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Advances in Bioresearch

## REVIEW ARTICLE

# Exploring the current trends of crop Nanotoxicity: Balancing Sustainable Agriculture and Human Health

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**ABSTRACT**
*With the advancement of nanotechnology in agriculture has sparked interest in their potential benefits, such as enhancing crop yield, improving pest control, and facilitating nutrient delivery. However, concerns regarding their toxicity to both plants and humans have raised important questions about the safety and sustainability of these technologies. Plant's exposed surface provideshuge interfaces to the air and soil environment. Thus, nanoparticles (NPs) are adsorbed to the plant surfaces, taken up through nano- or micrometer-scale openings and are translocated within the plant body. Persistent nanoparticles associated with plants enter the human food chain. This review explores the current trends in crop nanotoxicology, focusing on the balance between advancing agricultural practices and ensuring human and environmental health. By examining recent studies on the impact of nanoparticles on soil health, plant physiology, and food safety, this review article Shows the interactions between nanomaterials and biological systems. Furthermore, we discuss the need for comprehensive risk assessments, regulatory frameworks, and innovative approaches to mitigate the risks of nanomaterial use in agriculture. This article concludes by emphasizing the importance of fostering a multidisciplinary approach to nanotoxicology research, which is crucial to achieving the goals of sustainable agriculture and safeguarding human health in the face of emerging agricultural technologies.*
***Keywords:*** *Nanotoxicology, metal nanoparticles, Ecotoxicology, particle size, surface charge*

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## INTRODUCTION

Particulate matter in atmosphere is defined as particles between 0.1 and 10 mm in size [1]. Approximately 25% of all particulate matter is based on carbon and associated with exhaust from all kinds of gas and coal engines [4]. Various metals are found in particulate fractions in areas close to heavy metal industries, with abundant vehicle traffic or along main wind directions [4]. Much is known about the composition and location of particulate matter, whereas it is difficult to get information about the detailed size distribution. Particulate matter is usually divided into particles with a 50% cut-off aerodynamic diameter of less than 10 mm (PM10), less than 2.5 mm (PM2.5) and ultrafine particles (UP) less than 0.2 mm [1]. Given that NPs are defined as particles with at least two dimensions below 100 nm (i.e. 0.1 mm), only the last category is interesting to the field of Nanotoxicology [1]. NPs are generated during combustion processes and diverse naturally occurring abiotic and biotic chemical processes. Their commercial production has increased steadily, because they are used in many novel applications (e.g. as catalysts, semiconductors, drug carriers and in cosmetics) and the development of additional novel materials is likely. Due to above mentioned reasons, the particle load of the atmosphere, aquatic environment will increase in the future. Particle sizes of inorganic materials, such as sulfate, ammonium, nitrate, chloride and organic compounds range from 50 nm to 2 mm, with an average size of approximately 100 nm [2]. The maximum platinum (Pt) concentration was found to be approximately 40

pg/$m^3$ in urban sites with high traffic volume. For medium traffic volumes, metallic fractions are typically below detection limits. Particles smaller than 100 nm make up 3–8% of particles under 2.5 mm, with higher concentrations in summer. In summer, 50% of particles are carbon-based (organic and elemental) and 50% inorganic (mainly sulfate and ammonium), while in winter, carbon increases to 70% and inorganic decreases to 30% [3]. Catalysts release small nanocrystalline Pt particles, which are attached to aluminium oxide carrier particles with a diameter that is generally bigger than 10 mm. It is also assumed that a small fraction of Pt particles are oxidized, therefore becoming soluble in water. In this state, the particles are more hazardous to organic systems. Extensive data already exists on human and environmental hazards and exposures to NPs during their production, use, and recycling, including prolonged worker exposure, local population and consumer risks, and potential emissions from waste treatment facilities.[4]. Some NPs have novel properties that may bypass normal human defenses, often causing lung effects and inflammation, though the severity, long-term impact, and role of NP type and concentration remain unclear. [4]. While NPs offer medical benefits, their potential health risks, behavior in humans and the environment, distribution across ecosystems, and degradation mechanisms remain insufficiently understood [5]. Therefore, a comprehensive re-examination of NPs and nanotechnology is needed for more accurate utilization and sustainable development. In this review, we enumerate the applications of nanotechnology related to human health, including industrial, agricultural, and medical aspects.

## ENVIRONMENTAL TOXICITY OF NANOPARTICLES

### Types of nanoparticles in toxicological studies

Studied particles can be divided into carbon-based, oxides, metals and semiconductors. The physical and chemical characteristics of NPs relevant for toxicity to biosystems are: (i) average size; (ii) element composition; (iii) surface area; (iv) porosity; (v) surface charge; (vi) hydrodynamic diameter; (vii) aggregation propensity, and also (viii) stability and (ix) coating with cellular or other constituents as shown in figure 1. Nanoparticles tend to aggregate, a behavior that decisively affects their bioavailability, transport and reactivity. $SiO_2$ and $TiO_2$ are among the most commonly applied NPs in industry, followed by other metal oxide particles [4]. Approximately half of the large number of studies dealing with $TiO_2$ enumerate the toxic effects, whereas the other half report either has noor positive effects. These controversial results can be explained, if the concentrations, different experimental setups and systems used are taken into account. Test concentrations range from 1 to 1000 mg/ml, which have to be compared with a value of approximately 1 mg/$m^3$ total amount of naturally occurring ultrafine matter in the environment. Thus, these studies address the rare situation where organisms might be exposed to an acute and high dose of NPs. Although metal NPs still constitute negligible fractions in the ultrafine matter, they are often studied owing to their expected biological interactions [5]. For health reasons, most interesting are platinum group metals, which are contained in traffic exhaust together with metals, such as Fe, Co, Al, Pb, Cd, Zn, which either naturally occur in particulate matter or are highly toxic at low concentrations. The total amount of these materials emitted to the environment is supposed to be quite low. However, in future, these elements can accumulate and can cause toxicity due to bioaccumulation. Cd in particular is known to be highly toxic. Silver (Ag)-NPs are exploited in many industrial applications due to their bactericidal activity [6].

