An Overview of Nanotoxicological Effects Towards Plants, Animals, Microorganisms and Environment

V. Ananthi, K. Mohanrasu, T. Boobalan, K. Anand, M. Sudhakar, Anil Chuturgoon, V. Balasubramanian, R. Yuvakkumar and A. Arun

Abstract In recent years, nanotechnology has reached the limelight of research in applications of medicine and technology. Due to its onset, huge varieties of nanoparticles possessing significant characters are synthesized with broad application fields. Even though these particles are infesting our present life; conflictual views regarding their medical and biological effects are debatable. The non biodegradable nature and nanosize are the alarming features of the nanoparticles that confront potential threats to both environment and biomedical field on its expanding usage. NPs synthesized from heavy metals like lead, mercury and tin are proclaimed as stringent and stable compounds for degradation, hence results in environmental biohazards.

V. Ananthi · K. Mohanrasu
Department of Energy Science, Alagappa University, Karaikudi, Tamil Nadu 630003, India

V. Ananthi · K. Mohanrasu · T. Boobalan · V. Balasubramanian · A. Arun (✉)
Department of Microbiology, Alagappa University, Karaikudi, Tamil Nadu 630003, India
e-mail: arunalacha@gmail.com

V. Ananthi
Department of Microbiology, PRIST University, Madurai Campus, Madurai, Tamil Nadu 630562, India

K. Anand
Department of Chemical Pathology, School of Pathology, Faculty of Health Sciences and National Health Laboratory Service, University of the Free State, Bloemfontein, South Africa

A. Chuturgoon
Discipline of Medical Biochemistry, School of Laboratory of Medicine and Medical Sciences, College of Health Science, University of KwaZulu-Natal, Durban 4013, South Africa

M. Sudhakar
Polymers and Composites, Materials Science and Manufacturing Unit, Council for Scientific and Industrial Research (CSIR), Port Elizabeth 6001, South Africa

Department of Chemistry, Faculty of Science, Nelson Mandela University, P.O. Box 1600, Port Elizabeth 6000, South Africa

R. Yuvakkumar
Nano Materials Laboratory, Department of Physics, Alagappa University, Karaikudi, Tamil Nadu 630003, India

A. Krishnan and A. Chuturgoon (eds.), *Integrative Nanomedicine for New Therapies*, Engineering Materials,
https://doi.org/10.1007/978-3-030-36260-7_5

The extensive applications of silver nanoparticles in biosensing, cosmetics, medical devices, food and clothing products inflates its human exposure and obviously resulted in toxicity (short and long term). In vitro studies revealed various cytotoxic effects in the cells of mammals such as brain, liver, lung, skin, reproductive organs and vascular system. Furthermore, ingestion, inhalation or injection of nanoparticles in intraperitoneal region resulted in toxic effect of multiple organs inclusively brain. Accounting the metal nanoparticles biohazardous effects like ROS (Reactive oxygen species) generation, DNA damage, protein denaturation and lipid peroxidation has been proved on carbon based nanoparticles, organic lipid based nanoparticles, mineral based nanoparticles, nano diamonds, nano composites, etc. Although, nanotechnology has become an advent field of research nowadays, it is importing significant environmental and health hazards thus couldn't be beneficial to both society and economy.

Keywords Nano particles · Toxicity · Nano composites · Bioeconomy · Human health

1 Introduction

Existence of nanoparticles (NPs) is uncertain, over million years ago and their employment by humans is about thousands of years. Because of the accelerated human capacity in nanoparticle synthesis, enough attention has been directed on this type of particles. Due to their compelling potential of usage in wide areas like electrical industry, pharmaceuticals, cosmetics, medical and environmental applications, their respective investments are also growing worldwide (Guzman et al. 2006). The imperative fact about nanotechnology is the consideration of scientists as the lucid step of science to integrate biology, chemistry, physics, medicine and engineering (Chen and Mao 2007; Dahl et al. 2007; Vo-Dinh 2007; Janata 2008; Stewart et al. 2008).

The applications of nanotechnology has inclined greatly from the laboratory to economic market with huge interest scientifically through pharma industry. The particles right from the distinct nano to sub-micron sized were engaged widely in food, pharmaceuticals and cosmetics industries. In pharmaceutical industries nanoparticles were employed adversely as carriers of drug delivery, imaging, diagnostic agents of oncology and in diabetes. In the flourishing field of pharmaceuticals the nanotechnology are engaged with great potential through oral, dermal and injectable routes. As per FDA, 25 nanoparticles has been approved to use in enormous drug delivery systems, which implies its competency in treating diseases (infectious and non infectious). Nanomaterials are worn in numerous forms like nanotubes, nanomembranes, nanoparticles, nanofibers, liposomes, nanofilms etc. In pharmaceutical industries, lipid based nanoparticles (nanolipidsomes, lipid nanoparticles, nanoemulsions, lipid nanocapsules, lipid polymer nanoparticles), dendrimers, nanoshells and fullerenes were extensively studied in drug delivery systems of both academics and industries.

Apart from these, some emerging particles includes, metal nanoparticles, nanodiamonds, carbon nanotubes, graphene nanoparticles and quantum dots, they were used in diagnosis, drug delivery and imaging so as to achieve decisive targeting upon organs and cells.

The probable toxicity of metals that are accounted herein was well rooted since roman times and not new. Pedanius Dioscorides, the greek physician has previously described the probable effects of metals like mercury (Caley 1928), lead oxide (Osbaldeston and Wood 2000), copper silicate (Wisniak 2004), poisonous effects of Arsenic in yellow and red sulfur mines as referred by Strabo (Cilliers and Retief 2000) and demise of Alexander, the great as a consequence of drinking contaminated water of River Styx (Atkinson and Truter 2009). In the initial part of the present century, toxicity of metals and toxic effects of the excessive tiny particles were explored (Donaldson et al. 2001).

Expulsion of nanoparticles from consumer's body is pivotal. It is vital to determine the exceeding nanoparticles to overcome adverse effects (Kantiani et al. 2010). It was determined from the ancient times that dose of poison was ample to evoke a response. Nonetheless, size, physicochemical properties and mode of entry of nanoparticle will influences to determine persistence, hazard threat and biotoxicity so as to formulate and implement safety patterns (Scott-Fordsmand et al. 2014). The unwelcome consequences of the nanoparticle exposure are health ailments due to cytotoxicity, genotoxicity, cancer and autoimmune diseases.

The primary concern regarding the employment of metals within living organisms is their corroding and degrading ability results in diminished toughness, disintegration and weakening of accounted implants. Their activity would be diminished by the curtailing effects of biocompatibility and escalation of toxic effects (Burugapalli et al. 2016; Khodaei et al. 2016). The components like dissolved oxygen, soluble carbonates, nitrogen and electrolytes along with some physiological fluids (proteins, enzymes, organic acids and macromolecules), secretory compounds of inflammatory and fibrotic cells are responsible for progress of metal degradation which are made possible by the inhabitance of stress, strain and frictional forces.

Concerning on the biosafety of health and environmental issues into account the risk factors of NPs should be assessed prior to its application. Additionally, engineered nanoparticles could be released into the water bodies during the manufacturing and utilization processes unaviodably. Some environmental factors includes UV radiation, dissolved organic matter, ionic strength and pH could possibly react with the NPs, then the converted NPs make toxic effects on the concerning environment (El Badawy et al. 2010; Levard et al. 2012).

The undenied biocompatibility nature of NPs were contemporarily swamped off by the biotoxicity effects. Understanding of their properties relating to biological responses is vital so as to understand the flawless usage of nanoparticles. The mechanism of the nanoparticle reckons on respective factors like composition, chemical functions, shape along with its exclusive size and charge (Goodman et al. 2004; Roiter et al. 2009; Simon-Deckers et al. 2009; Xiao et al. 2012; Silva et al. 2014). Moreover, probable risk of nanoparticle resides on its respective particle size below 100 nm (nanoparticle). Based on the nanoparticle nature (metal or magnetic), the

breakdown mechanism that arise within the body results in unpredictable and noteworthy toxic effects. Since, NPs are involving in numerous catalytic and oxidative mechanisms in vivo, it is very hard to predict. Nanomaterials that exposing reactive surfaces with very high surface area are attractive for specific objectives. Beddoes et al. (2015) has conferred from both in vitro and in vivo examination of human cells along with membranes and succeedingly addressed that (a) Efficient translocation of nanoparticle through the membrane that resulting in cellular damage has been made possible by small NPs, whilst nanoparticles of large size displays active cellular uptake without toxic effects, (b) Disruption of membrane integrity was made by nanoparticles of positive charge rather than negative charged particles.

The nanomaterial field is very extensive with diverge toxicity, in the present review, few nanoparticle effects were highlighted as examples to predict the disturbances in biological systems. The study of nanoparticle toxicity towards any biological substances (animals and plants) are known as nanotoxicology, which comprises in vitro studies using cell lines of human or animal, in vivo experiments using human volunteers and animals, along with epidemiological data regarding the pollution of particle and studies of workers those who are exposed to nanoparticles (during welding, mining, etc.). Applications of nanoparticles are being inflated nowadays in agriculture field in the form of agrochemicals.

Toxicity induced by nanoparticle involves in evolution of oxidative stress (free radical or liberation of reactive oxygen species (ROS), genetic damage, inflammation and suppression of cell division which results in apoptosis. In addition, ROS stress accounts for fibrosis, inflammation, genotoxicity followed by carcinogenesis through the liberation of adverse cytokines. Above all the vital mechanism of toxicity resides on the reactive oxygen species generation, such that free radical possess detrimental impacts over biomolecules (DNA, lipids, proteins). Numerous biological mechanisms like endocytosis, phagocytosis with its processing (antigen presentation on MHC class molecules) and passive diffusion reckon on the particle size of nanoparticles (gold, silver, nickel, titanium, carbon nanotubes). The large surface area of NPs contributes to few toxic indications of biological molecules that confers oxidation results in DNA damage than the larger particles with similar size (Gatoo et al. 2014). The factor that contributes the difference between nanoparticle and large particle composed of same material are the quantum effects and its respective surface (Buzea and Pacheco 2017). The nanosized material displayed diverge properties (physical, chemical and mechanical) rather than the bulk sized particles. As a consequence of the proportion of atoms found exposed on the surface of the nanoparticle correlated with the interior surface escalates results in boost up of its physical (increased surface area along with volume ratio, and shortened melting point) and chemical properties (higher chemical reactivity). By the cause of the small size of the nanoparticles (gold, palladium and platinum), the electrons confined and possess quantized spectrum of energy, producing quantum size effects like magnetic moments.

The nanomaterials are prone to contaminate the vulnerable water ecosystem directly or indirectly so as their possible toxicity to aquatic biota should be evaluated. Adverse effects like inhibition of algal growth, behavioural changes associated with severe mortality rate in water fleas (*Daphnia* species), damage in fish brain cells and

changes in molecular biomarkers were explored. But, interaction of aquatic biota with nanomaterials, and their respective destiny in water is least recognized still. Along with the coastal progression, NiO nanoparticles separated during welding has turned into the vital sources of coastal pollution (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans). These NiO nanoparticles can be enforced as risk factors for the environment and health of human. The risk associated with inhalation of NiO nanoparticles by mammals were well established in in vitro assays (Oyabu et al. 2007).

Even though the nanoparticles acquire huge beneficial applications in the fields of agriculture, environment, medical diagnosis and treatment, some hazardous effects were also observed in animal models, human, plants, and water bodies of the environment. The fundamental complication explored by the nanoparticles are their ability to enter into the cells and concludes in cytotoxicity to inhibit their growth and development respectively. This chapter probes the biohazardous effects of different nanoparticles towards various hosts and habitat. Analysing those detrimental effects of nanoparticle would grant a wide view upon commercialization of nanoparticles in the field of agriculture, medicine and environment.

2 Factors Responsible for the Toxicity of Nanoparticles

The shape, size, surface charge, crystallinity, aggregation and surface coating of NPs are some of the factors responsible for the toxicity of nanoparticles.

The shape dependent toxicity is associated to the metal nanoparticles (gold, silver, nickel, titanium) and engineered particles (Carbon nanotubes). The nanoparticle entry into the cell by endocytosis and phagocytosis have serious impact due to the shape of the nanoparticles. For example spherical shaped nanoparticles are very prone to endocytosis when compared to other shapes of nanoparticles (Gatoo et al. 2014). Investigations revealed that the shape of the particle could affect the cellular level. K^+ ion channel blockage is three times higher by rod shaped Single walled nanotubes (SWNTs) than the spherical shaped C_{60} fullerene (Park et al. 2003). ZnO nanorods are confirmed to be more cytotoxic than the spherical ones (Hsiao and Huang 2011).

The size of nanoparticle is also inevitable in cytotoxic effects. Asbestos fibres of <2 μm size could cause asbestosis, whereas asbestos with <5 μm size cause mesothelioma and 10 μm sized asbestos would results in carcinoma (Lippmann 1990). Similarly 15 mm length TiO_2 fibres are more toxic than the 5 mm length fibres, which cause inflammatory response by alveolar macrophages in mice. Long multi walled carbon nanotubes (MWCNTs) can cause inflammatory response in abdominal cavity of mice than the small MWCNTs (Poland et al. 2008).

The surface charge of the nanoparticle employs vital impact over toxicity. The charge of the nanoparticle directs huge interactions like selective absorption, blood brain barrier integrity, plasma protein binding and membrane permeability. For example, negative charge carrying mammalian cell membranes improves interaction with cationic particles with the cells to a terrific degree than the negative or neutral

nanoparticles. Nonetheless greater cationic charge results in serious toxicity through hemolysis and aggregation of platelets (Gatoo et al. 2014). Silica NPs which carry positive charge are shown to induce ROS than the silica NPs with negative or neutral charge (Bhattacharjee et al. 2010).

Several studies have reported that TiO_2 (anatase form) could results in toxicity thereby inducing DNA damage with higher lipid peroxidation in the presence of light whereas the rutile form couldn't results in any toxic effects (Gurr et al. 2005).

Aggregation of particles could also conveys toxicity. Aggregation of the particles mostly imparts on the size, surface charge and particle composition. For example, aggregated carbon nanotubes (CNTs) will have more cytotoxic effect than the dispersed ones (Wick et al. 2007).

