Environ. Water Eng., 2025, 11(3), 403-428 https://doi.org/10.22034/ewe.2025.544576.2060

EWE

Environment and Water Engineering

Homepage: www.jewe.ir

ISSN: 2476-3683

Copper oxide nanoparticles in medicinal plant protection products: A review of soil ecotoxicology and threats to human health

Amin Pirmoghani [1], Diba Sheykhi Sanandaji [2], Hamzeh Salehzadeh [1], Hee-Jeong Choi [3], and Behzad Shahmoradi [1]

[1]Environmental Health Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran
[2]Department of Water Engineering, Faculty of Agriculture, University of Kurdistan, Sanandaj, Iran
[3]Department of Biomedical Science, Catholic Kwandong University, Gangneung-si, Republic of Korea

ARTICLE INFO

Paper Type: Review Paper

Received: 04 September 2025
Revised: 11 September 2025
Accepted: 14 September 2025
Published: 24 September 2025

Keywords
Copper-based Nanomaterials
Human Health
Medicinal Plants
Nanoparticle Toxicity
Synthesis

Corresponding author:
B. Shahmoradi
bshahmoradi@muk.ac.ir

ABSTRACT

The expanding application of nanoparticles raises significant concerns regarding their environmental, health, and safety implications. Copper oxide nanoparticles (CuO NPs), in particular, are being investigated for their potential in agriculture. This systematic review, conducted via a structured process of literature search, study selection, and data extraction from PubMed and Scopus databases, synthesizes current knowledge on this subject. Bibliometric analysis was performed using VOSviewer software. The findings indicate that CuO NPs can be internalized by medicinal plants, accumulating in various tissues with effects—both beneficial and detrimental—that are contingent upon plant species, nanoparticle concentration, and exposure duration. Internalized NPs can traverse cell membranes, localize within organelles, and interact with biomolecules like DNA, RNA, and proteins. Crucially, this bioaccumulation presents a potential route for human exposure through the food chain. Excessive intake beyond tolerance levels is associated with toxicological effects, including hemolysis, jaundice, liver cirrhosis, and mortality. This review underscores the necessity for further research to establish safe application methods and optimal concentrations for the sustainable use of CuO NPs in agricultural practices.

Highlights

- CuO-NPs are widely applied in industry, agriculture, and medicinal plants.
- Shape and size of CuO-NPs affect plant growth and medicinal properties.
- CuO-NPs accumulate in soil, influencing uptake and plant performance.
- Knowledge gaps remain on uptake thresholds and environmental toxicity.

How to cite this paper:
Pirmoghani, A., Sheykhi Sanandaji, D., Salehzadeh, H., Choi, H., & Shahmoradi, B. (2025). Copper oxide nanoparticles in medicinal plant protection products: A review of soil ecotoxicology and threats to human health. *Environment and Water Engineering*, *11*(3), 403-428. https://doi.org/10.22034/ewe.2025.544576.2060

1. Introduction

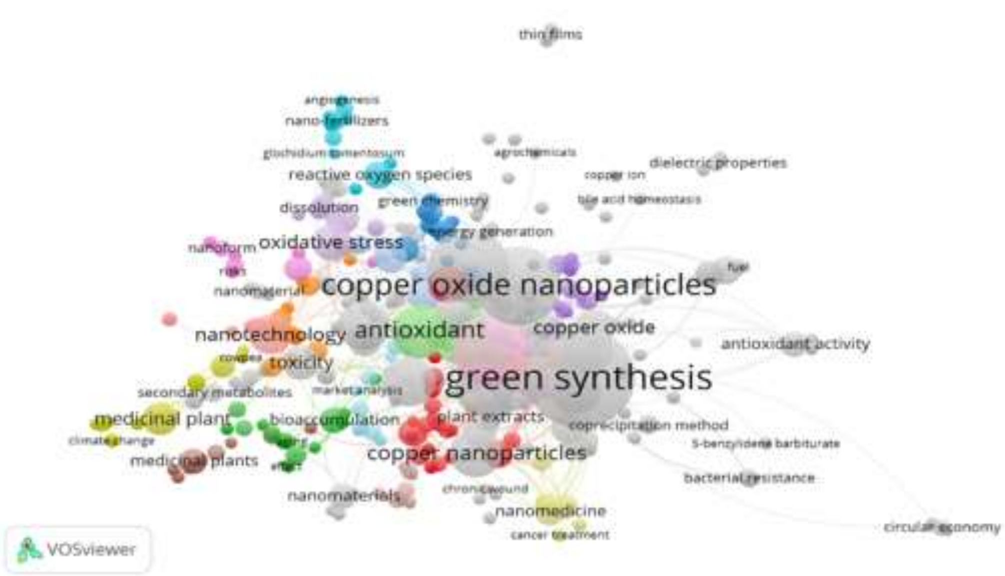
Recognizing the important role medicinal plants play in human health, their usage is ever-growing and there is renewed interest in finding ways to improve medicinal plant production using sustainable tools and strategies (Nekoukhou et al., 2024). Medicinal plants have therapeutic properties and phytotherapeutic effects due to the presence of specific biologically active secondary metabolites (Pirmoghani et al., 2019). Secondary metabolites serve as the main components for designing effective drugs today (Nazir et al., 2020). Although the use of chemical drugs has become common in recent decades, their harmful effects on life have caused humans to turn to medicinal plants again (Sonawane et al., 2022). According to the World Health Organization (WHO), it is estimated that more than 80% of the world's population in rural areas uses medicinal plants as primary treatment due to their direct availability (Yeboah et al., 2022). It is predicted that by 2050, the value of international trade in medicinal plants and their products will reach 5 trillion dollars (USD 5 trillion) (Zahra et al., 2019). Medicinal and industrial plants of rangelands are one of the most valuable resources in the vast range of natural resources (Lubbe & Verpoorte, 2011; Feng et al., 2023). Currently, medicinal plants account for a large part of agricultural production (Ahmed, 2023).

