guo, H. (2011). TiO_2 and ZnO nanoparticles negatively affect wheat growth and soil enzyme activities in agricultural soil. *Journal of Environmental Monitoring, 13,* 822–828.

Feng, X., Yan, Y., Wan, B., Li, W., Jaisi, D. P., Zheng, L., et al. (2016). Enhanced dissolution and transformation of ZnO nanoparticles: the role of inositol hexakisphosphate. *Environmental Science and Technology, 50,* 5651–5660.

Fernández-Luqueño, F., Medina-Pérez, G., López-Valdez, F., Gutiérrez-Ramírez, R., Campos-Montiel, R. G., Vázquez-Núñez, E., et al. (2018). Use of Agronanobiotechnology in the Agro-Food Industry to Preserve Environmental Health and Improve the Welfare of Farmers. In F. López-Valdez & F. Fernández-Luqueño (Eds.), *Agricultural Nanobiotechnology* (pp. 3–16). Cham: Springer.

Gajjar, P., Pettee, B., Britt, D. W., Huang, W., Johnson, W. P., & Anderson, A. J. (2009). Antimicrobial activities of commercial nanoparticles against an environmental soil microbe, *Pseudomonas putida* KT2440. *Journal of Biological Engineering, 3,* 9.

Gao, X., Avellan, A., Laughton, S., Vaidya, R., Rodrigues, S. M., Casman, E. A., et al. (2018). CuO nanoparticle dissolution and toxicity to wheat (*Triticum aestivum*) in rhizosphere soil. *Environmental Science and Technology, 52,* 2888–2897.

García-Gómez, C., Fernández, M. D., García, S., Obrador, A. F., Letón, M., & Babín, M. (2018). Soil pH effects on the toxicity of zinc oxide nanoparticles to soil microbial community. *Environmental Science and Pollution Research, 25,* 28140–28152.

Ge, Y., Schimel, J. P., & Holden, P. A. (2011). Evidence for negative effects of TiO_2 and ZnO nanoparticles on soil bacterial communities. *Environmental Science and Technology, 45,* 1659–1664.

Ghosh, M., Sinha, S., Jothiramajayam, M., Jana, A., Nag, A., & Mukherjee, A. (2016). Cyto-genotoxicity and oxidative stress induced by zinc oxide nanoparticle in human lymphocyte cells in vitro and *Swiss albino* male mice in vivo. *Food and Chemical Toxicology, 97,* 286–296.

Gogos, A., Thalmann, B., Voegelin, A., & Kaegi, R. (2017). Sulfidation kinetics of copper oxide nanoparticles. *Environmental Science: Nano, 4,* 1733–1741.

Gottschalk, F., Sonderer, T., Scholz, R. W., & Nowack, B. (2009). Modeled Environmental concentrations of engineered nanomaterials (TiO_2, ZnO, Ag, CNT, Fullerenes) for different regions. *Environmental Science and Technology, 43,* 9216–9222.

Hansen, S., Heggelund, L. R., Revilla Besora, P., Mackevica, A., Boldrin, A., & Baun, A. (2016). Nanoproducts–what is actually available to European consumers? *Environmental Science: Nano, 3,* 169–180.

Kasemets, K., Ivask, A., Dubourguier, H. C., & Kahru, A. (2009). Toxicity of nanoparticles of ZnO, CuO and TiO2 to yeast *Saccharomyces cerevisiae*. *Toxicology in Vitro, 23,* 1116–1122.

Katsumiti, A., Thorley, A. J., Arostegui, I., Reip, P., Valsami-Jones, E., Tetley, T. D., et al. (2018). Cytotoxicity and cellular mechanisms of toxicity of CuO NPs in mussel cells in vitro and comparative sensitivity with human cells. *Toxicology in Vitro, 48,* 146–158.

Keller, A. A., Adeleye, A. S., Conway, J. R., Garner, K. L., Zhao, L., Cherr, G. N., et al. (2017). Comparative environmental fate and toxicity of copper nanomaterials. *NanoImpact, 7,* 28–40.

Keller, A. A., & Lazareva, A. (2013). Predicted releases of engineered nanomaterials: From global to regional to local. *Environmental Science & Technology Letters, 1,* 65–70.

Keller, A. A., McFerran, S., Lazareva, A., & Suh, S. (2013). Global life cycle releases of engineered nanomaterials. *Journal of Nanoparticle Research, 15*(6), 1692.