The physiochemical properties of NPs like surface charge, chemical, magnetic, optical and electric charge can altered by the surface coating of the particles. These changes can eventually results in interactions with biomolecules to produce significant nanoparticle toxicity. For example, the presence of oxygen radicals with heavy metals and ozone on surface of nanoparticles results in ROS formation and triggers cell inflammation. In certain cases the surface coating is essential to subside the NP toxicity. For example, essential coating in quantum dots made them non toxic because of their hydrophobic metal core and toxic heavy metals like cadmium (Talkar et al. 2018).

3 Nanoparticles in Agriculture Field

3.1 Phytotoxicity of Nanoparticles

The efficient uptake of nanoparticle is very specific depending on the plants. The factors involved in uptake are type and physicochemical properties of the nanoparticle, species and substrate of the plants (Arruda et al. 2015; Zuverza-Mena et al. 2017). Translocation of nanoparticle within the plants are made by establishing complexes between root exudates and transporter proteins (Yadav et al. 2014). Roots could intake tiny nanoparticles through its pores (5–20 nm size) present in epidermal cell wall of roots (apoplast) (Deng et al. 2014). Larger particles will be blocked so that small particles pass the cell walls results in capillary forces as a result of osmotic pressure and finally reaches endodermis by diffusing through the apoplast (Lin et al. 2009; Deng et al. 2014). In plants, nanoparticles can be uptaken by symplastic pathway through the plasma membrane inner side. Migration of nanoparticles to neighbor cells occurs through 20–50 nm (diameter) plasmodesmata channels (Deng et al. 2014). One more possible way of nanoparticle entry is foliar via pores of stomata and could be translocated to other parts along with roots (Hong et al. 2014). Nanoparticles (silver, zinc oxide, iron oxide, ceria and titania) with huge range of size and composition can interact with plants by means of internalization into leaves (Chichiricco and Poma 2015). The nanoparticles react with organelles of cell and contributes in oxidative stress,

metabolic transformations and genotoxicity (Deng et al. 2014). Even though few nanoparticles exposes positivity on one extreme, also urges negative consequences on another extreme. For Example CeO nanoparticles (500 mg/kg) exposed to barley could boost up shoot biomass (300%) but no grain formation was possible (Rico et al. 2015).

3.2 Detrimental Effects of Nanoparticle on Biochemical Traits of Plants

Even though the plant nanoparticle interaction brings some beneficial effects, huge studies are found available in indicating the detrimental effects of nanoparticle towards plants. The detrimental effects upon biochemical traits involves in ROS generation, lipid peroxidation, decline transpiration rate, disruption in mitosis, cell wall breakdown, diminished content of chlorophyll and cutback photosynthesis (Tripathi et al. 2017). Exposure of carbon-based nanoparticles (CNTs, C_{60}) results in cellular toxicity of rice, onion and spinach respectively (Chen et al. 2010; Shen et al. 2010; Begum and Fugetsu 2012). TiO_2 exposure produces stress in cucumber (Servin et al. 2013). Exposure of NiO nanoparticles in tomato triggers stress which was followed by mitochondrial and cell damage (Faisal et al. 2013). TiO_2 exposure produces chloroplast damage and hence photosynthetic rate of spinach was also decreased. In green peas the chlorophyll is greatly affected by ZnO nanoparticles (Mukherjee et al. 2014).

3.3 Unfortunate Outcomes of Nanoparticles on Plant Morphological Changes

The morphological changes of plants include germination index (germination rate and time), biomass of shoot and root, morphology of root tip, root elongation, etc. (Deng et al. 2014). The phytotoxic nanoparticles includes gold, silver, copper oxide, zinc oxide, carbon nanotubes and alumina which produce detrimental effects on roots and shoots (Ghodake et al. 2011; Begum and Fugetsu 2012; Begum et al. 2012; Burklew et al. 2012; Dimkpa et al. 2013; Deng et al. 2014; Feichtmeier et al. 2015). Exposure of ZnO in soybean plant affects formation of seeds (Yoon et al. 2014). Gold nanoparticles exposure in tobacco plant urges necrosis in tissues (Sabo-Attwood et al. 2012). CNTs inclusion is found to be phytotoxic against cucumber, lettuce and red spinach by decreasing length of roots and shoot, at the same time no unfavourable effects were recognised in soybeans and chilli (Begum et al. 2014). By virtue of nanoparticle absorption by roots, numerous NPs contributes adverse effects to seedling during roots and shoot elongation. Nanoparticle phytotoxicity pertinent to inhibition of growth reveals biomass reduction, decrease in germination

and growth of leaf, reduced elongation of root, decreased root biomass, change in root tip morphology, and shoot growth, flowering delay and yield decrease (Tripathi et al. 2017). Silver nanoparticles exposure results in stunted germination of corn and rice (Pokhrel and Dubey 2013; Thuesombat et al. 2014) followed by reduction of mitotic index and fragmentations of chromosomes in onion (Kumari et al. 2009). Growth of rice, soybean, corn and cabbage plants were adversely inhibited by the exposure of ZnO nanoparticles (Lin and Xing 2007; Boonyanitipong et al. 2011; Xiang et al. 2015). Carbon-based nanoparticles like C_{60} and CNTs urges biomass reduction in zucchini (Stampoulis et al. 2009), followed by delay in flowering and diminished harvest (Lin et al. 2009). TiO_2 exposure towards corn brings about inhibition in growth of leaf with damage of DNA damage (Asli and Neumann 2009; Castiglione et al. 2011).

3.4 Genotoxic Effects of Nanoparticles in Plants

Because of tiny size, NPs can migrate into cells and evoke genetic response of plants. Numerous metal nanoparticles like, Ag, CuO, CeO, TiO_2, ZnO and CNTs triggers genotoxicity against huge plant varieties (Fava beans, Soybean, Buckwheat, Ryegrass, Radish, Tobacco, Onion) (Kumari et al. 2011; Atha et al. 2012; Burklew et al. 2012; Chichiricco and Poma 2015; Ghosh et al. 2015). Genotoxic effects of nanoparticle comprises mitotic index reduction, fragmented sticky chromosomes, gene alteration, chromosomal aberrations, damage of DNA structure and decline viability of cell (Tripathi et al. 2017). These effects were observed in garlic, onion and buckwheat as a consequence of ZnO exposure (Kumari et al. 2011; Shaymurat et al. 2012; Lee et al. 2013). Exposure of CuO to buckwheat and radish results in genotoxic effects (Atha et al. 2012; Lee et al. 2013). Various chromosomal aberrations (breaking of chromosome and nuclear blebbing) were resulted by titanium oxide nanoparticle exposure (Pakrashi et al. 2014). Accumulation of CNTs in onion plants ascertained both cytotoxic and genotoxic consequences, which includes alteration in morphology of cells, affecting function of mitochondria and membrane integrity, damage of DNA and chromosomal aberrations (Ghosh et al. 2015). CeO nanoparticles causes adverse effects in intake of nutrition along with genetic alterations of wheat, rice and cucumber (Hong et al. 2014; Rico et al. 2014; Zhao et al. 2014).

3.5 Depletion of Growth Nutrients in Plants Due to Nanoparticles

The plants and plant products like fruits are being consumed mainly for its nutrients and minerals. Exposure of nanoparticles could also results in altered nutrient content, flavor of fruit, performance of growth and antioxidant capability (Deng et al. 2014;

Petersen et al. 2014; Antisari et al. 2015). Hence, usage of agrichemicals composed of nanoparticles would affect nutrients of various crops like rice, soybean, corn, cucumber and tomato (Rico et al. 2013; Antisari et al. 2015; Zhao et al. 2014, 2015). Numerous metal nanoparticles (TiO, Ag, Co, Fe_3O_4, CeO_2 and Ni) exposure to tomato plants displays depletion of compounds like Mg, P and S (Antisari et al. 2015). Exposure of CeO_2 nanoparticles in rice harvest grains resulted in negotiable nutrition values which includes least amount of starch, antioxidants, glutelin, iron, lauric and valeric acid (Rico et al. 2013). Nanoceria exposed cucumber plants would produce fruits with altered Mo micronutrient, sugar, phenolic contents along with fractionation of protein (Zhao et al. 2014). Exposure of nanoceria to corn plant urges decreased yield and curtail calcium translocation to kernals provided by cob (Zhao et al. 2015). ZnO nanoparticles exposure to corn plants produce subtle effects on altered nutrient contents, and reduced photosynthesis as a result of chlorophyll content consequently reduction in yield (49%) (Zhao et al. 2015).

3.6 Transgenerational Effects in Plants by Nanoparticles

Nanoparticles can got concentrated within tissues of roots, seeds, fruits and leaves. Uptake of nanoparticles by seeds has revealed to produce transgenerational effects over few plants (Lin et al. 2009; Wang et al. 2013). The nanoparticles could be disseminated to the progenies of plants through seeds even without exposure of nanoparticles externally. C_{70} could be found in the rice plants even after second generation as black aggregates adjacent to vascular system of stems and leaf tissues (Lin et al. 2009). The second-generation tomato plants obtained after exposure of ceria nanoparticles to parent plants were found to be uncertain with decrease in biomass, declined transpiration of water and greater ROS amount (Wang et al. 2013). The impact of nanoparticles on plant is given in Fig. 1.

4 Nanoparticles on Humans and Animals

4.1 BioToxicity of Nanoparticles in Humans and Animals

The nanoparticles are inappropriate in some extent that some are beneficial agriculturally, nevertheless those are internalized within crops and toxic towards human and laboratory animals by some extent. The toxicity of nanoparticle on animals relies on their size that helps in entering into the organisms, reach circulatory system, translocation to various organs like brain, kidneys, spleen, liver finally enter cells and organelles (Buzea et al. 2007). Those adverse effects are correlated with inflammation and discrete diseases including cancer. Even though the nanotoxicology is

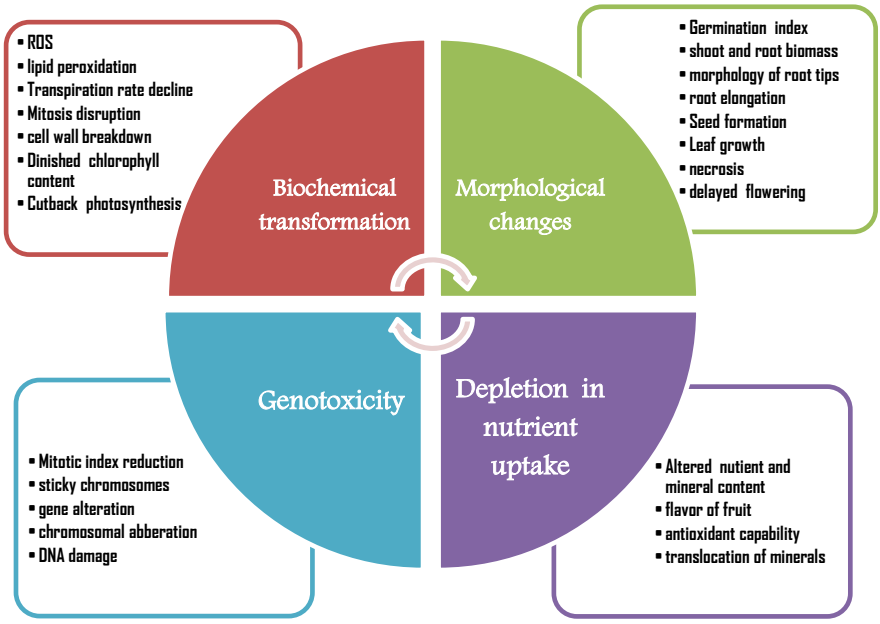

Fig. 1 Impacts of nanoparticles on plant growth, physicochemical and genetic activities

rather a new discipline, plenty of epidemiological investigation on toxicity of environmental nanoparticle towards human are elderly available. Some of the toxic effects of various nanoparticles tested against huge animal models and human cell lines were tabulated (Table 1).

4.2 Factors Affecting Biotoxicity of Nanoparticles—Physicochemical Characteristic

The determination of nanoparticle toxicity confides on the physico-chemical properties like shape, size, composition, porosity, hydrophobicity, surface area, aggregation, magnetic properties and electric charge (Buzea et al. 2007; Li et al. 2015; Silva et al. 2015; Schlinkert et al. 2015; Teske and Detweiler 2015). Same compound derived nanoparticles would exhibit diverse toxicity based on its distinction in size, surface charge and functionalization. Nanoparticles with similar size but with different material composition would also exhibit diverse toxicities obviously. Smaller size nanoparticles will have greater toxicities than the larger ones (Buzea et al. 2007). Simultaneously NPs (Titanium oxide) with same material composition but with varied crystalline forms (rutile and anatase forms) could exerts divergent properties and toxicity. Titania in rutile form (200 nm) would induce oxidative damage to DNA and cytotoxicity in bronchial epithelial cells of human, on the other hand anatase

form of titania could not (Gurr et al. 2005). Few NPs displays both hydrophobic and hydrophilic properties (Garcia-Ivars et al. 2015) which are modulated by the employed coating substances (Podila and Brown 2013) such as polyethylene glycol (PEG) provides hydrophilicity for the accompanying nanoparticle (Kettler et al. 2014). Charges of NPs either positive or negative charge is responsible to react with different biological systems (Gatoo et al. 2014; Salatin et al. 2015). For example NPs with positive charge would be attracted towards cell membranes carrying negative charge and results in cellular intake, which couldn't be made possible by nanoparticles with negative and neutral charge (Kettler et al. 2014). Investigations also revealed

Table 1 Biotoxicity of nanoparticles against model animals and human cell lines

Nanoparticle employed	Animal model/cell line	Toxic effects	Reference
SWCNTs	Rats	Interstitial inflammation and lesions	Lam et al. (2004)
	Kidney cells of human embryo	Cell proliferation inhibition Cell adhesive ability decrease	Cui et al. (2005)
	Lung fibroblast of chinese hamster (V79)	DNA damage	Kisin et al. (2007)
	Fibroblast cells of Mouse embryo	DNA damage	Yang and Watts (2005)
	Epithelial BEAS 2B cells of human	DNA damage	Lindberg (2009)
MWCNTs	Mouse embryonic stem cells	DNA damage	Zhu et al. (2007)
C_{60} fullerenes	Human lung adenocarcinoma	DNA polymerase inhibition (size dependent) Enhanced cytotoxicity	Song et al. (2012)
Citrate capped AgNPs	Rats	Induction of microvessel vascular endothelial cells inflammation Integrity of blood brain barrier affliction	Trickler et al. (2010)
AgNPs	Sprague Dawley rats	Locomotory activity diminishing Injury of central nervous system	Zhang et al. (2013)

(continued)

Table 1 (continued)

Nanoparticle employed	Animal model/cell line	Toxic effects	Reference
	Rats	Histopathological alterations (kidney, liver) swollen epithelium with cytoplasmic vacuolization Basement membrane thickening Mitochondrial cristae destruction Endosomes and lysosomes filled with AgNPs	Sarhan and Hussein (2014)
	Mice	Reduced hemoglobin content RNA transcription inhibition-red cell precursors Downregulation of hemoglobin level-fetal anemia Retardation of embryonic development	Wang et al. (2013)
	Human hepatoma cells	Cytotoxicity	Kim et al. (2009)
CoO	primary human immune cells	toxicity mediated with oxidative stress	Chattopadhyay et al. (2015)
MgO NPs	Vein endothelial and microvascular endothelial cell of human	Toxic effects on cells, oxidative stress	Ge et al. (2011), Sun et al. (2011)

that higher charge (positive and negative) imparts increased endocytic uptake mediated by receptors than the nanoparticles with neutral charge (Kettler et al. 2014). Toxicity of nanoparticles confides on internalization within the cells, such that gold nanoparticles with cationic property are toxic than the nanoparticles with anionic property (Goodman et al. 2004).