Cultivation and production of medicinal plants is not only a means to meet the increasing needs of the current and future pharmaceutical industries, but also a means to reduce the excessive exploitation of wild communities of these plants (Applequist et al., 2020). Therefore, their cultivation can be used to restore degraded areas (Marcelino et al., 2023). Plant metabolism is regulated by the presence of essential macronutrients and micronutrients, with micronutrients mainly involved in secondary metabolic and enzymatic processes (Bhat et al., 2020; Tariq et al., 2023). Nanoparticles can reduce biotic and abiotic stresses and improve morphological, physiological, and other biological parameters in medicinal plants and their production (Pandita, 2022). Nanoparticles act as new and effective inducers and increase the production of secondary metabolites in medicinal plants by creating oxidative stress (Javed et al., 2017). Inorganic materials such as metals and metal oxides have attracted much attention in the past decade due to their ability to withstand the conditions of synthesis (Abdallah et al., 2019). Several metal oxides such as TiO_2, NiO, ZnO, MgO, and CuO have been used in a wide range of different applications, not only because of their stability under operational conditions but also because of their safety (Maroufpoor et al., 2019). Among them, CuO NPs have attracted attention due to their diverse applications in agriculture, including nanofertilizers, nanopesticides, and nanosensors to improve and manage the harmful effects of pests on crops (Dorjee et al., 2023; Monreal et al., 2016). This nanoparticle is required for the normal growth and development of plants, and its deficiency affects younger leaves and reproductive organs when it is not bioavailable to plants (Yruela, 2005). However, it can be toxic to plants at high concentrations. For instance, foliar application of various concentrations of copper oxide nanoparticles (CuONPs) (0, 40, 80, 160, and 400 mg/L) to Dracocephalum moldavica [L.] resulted in a significant concentration-dependent increase in copper bioaccumulation in the shoot, along with elevated levels of flavonoids and anthocyanins, in response to CuONPs treatment (Nekoukhou et al., 2023). Likewise, in peppermint, at 1500 mg/L, CuONPs reduced α-phellandrene, limonene, and comphene content by 45, 43.8, and 17.2 %, respectively (Lafmejani et al., 2018; Nekoukhou et al., 2023). Excess can also negatively impact soil microbiome and other receptors (Alengebawy et al., 2021). Therefore, as nanotechnology continues to expand its positive applications, a proportionate level of responsibility is necessary to address and mitigate potential risks on the other side. The results of life cycle assessment study show that most nanoparticles are released during the use phase and after disposal (Nowack et al., 2015). Therefore, in the present study, the topic of Copper oxide nanoparticles in medicinal plant protection products: A review of soil ecotoxicology and threats to human health, was investigated.

2. Materials and Methods

In this review, we used keywords such as copper nanomaterials, copper nanocomposite synthesis methods, nanomaterial toxicity, factors affecting toxicity, and toxic effects on medicinal plants to find relevant articles. For this purpose, relevant articles published in various databases, including PubMed, Google Scholar, and Science Direct, were searched, and after finding relevant articles, first the title and abstract and then the full text were reviewed. Based on the inclusion criteria, studies whose main objective was the toxic effects of the use of copper oxide-based nanoparticles on medicinal plants were reviewed. Additionally, we utilized VOSviewer software to visualize and analyze the bibliometric Figures 1 and 2. The bibliometric parameters assessed with VOSviewer enabled us to identify key citations related to the primary research topics based on established criteria. VOSviewer has been widely applied in various studies for article evaluation and data visualization. As a result, extracted and cited 248 papers in this review.

Fig. 1 Network visualization of the keywords related to the CuO-NPs



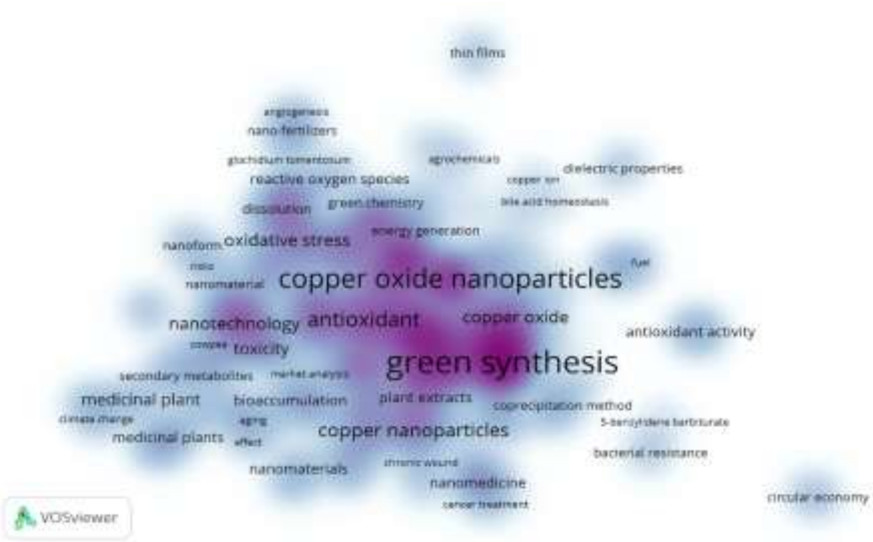


Fig. 2 Density visualization of keywords related to the CuO-NPs

2.1 Definition of Cu-based NPs

The physical and chemical nature of nanoparticles makes them highly reactive, thus they are used on an industrial scale and possess biological properties (Idrees et al., 2025; Sharafudheen et al., 2025). Nanoparticles can be classified into organic and inorganic forms. However, inorganic nanoparticles are generally classified as metals and metal oxides (Iranbakhsh et al., 2021). Metal nanoparticles (MNPs) include copper (Cu) and zinc (Zn), while metal oxide NPs (MONPs) are modified forms of their respective MNPs and include copper oxide (CuO), titanium oxide (TiO_2), etc (Rajput et al., 2019). Thus, they are endowed with high surface-to-volume ratios, along with reactivity, solubility, strength, and mobility, as well as unique interface effects and quantum properties (Croteau et al., 2014). Their fabrication has attracted the attention of researchers due to their wide applications, electrical, magnetic, optical, and physical properties (Zoolfakar et al., 2014).

Copper (Cu), a first-row transition metal with a molar mass of 63.5 g/mol, has some interesting physicochemical properties. In particular, Cu is attractive because of its high natural abundance and low cost (Deka et al., 2019). Cu-based NPs can promote and catalyze a variety of chemical reactions due to the different oxidation states of Cu (Cu0, CuI, and CuII), which facilitate reactivity through one- and two-electron pathways (Gawande et al., 2016). CuO is a p-type semiconductor with a band gap energy of 1.2 eV, making it one of the metal-based compounds in this class. The production and use of CuO NPs is of great importance from both a practical and a theoretical perspective (Moumen et al., 2022; Ali et al., 2024). CuO NPs have unique crystal structures and high surface areas, which make them highly valuable antimicrobial agents. These NPs are robust and stable, and have a longer half-life than other organic antimicrobial agents (Vaidehi et al., 2018). Therefore, the controlled production of CuO NPs with specific geometric shapes can be useful for creating new structures that exhibit improved properties (Velmurugan et al., 2024). Advanced materials processing technologies have emphasized the development of various types of composites to produce materials with improved mechanical, physical, chemical, and functional properties (Singh et al., 2023). One of the most prominent material systems in the past few decades is metal matrix composites (MMCs), in which two or more components are used to construct a new material (Shirvanimoghaddam et al., 2017). By formulating a composite, it is possible to utilize the unique advantages of different components in a complementary manner to overcome the limitations of each component (Surappa, 2003; Sharma et al., 2014). The development of nano/micro/macro composites, in particular (MMCs), significantly fulfills most of these requirements for strength and functional properties (Bansal et al., 2022). Recently, researchers have sought to achieve efficient performance of CuO NPs through metal doping. It has been shown that the incorporation of different metals significantly affects the structural, optical, electrical, magnetic, morphological, electrochemical, and dielectric properties of the resulting nanomaterials (Sarfraz et al., 2024). Transition metal doping offers a simple and effective way to tune the optical, electrical, and magnetic properties of CuO NPs (Singh et al., 2020).