Kranner, I., & Colville, L. (2011). Metals and seeds: biochemical and molecular implications and their significance for seed germination. *Environmental and Experimental Botany, 72,* 93–105.

Lalau, C. M., Mohedano Rde, A., Schmidt, E. C., Bouzon, Z. L., Ouriques, L. C., dos Santos, R. W., et al. (2015). Toxicological effects of copper oxide nanoparticles on the growth rate, photosynthetic pigment content, and cell morphology of the duckweed *Landoltia punctata*. *Protoplasma, 252,* 221–229.

Lee, S., Chung, H., Kim, S., & Lee, I. (2013). The genotoxic effect of ZnO and CuO nanoparticles on early growth of buckwheat, Fagopyrum Esculentum. *Water, Air, and Soil pollution, 224*(9), 1668.

Lin, D., & Xing, B. (2008). Root uptake and phytotoxicity of ZnO nanoparticles. *Environmental Science and Technology, 42,* 5580–5585.

Liu, J., Feng, X., Wei, L., Chen, L., Song, B., & Shao, L. (2016). The toxicology of ion-shedding zinc oxide nanoparticles. *Critical Reviews in Toxicology, 46,* 348–384.

Lofts, S., Criel, P., Janssen, C. R., Lock, K., McGrath, S. P., Oorts, K., et al. (2013). Modelling the effects of copper on soil organisms and processes using the free ion approach: Towards a multi-species toxicity model. *Environmental Pollution, 178,* 244–253.

Lopez-Moreno, M. L., De La Rosa, G., Hernandez-Viezcas, J. A., Castillo-Michel, H., Botez, C. E., Peralta-Videa, J. R., et al. (2010). Evidence of the differential biotransformation and genotoxicity of ZnO and CeO_2 NPs on soybean (*Glycine max*) plants. *Environmental Science and Technology, 44,* 7315–7320.

Loureiro, S., Tourinho, P. S., Cornelis, G., Van Den Brink, N. W., Díez-Ortiz, M., Vázquez-Campos, S., et al. (2018). *Nanomaterials as Soil Pollutants* (pp. 161–190). In Soil Pollution: From Monitoring to Remediation.

Lowry, G. V., Gregory, K. B., Apte, S. C., & Lead, J. R. (2012). Transformations of nanomaterials in the environment. *Environmental Science and Technology, 46,* 6893–6899.

Lu, X., Miousse, I. R., Pirela, S. V., Melnyk, S., Koturbash, I., & Demokritou, P. (2016). Short-term exposure to engineered nanomaterials affects cellular epigenome. *Nanotoxicology, 10,* 140–150.

Ma, R., Stegemeier, J., Levard, C., Dale, J. G., Noack, C. W., Yang, T., et al. (2014). Sulfidation of copper oxide nanoparticles and properties of resulting copper sulfide. *Environmental Science: Nano, 1,* 347–357.

Marschner, H. (1995). Diagnosis of Deficiency and Toxicity of Mineral Nutrients. In H. Marschner (Ed.), *Mineral Nutrition of Higher Plants* (2nd ed., pp. 461–479). London: Academic Press.

McGillicuddy, E., Murray, I., Kavanagh, S., Morrison, L., Fogarty, A., Cormican, M., et al. (2017). Silver nanoparticles in the environment: Sources, detection and ecotoxicology. *Science of the Total Environment, 575,* 231–246.

Mousavi, K. S. M., Lahouti, M., Ganjeali, A., & Entezari, M. H. (2015). Long-term exposure of rapeseed (*Brassica napus* L.) to ZnO nanoparticles: anatomical and ultrastructural responses. *Environmental Science and Pollution Research, 22,* 10733–10743.

Mudunkotuwa, I. A., Pettibone, J. M., & Grassian, V. H. (2012). Environmental implications of nanoparticle aging in the processing and fate of copper-based nanomaterials. *Environmental Science and Technology, 46,* 7001–7010.

Nowack, B., & Bucheli, T. D. (2007). Occurrence, behavior and effects of nanoparticles in the environment. *Environmental Pollution, 150,* 5–22.

Peng, C., Duan, D., Xu, C., Chen, Y., Sun, L., Zhang, H., et al. (2015). Translocation and biotransformation of CuO nanoparticles in rice (*Oryza sativa* L.) plants. *Environmental Pollution, 197,* 99–107.

Peng, Y. H., Tsai, Y. C., Hsiung, C. E., Lin, Y. H., & Shih, Y. H. (2017). Influence of water chemistry on the environmental behaviors of commercial ZnO nanoparticles in various water and wastewater samples. *Journal of Hazardous Materials, 322,* 348–356.