4.3 Mode of Internalization of Nanoparticles into Humans

By virtue of its tiny size, NPs could be ingested, inhaled or penetrated via the skin. The smaller nanoparticles will have higher accumulation within tissues (Sonavane et al. 2008). Accumulation of NPs within the body sites is resolved by its respective

composition and functional groups on surface. By means of the gastrointestinal and respiratory systems, the nanoparticles could hastily reaches circulatory and lymphatic system respectively (Landsiedel et al. 2012). It was revealed from various studies that the nanoparticles inhaled would accumulate in the lungs, some of them could reach alveoli based on their respective size and physicochemical properties, could also be systemic by translocating to other organ. These nanoparticles were found available in various parts like heart, brain, liver, spleen, thyroid, kidney, colon, bones along with lymphatic system and circulatory system (Johnston et al. 2010; Khlebtsov and Dykman 2011; Landsiedel et al. 2012; Anderson et al. 2015; Bruinink et al. 2015; Davidson et al. 2015; Geiser and Kreyling 2010; Gosens et al. 2015). Various types of NPs were found in the blood of many diseased patients (Gatti and Montanari 2006). Those nanoparticles combine with the plasma present in the circulatory system and results in the formation of protein corona which determine its toxicity and translocation. Later on, the nanoparticles reach and thereby acquire within various organs and tissues of heart, brain, liver, kidney, spleen, lymph nodes, bone marrow (Landsiedel et al. 2012; Sonavane et al. 2008).

The NPs enter through ingestion reach the gastrointestinal tract and are partially eliminated through feces, few get absorbed and found systematically (Hillyer and Albrecht 2001). It was evident from studies of animal model (in vitro and in vivo) that the nanoparticles could pass the placenta and reach fetus so as resulting in detrimental effects to pregnancy and fetus (Melnik et al. 2013; Semmler-Behnke et al. 2014; Snyder et al. 2015).

4.4 Cytotoxicity of Nanoparticles Towards Animals

Gold nanoparticle cytotoxicity depends on cell specificity and its coating upon surface respectively (Cheng et al. 2013; Schlinkert et al. 2015). These NPs internalized within the cells as a result of surface functions and by locations in mitochondria and lysosomes (Cheng et al. 2013), nuclei (Ojea-Jimenez et al. 2012) and vacuoles (Khlebtsov and Dykman 2011). In vivo studies of NPs in macrophages (spleen and liver kupffer cells) shown severe inflammation and liver cells apoptosis (Cho et al. 2009). Overexposure of silver nanoparticles in the form of wound dressings or drugs to humans undergo a condition called argyria (blue-gray discoloration of skin) associated with adverse toxic effects on liver (Christensen et al. 2010; Hadrup and Lam 2014). Exposure of silver nanoparticles would results in cardiac dysfunction in chicken, malformation of heart in fish and formation of thrombus in rats (Yu et al. 2016). Some studies represented that lungs and liver are the main targets of AgNPs exposure (Sung et al. 2008; Takenaka et al. 2001). Exposure of AgNPs on rat liver cells deplete antioxidant glutathione, decreased mitochondrial membrane potential and elevated ROS mediated by oxidative stress of liver cells (Hussain et al. 2005). Titanium oxide nanoparticle exposure develop arrhythmia in rats because of their direct contact with cardiac tissue (Savi et al. 2014). Titanium NPs on rodents heart tissue results in myocarditis, arrhythmia, vascular dysfunction, cardiac damage with

dysfunction, and some inflammatory responses (Yu et al. 2016). Degradation of DNA is possible with generation of oxygen species after copper nanoparticle exposure. As a result of in vivo experiments using mice, exploration of copper NPs translocate to organs like spleen, kidney and liver and finally results in inflammation of the respective organs (Magaye et al. 2012). Affirmatory effects of cerium oxide NPs on various cell lines would results in reactive oxygen species (ROS) and apoptosis (Mittal and Pandey 2014; Gagnon and Fromm 2015). Magnetic nanoparticles (Fe, Co and Ni) can be used in vivo imaging for diagnosis, more liable for aggregation, and finally results in inflammation followed by immune responses (Markides et al. 2012). Intravenous administration of ultrasmall supermagnetic iron oxide nanoparticles (USPION) in mice boost up blood clot formation followed by cardiac oxidative stress (Nemmar et al. 2016). Elicitation of nickel nanoparticles produce severe cytotoxic effects like oxidative stress which was followed by cell death (Magaye et al. 2012). Silicon nanoparticles could produce adverse cytotoxic effects on diverse human cell types like epithelial cells, platelets, microvascular endothelial cells, umbilical vein endothelial cells and aortic vessel cells (Yu et al. 2016). Exposure of carbon nanotubes (CNTs) in rodents produce consequences like thrombus formation, damage of placenta vessel, vasorelaxation, endothelial and cardiac dysfunction (Yu et al. 2016). Cytotoxic effects were observed in huge range of cell types like smooth muscle cells, blood cells, aortic endothelial cells, umbilical vein endothelial cells and microvascular endothelial cells of human (Yu et al. 2016). Even though, lack of action on cell viability or migration was observed, the platinum nanoparticle (Pt NPs) exposure produce some extent of activity in triggering toxicity towards primary keratinocytes and diminished metabolism of cells (Konieczny et al. 2013). Cytotoxic effects of Pt NPs resulted in accumulation in lysosomes and liberation of Pt^{2+} (Asharani et al. 2010).

4.5 Toxicity of Nanoparticles in Organ Development

Exposure of titanium oxide nanoparticle towards animal models would results in reduction of sperm production, alteration of neurobehaviour, abnormality in brain development of fetus, small fetuses, deformation of fetus and mortality (Savi et al. 2014).

4.6 Immunogenic Responses of Nanoparticles

Accumulation of AgNPs in the organs of immune system were followed by multiple organ (thymus, spleen, liver and kidney) damage (Wen et al. 2017). The reduced cell viability of alveolar macrophages and epithelial cells of lungs are possible on AgNPs exposure (Soto et al. 2007) Oxidative stress along with alveolar macrophage toxicity was observed in AgNPs by Carlson et al. (2008). Titanium oxide exposure

would cause toxicity which comprises effects of immune system (Savi et al. 2014). Exposure of ZnO NPs on rats and mice results in cardiac inflammation and apoptosis (Yu et al. 2016). Long term exposure of cobalt NPs were accompanied with immune system related health effects, skin, lungs and thyroid gland (Simonsen et al. 2012).

4.7 Genotoxic Effects of Nanoparticles

Injection of gold nanoparticles on rat samples (spleen and liver) produce changes in gene expression and results in lipid metabolism, defense response, detoxification, circadian rhythm and cell cycle (Balasubramanian et al. 2010). Genotoxic effects, because of chromosomal breakage is made possible by the exposure of nanoparticles to human (Wen et al. 2017). Silver nanoparticle exposure in chicken cause genotoxic effects (Yu et al. 2016). Intraperitoneal injection of AgNPs in mouse results in cytotoxic effects upon brain which are mediated by apoptosis, neurotoxicity with oxidative stress and change in genetic expression (Rahman et al. 2009). In addition to cytotoxic effects, some genotoxic effects were also observed in numerous cell lines as a result of titanium dioxide nanoparticles exposure (Gurr et al. 2005; Coccini et al. 2015; Yu et al. 2016). Zinc nanoparticle exposure to mice and rats were more probable to produce DNA damage (Yu et al. 2016). Administration of USPION intravenously to mice promote DNA damage (Nemmar et al. 2016). Exposure of nickel nanoparticle would bring about genotoxic effects as a result of cytotoxicity (Magaye et al. 2012). Alike production of cytotoxic effects by silicon nanoparticles, genotoxic effects were also possible on human cell types like, epithelial cells, aortic vessel cells, platelets, microvascular endothelial cells and umbilical vein endothelial cells (Yu et al. 2016). Genotoxic effects were observed followed by cytotoxic effects in huge range of cell types like smooth muscle cells, blood cells, umbilical vein endothelial cells, aortic endothelial cells and dermal microvascular endothelial cells of human (Yu et al. 2016). Exposure of platinum NPs displayed more detrimental effect on the stability of DNA (Konieczny et al. 2013).

4.8 Tumorigenesis in Animals by Nanoparticles

Nanoparticle could be vital for greater than 6 months within the body (Lin et al. 2015). Persistence for a longer time in the body would cause tissue inflammation injury and finally results in various diseases including cancer. The metallic nanoparticles residence in tissues aids tumorigenesis (Sighinolfi et al. 2016). Various studies are available to demonstrate the accumulation of nanoparticles within the tissues of patients infected with numerous diseases like pulmonary embolism, deep vein thrombosis, Hodgkin's lymphoma, prostrate cancer, renal failure, colon cancer, ulcerative colitis, emphysema, lung cancer, liver necrosis, asthma, stroke and Crohn's disease (Ballestri et al. 2001; Gatti and Rivasi 2002; Gatti 2004; Gatti and Montanari 2006;

Iannitti et al. 2010; Roncati et al. 2015a, b). Exposure of copper dust or fumes on copper smelter workers would expand cancer risk (Magaye et al. 2012). Dermal exposure and inhalation of magnetic nanoparticle (copper and nickel) results in cancer, lung fibrosis and skin allergies (Magaye et al. 2012). A detailed study on toxicity of CNTs revealed that its exposure would result in fibrosis and granulomas as consequences of carcinogenic and genotoxic effects (Aschberger et al. 2010).

5 Biohazards of Nanoparticle on Environmental Concern

The nanoparticles and their products enter the environment inevitably by means of washing, recycling and disposing (Kohler et al. 2008). The natural ecosystems are contaminated directly by the discharge of waste water and powder nanoparticles into the atmosphere. Unintentional release of AgNPs also results due to the activities like sampling, leaking and accidental release during transportation (Yu et al. 2013). Elemental silvers are found available in various forms as native silver (Leblanc and Lbouabi 1988; Lu et al. 2012) and as blends with metals like gold (Electrum) (Saunders et al. 2008; Denditius et al. 2011). Recently, AgNPs are extensively used in our day to day life with disinfectant sprays, outdoor paints, odour free socks, antimicrobial plastics and textiles. These nanoparticles reach the environment through scrapes, ageing of the materials and periodic washing of the materials. Liquid products like sprays and disinfectant are very rapid in entering the environment than the particles fixed to a solid cast like textiles and paints. The nanoparticles reacted to the sewage treatment plants could be used as fertilizers for agriculture land so as to reach the terrestrial system or groundwater system as leachate. Once the silver nanoparticles get released into the atmosphere, it could transport, disseminate and alter into various forms. The humans are exposed to nanoparticles through breathing, skin contact or eating. Environmentally exposed nanoparticles are associated with several neurodegenerative diseases (Alzheimer's disease, dementia and Parkinson's disease) (Calderon-Garciduenas et al. 2016; Chin-Chan et al. 2015; Gonzalez-Maciel et al. 2017). It was evident from the recent studies that the environmental polluted nanoparticle can translocate to the brain (adults and child) then enter cells and organelles and finally results in cellular damage with neurotoxicity (Gonzalez-Maciel et al. 2017). The exposure of AgNPs are manifested to affect huge number of aquatic and terrestrial habitats. They invade the embyos of zebrafish and results in growth interruption and abnormality. Acute and chronic studies deals with biological toxicities available based on organisms like algae, cladoceran and freshwater fishes. Over all, some iron nanostructures (iron oxide, ferrihydrite, lepidocrocite, hematite, maghemite, magnetite) are also naturally available in aquatic and terrestrial ecosystem (marine, rivers, lakes, springs, soils and sediments) and could possibly results in cytotoxic effects accompanied with ROS (Guo and Barnard 2013).

6 Hazardous Effects of Nanoparticles Towards Aquatic Organisms

The toxicity of various species in the aquatic system were studied by various researchers, among them the dominant species is fish followed by crustaceans, crabs and algal species. Their respective growth, organ development and reproductive behavior which were analysed by various studies and were tabulated (Table 2). The results revealed their lethality, behavioural change, toxicity and related stress. The environmental impact of a nanoparticle resides on various physical, chemical and biological parameters like shape, size, surface structure, surface charge, chemical composition, solubility aggregation and dispersion of nanoparticles (Navarro et al. 2008).