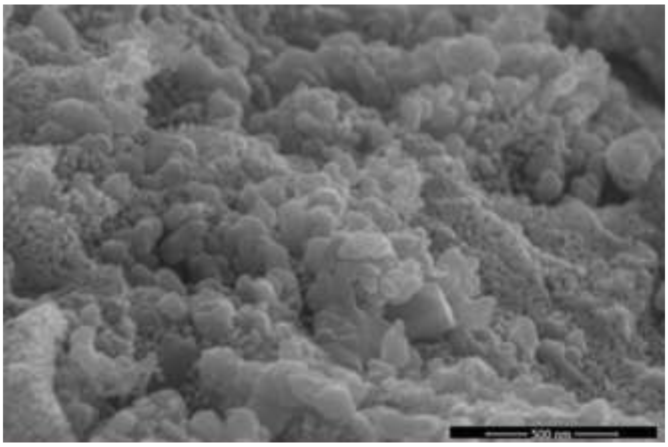
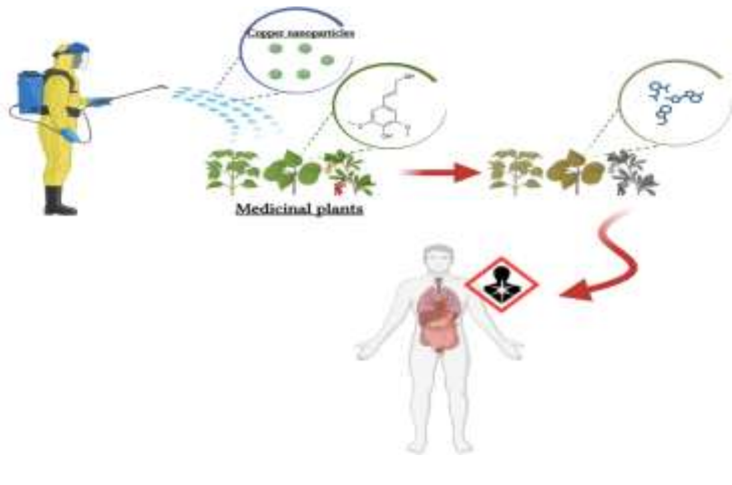


Fig. 3 Scanning electron micrograph of greenly synthesized CuO-NPs (Idrees et al., 2025).

2.2 Importance of toxicity effects on medicinal plants

One of the important aspects in studying the interaction of engineered CuO NPs with plants is the uptake and transport of these nanomaterials, which is of great importance due to the risk of accumulation of engineered nanomaterials in the food chain (Auffan et al., 2009). The increasing number of CuO NP products and their use leads to an increase in the release and accumulation of NPs in the environment, including soil (Zhou et al., 2020). In 2010, the annual global production of Cu-based NPs (including Cu and CuO nps) reached 2.0×10^5 kg/yr and is estimated to reach 1.6×10^6 kg/yr by 2025 (G. Huang et al., 2022). Global estimates of NP emissions show that soils (approximately 8–28%) receive the largest share, followed by emissions to aquatic and air environments (7 and 1.5% of the production volume, respectively) (Keller et al., 2013). Plants serve as the basis of terrestrial food and drug chains, provide oxygen, and play a key role in carbon sequestration (Wahab et al., 2023). Studies have shown that plants rapidly and completely absorb nanofertilizers (Elsayed et al., 2022). A study by Shi et al. (2014) investigating the phytotoxicity and accumulation of CuO NPs in *Elsholtzia splendens* (a Cu-tolerant plant) under hydroponic conditions showed that CuO NPs could be taken up by roots and transported to shoots in *E. splendens*. In addition, inhibition of seedling growth in mung bean plants treated with different concentrations of CuO NPs was observed (Lee et al., 2008). However, alongside these promising developments, there is a parallel increase in potential risks. Pollution caused by nanopollutants (NPOs), also known as “invisible pollution,” is considered the most serious type of pollution that needs to be controlled and managed (García-Mayagoitia et al., 2023). Therefore, CuO NPs induce oxidative stress in human pulmonary epithelial cells, increase toxicity, and can damage DNA and mitochondria, posing a serious threat to human health (Perreault et al., 2012). To control and eliminate these risks, environmental monitoring of CuO NPs is required, which provides research on their fate in the environment and residual concentrations in edible plant parts. This is particularly important in the case of aromatic medicinal plants, a large group of economically important plants that provide raw materials (roots, stems, leaves, and fruits) for the pharmaceutical, perfumery, food (dairy products), and cosmetic industries (Slikkerveer, 2006). CuO NPs may be toxic to non-target organisms due to their potential toxic effects (Ruiz et al., 2015; Grigore et al., 2016) Fig 4. The results suggest that specific concentrations of metal oxide NPs can impact the physiology of cells within the excretory system of various mammals, including humans, and pave the way for comparing the toxic effects between ions and nanoparticles for further nanotoxicological studies (Mavil-Guerrero et al., 2024).

Fig. 4 Pathways through which the toxicity of copper oxide-based nanoparticles affects humans



3. Overview of the impact of nanoparticles on plant growth and development

Nanotechnology is continuously offering new products and solutions in many branches of industry (Jośko et al., 2020). However, knowledge about the penetration and movement of Cu NPs within the plant is required before such applications can be developed (Salem et al., 2023).

3.1 Root intake and foliar application

The primary route of entry of CuNPs into plants is through their roots. 1) As plants absorb water and nutrients from the soil, CuNPs can be absorbed along with these essential resources. The porous structure of the root cell wall allows CuNPs to penetrate into the root tissues (Yusefi-Tanha et al., 2020). 2) In foliar application, nanoparticles enter the leaves mainly through stomata and are transported to different parts of the plant via apoplastic and symplastic routes (Hong et al., 2021). Therefore, the amount of NPs absorbed by plants on the leaf surface varies at different stages of growth and, after being internalized, can move upwards through the plant vascular system (Dev et al., 2017; Gao et al., 2023). 3) Movement within plant stems and leaves: After entering through the roots, CuNPs can be transported to other parts of the plant. This movement is carried out through vascular tissues, which include xylem and phloem. CuNPs move upward through xylem vessels from the root to the stem and leaves (Gao et al., 2023). This movement allows them to reach the aerial parts of the plant (Singh et al., 2024). These nanomaterials can also move downward from the leaves to other plant organs through the phloem. This bidirectional transport provides distribution throughout the plantn (Thiruvengadam et al., 2024).