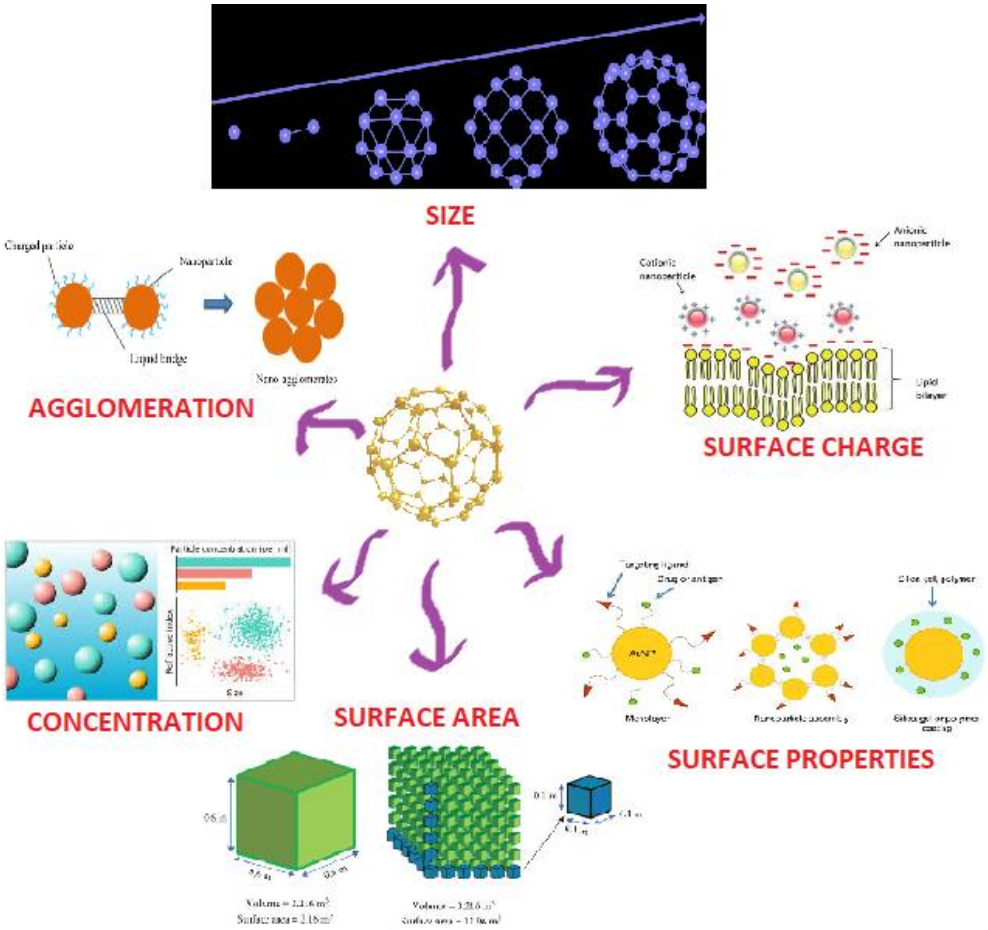


**Figure 1: The properties of nanoparticles that play role in toxicity issues:**

**Toxicokinetics of nanomaterials in plants**

There is no doubt that nanomaterials (NMs) are capable of delivering quality inputs into agricultural applications, but the doubt arises if those benefits far outweigh their negatives. Unlike certain other processes that involve fewer dynamic resources, interaction of nanomaterials (NMs) with plants is no trivial issue [7]. Given the reports on the negative effects of NMs on plants the possibility of affecting staple crops is not a theory anymore. Various adverse reactions have been reported in plants: Such as decreased growth, increased oxidative stress, chromosomal abnormalities, affected photosynthetic rates, disturbances in water transport and the water status of the plant, decline in the concentration of growth hormones such as IAA, metabolic disorders, mass intrusion in the transcriptional profile of a series of genes and increased susceptibility to natural toxins [8]. Depending on the experimental situation, the same NMs may indicate conflicting results. For instance, a researcher applied NMs biomanufacturer from Ag (Silver) to *Pennisetum glaucum*, this initially improved germination but later had a negative impact on seedling growth. A similar effect was reported in Ryegrass, Barley and Flax upon the application of Fe and Ag NMs too [9].

**BIOACCUMULATION AND DISTRIBUTION OF METAL-BASED NPS IN PLANTS**

Bioaccumulation factor (BAF) refers to the ratio of metal concentration in the plant tissue to its concentration in the environment. It is calculated to compare and analyze the differences of NPs uptake in higher plants. Investigations where separate root and shoot tissues were harvested from either in soil or hydroponic solution amended with NPs were selected to calculate tissue specific-BAFs [10]. Although direct comparisons across separate studies are still somewhat problematic, some interesting observations are evident. For example, as expected, the BAF in shoots and roots exposed to different strengths of Hoagland's solution amended with Ag NPs and cerium oxide nanoparticles ($CeO_2$ NPs) are higher than accumulation in plants grown in soil. Moreover, uptake of metal-based NPs in plants is influenced by nanoparticle size, as demonstrated in cucumber (*Cucumis sativus*) exposed to $CeO_2$ NPs (7 and 25 nm) [11], and annual ryegrass (*Lolium multifolrum*) exposed to Ag NPs (6 and 25 nm) as shown in figure 2 [11].