6.1 Cytotoxic Effects of Nanoparticles Against Algae

Nanoparticles are curious because of their high surface which can adsorb to pollutants, thereby alters its bioavailability along with the pollutants, and hence toxic to algae. Few heavy metals (Zn, Co, Cu, Ni, Pb and Cd) possess some detrimental effects towards algal growth, cell division, photosynthesis and primary metabolites elimination. The cytotoxicity is influenced by factors responsible for its conceivable mechanisms. Exposure of TiO_2 nanoparticles would entraps the algal cells thereby reducing the availability of light and subsidise toxicity to the algal cells (Aruoja et al. 2009). When compared with dark conditions, greater cytotoxicity was observed under light conditions. *Scenedesmus obliquus* produce serious ROS and increased membrane permeability while exposed to TiO_2 nanoparticles (Cherchi et al. 2011). Hazeem et al. (2016) reported that ZnO nanoparticles impose obscure effects upon marine algae thereby affecting its growth and chlorophyll a content during early stages of its growth respectively. Exposure of CuO nanoparticles produce adverse impacts on morphological, biochemical and physiological algae processes. The production of ROS, oxidative stress results in biomolecules (protein and lipids) damage, and finally reduced activity of glutathione activity was also happened (Melegari et al., 2013, Babu et al. 2014). As the concentration of CuO nanoparticles increased, metabolic activity of the cells were also decreased (Melegari et al. 2013) followed by damage of photosynthetic pigments in the presence of light meanwhile alters photosynthesis (Gouveia et al. 2013). The extent of DNA damage increases with higher concentration of CuO nanoparticles (Babu et al. 2014). Moreover, Cu NPs were found available in the cell membranes of algal cells at various sites while investigating the lipid peroxidation of cell membranes (Manusadzianas et al. 2012; Melegari et al. 2013). The GO exposure towards *Raphidocelis subcapitata* brought some adverse effects like oxidative stress and membrane damage (Nogueira et al. 2015). The pristine graphene exposure will results in inevitable disruption of cell wall and cell swelling (Pretti et al. 2014). The toxicity of nC_{60} nanoparticle was

Table 2 Toxicity of AgNPs on fresh water organisms

Nanoparticles employed	Organisms	Toxicity observed	Reference
AgNPs	*Danio rerio*	Increased rate of operculum movement and surface respiration, shows respiratory toxicity	Bilberg et al. (2012)
	Oryzias latipes	Multiple malformations during embryo development Decreased optic cup pigmentation, exophthalmia, abnormal finfold, anal swelling, head reduction and pericardial edema.	Wu et al. (2010)
	Pimephales promelas	Enter the embryos Induction of concentration-dependent increase in larval abnormalities, mostly edema	Laban et al. (2010)
	Zebrafish embryos	Heart rate- drop Increased mortality rate Delay in embryo hatching Organ deformities	Sutherland et al. (2010), Becker et al. (2011)
	Zebra fish	Oxidative stress, DNA damage and tumor formation risk	Asharani et al. (2008), Becker et al. (2011)
	Algae	Inhibition of photosynthesis	Tuominen et al. (2013)
C60 fullerenes	*Daphnia magna*	Elevated lipid peroxidation-cephalic ganglion and gills	Zhu et al. (2006)
Carbon nanotubes with fats	*Daphnia* sp.	Acute toxic effects	Roberts et al. (2007)
Carbon nanotubes	Fresh water crabs	Increased mortality	Templeton et al. (2006)
CNFs	*Klebsormidium flaccidum*	ROS production Promotion of physical damage to cells and inhibition of algae proliferation Induction of change in morphology, cell death	Munk et al. (2015)

(continued)

Table 2 (continued)

Nanoparticles employed	Organisms	Toxicity observed	Reference
GO	Green algae *Raphidocelis subcapitata*	Induction of ROS and film damage, results in toxic effects and the density of algae	Nogueira et al. (2015)
SWCNTs	*Chlorella vulgaris* *Raphidocelis subcapitata*	Restrain of growth	Sohn et al. (2015)
GONS, GOQD	*Chlorella* sp.	Reduced permeability of the cell Plasmolysis Increase of oxidative stress Mitochondrial membrane damage Inhibition of cell division and chlorophyll biosynthesis	Ouyang et al. (2015)
ZnO	*Chlorella vulgaris*	Distortion in morphological features Reduction in cell viability	Suman et al. (2015)
TiO_2 and C_{60}	*Daphnia magna*	Accumulates within digestive tract and other body parts	Becker et al. (2011), Johnston et al. (2012)
	Earthworm	Delay in reproduction	Hund-Rinke et al. (2012)
TiO_2	*Scenedesmus obliquus*	Production of ROS and increase in membrane permeability	Cherchi et al. (2011)
Nano zerovalent iron (nZVI)	Earthworm	Increased rate of mortality	Sevcu et al. (2011), Becker et al. (2011)
Nanodiamonds	Zebra fish	Malformations in embryo	Lin et al. (2016)
	Xenopus laevis	Increased embryo malformations decreased embryo survival rate	Marcon et al. (2010)
	Daphnia magna	Chronic toxicity of high concentrations resulted in reproduction inhibition and 100% mortality	Mendonça et al. (2011)
MgO	Zebrafish embryos	Inhibition of embryo hatchability	Ghobadian et al. (2015)

contributed by absorption and aggregation of the particles over the algal surface thereby hindering Mg^{2+} channels and triggering photosynthetic toxicity (Tao et al. 2016). The vital factor responsible for Au nanoparticle toxicity are bioavailability and biotoxicity. The electric charge present on its surface, for example positive charge functional group can employ toxicity on algae as it combined with the algae. The secondary factor that assimilate toxicity is its smaller hydrodynamic particle size (Garcia-Cambero et al. 2013). The exposure of AgNPs towards algae results in toxic effects including membrane adhesion, alteration in permeability and ion transport thereby expanding the porosity of cell, interruption in phosphate management of cell and DNA synthesis inhibition and ROS formation (Klaine et al. 2008). After exposure of AgNPs, deformation of algal cells from spindle to round was happened, ultimately results in cell lysis and collapse. The dose of the AgNPs is responsible for the severity of toxicity and algal viability, even more ionic silver exhibits extreme algal toxicity than AgNPs (He et al. 2012).

6.2 *Nanoparticles Effects on Terrestrial Species*

The released nanoparticles could be deposited in the terrestrial ecosystem like sewage and soil matrix thereby absorbed so as to interact soil organisms finally results in toxic effects. The routes of nanoparticle exposure includes nutrition absorption, body surface contact and through water. As per the observation of Yin et al. (2011) AgNPs coated with gummi arabicum inhibited the growth and morphological damage was triggered on *Lolium multiflorum*. Few terrestrial animals like nematodes and earthworms were chosen as the models for toxicity evaluation of AgNPs in soil due to high permeability of their skin. Exposure of AgNPs to *Eisenia fetida* earthworm resulted in growth and reproductive toxicity (Shoults-Wilson et al. 2011). Feeding *Acheta domesticus* (House cricket) with nanodiamond supplemented diet affected the insect development with oxidative damage followed by feeding disturbances (Karpeta-Kaczmarek et al. 2018). Some soil microbes which were exposed by AgNPs are found to be extremely sensitive and toxic.

6.3 *Cytotoxic Effects of Nanoparticles Against Beneficial Microbes and Protozoa*

Microorganisms are the unique nitrogen fixers and animal degraders found in nature, by the mean time these microbes were located at the end of the food chain to complete the cycle. Silver nanoparticles (AgNPs) has been acknowledged because of its antimicrobial (antibacterial and antifungal) activity so as to be used as agrochemicals extensively. Correspondingly, the AgNps sustenance in soil would have consequence upon beneficial microbiota of soil like nitrogen fixing bacteria, consecutively affects

physicochemical characteristics of both plants and soil (Anjum et al. 2013). Additionally the AgNPs interact with the bacterial cells and are toxic that finally results in death of microbes like *E. coli* (Lok et al. 2006). Exposure of inorganic nanoparticles like TiO_2, SO_2 and ZnO produce toxic effects upon bacteria which found to increase in the presence of light (Lovern and Klaper 2006). Death of microbes resulted by the cell membrane damage are made possible by the exposure of carbon nanomembranes (CNMs), could also vitally confides upon harmness to ecosystem, human health and finally resides in loss of biodiversity (Chen et al. 2017). Exposure of TiO_2 nanoparticles to *Saccharomyces cerevisiae* under dark condition results in toxic effect (Kasemets et al. 2009), whereas TiO_2 exposure towards *E. coli* and *Bacillus subtilis* results in growth inhibition (Erdem et al. 2015). CNMs also possibly induce ROS associated with lipid peroxidation, DNA damage, protein denaturation and finally cell death. The cells of protozoa could able to absorb carbon nanotubes resulting in accumulation within the mitochondrial cells (Zhu et al. 2006).

7 Future Perspectives

The experimental data which reveals the possible interaction between plant root and the nanoparticle is needed. Since the nanoparticles are widely consumed by human, their physical, chemical and biological interactions have to be studied keenly. Hence more prudential idea about interactions of nanoparticle with cells and their respective toxicity will be recognized. There is no detailed data regarding the consequences resulting from the chronic exposure of the nanoparticles to both environment and living beings.

8 Conclusion

Even though the utilization of nanoparticles has elevated in consumer and economical aspects, some detrimental consequences were also being faced by plants, animals, human and environment. This chapter explored the fragmentary views of discrepancy in practicing nanoparticle based on its toxicity and environmental hazards. If the nanoparticles are used as agrichemicals to boost up soil fertility some phytotoxic effects were also ascertained, which results in various diseases related to human and animals. Over exposure of nanoparticles to the environment will also pose catastrophic risks to the organisms residing in the environmental habitat.

Acknowledgements Authors thanks the financial support given by RUSA – Phase 2.0 grant sanctioned vide Letter No. F.24- 51/2014- U, Policy (TNMulti-Gen), Dept. of Edn. Govt. of India, Dt. 09.10.2018.

References

Anderson, D. S., Patchin, E. S., Silva, R. M., Uyeminami, D. L ., Sharmah, A., Guo, T., et al. (2015). Influence of particle size on persistence and clearance of aerosolized silver nanoparticles in the rat lung. *Toxicological Sciences, 144*, 366–381. https://doi.org/10.1093/toxsci/kfv005.

Anjum, N. A., Gill, S. S., Duarte, A. C, Perelra, E., & Ahmad, I. (2013). Silver nanoparticles in soil-plant systems. *Journal of Nanoparticle Research, 15*, 1896–1897. https://doi.org/10.1007/s11051-013-1896-7.

Antisari, L. V., Carbone, S., GattiA Vianello, G., Nannipieri, P., et al. (2015). Uptake and translocation of metals and nutrients in tomato grown in soil polluted with metal oxide (CeO_2, Fe_3O_4, SnO_2, TiO_2) or metallic (Ag Co, Ni) engineered nanoparticles. *Environmental Science and Pollution Research, 22*, 1841–1853. https://doi.org/10.1007/s11356-014-3509-0.

Arruda, S. C. C., Silva, A. L. D., Galazzi, R. M., Azevedo, R. A., & Arruda, M. A. (2015). Nanoparticles applied to plant science: A review. *Talanta, 131*, 693–705. https://doi.org/10.1016/j.talanta.2014.08.050.

Aruoja, V., Dubourguier, H. C., Kasemets, K., & Kahru, A. (2009). Toxicity of nanoparticles of CuO, ZnO and TiO to microalgae *Pseudokirchneriella subcapitata*. *Science of the Total Environment, 407*(4):1461–1468. https://doi.org/10.1016/j.scitotenv.2008.10.053.

Aschberger, K., Johnston, H. J., Stone, V., Aitken, R. J., Hankin, S. M., Peters, S. A., et al. (2010) Review of carbon nanotubes toxicity and exposure-appraisal of human health risk assessment based on open literature. *Critcal Reviews in Toxicology, 40*, 759–790. https://doi.org/10.3109/10408444.2010.506638.

Asharani, P. V., Wu, L. Y., Gong, Z., & Valiyaveettil, S. (2008). Toxicity of silver nanoparticles in zebrafish models. *Nanotechnology, 19*, 255102. https://doi.org/10.1088/0957-4484/19/25/255102.

Asharani, P. V., Xinyi, N., Hande, M. P., & Valiyaveettil, S. (2010). DNA damage and p53-mediated growth arrest in human cells treated with platinum nanoparticles. *Nanomedicine, 5*, 51–64. https://doi.org/10.2217/nnm.09.85.

Asli, S., & Neumann, P. M. (2009). Colloidal suspensions of clay or titanium dioxide nanoparticles can inhibit leaf growth and transpiration via physical effects on root water transport. *Plant Cell & Environment, 32*, 577–584. https://doi.org/10.1111/j.1365-3040.2009.01952.x.

Atha, D. H., Wang, H. H., Petersen, E. J., Cleveland, D., Holbrook, R. D., Jaruga, P., et al. (2012). Copper oxide nanoparticle mediated DNA damage in terrestrial plant models. *Environment Science & Technology, 46*, 1819–1827. https://doi.org/10.1021/es202660k.

Atkinson, J., & Truter, E. (2009). Alexander's last days: malaria and mind games. *Acta Classica, 52*, 23–46.

Babu, M. Y., Palanikumar, L., Nagarani, N., Devi, V. J., Kumar, S. R., Ramakritinan, C. M., et al. (2014). Cadmium and copper toxicity in three marine macroalgae: evaluation of the biochemical responses and DNA damage. *Environmental Science and Pollution Research, 21*, 9604–9616. https://doi.org/10.1007/s11356-014-2999-0.

Balasubramanian, S. K., Jittiwat, J., Manikandan, J., Ong, C. N., Yu, L. E., & Ong, W. Y. (2010). Biodistribution of gold nanoparticles and gene expression changes in the liver and spleen after intravenous administration in rats. *Biomaterials, 31*, 2034–2042. https://doi.org/10.1016/j.biomaterials.2009.11.079.

Ballestri, M., Baraldi, A., Gatti, A. M., Furci, L., Bagni, A., Loria, P., et al. (2001). Liver and kidney foreign bodies granulomatosis in a patient with malocclusion, bruxism, and worn dental prostheses. *Gastroenterology, 121*, 1234–1238. https://doi.org/10.1053/gast.2001.29333.

Becker, H., Herzberg, F., Schulte, A., & Kolossa-Gehring, M. (2011). The carcinogenic potential of nanomaterials, their release from products and options for regulating them. *International Journal of Hygiene and Environmental Health, 214*(3): 231–238. https://doi.org/10.1016/j.ijheh.2010.11.004.

Beddoes, C. M., Case, C. P., & Briscoe, W. H. (2015). Understanding nanoparticle cellular entry: A physicochemical perspective. *Advances in Colloid and Interface Science, 218*, 48–68. https://doi.org/10.1016/j.cis.2015.01.007.

Begum, P., & Fugetsu, B. (2012). Phytotoxicity of multi-walled carbon nanotubes on red spinach (*Amaranthus tricolor* L) and the role of ascorbic acid as an antioxidant. *Journal of Hazardous Materials, 243*, 212–222. https://doi.org/10.1016/j.jhazmat.2012.10.025.