3.2 Effect of Cu NPs on plant growth and development

1) Cu plays an important role in plant growth, metabolism, and defense (Elbanna et al., 2024). Generally, both the reduced (Cu^+) and oxidized (Cu^{2+}) forms of Cu are used in agriculture. Cu participates as a metal cofactor in various metabolic pathways in plants, including electron transport and oxidative stress response; 2) In chloroplasts, Cu is a component of plastocyanin (Pc), an essential protein in early photosynthetic reactions. In addition, it in the structure of Cu/Zn superoxide dismutase (Cu/Zn-SOD) helps to protect against reactive oxygen species produced during photosynthesis (Michiels et

al., 1994). Rahmani et al. (2016) reported that ZnO and Cu NPs at a concentration of 10 mg/L increased the growth of the *Brassica napus L.* oilseed plant. Meanwhile, they found that exposing germinated rapeseed seeds to NPs caused changes in the transcript levels of all four genes including Auxin Responsive Protein, protein kinase, MPK3 and MPK4 in root and stem tissues.

3.3 Sources of CuO-based NPs

In principle, any soluble Cu salt can be used as a precursor for the preparation of CuO nanostructures without modification or with minimal modification. Various Cu salts such as copper chloride ($CuCl_2$), copper nitrate ($Cu(NO_3)_2$), copper sulfate ($Cu(SO_4)_2$), and copper acetate ($Cu(CH_3COO)_2$) have been used to prepare CuO NPs (Siddiqui et al., 2016). The use of microorganisms such as bacteria, yeasts, algae, fungi, and actinomycetes in the biosynthesis of metal nanoparticles has been reported in the literature (Mandal et al., 2006) Fig 5. Rubilar et al. studied the synthesis of Cu NPs by bacteria, fungi, and plant extracts and reported that biosynthesis is a cost-effective, simple, and non-polluting process (Rubilar et al., 2013). Labaran et al. (2024) investigated the use of *Alstonia scholaris* for the biosynthesis of Cu NPs and its antimicrobial studies. The observed color changes confirmed the successful formation of Cu NPs and Cu had the highest relative abundance of 67.41 wt%, confirming the colloidal purity of Cu NPs. This material can be used as an antimicrobial, antibacterial and antifungal agent, etc (Naika et al., 2015 Naika). Cu and Cu-based compounds have effective biocidal properties, which are commonly used in insecticide formulations and some hygiene applications (Borkow & Gabbay, 2009).

Fig. 5 Flow chart showing the protocol for the biosynthesis of CuO-NPs

3.4 Common methods of synthesizing Cu-based NPs

Cu NPs can be synthesized through various methods. The most common methods for synthesizing Cu NPs include: 1) chemical reduction method, which is a widely used method for synthesizing Cu NPs and involves the reduction of Cu salts, such as copper sulfate or copper chloride, using reducing agents such as sodium borohydride, hydrazine, or ascorbic acid (Ravele et al., 2022): 2) thermal decomposition method, in which copper-based precursors, such as copper acetate or copper acetylacetonate, are thermally decomposed to produce copper nanoparticles. The decomposition process is carried out in the presence of stabilizing agents or surfactants to control the size and morphology of the nanoparticles (Betancourt-Galindo et al., 2014): 3) electrochemical synthesis, which involves the reduction of copper ions at the electrode surface to form Cu NPs. The size and morphology of the nanoparticles can be controlled by adjusting electrochemical parameters such as current density, potential, and electrolyte composition (Kokorekin et al., 2017): 4) biological synthesis, in this approach, natural organisms such as bacteria, fungi, enzymes or plant extracts are used to synthesize Cu NPs. The biomolecules present in these organisms act as reducing and stabilizing agents, leading to the formation of Cu NPs (Shobha et al., 2014). Green synthesis of Cu NPs is an ecofriendly approach. These biomolecules act as metal ion reducing agents and capping agents to minimize the aggregation of nanoparticles, thus improving the biological potential (Singh et al., 2019). This method usually involves the reduction of Cu salts using plant extracts, microbial cultures or other bio-derived compounds that act as both reducing and stabilizing agents (Asemani & Anarjan, 2019; Fouda et al., 2022). Green synthesis of Cu NPs is advantageous because it is a sustainable, cost-effective and non-toxic process compared to conventional chemical synthesis methods (Akintelu et al., 2020). Nguyen et al. (2018) reported that CuO NPs produced by *P. acerifolium* are more stable and exhibit less toxicity to the unicellular *Chlamydomonas reinhardtii* alga. CuO NPs produced using this method have various applications, including catalysis, antimicrobial coatings, and medical applications such as cancer treatment, antifungal and antibacterial properties, and drug delivery, in addition to their use as insecticides and seed priming (Jayarambabu et al., 2020; Geremew et al., 2024). In this regard, several plants have been investigated for the synthesis of CuO NPs Table 1.

Table 1 Studies on plant-mediated synthesis of CuO NPs, their morphology and various applications

Plant	Part of plant used	Active compounds	morphology and size	Various applications	Ref.
Rosmarinus Officinalis	leaf	Polyphenols	crystalline 20-30 nm	These green methods are low cost, fast, efûcient, and generally lead to the formation of crystalline nanostructures with a variety of shapes.	(Mohammad Shafiee et al., 2016)
Eichhornia crassipes	leaf	flavonoids, proteins and other functional groups present	spherical 28 ± 4 nm	antifungal activity against plant pathogens.	(Vanathi et al., 2016)
Aloe barbadensis Miller	leaf	flavonoids, proteins	Crystalline 15and 30 nm	health related applications of CuO nanoparticles	(Gunalan et al., 2012)
Ixoro coccinea	leaf	alcohols and phenolic	Spherica l80–110 nm	Environmental friendly method	(Vishveshvar et al., 2018)
Piper betle	leaf	various phytochemicals	Spherical 10 to 50 nm	antibacterial potential	(Ahmad et al., 2024)
basil extract	dry matter of the plant	flavonoid	quasi-spherical -less than 100nm	nanofertilizers on the morphological and biochemical attributes of plant	(Abbasifar et al., 2020)
Achillea fragrantissima- Nigella sativa	whole plant - seeds	phytochemicals	semi-spherical range of 15–40 nm in size	Their Effects as Larvicidal, Molluscicidal and Antimicrobial Agents	(Al-Ghabban & Eldiasty, 2022)
Macroptilium Lathyroides (L)	leaf extract	flavonoids, polyphenols, terpenoids, saponins, and alkaloids	formed CuO NPs is found to be spherical shaped crystals with the size between 6 nm to 32 nm and the average size 18.9 nm	biological applications such as antioxidant, antibacterial, cytotoxicity, anticancer and antifungal behaviours	(Prabu & Losetty, 2024)
Eryngium foetidum	leaf extract	olyphenols, carbohydrates, flavonoids	Rod-shaped- size ranged from 7 to 23 nm with an average size of 16.49 nm	Anticancer, antimicrobial and antioxidant activity	(Daimari & Deka, 2024)
Plectranthus amboinicus	leaf extract	Monoterpenoids, Geranyl acetate	spherical, circular-shaped nanoparticles with size in 5–30 nm range	anti-larvicidal activity manifested the potent inhibition on Anopheles subpictus .	(Velsankar et al., 2020)
Panicum sumatrense	extract seeds	diethyl phthalate	rectangular shaped nanoparticles and their average particle size was in between 15 and 35 nm	applied as a biocompatible, cost-effective insecticides, drugs and fertilizers.	(Velsankar et al., 2022)
Capsicum frutescens	leaf extract	phytochemicals	micrographs illustrated the spherical and rectangular-rod shaped nanoparticles with its diameter (width) ranging from 20 to 40 nm	The antibacterial and biofilm activities against Gram-positive (Bacillus anthracis, and Listeria monocytogenes) and Gram-negative (Klebsiella pneumoniae)	(Velsankar et al., 2021)