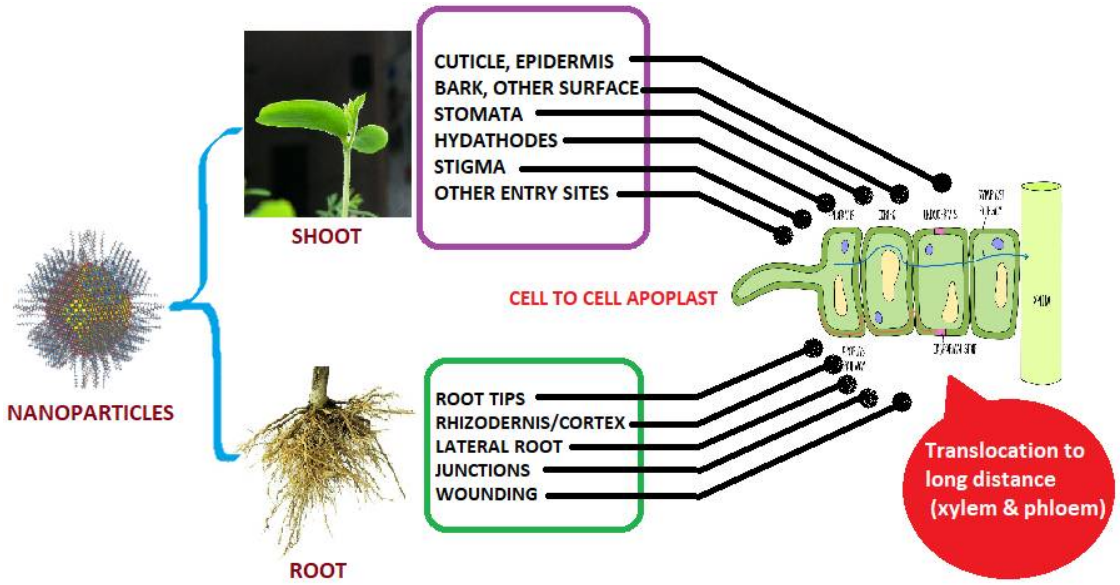


**Figure 2: Pathways of nanoparticles association, uptake and translocation in plants**

Interestingly, ZnO NPs (zinc oxide nanoparticles) seem to behave differently with regard to exposure medium [12]. In a study the BAF in both roots and shoots of perennial ryegrass (*Lolium perenne*) and velvet mesquite (*Prosopis julif lora-velutina*) are lower than that of edible crops (soybean, corn, wheat, and green peas) grown in soil.The impact of NPs on plants depends on their transport, translocation, and accumulation in plant tissues. Transmission electron microscopy (TEM) is commonly used to detect NPs in plant cells. Metal-based NPs in soil or medium can enter roots through the epidermis, move through the cortex, and distribute to stems and leaves via the xylem and phloem [13]. For instance, $CeO_2$ NPs in corn roots were mainly transported via the apoplastic route, while lanthanum oxide NPs followed a similar pattern in cucumber. Fluorescent-labeled mesoporous silica NPs showed accumulation in the Casparian strip, preventing upward translocation. Superparamagnetic iron oxide NPs in soybean and ZnO NPs in corn moved through xylem, while Au NPs were found in both phloem and xylem in cottonwood plant, suggesting both pathways are involved in NPs transport. In agriculture, NPs are used as pesticides and herbicides for their antimicrobial properties, often applied via foliar spray. NPs absorbed through leaves can be redistributed to roots via phloem vessels. For example, $CeO_2$ and CaO NPs translocated to roots in cucumber and groundnut after foliar application. However, $CeO_2$ NPs did not penetrate cucumber root cells in hydroponic conditions, only aggregating on the root surface [14]. Studies have shown that CuO and $TiO_2$ NPs localized in plant cell spaces, such as vacuoles and chloroplasts in wheat and in root cytoplasm of maize. NiO NPs in tomato roots were found in intercellular spaces or vacuoles though confirmation was not obtained. While the translocation of trace metal oxide NPs is well-studied, the information on the distribution of REE NPs remains unclear. Micro X-ray fluorescence (μXRF) and X-ray absorption spectroscopy (XAS) can also trace the distribution of metal elements in plants [15]. For example, ZnO NPs in velvet mesquite accumulated in the root cortex and leaf vascular tissues, and $CeO_2$ NPs were found in rice root transport systems. The size of NPs also affects their accumulation location; smaller 14 nm $TiO_2$ NPs accumulate in rice and rapeseed root parenchyma while larger 25 nm NPs are in the root vascular cylinder. Crystal phase also matters—anatase-$TiO_2$ NPs accumulate in cucumber xylem while rutile-$TiO_2$ NPs are found in the phloem [16].

## BIOTRANSFORMATION OF METAL-BASED NPS INSIDE PLANTS

Metal-based NPs can release ions into the soil or medium so experiments assessing the effects of NPs on plants must include ion controls to properly evaluate the role of particle size and dissolution in plant damage. X-ray absorption spectroscopy (XAS) can help assess biotransformation of NPs in plants. For instance, X-ray absorption near edge structure (XANES) analysis of alfalfa exposed to Au(III) showed conversion to Au in both roots and shoots, confirmed by TEM and X-ray EDS [17]. Studies using XAS have also revealed metal speciation in plants, such as Ce (IV) in soybean tissues exposed to $CeO_2$ NPs, while no ZnO NPs were found indicating significant transformation of zinc. This study shows that nanotoxicity can arise from either the NPs themselves or metal ions released from them. ZnO NPs, for example, can release up to 19% of Zn ions at pH 7.5 which can explain the absence of ZnO NPs in planta in this study [18]. Other studies have found $CeO_2$ NPs accumulating in the roots of various edible plants. Both Ce and Zn can

accumulate in soybean pods but without controlling the metal ions, the source of the metals remains unclear. Some REE NPs, like $CeO_2$partially transform into phosphate precipitates in cucumber though most often NPs remain as such. Similarly, Zn-phosphate formed from ZnO NPs accumulated in wheat shoots, but no ZnO NPs were detected. ZnO NPs can quickly transform into Zn ions in soil, while CuO NPs were detected in wheat shoots grown in amended sand. Shukla et al., (2024) found that CuO NPs in *Elsholtzia splendens* can transform into Cu-alginate, Cu-oxalate and Cu-cysteine, though it's unclear whether Cu NPs or ions are taken up first. More research is needed to understand the mechanisms and timing of NPs transformation in plants. XANES can help explore NPs behavior in plants but the key issue remains understanding the biotransformation mechanisms in both the growth media and plants. Currently, $CeO_2$ NPs accumulate in many plant species, but transformation is limited, while ZnO NPs primarily release metal ions that results in abiotic stress in plants [19]. The exact process by which ZnO NPs transform into ions is unclear. Two hypotheses exist: a) ZnO NPs release metal ions in the substrate which are then taken up by the plant and the ions may or may not be reduced back to NP form inside the plant; b) ZnO NPs enter the plant directly and dissolve into ions through species-specific processes. Both the mechanisms help us explain the detection of NPs inside plants [20].