Perreault, F., Samadani, M., & Dewez, D. (2014). Effect of soluble copper released from copper oxide nanoparticles solubilisation on growth and photosynthetic processes of *Lemna gibba* L. *Nanotoxicology, 8,* 374–382.

Philippe, A., & Schaumann, G. E. (2014). Interactions of dissolved organic matter with natural and engineered inorganic colloids: A review. *Environmental Science and Technology, 48,* 8946–8962.

Piccinno, F., Gottschalk, F., Seeger, S., & Nowack, B. (2012). Industrial production quantities and uses of ten engineered nanomaterials in Europe and the world. *Journal of Nanoparticle Research, 14*(9), 1109.

Priester, J. H., Moritz, S. C., Espinosa, K., Ge, Y., Wang, Y., Nisbet, R. M., et al. (2017). Damage assessment for soybean cultivated in soil with either CeO_2 or ZnO manufactured nanomaterials. *Science of the Total Environment, 579,* 1756–1768.

Qiu, H., & Smolders, E. (2017). Nanospecific phytotoxicity of CuO nanoparticles in soils disappeared when bioavailability factors were considered. *Environmental Science and Technology, 51,* 11976–11985.

Rai, M., Ingle, A., Pandit, R., Paralikar, P., Shende, S., Gupta, I., et al. (2018). Copper and copper nanoparticles: Role in management of insect-pests and pathogenic microbes. *Nanotechnology Reviews, 7,* 303–315.

Rajput, V. D., Minkina, T. M., Behal, A., Sushkova, S. N., Mandzhieva, S., Singh, R., et al. (2018a). Effects of zinc-oxide nanoparticles on soil, plants, animals and soil organisms: A review. *Environmental Nanotechnology, Monitoring & Management, 9,* 76–84.

Rajput, V. D., Minkina, T., Fedorenko, A., Mandzhieva, S., Sushkova, S., Lysenko, V., et al. (2018b). Destructive effect of copper oxide nanoparticles on ultrastructure of chloroplast, plastoglobules and starch grains in spring barley (*Hordeum sativum* distichum). *International Journal of Agriculture and Biology, 21,* 171–174.

Rajput, V., Minkina, T., Fedorenko, A., Sushkova, S., Mandzhieva, S., Lysenko, V., et al. (2018d). Toxicity of copper oxide nanoparticles on spring barley (*Hordeum sativum* distichum). *Science of the Total Environment, 645,* 1103–1113.

Rajput, V. D., Minkina, T., Fedorenko, A., Tsitsuashvili, V., Mandzhieva, S., Sushkova, S., & Azarov, A. (2018b). *Metal oxide nanoparticles: Applications and effects on soil ecosystems*. In "Soil Contamination: Sources, Assessment and Remediation", Nova Science Publisher, pp. 81–106.

Rajput, V. D., Minkina, T., Sushkova, S., Tsitsuashvili, V., Mandzhieva, S., Gorovtsov, A., et al. (2017a). Effect of nanoparticles on crops and soil microbial communities. *Journal of Soils and Sediments, 18,* 2179–2187.

Rajput, V. D., Minkina, T., Suskova, S., Mandzhieva, S., Tsitsuashvili, V., Chapligin, V., et al. (2017b). Effects of copper nanoparticles (CuO NPs) on crop plants: A mini review. *BioNanoScience, 8,* 36–42.

Raliya, R., Saharan, V., Dimkpa, C., & Biswas, P. (2017). Nanofertilizer for precision and sustainable agriculture: current state and future perspectives. *Journal of Agricultural and Food Chemistry, 66*(26), 6487–6503.

Rawat, S., Pullagurala, V. L. R., Hernandez-Molina, M., Sun, Y., Niu, G., Hernandez-Viezcas, J. A., et al. (2018). Impacts of copper oxide nanoparticles on bell pepper (*Capsicum annum* L.) plants: a full life cycle study. *Environmental Science: Nano, 5,* 83–95.

Rico, C. M., Majumdar, S., Duarte-Gardea, M., Peralta-Videa, J. R., & Gardea-Torresdey, J. L. (2011). Interaction of nanoparticles with edible plants and their possible implications in the food chain. *Journal of Agricultural and Food Chemistry, 59,* 3485–3498.