Plant	Part of plant used	Active compounds	morphology and size	Various applications	Ref.
Azadirachta indica	leaf extract	flavonoids, proteins, terpenoids, polyphenols	particles are crystalline, cubical shape with the average size 48 nm and highly stable	Development of an eco-friendly process	(Nagar & Devra, 2018)
garlic	extracts of garlic husk	Flavonoids	crystalline size of 14 nm	activity against Gram-positive (Escherichia coli, Vibrio cholera) and Gram-negative (Bacillus cereus, Staphylococcus aureus) microorganisms	(Senthilkumar et al., 2024)
Foenum-Graecum	seed extract	phytochemicals	Average crystallite size of the CuO NPs is about 36 nm.	experimentation -Drug delivering agent	(Rinita et al., 2023)
Eucalyptus Globoulus	leaf extract	polyphenols	nanoparticles are spherical and have a mean particle size of 88 nm	To optimize dye removal efficiency,	(Alhalili, 2022Alhalili)
foenum-graecum	seed extract	phytochemicals	spherical forms- small crystallite size of 6.23 nm,	Notably, our findings highlight the exceptional photocatalytic activity of these NPs, particularly in the degradation of the resilient MG dye under UV irradiation.	(Kumar et al., 2024)
Piper retrofractum Vahl	fruit extracts	phenol compounds	spherical forms- crystalline size of 2–10 nm	The synthesized CuNPs have relatively good stability and could inhibit Escherichia coli and Staphylococcus aureus.	(Amaliyah et al., 2020)
Inula graveolens	whole aerial part of plant	is rich in pharmacologically active compounds such as terpenoids (including sesquiterpene lactones and dimers, diterpenes, and triterpenoids	were found to be around 20 nm in size and spherical in shape	have potential as antimicrobial, antioxidant, and anticancer agents and as efficient adsorbents.	(Alangari et al., 2024)
Gloriosa superba L.	Leaves	alkaloid	spherical in shape, and the size is found to be in the range 5–10 nm.	activity against pathogenic bacterial	(Naika et al., 2015)

3.5 Applications of CuO NPs

3.5.1 Agriculture

Cu NPs interact with plant pathogens and plants themselves in a variety of ways, which reduces the chance of developing resistant strains of the pathogen (Khan et al., 2022). Engineered Cu-based NPs have several advantages: i) Antimicrobial action: Cu NPs exhibit potent antimicrobial properties at concentrations considered safe for humans and the environment (DeAlba-Montero et al., 2017): ii) Low production cost: The starting materials and production methods for these nanoparticles are inexpensive (Ojha et al., 2017): iii) Green synthesis: In addition to traditional chemical methods, green routes including biogenic methods allow for the sustainable preparation of Cu-based NPs (Thiruvengadam et al., 2019): iv) Historically, Cu has been used in agriculture as a key component of fungicides to combat plant diseases. However, recent advances in the design of Cu-based NPs have opened up new avenues for crop protection and (Viet et al., 2016): v) Compared to bulk copper, these nanoparticles show superior results with less toxic effects (Gomes et al., 2022).

3.5.2 Seed priming

In many medicinal plants, seed survival, germination, and rapid seedling propagation are major challenges due to seed dormancy, hard seed coat, and slow seedling growth rate (Soltani & Soltani, 2015). By definition, pre-sowing seed treatment is a process by which seeds undergo the initial stages of germination but do not germinate due to low water uptake (Paparella et al., 2015), and it induces changes in metabolic and signaling processes to activate the early stages of seed germination, thereby increasing germination rate, growth, and crop quality .

Since plant species are physiologically diverse, nanopriming has been effective in these areas mainly due to its small size and unique physicochemical properties (Bambharoliya et al., 2025). Several studies have shown that NPs have the ability to penetrate the seed coat and increase water uptake, which enhances germination and growth (Abbasi Khalaki et al., 2021; Amin & Aziz, 2025). Proline, a highly soluble molecule with low molecular weight, provides a defense mechanism against stress in plants through cellular osmotic adjustments to maintain membrane integrity and enzyme/protein stabilization. Studies have also reported an increase in proline content in mustard plants when treated with CuO NPs as a foliar spray (Faraz et al., 2022). Also, studies conducted in Table 2 point to a number of benefits of nano-priming seeds, including increased plant growth and development, increased productivity, reduced use of pesticides and fertilizers by modulating biochemical pathways, balance between reactive oxygen species and plant growth hormones, and improved resistance to stress and disease.

Table 2 Applications of CuO NPs in various fields

Summary of positive results	Plant species	Usage		Ref.
		Medicine	oilseed	
Can be effectively used to increase the performance of B. juncea	Brassica juncea	✓		(Faraz et al., 2023)
seed germination and cyto-physiological responses	Fenugreek	✓		(Kavitha et al., 2022)
Potential variation in biochemical constituents	Peanut plant leaves		✓	(Suresh et al., 2016)
It improved the plant's water use efficiency, and by creating a better root-to-stem ratio, it helped the plant become more resistant to water shortages.	Maize		✓	(Gomes et al., 2024)
Some growth and physiological parameters	Brassica napus		✓	(Rahmani et al., 2016)
Molecular level responses	Arabidopsis	✓		(Prakash et al., 2014)
Morphological, physiological and molecular level effects	seed crop Brassica juncea L		✓	(Nair & Chung, 2015b)
Improved photosynthetic activity	Elodea densa Planch	✓		(Nekrasova et al., 2011)
Highest rate of seeds germination were a chieved	Echinacea purpurea	✓		(Ahmed & Omran, 2024)
Lowest treatment concentration (3 µM, Cu) stimulated potassium absorption.	Matricaria chamomilla	✓		(Kováčik et al., 2008)

3.6 Phytotoxic activity and applications

Cu-based NPs have been studied particularly in pest management due to their phytotoxic activity. Common forms of these materials include copper sulfate ($CuSO_4$), copper oxide (CuO/Cu_2O), and copper hydroxide ($Cu(OH)_2$). These nanoparticles can inhibit the development of pathogenic microorganisms and limit their spread among agricultural crops (Gabal et al., 2018). Researchers have investigated greenly synthesized Cu NPs as potential antifungal agents, emphasizing their role in protecting crops against pests and diseases (Liu et al., 2022). Ultimately, the design and application of Cu-based NPs offer promising solutions for sustainable agriculture. Their antimicrobial properties, low cost, and environmentally friendly synthesis methods make them valuable tools in pest management (Feigl, 2023).