## NANOPARTICLES UPTAKE AND TRANSLOCATION IN PLANT SYSTEMS

NPs are adsorbed to plant surfaces and taken up through plant openings at the nano- or micrometer scale. Several predicted pathways exist for NPs association and uptake. The aboveground plant surface, especially in species with high leaf area indices (LAI) exposes large areas to NP deposition. Plant shoots are lipophilic due to cuticular waxes, and structures like trichomes and epicuticular cavities that may increase NP deposition [21]. A study with maize plants exposed to aerosol $CeO_2$-NPs found that NPs tightly associated with the plants, though it couldn't distinguish between surface adsorption and structural incorporation. NP uptake in plants occurs through various pathways that are influenced by NP size and surface properties. Small, lipophilic NPs can penetrate the cuticle's apolar fluid areas, while larger NPs may enter through cuticle-free areas like hydathodes, stigma, and stomata. Stomata, with apertures up to 10 μm, facilitate NP entry, as seen with airborne $CeO_2$-NPs in *Vicia faba* leaves. The physical properties of the cuticle which change with temperature affect NP interaction and penetration although this process hasn't been fully analyzed [22]. Newly developed leaves did not contain detectable levels of Ce, suggesting no significant long-distance translocation of $CeO_2$ through the phloem. Similarly, no Ce was found in aboveground organs after 14 days of $CeO_2$-NP irrigation. NPs that enter leaves via stomates are deposited on cell walls or neighboring cells and must pass through the cell wall to reach the protoplast. Cell walls typically have pore sizes of 3.5–5.2 nm allowing only NPs smaller than 5 nm to pass efficiently. However, cell wall defects may enable larger NPs to cross the plasma membrane. Alizarin red S-labeled $TiO_2$-NPs (3 nm) in *Arabidopsis* seedlings showed tissue and cell-specific distribution, traversing the cell wall and localizing in epidermal cells and vacuoles [23]. In maize, NPs smaller than 4.9 nm can pass through xylem pits, while particles larger than 20 nm are blocked. The size exclusion limit for primary cell walls is around 3.5 nm, though xylem pit sizes vary widely across species, with some, like *Abies nordmanniana* and *Eucalyptus regnans* having much larger pit sizes. Once NPs reach the xylem, movement between vessels is possible, as these vessels serve as open conduits for particle and bacterial spread in plants. For example, 1.0 μm polystyrene microspheres moved from petioles into leaf veins in vine leaves. However, this connectivity can vary across species and pit membranes may restrict larger NPs from moving freely through the xylem in some species[24].

## PHYTOTOXICITY AND NANOPARTICLES

### Effect of NPs on morphology and physiology of plants

NP exposure has caused morphological changes in plant roots. In annual ryegrass exposed to 40 mg/L Ag NPs, damaged root caps and vacuolated cortical cells were observed. Similarly, $Yb_2O_3$ NPs induced severe cellular changes in the meristem and root cap of cucumber. A tunneling-like effect causing cellular disintegration was observed in maize root tip cells treated with 1000 μg/mL ZnO NPs [25]. However, it's unclear whether root morphological changes depend on the type of metal-based NPs or plant species. Further research is needed to understand if these changes like vacuolated cortical cells serve as a defense mechanism against NPs-induced stress, as vacuoles store toxic substances. Nanotoxicity of metal-based NPs in plants can cause root length inhibition, reduced biomass, altered transpiration rates, and developmental delays as shown in figure 3. Once inside plant tissues, NPs can disrupt chlorophyll synthesis leading to significant reductions in chlorophyll content as seen in wheat exposed to CuO and ZnO NPs. Similar effects were observed in green peas treated with ZnO NPs and tomatoes exposed to Ag NPs [26]. Ag NPs exposure inhibited chlorophyll b content in rice, while different NPs can have varying

effects on the same plant species. In soybean, exposure to $CeO_2$ and ZnO NPs did not significantly affect chlorophyll content. Additionally, some NPs like Au, $TiO_2$ and ZnO increased chlorophyll content in mustard, cucumber and clusterbean respectively. Lipid peroxidation indicates cell membrane damage caused by ROS leading to ion leakage and potential cell death. CuO and ZnO NPs at 500 mg/kg induced lipid peroxidation in sand-grown wheat, although ion leakage was not assessed in the study. A study on corn exposed to $CeO_2$ NPs showed that lipid peroxidation caused ion leakage. However, Rico et al. found no increase in lipid peroxidation in rice treated with $CeO_2$ NPs (0–500 mg/L), though ion leakage occurred at higher concentrations [27]. Metal-based NPs can disrupt nutrient transport and assimilation in plants potentially causing more harm than ROS-related effects. $CeO_2$ NPs significantly reduced $N_2$ fixation in soybean nodules leading to growth reduction from N deficiency while ZnO NPs had no such effect. Additionally, $CeO_2$ NPs can bind to phosphorus reducing its bioavailability and causing nutrient deprivation. $TiO_2$ NPs at 500 mg/L increased P and K availability in cucumber fruit. In *Arabidopsis*, Au NPs downregulated genes for metal transporters (e.g., Zn, Na, Ca, Cu, Fe, Mn) and aquaporins, possibly as a defense to limit Au uptake and reduce phytotoxicity. While NPs may disrupt ion channels, studying gene regulation in nutrient transport could clarify their positive and negative impacts on plant growth [28].