Begum, P., Ikhtiari, R., & Fugetsu, B. (2014). Potential impact of multi-walled carbon nanotubes exposure to the seedling stage of selected plant species. *Nanomaterials, 4*, 203–221. https://doi.org/10.3390/nano5010268.

Begum, P., Ikhtiari, R., Fugetsu, B., Matsuoka, M., TsukasaAkasaka, T., & Watari, F. (2012). Phytotoxicity of multi-walled carbon nanotubes assessed by selected plant species in the seedling stage. *Applied Surface Science, 262*, 120–124. https://doi.org/10.1016/j.apsusc.2012.03.028.

Bhattacharjee, S., Haan, L. H. J. D., Evers, N. M., Jiang, X., Marcelis, A. T, Zuilhof, H., et al. (2010). Role of surface charge and oxidative stress in cytotoxicity of organic monolayer-coated silicon nanoparticles towards macrophage NR8383 cells. *Particle and Fibre Toxicology, 7*, 25.http://dx.doi.org/10.1186/1743-8977-7-25.

Bilberg, K., Hovgaard, M. B., Besenbacher, F., & Baatrup, E. (2012). In vivo toxicity of silver nanoparticles and silver ions in zebrafish (*Danio rerio*). *Journal of Toxicology, 2012*, 293784–293784. https://doi.org/10.1155/2012/293784.

Boonyanitipong, P., Kositsup, B., Kumar, P., Baruah, S., & Dutta, J. (2011). Toxicity of ZnO and TiO_2 nanoparticles on germinating rice seed *Oryza sativa* L. *International Journal of Bioscience, Biochemistry and Bioinformatics, 1*(4), 282–285. https://doi.org/10.7763/IJBBB.2011.V1.53.

Bruinink, A., Wang, J., & Wick, P. (2015). Effect of particle agglomeration in nanotoxicology. *Archives of Toxicology, 89*, 659–675. https://doi.org/10.1007/s00204-015-1460-6.

Burklew, C. E., Ashlock, J., Winfrey, W. B., & Zhang, B. (2012). Effects of aluminum oxide nanoparticles on the growth, development, and microRNA expression of tobacco (*Nicotiana tabacum*). PLoS One7. https://doi.org/10.1371/journal.pone.0034783.

Burugapalli, K., Razavi, M., Zhou, L., & Huang, Y. (2016). In vitro cytocompatibility study of a medical ß-type Ti-35.5 Nb-5.7 Ta titanium alloy. *Journal of Biomaterials and Tissue Engineering, 6*, 141–8. https://doi.org/10.1166/jbt.2016.1424.

Buzea, C., & Pacheco, I. (2017). Nanomaterials and their classification. In: Shukla, A.K. (Ed) EMR/ESR/EPR spectroscopy for characterization of nanomaterials, Advanced structured materials, Vol. 62, pp. 3–45. New York: Springer. ISBN 978-981-10-6214-8.

Buzea, C., Pacheco, I. I, Robbie, K. (2007). Nanomaterials and nanoparticles: Sources and toxicity. Biointerphases 2:MR17–MR71. https://doi.org/10.1116/1.2815690.

Calderon-Garciduenas, L., Reynoso-Robles, R., Vargas-Martinez, J., Gómez-Maqueo-Chew, A., Pérez-Guillé, B., Mukherjee, P.S., et al. (2016). Prefrontal white matter pathology in air pollution exposed Mexico City young urbanites and their potential impact on neurovascular unit dysfunction and the development of Alzheimer's disease. *Environmental Research, 146*, 404–417. https://doi.org/10.1016/j.envres.2015.12.031.

Caley, E. R. (1928). Mercury and its compounds in ancient times. *Journal of Chemical Education, 5*(4), 419. https://doi.org/10.1021/ed005p419.

Carlson, C., Hussain, S. M., Schrand, A. M., Braydich-Stolle, L. K., Hess, K. L., Jones, R. L., et al. (2008). Unique cellular interaction of silver nanoparticles: size-dependent generation of reactive oxygen species. *The Journal of Physical Chemistry B, 112*, 13608–13619. https://doi.org/10.1021/jp712087m.

Castiglione, M. R, Giorgetti, L., Geri, C., & Cremonini, R. (2011). The effects of nano-TiO2 on seed germination,development and mitosis of root tip cells of Vicia narbonensis L. and Zea mays L. *Journal of Nanoparticle Research, 13*, 2443–2449. https://doi.org/10.1007/s11051-010-0135-8.

Chattopadhyay, S., Dash, S. K, Tripathy, S., Das, B., Mandal, D., Pramanik, P., et al. (2015). Toxicity of cobalt oxide nanoparticles to normal cells; an in vitro and in vivo study. *Chemical Biological Interactions, 226*, 58-71. https://doi.org/10.1016/j.cbi.2014.11.016.

Chen, M., Qin, X., & Zeng, G. (2017). Biodiversity change behind wide applications of nanomaterials? *Nano Today, 17*, 11-13. https://doi.org/10.1016/j.nantod.2017.09.001.

Chen, R., Ratnikova, T. A., Stone, M. B., Lin, S., Lard, M., Huang, G., et al. (2010). Differential uptake of carbon nanoparticles by plant and mammalian cells. *Small, 6*, 612–617. https://doi.org/10.1002/smll.200901911.

Chen, X., & Mao, S. S. (2007). Titanium dioxide nanomaterials: Synthesis, properties, modifications, and applications. *Chemical Reviews, 107*, 2891–2959. https://doi.org/10.1021/cr0500535.

Cheng, L. C., Jiang, X., Wang, J., Chen, C., & Liu, R. S. (2013). Nano-bio effects: interaction of nanomaterials with cells. *Nanoscale, 5*, 3547–3569 (2013). https://doi.org/10.1039/c3nr34276j.

Cherchi, C., Chernenko, T., Diem, M., & Gu, A. Z. (2011). Impact of nano titanium dioxide exposure on cellular structure of Anabaena variabilis and evidence of internalization. *Environmental Toxicology and Chemistry, 30*(4), 861–869. https://doi.org/10.1002/etc.445.

Chichiricco, G., & Poma, A. (2015). Penetration and toxicity of nanomaterials in higher plants. *Nanomaterials, 5*, 851–873. https://doi.org/10.3390/nano5020851.

Chin-Chan, M., Navarro-Yepes, J., & Quintanilla-Vega, B. (2015). Environmental pollutants as risk factors for neurodegenerative disorders: Alzheimer and Parkinson diseases. *Frontiers in Cellular Neuroscience, 9*, 124. https://doi.org/10.3389/fncel.2015.00124.

Cho, W. S., Cho, M. J., Jeong, J., Choi, M., Cho, H.Y., Han, B.S., et al. (2009). Acute toxicity and pharmacokinetics of 13 nm-sized PEG-coated gold nanoparticles. *Toxicology and Applied Pharmacology, 236*, 16–24. https://doi.org/10.1016/j.taap.2008.12.023.

Christensen, F. M., Johnston, H. J., Stone, V., Aitken, R. J., Hankin, S., Peters, S., et al. (2010). Nano-silver – feasibility and challenges for human health risk assessment based on open literature. *Nanotoxicology, 4*, 284–295. https://doi.org/10.3109/17435391003690549.

Cilliers, L., & Retief, F. P. (2000). Poisons, poisoning and the drug trade in ancient Rome. *Akroterion, 45*, 87–88. https://doi.org/10.7445/45-0-166.

Coccini, T., Grandi, S., Lonati, D., Locatelli, C., & De Simone, U. (2015). Comparative cellular toxicity of titanium dioxide nanoparticles on human astrocyte and neuronal cells after acute and prolonged exposure. *Neurotoxicology, 48*, 77–89. https://doi.org/10.1016/j.neuro.2015.03.006.

Cui, D., Tian, F., Ozkan, C. S., Wang, M., & Gao, H. (2005). Effect of single wall carbon nanotubes on human HEK293 cells. Toxicology Letters 155(1), 73–85. https://doi.org/10.1016/j.toxlet.2004.08.015.

Dahl, J. A., Maddux, B. L. S., & Hutchison, J. E. (2007). Toward greener nanosynthesis. *Chemical Reviews, 107*, 2891–2959. https://doi.org/10.1021/cr0500535.

Davidson, R. A, Anderson, D. S, Van Winkle, L. S, Pinkerton, K. E, & Guo, T. (2015). Evolution of silver nanoparticles in the rat lung investigated by X-ray absorption spectroscopy. *The Journal of Physical Chemistry A, 119*, 281–289. https://doi.org/10.1021/jp510103m.

Denditius, A. P., Utsunomiya, S., Reich, M., Kesler, S. E., Ewing, R. C., Hough, R., et al. (2011). Trace metal nanoparticles in pyrite. *Ore Geology Reviwes, 42*(1), 32–46. https://doi.org/10.1016/j.oregeorev.2011.03.003.

Deng, Y. Q., White, J. C., & Xing, B. S. (2014). Interactions between engineered nanomaterials and agricultural crops: Implications for food safety. *Journal of Zhejiang University SCIENCE A, 15*, 552–572. https://doi.org/10.1631/jzus.A1400165.

Dimkpa, C. O., McLean, J. E., Martineau, N., Britt, D. W., Haverkamp, R., & Anderson, A. J. (2013). Silver nanoparticles disrupt wheat (*Triticum aestivum* L.) growth in a sand matrix. *Environmental Science Technology, 47*, 1082–1090. https://doi.org/10.1021/es302973y.

Donaldson, K., Stone, V., Clouter, A., Renwick, L., & MacNee, W. (2001). Ultrafine particles. *Occupational and Environmental Medicine, 58*(3), 211–216.

El Badawy, A. M., Luxton, T. P, Silva, R. G, Scheckel, K. G, Suidan, M. T, Tolaymat, T. M (2010). Impact of environmental conditions (pH, ionic strength, and electrolyte type) on the surface charge and aggregation of silver nanoparticles suspensions. *Environmental Science & Technology, 44*, 1260-1266. https://doi.org/10.1021/es902240k.

Erdem, A., Metzler, D. M, Cha, D. K, & Huang, C. P. (2015). The short-term toxic effects of TiO_2. Environ nanoparticles toward bacteria through viability, cellular respiration, and lipid peroxidation. *Science Pollution Research, 22*, 17917–17924. https://doi.org/10.1007/s11356-015-5018-1.

Faisal, M., Saquib, Q., Alatar, A. A., Al-Khedhairy, A. A., Hegazy, A. K., & Musarrat, J. (2013). Phytotoxic hazards of NiO-nanoparticles in tomato: a study on mechanism of cell death. *Journal of Hazardous Materials, 250*, 318–332. https://doi.org/10.1016/j.jhazmat.2013.01.063.

Feichtmeier, N. S., Walther, P., & Leopold, K. (2015). Uptake, effects, and regeneration of barley plants exposed to gold nanoparticles. *Environmental Science Pollution Research, 22*, 8549–8558. https://doi.org/10.1007/s11356-014-4015-0.

Gagnon, J., & Fromm, K. M. (2015). Toxicity and protective effects of cerium oxide nanoparticles (Nanoceria) depending on their preparation method, particle size, cell type, and exposure route. *European Journal of Inorganic Chemistry*, 4510–4517. https://doi.org/10.1002/ejic.201500643.

Garcia-Cambero, J. P., Nunez Garcia, M., Lopez, G. D., Herranz, A. L., Cuevas, L., Perez-Pastrana, E., et al. (2013). Converging hazard assessment of gold nanoparticles to aquatic organisms. *Chemosphere, 93*(6), 1194–1200. https://doi.org/10.1016/j.chemosphere.2013.06.074.

Garcia-Ivars, J., Iborra-Clar, M. I., Alcaina-Miranda, M .I., & Van Der Bruggen, B. (2015). Comparison between hydrophilic and hydrophobic metal nanoparticles on the phase separation phenomena during formation of asymmetric polyethersulphone membranes. *Journal of Membrane Science, 493*, 709–722. https://doi.org/10.1016/j.memsci.2015.07.009.

Gatoo, M. A., Naseem, S., Arfat, M. Y., Dar, A. M., Qasim, K., & Zubair, S. (2014). Physicochemical properties of nanomaterials: implication in associated toxic manifestations. *Biomedical Research International, 2014*, 498420. https://doi.org/10.1155/2014/498420.

Gatti, A. M. (2004). Biocompatibility of micro- and nano-particles in the colon. Part II. *Biomaterials, 25*, 385–392. https://doi.org/10.1016/s0142-9612(03)00537-4.

Gatti, A. M., & Montanari, S. (2006). Retrieval analysis of clinical explanted vena cava filters. *Journal of Biomedical Materials Research Part B 77B*, 307–314. https://doi.org/10.1002/jbm.b.30361.

Gatti, A. M., & Rivasi, F. (2002). Biocompatibility of micro- and nanoparticles. Part I: in liver and kidney. *Biomaterials, 23*, 2381–2387. https://doi.org/10.1016/s0142-9612(01)00374-x.

Ge, S., Wang, G., Shen, Y., Zhang, Q., Jia, D., Wang, H., et al. (2011). Cytotoxic effects of MgO nanoparticles on human umbilical vein endothelial cells in vitro. *IET Nanobiotechnology, 5*(2), 36–40. https://doi.org/10.1049/iet-nbt.2010.0022.

Geiser, M., & Kreyling, W. G. (2010). Deposition and biokinetics of inhaled nanoparticles. *Particle and Fibre Toxicology, 7*, 2.https://doi.org/10.1186/1743-8977-7-2.

Ghobadian, M., Nabiuni, M., Parivar, K., Fathi, M., & Pazooki, J. (2015). Toxic effects of magnesium oxide nanoparticles on early developmental and larval stages of zebrafish (*Danio rerio*). *Ecotoxicology and Environmental Safety, 122*(1), 260–267. https://doi.org/10.1016/j.ecoenv.2015.08.009.

Ghodake, G., Seo, Y. D., & Lee, D. S. (2011). Hazardous phytotoxic nature of cobalt and zinc oxide nanoparticles assessed using *Allium cepa*. *Journal of Hazardous Materials, 186*, 952–955. https://doi.org/10.1016/j.jhazmat.2010.11.018.