3.6.1 Nanoparticles and herbal medicine

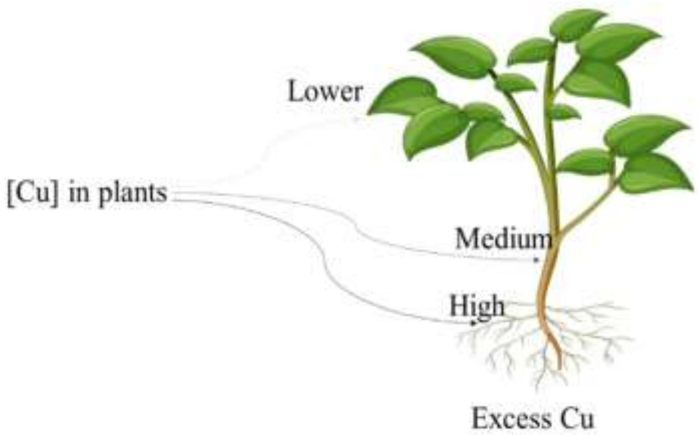
The innovative physical and chemical properties of nanomaterials potentially provide applications in various medical fields, including antidiabetic, anti-inflammatory, and antioxidant activity (Ringu et al., 2024). Also, in recent years, the rapid growth of the global nanomaterials market has stimulated research on the potential use of copper nanoparticles for diagnostics, biomarkers, drug development and delivery, cell labeling, cancer therapy, and wound healing of antiviral and antimicrobial agents (Antonio-Pérez et al., 2023). And due to antibiotic resistance, nanoparticles have been incorporated as antibacterial agents in the development of various products such as burn and wound treatment creams and skin care products (Salvioni et al., 2021; Ermini et al., 2023). In a study, products with copper-containing surfaces can be used for sterilization processes in hospitals, and the use of copper-containing alloys may limit the spread of multidrug-resistant bacteria in hospitals (Mikolay et al., 2010). Copper and its alloys are able to kill 99.9% of pathogenic bacteria within 2 hours and were recognized by the Environmental Protection Agency (EPA) as the first effective metal antimicrobial agents in 2008 (Robinson et al., 2024). However, changing the membrane potential (depolarisation) is considered as the main method for causing toxicity by copper (Mitra et al., 2019). Also, CuONPs are made extracellularly or intracellularly by various biological organisms such as bacteria, fungi, actinomycetes, algae and plants (Al-Ghabban & Eldiasty, 2022).

3.6.2 Toxicity Effects on Medicinal Plants

The toxicity of CuO NPs depends on their shape and surface properties, as both can affect the interaction of nanoparticles with cells as well as the rate of penetration into cells (Jampilek & Králová, 2015). Phytotoxicity: Cu NPs can have adverse effects on plant health and lead to phytotoxicity Fig 6. Some of the toxicities caused to plants include: 1) inhibition of plant growth- Cu NPs may inhibit plant growth by disrupting cellular processes, affecting nutrient uptake, and altering hormonal balance (Wang et al., 2020): 2) alterations in plant cell structure- Cu NPs can damage cell membranes, organelles, and cell walls, altering plant integrity (Da Costa & Sharma, 2016): 3) oxidative stress- Cu NPs produce reactive oxygen species (ROS), which cause oxidative stress. ROS can damage proteins, lipids, and DNA of plant cells (Nair & Chung, 2015a): 4) Genotoxic damage- Cu NPs may cause genetic mutations or DNA damage, which affects plant reproduction and overall fitness (Abdelkader et al., 2022).

Some medicinal plants, such as *Hypericum perforatum L.* or *Matricaria recutita L.*, are resistant to excess metals and accumulate high concentrations of toxic metals in their aerial parts/leaves (Masarovičová et al., 2010; Szőllősi et al., 2020). Therefore, to ensure food safety, cultivation of medicinal plants for commercial use under natural conditions should be carried out in soils uncontaminated by toxic metals (Šalamon et al., 2007). In addition, metals and metal oxides at the nanoscale can also be cytotoxic and genotoxic, causing cell cycle arrest and apoptosis induction, as well as serious DNA damage (Cavallo et al., 2023). Therefore, for each plant species, it is necessary to determine the concentrations that have plant growth-stimulating effects as well as plant growth-inhibitory effects. CuO NPs at different concentrations (0, 2, 4, 8, and 16 mg/L) were investigated on mustard plant growth. The results showed that among different concentrations of CuO NPs, 8 mg/L was the most optimal foliar spray treatment, as CuO NPs interacted with meristematic cells and initiated biochemical pathways that increased growth characteristics, but at higher concentrations it was proven to be inhibitory and decreased proline levels (Faraz et al., 2022). According to the study by Naderi et al. two foliar sprays CuO NPs (at the five-leaf stage and before flowering) with concentrations of 5 and 10 mg/L positively affected biomass, height, grain yield, and harvest index of fennel plant. In contrast, foliar application with a concentration of 20 mg/l of showed lesser effects on most of the above traits and the essential oil content of the plant compared to the 5 and 10 mg/L concentrations. Therefore, the use of an appropriate concentration of copper oxide nanoparticles improves plant tolerance, grain yield, and essential oil content of the aerial parts of fennel under drought stress (Naderi & Amooaghaie, 2023).

Fig. 6 Cu accumulates to a greater extent in the root, stem, and leaves



3.6.3 Impact on plant physiology, growth, and yield

The size and nature of the nanoparticles, the method of application, environmental conditions, rhizosphere and phyllosphere environment, and plant species are the main factors affecting the performance, and these superior properties of nanoparticles can enhance plant metabolism (Zhao et al., 2010). Since the size of NPs is very small; once inside plants, they allow for multiple applications (Cifuentes et al., 2010), they can cross the cell membrane and enter with various organelles and biomolecules such as DNA, RNA, and proteins, and can also transport DNA and chemicals into the plant cell (Nikalje, 2015). In studies reviewed by Atha et al. (2012), it was shown that CuO-NPs cause DNA damage in plants. Significant accumulation of mutagenic and oxidatively modified DNA lesions (7,8-dihydro-8-oxoguanine;2,6-diamino-4-hydroxy-5-formamidopyrimidine;4,6-diamino-5 formamidopyrimidine) and severe inhibition of plant growth were observed under controlled conditions *in vitro*. Keller et al. (2017) reported that Cu NPs effectively control pests when used as pesticides in agriculture. However, even at low doses (5–20 mg Cu per plant), there are metabolic effects due to Cu accumulation and production of reactive oxygen species (ROS).