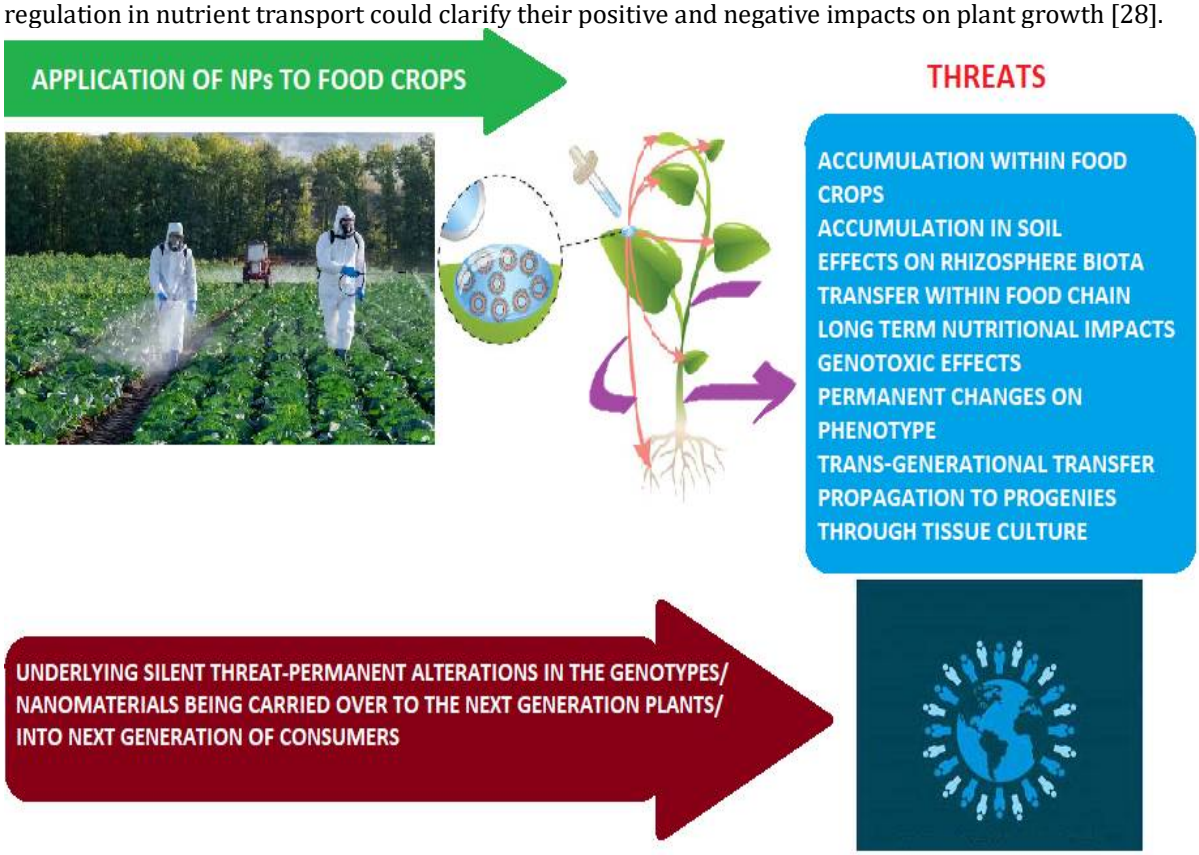


**Figure 3: The silent threats facing the application of NMs to staple food crops.**

**Molecular effects of Metal-Based nanoparticles in Higher Plants**

While metal-based NPs are known to cause oxidative stress through reactive oxygen species (ROS) production, less is known about their potential for DNA damage. A study on CuO NPs exposure in *Raphanus sativus* (radish) and *Lolium perenne* (ryegrass) measured levels of oxidatively modified bases, which can cause genetic mutations, after exposure to various concentrations of CuO NPs (10–1000 mg/L). CuO NP exposure significantly increased DNA lesions in plants with more lesions as the concentration rose [29]. The Comet assay showed $TiO_2$ NPs caused DNA damage in onion, with tail DNA nearly three times higher than the control after 24 hours. DNA damage was also observed in tomato and onion exposed to NiO and Ag NPs, respectively. Additionally, the mitotic index, chromosomal aberrations, and micronuclei induction provide further evidence of NP genotoxicity in plants. A dose-dependent relationship between mitotic index (MI) and exposure to Ag NPs and ZnO NPs was observed in broad bean and onion [30]. Similar responses were seen in $TiO_2$ NP-treated Narbon bean, maize and onion exposed to Ag NPs [31]. The RAPD assay revealed DNA instability in soybean treated with ZnO and $CeO_2$ NPs with nanoceria causing DNA alterations at 2000 and 4000 mg/L. While DNA damage from metal-based NPs in plants is documented, further research is needed on the mechanisms, severity and repair.

Additionally, studying plants' combined responses at the transcriptome, proteome and metabolome level is crucial for a deeper understanding [31].