Ghosh, M., Bhadra, S., Adegoke, A., Bandyopadhyay, M., & Mukherjee, A. (2015). MWCNT uptake in *Allium cepa* root cells induces cytotoxic and genotoxic responses and results in DNA hypermethylation. *Mutation Research, 774*, 49–58. https://doi.org/10.1016/j.mrfmmm.2015.03.004.

Gonzalez-Maciel, A., Reynoso-Robles, R., Torres-Jardon, R., Mukherjee, P. S., & Calderón-Garcidueñas, L. (2017). Combustion-derived nanoparticles in key brain target cells and organelles in young urbanites: culprit hidden in plain sight in Alzheimer's disease development. *Journal of Alzheimer's Disease, 59*, 189–208. https://doi.org/10.3233/jad-170012.

Goodman, C. M., McCusker, C. D., Yilmaz, T., & Rotello, V. M. (2004). Toxicity of gold nanoparticles functionalized with cationic and anionic side chains. *Bioconjugate Chemistry, 15*, 897–900. https://doi.org/10.1021/bc049951i.

Gosens, I., Kermanizadeh, A., Jacobsen, N. R., Lenz, A .G., Bokkers, B., de Jong, W. H., et al. (2015). Comparative hazard identification by a single dose lung exposure of zinc oxide and silver nanomaterials in mice. *PLoS One, 10*, e0126934. https://doi.org/10.1371/journal.pone.0126934.

Gouveia, C., Kreusch, M., Schmidt, É. C., Felix, M. R., Osorio, L. K., Pereira, D. T., et al. (2013). The effects of lead and copper on the cellular architecture and metabolism of the red alga *Gracilaria domingensis*. *Microscopy and Microanalysis, 19*(3), 513–524. https://doi.org/10.1017/S1431927613000317.

Guo, H., & Barnard, A. S (2013). Naturally occurring iron oxide nanoparticles: morphology, surface chemistry and environmental stability. *Journal of Materials Chemistry A, 1*, 27-42. https://doi.org/10.1039/c2ta00523a.

Gurr, J. R, Wang, A. S, Chen, C. H, & Jan, K. Y. (2005). Ultrafine titanium dioxide particles in the absence of photoactivation can induce oxidative damage to human bronchial epithelial cells. *Toxicology, 213*, 66–73. http://dx.doi.org/ https://doi.org/10.1016/j.tox.2005.05.007.

Guzman, K. A. D., Taylor, M. R., & Banfield, J. F. (2006). Environmental risks of nanotechnology: National nanotechnology initiative funding, 2000–2004. *Environment Science Technology, 40*, 1401–1407. https://doi.org/10.1021/es0515708.

Hadrup, N., & Lam, H. R. (2014). Oral toxicity of silver ions, silver nanoparticles and colloidal silver – a review. *Regulatory Toxicology and Pharmacology, 68*, 1–7. https://doi.org/10.1016/j.yrtph.2013.11.002.

Hazeem, L. J., Bououdina, M., Rashdan, S., Brunet, L., Slomianny, C., & Boukherroub, R. (2016). Cumulative effect of zinc oxide and titanium oxide nanoparticles on growth and chlorophyll a content of *Picochlorum sp*. *Environmental Science and Pollution Research International, 23*(3), 2821–2830. https://doi.org/10.1007/s11356-015-5493-4.

He, D., Dorantes-Aranda, J. J, & Waite, T. D. (2012). Silver nanoparticle-algae interactions: oxidative dissolution, reactive oxygen species generation and synergistic toxic effects. *Environmental Science Technology, 46*(16), 8731–8738. https://doi.org/10.1021/es300588a.

Hillyer, J. F., & Albrecht, R. M. (2001). Gastrointestinal persorption and tissue distribution of differently sized colloidal gold nanoparticles. *Journal of Pharmaceutical Sciences, 90*, 1927–1936. https://doi.org/10.1002/jps.1143.Abs.

Hong, J., Peralta-Videa, J. R., Rico, C., Sahi, S., Viveros, M. N., Bartonjo, J., et al. (2014). Evidence of translocation and physiological impacts of foliar applied CeO nanoparticles on cucumber (*Cucumis sativus*) plants. *Environmental Science Technology, 48*, 4376–4385. https://doi.org/10.1021/es404931g.

Hsiao, I. L., & Huang, Y. J. (2011). Effects of various physicochemical characteristics on the toxicities of ZnO and TiO2 nanoparticles toward human lung epithelial cells. *Science of the Total Environment, 409*, 1219–1228. https://doi.org/10.1016/j.scitotenv.2010.12.033.

Hund-Rinke, K., Schlich, K., & Klawonn, T. (2012). Influence of application techniques on the ecotoxicological effects of nanomaterials in soil. *Environmental Sciences Europe, 24*(1), 30. http://dx.doi.org /https://doi.org/10.1186/2190-4715-24-30.

Hussain, S. M., Hess, K. L., Gearhart, J. M., Geiss, K. T, & Schlager, J. J. (2005). In vitro toxicity of nanoparticles in BRL 3A rat liver cells. *Toxicology in Vitro, 19*, 975 –983. https://doi.org/10.1016/j.tiv.2005.06.034.

Iannitti, T., Capone, S., Gatti, A., Capitani, F., Cetta, F., & Palmieri, B. (2010). Intracellular heavy metal nanoparticle storage: progressive accumulation within lymph nodes with transformation from chronic inflammation to malignancy. *International Journal of Nanomedicine, 5*, 955–960. https://doi.org/10.2147/ijn.s14363.

Janata, J. (2008). Introduction: Modern topics in chemical sensing. *Chemical Reviews, 108*, 327–328. https://doi.org/10.1021/cr0680991.

Johnston, H., Pojana, G., Zuin, S., Jacobsen, N. R, Møller, P., Loft, S., et al. (2012). Engineered nanomaterial risk. Lessons learnt from completed nanotoxicology studies: Potential solutions to current and future challenges. *Critical Reviews in Toxicology, 43*(1), 1–20. http://dx.doi.org /https://doi.org/10.3109/10408444.2012.738187.

Johnston, H. J., Hutchison, G., Christensen, F. M., Peters, S., Hankin, S., & Stone, V. (2010). A review of the in vivo and in vitro toxicity of silver and gold particulates: particle attributes and biological mechanisms responsible for the observed toxicity. *Critical Reviews in Toxicology, 40*, 328–346. https://doi.org/10.3109/10408440903453074.

Kantiani, L., Llorca, M., Sanchi Sandaloval, J., Farre, M., & Barcelo, D. (2010). Emerging food contaminants: A review. *Analytical and Bioanalytical Chemistry, 398*(6), 2413–2427.https://doi.org/10.1007/s00216010-3944-9.

Karpeta-Kaczmarek, J., Kędziorski, A., Augustyniak-Jabłokow, M. A., Dziewięcka, M., & Augustyniak, M. (2018). Chronic toxicity of nanodiamonds can disturb development and reproduction of *Acheta domesticus* L. *Environmental Research, 166*, 602–609. https://doi.org/10.1016/j.envres.2018.05.027.

Kasemets, K., Ivask, A., Dubourguier, H., & Kahru, A. (2009). Toxicity of nanoparticles of ZnO, CuO and TiO2 to yeast *Saccharomyces cerevisiae*. *Toxicology in Vitro, 23*, 1116–1122. https://doi.org/10.1016/j.tiv.2009.05.015.

Kettler, K., Veltman, K., van de Meent, D., van Wezel, A., & Hendriks, A. J. (2014). Cellular uptake of nanoparticles as determined by particle properties, experimental conditions, and cell type. *Environmental Toxicology and Chemistry, 33*, 481–492. https://doi.org/10.1002/etc.2470.

Khlebtsov, N., & Dykman, L. (2011). Biodistribution and toxicity of engineered gold nanoparticles: a review of in vitro and in vivo studies. *Chemical Society Reviews, 40*, 1647–1671. https://doi.org/10.1039/c0cs00018c.

Khodaei, M., Meratian, M., Savabi, O., & Razavi, M. (2016). The effect of pore structure on the mechanical properties of titanium scaffolds. *Materials Letters, 171*, 308–311. https://doi.org/10.1016/j.matlet.2016.02.101.

Kim, S., Choi, J. E., Choi, J., Chung, K. H., Park, K., Yi, J., et al. (2009). Oxidative stress-dependent toxicity of silver nanoparticles in human hepatoma cells. *Toxicology in Vitro, 23*, 1076–1084. https://doi.org/10.1016/j.tiv.2009.06.001.

Kisin, E. R., Murray, A. R, Keane, M. J, Shi, X. C, Schwegler-Berry, D., Gorelik, O., et al. (2007). Single-walled carbon nanotubes: Geno- and cytotoxic effects in lung fibroblast V79 cells. *Journal of Toxicology and Environmental Health, Part A, 70* (24), 2071–2079. https://doi.org/10.1080/15287390701601251.

Klaine, S. J., Alvarez, P. J. J., Batley, G. E., Fernandes, T. F., Handy, R. D., Lyon, D. Y., et al. (2008). Nanomaterials in the environment: Behavior, fate, bioavailability, and effects. *Environmental Toxicology and Chemistry, 27*, 1825–1851. https://doi.org/10.1897/08-090.1.

Kohler, A. R., Som, C., Helland, A., & Gottschalk, F. (2008). Studying the potential release of carbon nanotubes throughout the application life cycle. *Journal of Cleaner Production, 16*, 927–937. https://doi.org/10.1016/j.jclepro.2007.04.007.

Konieczny, P., Goralczyk, A. G., Szmyd, R., et al. (2013). Effects triggered by platinum nanoparticles on primary keratinocytes. *International Journal of Nanomedicine, 8*, 3963–3975. https://doi.org/2147/IJN.S49612.

Kumari, M., Khan, S. S, Pakrashi, S., Mukherjee, A., & Chandrasekaran, N. (2011). Cytogenetic and genotoxic effects of zinc oxide nanoparticles on root cells of *Allium cepa*. *Journal of Hazardous Materials, 190*, 613–621. https://doi.org/10.1016/j.jhazmat.2011.03.095.

Kumari, M., Mukherjee, A., & Chandrasekaran, N. (2009). Genotoxicity of silver nanoparticles in *Allium cepa*. *Science of the Total Environment, 407*, 5243–5246. https://doi.org/10.1016/j.scitotenv.2009.06.024

Laban, G., Nies, L. F., Turco, R. F., Bickham, J. W., & Sepulveda, M. S. (2010). The effects of silver nanoparticles on fathead minnow (*Pimephales promelas*) embryos. *Ecotoxicology, 19*(1), 185–195. https://doi.org/10.1007/s10646-009-0404-4.

Lam, C., James, J. T., McCluskey, R., & Hunter R. L. (2004). Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intractracheal instillation. *Toxicological Sciences, 77*(1), 126–134. https://doi.org/10.1093/toxsci/kfg243.

Landsiedel, R., Fabian, E., Ma-Hock, L., van Ravenzwaay, B., Wohlleben, W., Wiench, K., et al. (2012). Toxico-/biokinetics of nanomaterials. *Archives of Toxicology, 86*, 1021–1060. https://doi.org/10.1007/s00204-012-0858-7.

Leblanc, M., & Lbouabi, M. (1988). Native silver mineralization along a rodingite tectonic contact between serpentinite and quartz diorite (Bou-Azzer, Morocco). *Economic Geology, 83*(7), 1379–1391. https://doi.org/10.2113/gsecongeo.83.7.1379.

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, & Soil Pollution, 224*(11). https://doi.org/10.1007/s11270-013-1668-0.

Levard, C., Hotze, E. M., Lowry, G. V., & Brown Jr., G. E. (2012). Environmental transformations of silver nanoparticles: Impact on stability and toxicity. *Environmental Science & Technology, 46*, 6900–6914. https://doi.org/10.1021/es2037405.

Li, X., Liu, W., Sun, L., Aifantis, K. E, Yu, B., Fan, Y., et al. (2015). Effects of physicochemical properties of nanomaterials on their toxicity. *Journal of Biomedical Materials Research Part A, 103*, 2499–2507. https://doi.org/10.1002/jbm.a.35384.

Lin, D. H., & Xing, B. S. (2007). Phytotoxicity of nanoparticles: inhibition of seed germination and root growth. *Environmental Pollution, 150*, 243–250. https://doi.org/10.1016/j.envpol.2007.01.016.

Lin, S. J., Reppert, J., Hu, Q., Hudson, J. S., Reid, M. L., Ratnikova, T. A., et al. (2009). Uptake, translocation, and transmission of carbon nanomaterials in rice plants. *Small, 5*, 1128–1132. https://doi.org/10.1002/smll.200801556.

Lin, Y. C., Wu, K. T., Lin, Z. R., Perevedentseva, E., Karmenyan, A., Lin, M. D., et al. (2016). Nanodiamond for biolabelling and toxicity evaluation in the zebrafish embryo in vivo. *Journal of Biophotonics, 9*(8), 827–836. https://doi.org/10.1002/jbio.201500304.

Lin, Z. M., Monteiro-Riviere, N. A., & Riviere, J. E. (2015). Pharmacokinetics of metallic nanoparticles. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 7*, 189–217. https://doi.org/10.1002/wnan.1304.

Lindberg, H. K., Falck, G. C., Suhonen, S., Vippola, M., Vanhala, E., Catalán J., et al. (2009). Genotoxicity of nanomaterials: DNA damage and micronuclei induced by carbon nanotubes and graphite nanofibres in human bronchial epithelial cells in vitro. *Toxicology Letters, 186*(3), 166–173. https://doi.org/10.1016/j.toxlet.2008.11.019.

Lippmann, M. (1990). Effects of fiber characteristics on lung deposition, retention, and disease. *Environmental Health Perspectives, 88*, 311–317 (1990). https://doi.org/10.1289/ehp.9088311.

Lok, CN., Ho, CM., Chen, R., He, Q. Y., Yu, W. Y., Sun, H., et al. (2006). Proteomic analysis of the mode of antibacterial action of silver nanoparticles. *Proteome Research, 5*(4): 916–924. https://doi.org/10.1021/pr0504079.

Lovern, S. B., & Klaper, R. (2006). Daphnia magna mortality when exposed to titanium dioxide and fullerene (C60) nanoparticles. *Environmental Toxicology and Chemistry, 25*(4): 1132–1137. https://doi.org/10.1897/05-278r.1.