3.6.4 Mechanisms of toxicity at the cellular and molecular levels

At least three distinct mechanisms are involved in the toxicity of nanoparticles (Brunner et al., 2006). First, ions released from nanoparticles are released into the environment. For example, Cu ions (Cu^+) released from Cu NPs or other toxic ions released from dissolved nanoparticles, which can contribute to DNA damage. Fe^{2+}, Ag^+, Cu^+, Mn^{2+}, Cr^{5+}, and Ni^{2+} are effective metal ions in the production of reactive oxygen species through Fenton-type reactions (Kruszewski et al., 2011). These ions can also bind to DNA bases (Robertazzi & Platts, 2006). Second, reactive oxygen species (ROS) are produced through surface reactions. Several studies have suggested a possible chemical reaction of hydrogen peroxide (H_2O_2) with Cu NPs, which is estimated to lead to the formation of Cu+ inside the cell (Liang et al., 2018). Third, the direct physical interaction of nanoparticles with physiological targets can be attributed to the interaction of carbon nanotubes with membranes and DNA. Cu NPs can also interact with mitochondria and other cellular components and disrupt their function. As reported, Cu NPs cause the production of reactive oxygen species, which can lead to DNA damage, by disrupting the mitochondrial respiratory chain and disrupting ATP synthesis (Lerner et al., 2016; Zhou et al., 2021).

3.6.5 Mechanisms of Toxicity

CuO NPs have been reported to affect plant growth by reducing germination rate, biomass reduction, root and shoot length, altering photosynthesis and transpiration rate, inhibiting chromatin compaction, and lipid peroxidation (Karlsson et al., 2009). Xiong et al. showed that most CuO NPs deposited as micrometer-sized aggregates either on the leaf surface or in stomata and could also block stomata. The stomatal opening also similarly changed shape to abiotic stress (Xiong et al., 2019). CuO NPs accumulation exhibited a disordered substructure in leaves, especially in the photosynthetic apparatus, by reducing the number of thylakoids per grain, plastoglobules, starch content, and stomatal opening (Olchowik et al., 2017). Genetic studies on Arabidopsis thaliana have shown that at a concentration of 0.2 mg/L, CuO NPs do not affect the expression of genes related to oxidative stress responses, sulfur uptake, glutathione, and proline biosynthesis, whereas gene expression is upregulated at higher concentrations (Prakash et al., 2014). It has also been observed that CuO NPs negatively affect photosynthetic activity by inactivating the reaction centers of photosystem II (PS II), reducing electron transport, the number of thylakoids per grain, the rate of photosynthesis, photosynthetic pigments, transpiration rate, and stomatal conductance (Perreault et al., 2014). Phytohormones have also been observed to change in response to CuO NPs (Le Van et al., 2016; Nair & Chung, 2017).

3.7 Factors affecting the uptake and accumulation of CuO NPs in plants

CuO NPs can enter plant cells through endocytosis or non-endocytotic penetration. They can be taken up by roots and transported to the stems through the vascular system (Doherty & McMahon, 2009; Milewska-Hendel et al., 2019). However, their effects on plant metabolism and growth depend on the hydrodynamic size, surface chemistry, concentration, and chemical conditions of the subcellular deposition site of CuO NPs (Dietz & Herth, 2011). Within leaves, the cell wall is a biological barrier with hydrophobic and hydrophilic components, with the waxy cuticle of the leaf epidermis and stomata being the main routes for delivery of nanomaterials to plant leaves (Hu et al., 2020). In a study by Sutulienė et al. (2024), they investigated the effects of different HPS and LED lights combined with CuO NPs on the plant (Mesembryanthemum). When plants were combined with CuO NPs and HPS lighting, Cu accumulation was higher.

3.7.1 Role of nanoparticle size, concentration, and exposure duration in toxicity effects

Nanomaterials behave differently from their bulk counterparts for two reasons: A: Surface effect (increased fraction of surface atoms in nanoparticles). B: Quantum effects (physical properties of electrons with decreasing particle size) (Roduner, 2006), which can affect the chemical reactivity of materials and lead to interactions with living organisms (Farré et al., 2011) Fig 7. The smaller size of CuO NPs is associated with greater surface reactivity, which can increase the bioavailability of nanoparticles compared with their ionic counterparts or bulk samples (Ju et al., 2022).

Fig. 7 Physicochemical properties of nanomaterials

The potential toxicity of Cu NPs on plant metabolism, defense systems, and growth may depend on the method of application, the concentration used, particle size, morphology, composition, and surface chemistry properties, including the chemical environment, intracellular locations, and plant species (Lin & Xing, 2008; Nuruzzaman et al., 2016). Jampílek & Kráľová (2019) reported that higher concentrations of nanoscale materials have adverse effects on plants and algae, can impair their photosynthetic performance, inhibit photosynthetic electron transport or CO_2 reduction by suppressing Rubisco activity, and enhance the production of reactive oxygen species. Accordingly, Cu NPs, similar to other nanomaterials, are likely to enter the environment and enter the human body through various routes such as wastewater, leakage during transportation and storage, consumer products and disposal, etc (Chen et al., 2006; Jain et al., 2021). CuO NPs cause dose-dependent pulmonary toxicity after inhalation (Gosens et al., 2021). It is well known that CuO NPs are highly toxic in vitro. In human alveolar epithelial cells, the mechanism of toxicity is most likely related to oxidative stress caused by intracellular soluble copper ions, ultimately leading to apoptotic or autophagic cell death (Moschini et al., 2023). If copper intake exceeds the human tolerance level, it causes toxic effects such as hemolysis, jaundice, liver cirrhosis, and even death (Zietz et al., 2003). The results of a study showed that copper intake at high concentrations caused negative effects on lipid profiles, which were associated with oxidative stress and decreased antioxidant enzyme activity (Galhardi et al., 2004).

3.7.2 Approaches to reduce the toxicity of CuO-based NPs on medicinal plants

3.7.1 Microbial synthesis

The environmentally friendly synthesis of CuO NPs is a challenging field in nanobiotechnology and is presented as a promising alternative to chemical routes because it avoids the production of secondary pollutants that affect the environment (Ibraheem et al., 2016). A large amount of CuO NPs is synthesized annually, but only a few of them are usefully utilized. Synthesized nanoparticles with desired morphology, size, and stability can enhance their overall quality for future applications (Govindaraju et al., 2008). Singh et al. (2010) found that microbial synthesis of CuO NPs using *E. coli* not only plays a role in the reduction of Cu(II) to CuO NPs, but also plays an important role in stabilizing the formed nanoparticles at room temperature. The formed CuO NPs had variable sizes and shapes. Bacteria-mediated biosynthesis offers a promising approach for scaling up the synthesis of commercially and technologically important MNPs and MONPs. This is an ecofriendly and safe approach to synthesize CuO NPs without the involvement of any toxic or stabilizing chemicals (Rautaray et al., 2003). Castro et al. reported a rapid and green synthesis method to obtain CuO NPs using protein fragments isolated from the aqueous extract of the brown alga *Macrocystis pyrifera* as reducing and capping agents. The use of water-soluble proteins from brown algae represents a green and facile method for the synthesis of homogeneous nanosized CuO NPs that exhibit high stability (Araya-Castro et al., 2020). Furthermore, the use of fabricated Cu and CuO NPs as biomedical, environmental remediation, and agricultural applications is also essential. Attention should be focused on their biocompatibility (Roy & Rhim, 2019). Physicochemical methods use toxic chemicals and energy-intensive routes, which makes these options environmentally hazardous and prevents their application for biomedical and clinical applications.