## EXTRINSIC TOXICOLOGICAL ANALYSIS OF NANOMATERIALS

### Ex-vivo evaluations including nanometrology

For nanoparticle detection and characterization, techniques like transmission electron microscopy (TEM), nano tracking analysis (NTA), and field flow fractionation with ICP-MS are essential. Analyzing engineered nanomaterials (ENMs) and their potential toxicity is also required using biological dose-response metrics. Effective characterization of nanomaterials (NMs) is hindered by challenges like low exposure concentrations, high background colloidal materials, and limitations in isolating NMs without artifacts [32]. While various methods exist, results are often controversial, and no standard methods have been established. Additionally, NMs may be coated with proteins and biomolecules, making pre-coating physical and chemical characterizations inadequate. The agglomeration and floating of nanomaterials (NMs) in liquids depend on the dispersion method used. Agglomeration reduces surface area, size and density, decreasing NM effectiveness. Larger NM diameters increase sedimentation rates, with a 5-fold increase in size causing a 50-fold higher settling rate impacting the in vitro dose availability. El-Kady et al., (2023) noted that high NM doses may cause physical overload effects, often mistaken for toxicity. Cell internalization and translocation depend on NM properties and the dose delivered. Matching in vivo and in vitro exposure is rarely done due to lack of accessible tools. Hybrid in vitro dosimetric methods combining NM suspension characterization and numerical fate models are recommended. Nanomaterials also play role in contamination transport, as it has been seen that highest exposure to pristine nanomaterials (NMs) happens during production. For example, carbon nanotubes (CNTs) are compared to other toxic high-aspect-ratio materials. In groundwater, mineral NMs transport contaminants like Plutonium and iron over long distances, as seen in polluted sites in Russia and Nevada [33]. Engineered nanoparticles (ENPs) can move as particles or aggregates and their transformation in biological and environmental matrices—such as coating changes, dissolution or aggregation affect detection. Methods like field flow fractionation can be less effective due to changes in diffusion and surface charge. Biological transformations including redox reactions and reactive oxygen species generation alter CNT properties like charge, stability, and absorption. Numerical modeling like a 1D MATLAB model tracks NM transport, settling and concentration over time [34]. Techniques such as DLS, AUC, hydrodynamic chromatography, and nanoparticle tracking analyze size distribution. The ISDD model calculates surface area, particle number and sedimentation. Due to the widespread production of NMs, their toxicity is hard to generalize and coating can alter their properties. Research should clearly state methods for determining physicochemical characteristics and dispersion. Labeling NMs with biocompatible markers helps study their fate in biological tissues [35].

### In vivo toxicity analyses

### Microscopic assessments and growth parameters

Microscopic studies have tracked NMs inside plant cells. For example, Se NPs in roots appeared as bright green spots under fluorescent microscopy. Similar results were observed in soybeans with magnetite nanoparticles. These NPs likely penetrate through semi-permeable membranes or capillary forces. $TiO_2$ NPs were also detected in *S. polyrrhiza* and super magnetic oxide NPs in Glycine max using fluorescence microscopy [36]. Translocation in plants depends on NP properties, with $TiO_2$ NPs' structure aiding their entrance. ZnSe NPs were internalized in *L. minor* roots in a concentration-dependent manner. NPs enter through endocytosis, pores, plasmodesmata, and openings like hydathodes and stomata. For example, CdSe/ZnS QDs were detected in *Medicago sativa* cell cultures, while CuO NPs in *S. polyrrhiza*and CdSe NPs in *L. minor* roots appeared as bright spots under fluorescence microscopy [36]. Mercaptopropionic acid-coated CdSe/ZnS QDs and Pt NPs were found in the cytosol, cell wall and organelles of *Medicago sativa* [37]. Se NPs capped with L-cysteine and tannic acid was detected in the cell wall and cytoplasm of ***L. minor*** causing ER and mitochondrial damage. Similarly, ZnO NPs caused organelle destruction in *Fagopyrum esculentum* [37]. NPs-induced ER stress is linked to cytotoxicity and apoptosis as seen with Ag NPs in human THP-1 monocytes. A study showed that L-cysteine and tannic acid-capped Se NPs reduced the relative frond number, frond size, and both fresh and dry weights of *L. minor* over time, with tannic acid-capped Se NPs causing greater growth inhibition. Similar results were observed with ZnSe and CdSe NPs, affecting the same growth parameters in *L. minor* [38]. Phytotoxicity was observed in plants treated with ZnSe, CdSe, CdS, Ag, $Nd_2O_3$ NPs, and Ag NP-CTAB, leading to growth inhibition in *S. polyrrhiza*, *L. minor*, *Phaseolus radiatus*, *pumpkin*, and *Allium cepa*. The toxicity was linked to protein denaturation reduced photosynthesis, gene expression changes and NPs aggregation impacting growth parameters like relative frond number, frond length, and dry weight, especially with $TiO_2$ NPs.CuO

NPs negatively affected *Landoltia punctata*, *L. minor* and *L. gibba*, while Ag NPs harmed *Medicago sativa* [39].CuO NPs were toxic to *S. polyrrhiza* at concentrations >0.5 mg/L and CdSe NPs reduced ***C. vulgaris*** cell numbers. Similarly, *Phaeodactylumtricornutum* and *Nannochloropsisoculata* exposed to $TiO_2$ and CuO NPs showed reduced cell numbers. NPs can block light access (shading effect) and inhibit nutrient uptake leading to ROS production and growth inhibition [40].

**Effect of NPs on Photosynthesis**

Studies show that exposure to NPs like Se, ZnSe and Ag NPs reduces chlorophyll a, b, and total chlorophyll in plants like *L. minor* and *Arabidopsis thaliana* with more severe effects from tannic acid capped Se NPs. Carotenoid content remains unchanged or declines with ZnSe NPs. This reduction in chlorophyll is linked to decreased biomass, oxidative stress and reduced photosynthesis impacting carbon fixation. Similar effects were observed in *S. polyrrhiza* exposed to $TiO_2$, CuO, Ag and Zn NPs [41]. Studies on various duckweeds like *Landoltia punctata*, *Hydrilla verticillata*, and *Salvinia natans* exposed to CuO, ZnO, and CdS NPs showed reduced chlorophyll levels [41]. $Zn^{2+}$ ions from ZnSe NPs may replace $Mg^{2+}$ in chlorophyll, disrupting photosynthesis. However, low CdSe NP concentrations (1 mg/L) increased chlorophyll, carotenoids, and anthocyanins, with higher concentrations (>2.5 mg/L) causing reductions. Some studies, like those on *C. vulgaris* showed enhanced stress defense but higher stress levels harmed photosynthetic structures. Contradictory findings include $TiO_2$ NPs increasing chlorophyll in *Lemna minor*[42].