Lu, R., Mao, J. W., Gao, J. J., Su, H. M., & Zheng, J. H. (2012). Geological characteristics and occurrence of silver in Xiabao Ag-Pb-Zn deposit, Lengshuikeng ore field, Jiangxi Province. East China. *Acta Petrologica Sinica, 28*(1), 105–121 (2012). https://doi.org/10.1007/s00126-014-0521-8.

Magaye, R., Zhao, J., Bowman, L., & Ding, M. (2012). Genotoxicity and carcinogenicity of cobalt-, nickel- and copper-based nanoparticles. *Experimental and Therapeutic Medicine, 4*, 551–561. https://doi.org/10.3892/etm.2012.656.

Manusadzianas, L., Caillet, C., Fachetti, L., Gylyte, B., Grigutyte, R., Jurkoniene, S., et al. (2012). Toxicity of copper oxide nanoparticle suspensions to aquatic biota. *Environmental Toxicology and Chemistry, 31*(1), 108–114. https://doi.org/10.1002/etc.715.

Marcon, L., Riquet, F., & Szunerits, S. (2010). Cellular and in vivo toxicity of functionalized nanodiamond in *Xenopus* embryos. *Journal of Materials Chemistry, 20*, 8064–8069. https://doi.org/10.1039/c0jm01570a.

Markides, H., Rotherham, M., & El Haj, A. J. (2012). Biocompatibility and toxicity of magnetic nanoparticles in regenerative medicine. *Journal of Nanomaterials*, 614094. https://doi.org/10.1155/2012/614094.

Melegari, S. P., Perreault, F., Costa, R. H. R., Popovic, R., & Matias, W. G. (2013). Evaluation of toxicity and oxidative stress induced by copper oxide nanoparticles in the green alga *Chlamydomonas reinhardtii*. *Aquatic Toxicology, 142–143*(4), 431–440. https://doi.org/10.1016/j.aquatox.2013.09.015.

Melnik, E. A., Buzulukov, Y. P., Demin, V. F., Demin, V. A., Gmoshinski, I. V., Tyshko, N. V., et al. (2013). Transfer of silver nanoparticles through the placenta and breast milk during in vivo experiments on rats. *Acta Naturae, 5*, 107–115.

Mendonça, E., Diniz, M., Silva, L., Peres, I., Castro, L., Correia, J. B., et al. (2011). Effects of diamond nanoparticle exposure on the internal structure and reproduction of *Daphnia magna*. *Journal of Hazardous Materials, 186*(1), 265–271. https://doi.org/10.1016/j.jhazmat.2010.10.115.

Mittal, S., & Pandey, A. K. (2014). Cerium oxide nanoparticles induced toxicity in human lung cells: Role of ROS mediated DNA damage and apoptosis. *Biomedical Research International*, 891934. https://doi.org/10.1155/2014/891934.

Mukherjee, A., Peralta-Videa, J. R., Bandyopadhyay, S., Rico, C. M., Zhao, L., & Gardea-Torresdey, J. L. (2014). Physiological effects of nanoparticulate ZnO in green peas (*Pisum sativum* L.) cultivated in soil. *Metallomics, 6*, 132–138. https://doi.org/10.1039/c3mt00064h.

Munk, M., Brandao, H. M., Nowak, S., Mouton, L., Gern, J. C., Guimaraes, A.S., et al. (2015). Direct and indirect toxic effects of cotton-derived cellulose nanofibres on filamentous green algae. *Ecotoxicology and Environmental Safety, 122*, 399–405. https://doi.org/10.1016/j.ecoenv.2015.09.001.

Navarro, E., Baun, A., Behra, R., Hartmann, N. B., Filser, J., Miao, A. J., et al. (2008). Environmental behavior and ecotoxicity of engineered nanoparticles to algae, plants, and fungi. *Ecotoxicology, 17*(5), 372–386. https://doi.org/10.1007/s10646-008-0214-0.

Nemmar, A., Beegam, S., Yuvaraju, P., Yasin, J., Tariq, S., Attoub, S., et al. (2016). Ultrasmall superparamagnetic iron oxide nanoparticles acutely promote thrombosis and cardiac oxidative stress and DNA damage in mice. *Particle and Fibre Toxicology, 13*, 22. https://doi.org/10.1186/s12989-016-0132-x.

Nogueira, P. F., Nakabayashi, D., & Zucolotto, V. (2015). The effects of graphene oxide on green algae *Raphidocelis subcapitata*. *Aquatic Toxicology, 166*, 29–35. https://doi.org/10.1016/j.aquatox.2015.07.001.

Ojea-Jimenez, I., Garcia-Fernandez, L., Lorenzo, J., & Puntes, V. F. (2012). Facile preparation of cationic gold nanoparticle-bioconjugates for cell penetration and nuclear targeting. *ACS Nano, 6*, 7692–7702. https://doi.org/10.1021/nn3012042.

Osbaldeston, T. A., & Wood, R. P. A. (2000). Dioscorides De Materia Medica: Being an Herbal with Many Other Medicinal Materials Written in Greek in the First Century of the Common Era; a New Indexed Version in Modern English, pp. 2–11. Johannesburg: IBIDIS.

Ouyang, S., Hu, X., & Zhou, Q. (2015). Envelopment–Internalization Synergistic Effects and Metabolic Mechanisms of Graphene Oxide on Single-Cell *Chlorella vulgaris* are Dependent on the Nanomaterial Particle Size. *ACS Applied Materials & Interfaces, 7*, 18104–18112. https://doi.org/10.1021/acsami.5b05328.

Oyabu, T., Ogami, A., Morimoto, Y., Shimada M., Lenggoro, W., Okuyama, K., et al. (2007). Biopersistence of inhaled nickel oxide nanoparticles in rat lung. *Inhalation Toxicology, 19 (Suppl 1)*, 55–58. https://doi.org/10.1080/08958370701492995.

Pakrashi, S., Jain, N., Dalai, S., Jayakumar, J., Chandrasekaran, P., Ashok, M., et al. (2014). In vivo genotoxicity assessment of titanium dioxide nanoparticles by *Allium cepa* root tip assay at high exposure concentrations. *PLoS One, 9*, 12. https://doi.org/10.1371/journal.pone.0087789.

Park, K. H., Chhowalla, M., Iqbal, Z., & Sesti, F. (2003). Single-walled carbon nanotubes are a new class of ion channel blockers. *Journal of Biological Chemistry, 278*, 50212–50216. http://dx.doi.org/ https://doi.org/10.1074/jbc.m310216200.

Petersen, E. J, Henry, T. B., Zhao, J., MacCuspie, R. I., Kirschling, T. L., Dobrovolskaia, M. A., et al. (2014). Identification and avoidance of potential artifacts and misinterpretations in nanomaterial ecotoxicity measurements. *Environmental Science Technology, 48*, 4226–4246. https://doi.org/10.1021/es4052999.

Podila, R., & Brown, J. M. (2013). Toxicity of engineered nanomaterials: A physicochemical perspective. *Journal of Biochemical and Molecular Toxicology, 27*, 50–55. https://doi.org/10.1002/jbt.21442.

Pokhrel, L. R., & Dubey, B. (2013). Evaluation of developmental responses of two crop plants exposed to silver and zinc oxide nanoparticles. *Science of the Total Environment, 452*, 321–332. https://doi.org/10.1016/j.scitotenv.2013.02.059.

Poland, C. A., Duffin, R., Kinloch, I., Maynard, A., Wallace, W. A., Seaton, A., et al. (2008). Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. *Nature Nanotechnology, 3*, 423–428. https://doi.org/10.1038/nnano.2008.111.

Pretti, C., Oliva, M., Pietro, R. D., Monni, G., Cevasco, G., Chiellini, F., et al. (2014). Ecotoxicity of pristine graphene to marine organisms. *Ecotoxicology and Environmental Safety, 101*, 138–145. https://doi.org/10.1016/j.ecoenv.2013.11.008.

Rahman, M. F., Wang, J., Patterson, T. A., Saini, U. T., Robinson, B. L., Newport, G. D., et al. (2009). Expression of genes related to oxidative stress in the mouse brain after exposure to silver nanoparticles. *Toxicology Letters, 187*, 15–21. https://doi.org/10.1016/j.toxlet.2009.01.020.

Rico, C. M., Barrios, A. C., Tan, W., Rubenecia, R., Lee, S. C., Varela-Ramirez, A., et al. (2015). Physiological and biochemical response of soil-grown barley (*Hordeum vulgare* L.) to cerium oxide nanoparticles. *Environmental Science and Pollution Research, 22*, 10551–10558. https://doi.org/10.1007/s11356-015-4243-y.

Rico, C. M., Lee, S. C., Rubenecia, R.,Mukherjee, A.,Hong, J., Peralta-Videa, J. R., et al. (2014). Cerium oxide nanoparticles impact yield and modify nutritional parameters in wheat (*Triticum aestivum* L.). *Journal of Agricultural and Food Chemistry, 62*, 9669–9675. https://doi.org/10.1021/jf503526r.

Rico, C. M., Morales, M. I., Barrios, A. C., McCreary, R., Hong, J., & Lee, W. Y., et al. (2013). Effect of cerium oxide nanoparticles on the quality of rice (Oryza sativa L.) grains. *Journal of Agricultural and Food Chemistry, 61*, 11278–11285. https://doi.org/10.1021/jf404046v.

Roberts, A. P., Mount, A. S., Seda, B., Souther, J., Qiao, R., Lin, S., et al. (2007). In vivo biomodification of lipid-coated carbon nanotubes by *Daphnia magna*. *Environmental Science Technology, 41*(8), 3025–3029. https://doi.org/10.1021/es062572a.

Roiter, Y., Ornatska, M., Rammohan, A. R., Balakrishnan, J., Heine, D. R., & Minko, S. (2009). Interaction of lipid membrane with nanostructured surfaces. *Langmuir, 25*, 6287–6299. https://doi.org/10.1021/la900119a.

Roncati, L., Gatti, A. M., Capitani, F., Barbolini, G., Maiorana, A., & Palmieri, B. (2015a). Heavy metal bioaccumulation in an atypical primitive neuroectodermal tumor of the abdominal wall. *Ultrastructural Pathology, 39*, 286–292. https://doi.org/10.3109/01913123.2015.1013655.

Roncati, L., Gatti, A. M., Pusiol, T., Barbolini, G., Maiorana, A., & Montanari, S. (2015b). ESEM detection of foreign metallic particles inside ameloblastomatous cells. *Ultrastructural Pathology, 39*, 329–335. https://doi.org/10.3109/01913123.2015.1042608.

Sabo-Attwood, T., Unrine, J. M., Stone, J. W., Murphy, C. J., Ghoshroy, S., Blom, D., et al. (2012). Uptake, distribution and toxicity of gold nanoparticles in tobacco (*Nicotiana xanthi*) seedlings. *Nanotoxicology, 6*, 353–360 (2012). https://doi.org/10.3109/17435390.2011.579631.

Salatin, S., Dizaj, S. M., & Khosroushahi, A. Y. (2015). Effect of the surface modification, size, and shape on cellular uptake of nanoparticles. *Cell Biology International, 39*, 881–890. https://doi.org/10.1002/cbin.10459.

Sarhan, O. M. M., & Hussein, R. M. (2014). Effects of intraperitoneally injected silver nanoparticles on histological structures and blood parameters in the albino rat. *International Journal of Nanomedicine, 9*, 1505–1517. https://doi.org/10.2147/ijn.s56729.

Saunders, J. A., Unger, D. L., Kamenov, G. D., Fayek, M., Hames, W. E., & Utterback, W. C. (2008). Genesis of middle miocene yellowstone hotspot-related bonanza epithermal Au-Ag

deposits, Northern Great Basin, USA. Mineralium Deposita, 43(7), 715–734. https://doi.org/10.1007/s00126-008-0201-7.

Savi, M., Rossi, S., Bocchi, L., Gennaccaro, L., Cacciani, F., Perotti, A., et al. (2014). Titanium dioxide nanoparticles promote arrhythmias via a direct interaction with rat cardiac tissue. *Particle Fibre and Toxicology, 11*, 63. https://doi.org/10.1186/s12989-014-0063-3.

Schlinkert, P., Casals, E., Boyles, M., Tischler, U., Hornig, E., Tran, N., et al. (2015). The oxidative potential of differently charged silver and gold nanoparticles on three human lung epithelial cell types. *Journal of Nanobiotechnology, 13*(1). https://doi.org/10.1186/s12951-014-0062-4.

Scott-Fordsmand, J. J., Pozzi-Mucelli, S., Tran, L., Aschberger, K., Sabella, S., Vogel, U., et al. (2014). A unified framework for nanosafety is needed. *Nano Today, 9*(5), 546–549. https://doi.org/10.1016/j.nantod.2014.07.001.

Semmler-Behnke, M., Lipka, J., Wenk, A., Hirn, S., Schäffler, M., Tian, F., et al. (2015). Size dependent translocation and fetal accumulation of gold nanoparticles from maternal blood in the rat. *Particle and Fibre Toxicology, 11*, 33. https://doi.org/10.1186/s12989-014-0033-9.

Servin, A. D., Morales, M. I., Castillo-Michel, H., Hernandez-Viezcas, J. A., Munoz, B., Zhao, L., et al. (2013). Synchrotron verification of TiO accumulation in cucumber fruit: A possible way of TiO_2 nanoparticle transfer from soil into the food chain. *Environmental Science & Technology, 47*, 11592–11598. https://doi.org/10.1021/es403368j.

Sevcu, A., El-Temsah, Y. S., Joner, E. J., Cernik, M. (2011). Oxidative stress induced in microorganisms by zero-valent iron nanoparticles. *Microbes and Environments, 26*(4), 271–281. https://doi.org/10.1264/jsme2.ME11126.

Shaymurat, T., Gu, J. X., Xu, C. S., Yang, Z., Zhao, Q., Liu, Y., et al. (2012). Phytotoxic and genotoxic effects of ZnO nanoparticles on garlic (*Allium sativum* L.): A morphological study. *Nanotoxicology, 6*, 241–248. https://doi.org/10.3109/17435390.2011.570462.

Shen, C. X., Zhang, Q. F., Li, J. A., Bi, F. C., Yao, N. (2010). Induction of programmed cell death in Arabidopsis and rice by single-wall carbon nanotubes. *American Journal of Botany, 97*, 1602–1609. https://doi.org/10.3732/ajb.1000073.