Rui, M., Ma, C., White, J. C., Hao, Y., Wang, Y., Tang, X., et al. (2018). Metal oxide nanoparticles alter peanut (*Arachis hypogaea* L.) physiological response and reduce nutritional quality: a life cycle study. *Environmental Science: Nano, 5,* 2088–2102.

Servin, A. D., Pagano, L., Castillo-Michel, H., De la Torre-Roche, R., Hawthorne, J., Hernandez-Viezcas, J. A., et al. (2017). Weathering in soil increases nanoparticle CuO bioaccumulation within a terrestrial food chain. *Nanotoxicology, 11,* 98–111.

Shah, V., Luxton, T. P., Walker, V. K., Brumfield, T., Yost, J., Shah, S., et al. (2016). Fate and impact of zero-valent copper nanoparticles on geographically-distinct soils. *Science of the Total Environment, 573,* 661–670.

Shaw, A. K., & Hossain, Z. (2013). Impact of nano-CuO stress on rice (*Oryza sativa* L.) seedlings. *Chemosphere, 93,* 906–915.

Simonin, M., & Richaume, A. (2015). Impact of engineered nanoparticles on the activity, abundance, and diversity of soil microbial communities: A review. *Environmental Science and Pollution Research, 22,* 13710–13723.

Singh, D., & Kumar, A. (2016). Impact of irrigation using water containing CuO and ZnO nanoparticles on *Spinach oleracea* grown in soil media. *Bulletin of Environmental Contamination and Toxicology, 97,* 548–553.

Singh, D., & Kumar, A. (2018). Investigating long-term effect of nanoparticles on growth of *Raphanus sativus* plants: a trans-generational study. *Ecotoxicology, 27,* 23–31.

Soni, D., Naoghare, P. K., Saravanadevi, S., & Pandey, R. A. (2015). Release, Transport and Toxicity of Engineered Nanoparticles. In D. M. Whitacre (Ed.), *Reviews of Environmental Contamination and Toxicology* (pp. 1–47). Cham: Springer International Publishing.

Strambeanu, N., Demetrovici, L., & Dragos, D. (2015). *Natural Sources of Nanoparticles*, In book: M. Lungu et al. (eds.), Nanoparticles' Promises and Risks, Springer International Publishing Switzerland, pp. 9–19.

Sturikova, H., Krystofova, O., Huska, D., & Adam, V. (2018). Zinc, zinc nanoparticles and plants. *Journal of Hazardous Materials, 349,* 101–110.

Sun, T. Y., Bornhoft, N. A., Hungerbuhler, K., & Nowack, B. (2016). Dynamic probabilistic modeling of environmental emissions of engineered nanomaterials. *Environmental Science and Technology, 50,* 4701–4711.

Tiede, K., Boxall, A. B., Tear, S. P., Lewis, J., David, H., & Hassellov, M. (2008). Detection and characterization of engineered nanoparticles in food and the environment. *Food Additives & Contaminants: Part A: Chemistry, Analysis, Control, Exposure & Risk Assessment, 25,* 795–821.

Tiede, K., Hanssen, S. F., Westerhoff, P., Fern, G. J., Hankin, S. M., Aitken, R. J., et al. (2016). How important is drinking water exposure for the risks of engineered nanoparticles to consumers? *Nanotoxicology, 10,* 102–110.

Tolaymat, T., El Badawy, A., Genaidy, A., Abdelraheem, W., & Sequeira, R. (2017). Analysis of metallic and metal oxide nanomaterial environmental emissions. *Journal of Cleaner Production, 143,* 401–412.

Ude, V. C., Brown, D. M., Viale, L., Kanase, N., Stone, V., & Johnston, H. J. (2017). Impact of copper oxide nanomaterials on differentiated and undifferentiated Caco-2 intestinal epithelial cells; assessment of cytotoxicity, barrier integrity, cytokine production and nanomaterial penetration. *Particle and Fibre Toxicology, 14,* 31.

Umar, H., Kavaz, D., & Rizaner, N. (2019). Biosynthesis of zinc oxide nanoparticles using *Albizia lebbeck* stem bark, and evaluation of its antimicrobial, antioxidant, and cytotoxic activities on human breast cancer cell lines. *International Journal of Nanomedicine, 14,* 87–100.

Vance, M. E., Kuiken, T., Vejerano, E. P., McGinnis, S. P., Hochella, M. F., Jr., Rejeski, D., et al. (2015). Nanotechnology in the real world: Redeveloping the nanomaterial consumer products inventory. *Beilstein Journal of Nanotechnology, 6,* 1769–1780.