**MITIGATION PATHWAYS IN PLANTS AGAINST TOXIC EFFECTS OF NANOPARTICLES**

**Detoxification pathways in Plants**

Under normal conditions, ROS are byproducts of metabolic processes in organelles like chloroplasts, mitochondria and peroxisomes. Membrane integrity can be assessed by malondialdehyde accumulation. The production of Malondialdehyde (MDA) occurs when unsaturated fatty acids in phospholipids undergo peroxidation due to ROS generated by NPs, leading to lipid peroxidation. MDA levels correlate with ROS accumulation and can cause protein and DNA denaturation. Studies showed increased MDA in ***L. minor*** exposed to Se, ZnSe, and CdSe NPs, as well as in *B. rapa* and lettuce exposed to Ag and $CeO_2$ NPs [42]. Plants remove ROS produced by NPs, but excessive ROS can damage biomolecules and kill cells [43]. These ROS are regulated by antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and ascorbate peroxidase (APX) to prevent oxidative damage. However, abiotic stresses (e.g., salt, temperature, heavy metals) can lead to excessive ROS production, causing damage to plant biomolecules. The main types of ROS are singlet oxygen ($1O_2$), superoxide ($O_2^-$), hydrogen peroxide ($H_2O_2$), and hydroxyl radicals (HO•) [44]. To reduce ROS toxicity in plants, antioxidant enzymes like SOD convert toxic ROS ($O2^-$) to less harmful $H_2O_2$. However, $H_2O_2$ can trigger the Fenton reaction, generating highly reactive hydroxyl radicals (HO•) in the presence of metal ions ($Fe^{2+}$, $Cu^{2+}$) which cause irreversible damage to lipids, DNA and proteins. While HO• has not been directly measured in plants exposed to metal-based NPs, $H_2O_2$ levels can be used to assess ROS production, with varied responses observed in rice cultivars exposed to $CeO_2$ NPs. In rice cultivar "Neptune" $H_2O_2$ levels were nearly three times higher than the control after exposure to 500 mg/L $CeO_2$ NPs, while "Cheniere" showed no significant difference. However, at a lower dose (62.5 mg/L), both cultivars scavenged $H_2O_2$ [44]. Venugopol et al., (2024) found that $CeO_2$ NPs at 50 mg/L could reduce ROS via a Fenton-type reaction. Wang (2022) reported that corn exposed to $CeO_2$ NPs showed effective antioxidant defense through CAT and APX, with $H_2O_2$ concentrated in epidermal, parenchyma and bundle sheath cells. Antioxidant enzymes like SOD, CAT, APX and GPX help detoxify ROS in plants. SOD comes in three types (Fe-SOD, Mn-SOD, Cu-Zn-SOD) that convert $O_2^-$ to $H_2O_2$. These excess $H_2O_2$ produced from SOD or abiotic stress gets detoxified by enzymes like CAT which converts $H_2O_2$ to $H_2O$ and $O_2$. APX converts $H_2O_2$ to $H_2O$ through ascorbate oxidation producing malondialdehyde (MDA) and dehydrogenase activity (DHA), which are recycled to generate more ascorbate [45]. This process is part of the ascorbate-glutathione cycle, involving glutathione (GSH). GSH can also directly transform $H_2O_2$. Additionally, glutathione peroxidase (GPX) catalyzes the conversion of $H_2O_2$ into glutathione disulfide (GSSG), which is then reduced by glutathione reductase (GR). The role of antioxidant enzymes in response to metal-based NPs has been studied with CAT and APX activities examined in various plants. In rice cultivar “Cheniere,” APX activity remained unaffected by $CeO_2$ NPs until 500 mg/L, while APX and GPX increased significantly in the roots at this concentration. Root CAT activity decreased suggesting that ROS detoxification may involve the ascorbate-glutathione and glutathione peroxidase cycles. In contrast, CAT activity in rice cultivar “Neptune” varied with $CeO_2$ NPs exposure [46].

**Role of GSH Biosynthesis Pathway Anthocyanin and Heat Shock Proteins (HSPs)**

GSH is a key antioxidant involved in the defense against oxidative stress from heavy metal exposure. Its biosynthesis begins with sulfur assimilation and involves cysteine synthase, γ-glutamylcysteine synthase, and glutathione synthase [47]. GSH scavenges ROS and is oxidized to GSSG, which is recycled by glutathione reductase (GR). Phytochelatins (PCs), derived from GSH, also help detoxify heavy metals by chelating metal ions for storage in vacuoles and the cell wall.The GSH biosynthesis pathway plays a key role in heavy metal detoxification. Overexpressing the γECS gene in Arabidopsis shoots led to increased GSH and phytochelatins (PCs) production, enhancing metal tolerance to arsenic (As) and mercury (Hg). Similarly, studies on Abyssinian mustard showed upregulation of genes involved in sulfur assimilation and GSH biosynthesis when exposed to arsenic (As) and chromium (Cr) [48]. Anthocyanin, a nonenzymatic antioxidant, is widely distributed in plant cells especially in the vacuole where it scavenges free radicals and chelates metals under abiotic stresses. Additionally, the production of molecular chaperones like HSPs helps plants defend against oxidative and abiotic stresses such as heat, drought, salt and heavy metals. The role of HSPs in response to NPs exposure is not well understood but it is expected to resemble their role in other oxidative stresses [48].