Shoults-Wilson, W. A., Reinsch, B. C., Tsyusko, O. V., Bertsch, P. M., Lowry, G. V., & Unrine, J. M. (2011). Role of particle size and soil type in toxicity of silver nanoparticles to earthworms. *Soil Science Society of America Journal, 75*(2), 365–377. https://doi.org/10.2136/sssaj2010.0127nps.

Sighinolfi, G. L., Artoni, E., Gatti, A. M., Corsi, L. (2016). Carcinogenic potential of metal nanoparticles in BALB/3T3 cell transformation assay. *Environmental Toxicology, 31*, 509–519 (2016). https://doi.org/10.1002/tox.22063.

Silva, R. M., Anderson, D. S., Franzi, L. M., Peake, J. L., Edwards, P. C., Van Winkle, L. S., et al. (2015). Pulmonary effects of silver nanoparticle size, coating, and dose over time upon intratracheal instillation. *Toxicological Sciences, 144*, 151–162 (2015). https://doi.org/10.1093/toxsci/kfu265.

Silva, T., Pokhrel, L. R., Dubey, B., Tolaymat, T. M., Maier, K. J., & Liu, X. (2014). Particle size, surface charge and concentration dependent ecotoxicity of three organo-coated silver nanoparticles: Comparison between general linear model-predicted and observed toxicity. *Science of the Total Environment, 468–469*, 968–976.https://doi.org/10.1016/j.scitotenv.2013.09.006.

Simon-Deckers, A., Loo, S., Mayne-L'hermite, M., Herlin-Boime, N., Menguy, N., Reynaud, C., et al. (2009). Size-composition-and shape-dependent toxicological impact of metal oxide nanoparticles and carbon nanotubes toward bacteria. *Environmental Science & Technology, 43*, 8423–8429. https://doi.org/10.1021/es9016975.

Simonsen, L. O., Harbak, H., & Bennekou, P. (2012). Cobalt metabolism and toxicology—a brief update. *Science of the Total Environment, 432*, 210–215. https://doi.org/10.1016/j.scitotenv.2012.06.009.

Snyder, R. W., Fennell, T. R., Wingard, C. J., Mortensen, N. P., Holland, N. A., Shannahan, J. H., et al. (2015). Distribution and biomarker of carbon-14 labeled fullerene C-60 (C-14(U) C-60) in pregnant and lactating rats and their offspring after maternal intravenous exposure. *Journal of Applied Toxicology, 35*, 1438–1451. https://doi.org/10.1002/jat.3177.

Sohn, E. K., Chung, Y. S., Johari, S. A., Kim, T. G., Kim, J. K., Lee, J. H., et al. (2015). Acute toxicity comparison of single-walled carbon nanotubes in various freshwater organisms. *Biomed Research Internatinal, 2015*, 1–7. https://doi.org/10.1155/2015/323090.

Sonavane, G., Tomoda, K., & Makino, K. (2008). Biodistribution of colloidal gold nanoparticles after intravenous administration: Effect of particle size. *Colloidal and Surfaces B: Biointerfaces, 66*, 274–280. https://doi.org/10.1016/j.colsurfb.2008.07.004.

Song, H., Wang, G., He, B., Li, L., Li, C., Lai, Y., et al. (2012). Cationic lipid-coated PEI/DNA polyplexes with improved efficiency and reduced cytotoxicity for gene delivery into mesenchymal stem cells. *International Journal of Nanomedicine, 7*, 4637–4648. https://doi.org/10.2147/ijn.s33923.

Soto, K., Garza, K. M., & Murr, L. E. (2007). Cytotoxic effects of aggregated nanomaterials. *Acta Biomaterialia, 3*, 351–358. https://doi.org/10.1016/j.actbio.2006.11.004.

Stampoulis, D., Sinha, S. K., & White, J. C. (2009). Assay-dependent phytotoxicity of nanoparticles to plants. *Environmental Science & Technology, 43*, 9473–9479. https://doi.org/10.1021/es901695c.

Stewart, M. E., Anderton, C. R., Thompson, L. B., Maria. J., Gray, S. K., Rogers, J. A, et al. (2008). Nanostructured plasmonic sensors. *Chemical Reviews, 108*, 494–521. https://doi.org/10.1021/cr068126n.

Suman, T. Y., Radhika Rajasree, S. R., & Kirubagaran, R. (2015). Evaluation of zinc oxide nanoparticles toxicity on marine algae *Chlorella vulgaris* through flow cytometric, cytotoxicity and oxidative stress analysis. *Ecotoxicology and Environmental Safety, 113*, 23–30. https://doi.org/10.1016/j.ecoenv.2014.11.015.

Sun, J., Wang, S. C., Zhao, D., Hun, F. H., Weng, L., & Liu, H. (2011). Cytotoxicity, permeability, and inflammation of metal oxide nanoparticles in human cardiac microvascular endothelial cells. *Cell Biology and Toxicoogy, 27*(5), 333–342. https://doi.org/10.1007/s10565-011-9191-9.

Sung, J. H., Ji, J. H., Yun, J. U., Kim, D. S., Song, M. Y., Jeong, J., et al. (2008). Lung function changes in Sprague-Dawley rats after prolonged inhalation exposure to silver nanoparticles. *Inhalation Toxicology, 20*, 567–74. https://doi.org/10.1080/08958370701874671.

Sutherland, W. J., Clout, M., Côté, I. M., Daszak, P., Depledge, M. H., Fellman, L., et al. (2010). A horizon scan of global conservation issues for 2010.*Trends in Ecology & Evolution, 25*(1), 1–7. https://doi.org/10.1016/j.tree.2009.10.003.

Takenaka, S., Karg, E., Roth, C., Schulz, H., Ziesenis, A., Heinzmann, U., et al. (2001). Pulmonary and systemic distribution of inhaled ultrafine silver particles in rats. *Environmental Health Perspectives, 4*, 547–551. https://doi.org/10.1289/ehp.01109s4547.

Talkar, S., Dhoble, S., Majumdar, A., & Patravale, V. (2018). Transmucosal nanoparticles: Toxicological overview. *Cellular and Molecular Toxicology of Nanoparticles, Advances in Experimental Medicine and Biology, 1048*, 37–57.https://doi.org/10.1007/978-3-319-72041-8-3.

Tao, X., Li, C., Zhang, B., & He, Y. (2016). Effects of aqueous stable fullerene nanocrystals (nC_{60}) on the food conversion from Daphnia magna to Danio rerio in a simplified freshwater food chain. *Chemosphere, 145*, 157–162. https://doi.org/10.1016/j.chemosphere.2015.11.036.

Templeton, R. C., Ferguson, P. L., Washburn, K. M., Scrivens, W. A., & Chandler, G. T. (2006). Life-cycle effects of single-walled carbon nanotubes (SWNTs) on an estuarine meiobenthic copepod. *Environmental Science & Technology, 40*, 7387–7393. https://doi.org/10.1021/es060407p.

Teske, S. S., & Detweiler, C. S. (2015). The biomechanisms of metal and metal-oxide nanoparticles interactions with cells. *International Journal of Environmental Research and Public Health, 12*, 1112–1134. https://doi.org/10.3390/ijerph120201112.

Thuesombat, P., Hannongbua, S., Akasit, S., & Chadchawan, S. (2014). Effect of silver nanoparticles on rice (*Oryza sativa* L. cv. KDML 105) seed germination and seedling growth. *Ecotoxicology and Environmental Safety, 104*, 302–309. https://doi.org/10.1016/j.ecoenv.2014.03.022.

Trickler, W. J., Lantz, S. M., Murdock, R. C., Schrand, A. M., Robinson, B. L., Newport, G. D., et al. (2010). Silver nanoparticle induced blood-brain barrier inflammation and increased permeability in primary rat brain microvessel endothelial cells. *Toxicological Science, 118*, 160–170. https://doi.org/10.1093/toxsci/kfq244.

Tripathi, D. K., Singh, S., Singh, S., Pandey, R., Singh, V. P., Sharma, N. C., et al. (2017). An overview on manufactured nanoparticles in plants: uptake, translocation, accumulation and phytotoxicity. *Plant Physiology and Biochemistry, 110*, 2–12. https://doi.org/10.1016/j.plaphy.2016.07.030.

Tuominen, M., Schultz, E., & Sillanpaa, M. (2013). Toxicity and stability of silver nanoparticles to the green alga. *Pseudokirchneriella subcapitata* in boreal freshwater samples and growth media. *Nanomaterials and Environment, 1*, 48–57. https://doi.org/10.2478/nanome-2013-0004.

Vo-Dinh, T. (2007). Nanotechnology in biology and medicine: Methods, devices, and applications. In T. Vo-Dinh (Ed.). Boca Raton, FL: CRC Press. ISBN-13: 978-0849329494.

Wang, Q., Ebbs, S. D., Chen, Y. S., & Ma, X. (2013). Trans-generational impact of cerium oxide nanoparticles on tomato plants. *Metallomics, 5*, 753–759. https://doi.org/10.1039/c3mt00033h.

Wen, H., Dan, M., Yang, Y., Lyu, J., Shao, A., Cheng, X., et al. (2017). Acute toxicity and genotoxicity of silver nanoparticle in rats. *PLoS One, 12*, e0185554. https://doi.org/10.1371/journal.pone.0185554.

Wick, P., Manser, P., Limbach, L., Dettlaff-Weglikowska, U., Krumeich, F., Roth, S., et al. (2007). The degree and kind of agglomeration affect carbon nanotube cytotoxicity. *Toxicology Letters, 168*, 121–131. https://doi.org/10.1016/j.toxlet.2006.08.019.

Wisniak, J. (2004). Dyes from antiquity to synthesis. *Indian Journal of History of Science, 39*(1), 75–100.

Wu, Y., Zhou, Q., Li, H., Liu, W., Wang, T., & Jiang, G. (2010). Effects of silver nanoparticles on the development and histopathology biomarkers of Japanese medaka (Oryzias latipes) using the partial-life test. *Aquatic Toxicology, 100*(2), 160–167. https://doi.org/10.1016/j.aquatox.2009.11.014.

Xiang, L., Zhao, H. M., Li, Y. W., Huang, X. P., Wu, X. L., Zhai, T., Yuan, Y., et al. (2015). Effects of the size and morphology of zinc oxide nanoparticles on the germination of Chinese cabbage seeds. *Environmental Science and Pollution Research, 22*, 10452–10462. https://doi.org/10.1007/s11356-015-4172-9.

Xiao, X., Montaño, G. A., Edwards, T. L., Allen, A., Achyuthan, K. E., Polsky, R., et al. (2012). Surface charge dependent nanoparticle disruption and deposition of lipid bilayer assemblies. *Langmuir, 28*, 17396–403. https://doi.org/10.1021/la303300b.

Yadav, T., Mungray, A. A., & Mungray, A. K. (2014). Fabricated nanoparticles: current status and potential phytotoxic threats. In: D. M. Whitacre (Ed.), *Reviews of environmental contamination and toxicology*, Vol. 230. Springer, ISBN 978-3-319-04411-8.

Yang, L., & Watts, D. J. (2005). Particle surface characteristics may play an important role in phytotoxicity of alumina nanoparticles. *Toxicology Letters, 158*(2), 122–132. https://doi.org/10.1016/j.toxlet.2005.03.003.

Yin, L., Cheng, Y., Espinasse, B., Colman, B. P., Auffan, M., Wiesner, M., et al. (2011). More than the ions: The effects of silver nanoparticles on *Lolium multiflorum*. *Environmental Science & Technology, 45*(6), 2360–2367. https://doi.org/10.1021/es103995x.

Yoon, S. J., Kwak, J. I., Lee, W. M., Holden, P. A., & An, Y. J. (2014). Zinc oxide nanoparticles delay soybean development: a standard soil microcosm study. *Ecotoxicology and Environmental Safety*, *100*, 131–137. https://doi.org/10.1016/j.ecoenv.2013.10.014.

Yu, S. J., Yin, Y. G., & Liu, J. F. (2013). Silver nanoparticles in the environment. *Environmental Science: Processes & Impacts, 15*(1), 78–92. https://doi.org/10.1039/C2EM30595J.

Yu, X. H., Hong, F. S., & Zhang, Y. Q. (2016). Bio-effect of nanoparticles in the cardiovascular system. *Journal of Biomedical Materials Research Part A, 104*, 2881–2897. https://doi.org/10.1002/jbm.a.35804.

Zhang, Y., Ferguson, S. A., Watanabe, F., Jones, Y., Xu, Y., Biris, A. S., et al. (2013). Silver nanoparticles decrease body weight and locomotor activity in adult male rats. *Small, 9*(9–10), 1715–1720. https://doi.org/10.1002/smll.201201548.

Zhao, L. J., Peralta-Videa, J. R., Rico, C. M., Hernandez-Viezcas, J. A., Sun, Y., Niu, G., et al. (2014). CeO and ZnO nanoparticles change the nutritional qualities of cucumber (*Cucumis sativus*). *Journal of Agriculture and Food Chemistry, 62*, 2752–2759. https://doi.org/10.1021/jf405476u.

Zhao, L. J., Sun, Y. P., Hernandez-Viezcas, J. A., Hong, J., Majumdar, S., Niu, G., et al. (2015). Monitoring the environmental effects of CeO and ZnO nanoparticles through the life cycle of corn (*Zea mays*) plants and in situ mu-XRF mapping of nutrients in kernels. *Environmental Science & Technology, 49*, 2921–2928. https://doi.org/10.1021/es5060226.

Zhu, L., Chang, D. W., Dai, L., & Hong, Y. (2007). DNA damage induced by multiwalled carbon nanotubes in mouse embryonic stem cells. *Nano Letters, 7*, 3592–3597. https://doi.org/10.1021/nl071303v.

Zhu, S., Oberdörster, E., & Haasch, M. L. (2006). Toxicity of an engineered nanoparticle (fullerene, C_{60}) in two aquatic species, *Daphnia* and fathead minnow. *Marine Environmental Research, 62*(1), S5–S9. https://doi.org/10.1016/j.marenvres.2006.04.059.

Zuverza-Mena, N., Martínez-Fernández, D., Du, W., Hernandez-Viezcas, J. A., Bonilla-Bird, N., López-Moreno, M. L., et al. (2017). Exposure of engineered nanomaterials to plants: Insights into the physiological and biochemical responses—A review. *Plant Physiology and Biochemistry*, *110*, 236–264. https://doi.org/10.1016/j.plaphy.2016.05.037.