Wang, S., Li, Z., Gao, M., She, Z., Ma, B., Guo, L., et al. (2017a). Long-term effects of cupric oxide nanoparticles (CuO NPs) on the performance, microbial community and enzymatic activity of activated sludge in a sequencing batch reactor. *Journal of Environmental Economics and Management, 187,* 330–339.

Wang, X., Ma, R., Cui, D., Cao, Q., Shan, Z., & Jiao, Z. (2017b). Physio-biochemical and molecular mechanism underlying the enhanced heavy metal tolerance in highland barley seedlings pre-treated with low-dose gamma irradiation. *Scientific Reports, 7,* 14233.

Wang, Z., von dem Bussche, A., Kabadi, P. K., Kane, A. B., & Hurt, R. H. (2013). Biological and environmental transformations of copper-based nanomaterials. *ACS Nano, 7,* 8715–8727.

Wang, X., Yang, X., Chen, S., Li, Q., Wang, W., Hou, C., et al. (2015). Zinc oxide nanoparticles affect biomass accumulation and photosynthesis in Arabidopsis. *Frontiers in Plant Science, 6,* 1243.

Wang, M., Yang, Q., Long, J., Ding, Y., Zou, X., Liao, G., et al. (2018). A comparative study of toxicity of TiO(2), ZnO, and Ag nanoparticles to human aortic smooth-muscle cells. *International Journal of Nanomedicine, 13,* 8037–8049.

Wu, S. G., Huang, L., Head, J., Chen, D. R., Kong, I. C., & Tang, Y. J. (2012). Phytotoxicity of metal oxide nanoparticles is related to both dissolved metals ions and adsorption of particles on seed surfaces. *Journal of Petroleum & Environmental Biotechnology, 3,* 126.

Xu, L. (2018). Adsorption and inhibition of CuO nanoparticles on Arabidopsis thaliana root. *IOP Conference Series: Earth and Environmental Science, 113,* 012230.

Xu, C., Peng, C., Sun, L., Zhang, S., Huang, H., Chen, Y., et al. (2015). Distinctive effects of TiO_2 and CuO nanoparticles on soil microbes and their community structures in flooded paddy soil. *Soil Biology & Biochemistry, 86,* 24–33.

Yang, Z., Chen, J., Dou, R., Gao, X., Mao, C., & Wang, L. (2015). Assessment of the phytotoxicity of metal oxide nanoparticles on two crop plants, maize (*Zea mays* L.) and rice (*Oryza sativa* L.). *International Journal of Environmental Research and Public Health, 12,* 15100–15109.

You, T., Liu, D., Chen, J., Yang, Z., Dou, R., Gao, X., et al. (2017). Effects of metal oxide nanoparticles on soil enzyme activities and bacterial communities in two different soil types. *Journal of Soils and Sediments, 18,* 211–221.

Zhang, Z., Ke, M., Qu, Q., Peijnenburg, W., Lu, T., Zhang, Q., et al. (2018a). Impact of copper nanoparticles and ionic copper exposure on wheat (*Triticum aestivum* L.) root morphology and antioxidant response. *Environmental Pollution, 239,* 689–697.

Zhang, J., Wang, B., Wang, H., He, H., Wu, Q., Qin, X., et al. (2018b). Disruption of the superoxide anions-mitophagy regulation axis mediates copper oxide nanoparticles-induced vascular endothelial cell death. *Free Radical Biology and Medicine, 129,* 268–278.

Zhang, J., Zou, Z., Wang, B., Xu, G., Wu, Q., Zhang, Y., et al. (2018c). Lysosomal deposition of copper oxide nanoparticles triggers HUVEC cells death. *Biomaterials, 161,* 228–239.

Zhao, L., Hu, J., Huang, Y., Wang, H., Adeleye, A., Ortiz, C., et al. (2017). (1)H NMR and GC-MS based metabolomics reveal nano-Cu altered cucumber (*Cucumis sativus*) fruit nutritional supply. *Plant Physiology and Biochemistry, 110,* 138–146.

Zuverza-Mena, N., Medina-Velo, I. A., Barrios, A. C., Tan, W., Peralta-Videa, J. R., & Gardea-Torresdey, J. L. (2015). Copper nanoparticles/compounds impact agronomic and physiological parameters in cilantro (*Coriandrum sativum*). *Environmental Science: Processes & Impacts, 17,* 1783–1793.