**POTENTIAL RISKS OF METAL-BASED NANOPARTICLES IN FOOD CHAIN AND HUMAN HEALTH**

Metal-based NPs can accumulate at each trophic level in the food web once released into the environment. While heavy metals like Hg, Cd and As are known to bioaccumulate, knowledge of metal-based NPs' trophic transfer is limited. Several studies have explored their transfer of trophic level in simple food chains [49]. In the aquatic food chain, $CeO_2$ NPs did not show significant differences in concentration between phytoplankton and mussels, whether ingested from water or sorbed to phytoplankton. $TiO_2$ NPs were not biomagnified in ciliated protozoa and microbes, although they were internalized by protozoa. Similarly, no biomagnification of $TiO_2$ NPs from daphnia to zebrafish or quantum dots from zooplankton to zebrafish was observed. Holbrook et al. observed similar patterns of NP accumulation from E. coli to ciliate and to rotifer [50]. While NPs accumulate at each trophic level, no biomagnification occurred, possibly because predators excrete toxins through feces, reducing toxicity. However, Werlin et al. found higher concentrations of CdS quantum dots (QDs) in protozoa than in bacteria, providing evidence for biomagnification. Biomagnification of NPs in aquatic food chains may depend on the type of NP and biota. Few studies have investigated trophic transfer of metal-based NPs in terrestrial food chains. A study showed biomagnification of Au NPs from tobacco-to-tobacco hornworm [50]. Another study found that while Au concentration decreased from soil to earthworms to bullfrogs, bioavailability in bullfrogs was higher through dietary uptake from earthworms [50]. Both studies lacked evidence on whether Au was excreted in feces that may have indicated bioaccumulation. Particle size may influence the accumulation and trophic transfer of NPs. For example, high Ce levels were found in cricket tissues and feces when fed on $CeO_2$ NPs-treated zucchini suggesting herbivores may excrete toxins to reduce nanotoxicity. Similarly, QD was observed in the grass of *Trichoplusiani* fed on QD-treated Arabidopsis. However, more research is needed to understand the biomagnification and trophic level transfer of metal-based NPs in food chains. [51].

**Lung inflammations**

The disturbance of lung inflammation caused by nanoparticles is closely related to their physicochemical properties. First, research based on carbon black (CB) nanoparticles $TiO_2$ nanoparticles, and silica-dioxide nanoparticles has confirmed that the smaller the particle size of nanoparticles, easier it may cause or aggravate lung inflammation. When the weight of nanoparticles is equal, the airway exposure to 14-nm CB nanoparticles strongly aggravates LPS-induced pulmonary edema and lung inflammation while 56-nm nanoparticles do not show obvious effects. Also studies showed 20nm silica NP induced lung inflammation in rats after repeated exposure for 14 days but 50nm silica NP failed to induce any response. Also as compared with the cells treated with 50-nm silica nanoparticles, the structural damage of organelles in the cells treated with 20-nm silica nanoparticles is more and the increase of mitochondrial membrane potential and mitochondrial calcium accumulation is only observed in 20-nm silica nanoparticle-treated cells. The lung inflammation induced by 20-nm silica nanoparticles may be related to the paraptosis of alveolar macrophages [52].

**Cardiovascular system**

The study conducted by He et al., (2021) suggests problems with direct cardiovascular effects of translocated nanoparticles or the systemic inflammation mechanisms, a neurogenic mechanism has been proposed. Indeed, epidemiological studies have shown that particulate air pollution exposure is associated with indicators of impacted autonomic input to the heart, resulting in increased heart rate, decreased heart rate variability and increased cardiac arrhythmias Furthermore, epidemiological studies

also demonstrate that short-term exposure to fine particulate pollutants can lead to an autonomic imbalance which results in vasoconstriction and high blood pressure. The growing body of evidence obtained from epidemiological studies strongly suggests that a neuron-regulated pathway may play a crucial role in regulating cardiovascular function after pulmonary exposure to engineered nanoparticles [53].

**DNA damage and cell death**

DNA damage and other stresses can trigger a highly specific survival response that inhibits cellular metabolism and growth, enhances defenses and maintains cellular integrity. A number of studies have shown that NP exposure causes DNA damage across cellular barriers. He et al. (2020) showed that CuO-NPs induced oxidative DNA damage and cell death in human umbilical vein endothelial cells (HUVECs) through copper ion-mediated p38 MAPK activation. In addition, many NPs can induce DNA damage, such as Au-NPs, Hafnium oxide NPs, Ag-NPs, sulfur NPs, indium NPs, polystyrene NPs, and so on [54].

**Reproductive effects**

Nanoparticles can alter the level of sex hormone directly by triggering secretory cells such as thecal cells, follicle cells, granule cells, and corpus luteum or via the hypothalamic pituitary gonadal axis. Some nanoparticles can reach the foetus by passive diffusion or endocytosis, causing fetal inflammation, apoptosis, genotoxicity, reproductive deficit, lower weight, cytotoxicity, immunodeficiency, neurological damage and other effects [54]. The primary female sex hormones in female are estrogen and progesterone which are mostly produced in the ovaries or placenta during pregnancy in human. Some data suggest that certain nanoparticles can change the gene expression that encodes proteins involved in steroidogenesis, such as ovarian genes essential for the synthesis of estrogen and/or progesterone [55].

## CONCLUSION AND FUTURE PERSPECTIVES

The environmental toxicological studies are important for human survival on earth. In this review, nanomaterials toxicity has been investigated broadly since the potential hazards arising from NMs are vast and are getting greater every day due to the increasing consumption of NMs. The adverse effects can reduce the green life mass on earth which would be a disaster.Most studies on nanoparticle (NP) toxicity in plants focus on parameters like germination and growth. Future research should align with current risk assessments, considering NP properties, transformation, environmental fate, human exposure, ecological effects, human health and NP life cycles. Nanomaterials may affect crop yield and disrupt microorganisms in the rhizosphere and endosphere, which are vital for carbon and nitrogen cycles. Addressing knowledge gaps in nanomaterial fate and effects is essential for accurate risk assessments for human health and the environment.

## AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data.They took part in drafting the article or revising it critically for important intellectual content, agreed to submit to the current journal. They all gave final approval of the version to be published and agree to be accountable for all aspects of the work.

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## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest related to the content of this review article. No financial or personal relationships with other people or organizations could have influenced the work presented in this article. All opinions expressed are those of the authors and do not reflect the views or interests of any affiliated institutions or funding organizations.

## ETHICAL APPROVALS

This article does not include experiments on animals or human subjects

## DATA AVAILABILITY

All the data is available with the authors and shall be provided upon request


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## USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript and no images were manipulated using AI.

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