3.7.2 Concentration

Many laboratory studies have shown dose-dependent phytotoxicity of CuO NPs. Root shortening occurs in a range of plants grown in hydroponic, sand and soil conditions after exposure to CuO NPs (Adams et al., 2017). Therefore, knowledge of the concentration used is very important when using these materials. Kavitha et al. (2022) reported that the use of CuO NPs at concentrations of 10 mg/L on seed germination of fenugreek and *Vigna radiata* had a positive effect on germination and cellular physiology of fenugreek. Therefore, CuO NPs at low concentrations perform better in plant species. Yadav et al.'s study on the effects of cyanobacterial-based CuO NPs at different concentrations (5, 10, and 15 mg/L) showed that the use of nanoparticle formulations significantly enhanced plant growth under hydroponic conditions (Yadav et al., 2024). Chang et al. (2024) also reported that Cu^{2+} amendment at low and medium concentrations resulted in the agglomeration and adsorption of CuO NPs in alkaline soils, but decreased at high concentrations. These findings provide important insights into the fate of CuO NPs in soil environments, with significant implications for environmental risk assessment and soil amendment strategies. Although biofabrication of MNPs from plants and microorganisms does not leave toxic residues in the environment, their safe disposal is essential and special attention should be paid to their biocompatibility (Siddiqi & Husen, 2020).

3.7.3 Surface to volume ratio

As mentioned, several routes for the uptake of NPs by plant cells have been proposed. CuO NPs can enter plant cells by binding to carrier proteins, through aquaporins, ion channels, or endocytosis, by creating new pores, or by binding to organic chemicals in the environment (Watanabe et al., 2008; Kurepa et al., 2010). Due to the increased surface-to-mass ratio of nanoparticles compared with bulk metals, they are thought to be more reactive with their surroundings (Parveen et al., 2016).

Therefore, surfactants or functional groups are added to the surface of nanoparticles to reduce their activity of nanoparticles, thereby reducing toxicity (Rico et al., 2011). In a study by Huang et al. (2022), it was reported that surface coatings with trisodium citrate (TC) and polyethylene glycol (PEG) could reduce the health risks of CuO NPs to adults and increase the safety of CuO nanofertilizer application. This suggests that the coating can be designed to target nanoparticles to a specific part of the plant.

3.7.4 Morphology changes of NPs

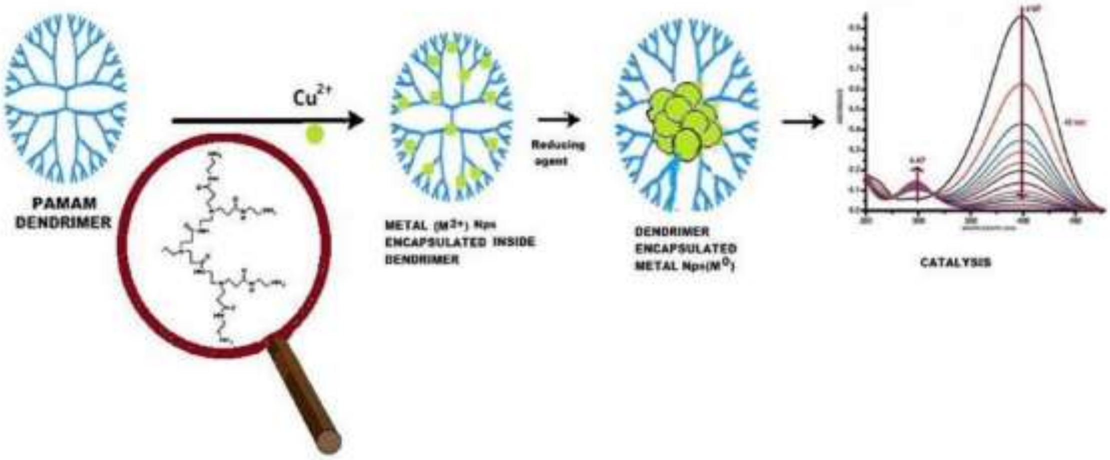
Further research shows, some shapes of nanomaterials can be more toxic, for example, sharper shapes may be more toxic and spherical shapes may be less toxic (Helmlinger et al., 2016). In addition, rod-shaped nanomaterials such as carbon nanotubes are more toxic than spherical nanoparticles due to their ability to enter the cell membrane and cause mechanical damage (Deline et al., 2020). CuO NPs synthesized using *Heliotropium bacciferum* plant extract with spherical morphology and an average particle diameter of 24.8 nm have been used as antifungal biological control agents and also for various sustainable agricultural applications (Hamdy et al., 2024). Moreover, smaller-sized nanomaterials will have the ability to cross the biological barriers of the body, interact with cells and cellular components, and cause toxicity. Meanwhile, smaller-sized nanoparticles will have a higher surface-to-volume ratio, which will cause more activity of the nanoparticles and the production of more amounts of reactive oxygen species (Carlson et al., 2008; Canaparo et al., 2020). Hence, smaller sizes will cause cytotoxicity (Sohaebuddin et al., 2010; Wei et al., 2014). Therefore, changing the morphology of nanomaterials can change their toxicity. In addition, temperature has a significant effect on the morphology and size of nanoparticles. Mott et al. (2007) investigated that the size, shape, and stability of Cu NPs strongly depend on the reaction temperature, such that the particle size increases almost linearly with increasing reaction temperature.

3.7.5 Addition of organic compounds to the surface of NPs

By adding compounds such as polymers to the surface of nanomaterials, the toxicity of nanomaterials can be reduced (Nikzamir et al., 2021; Wang et al., 2022). The base of the nanoparticles should be chosen to have lower toxicity; for example, instead of using Cu NPs, chemical compounds with less toxicity should be used (Nel et al., 2006; Jeevanandam et al., 2018). The addition of biostable polymers, proteins, and small organic molecules can prevent the aggregation of nanoparticles, affect the surface charge and reactivity of the nanomaterial surface, and reduce reactive oxygen species and oxidative stress (Sanità et al., 2020; Kumar et al., 2021). Fig 8 The results of a study showed that the surfactant

Bis(ethylhexyl)hydrogen phosphate HDEHP is very effective in resisting the oxidation of Cu NPs in nonpolar solvents (Song et al., 2004). Therefore, it can lead to a decrease in the oxidation of Cu in solvents and the entry of Cu into the solvent, followed by toxicity to the environment and living organisms.

Fig. 8 Use of PAMAM dendrimer to encapsulate copper (Cu^{2+}) metal ions



3.7.6 Potential benefits and risks of nanoparticle application in agriculture

3.7.6.1 Benefits

CuO NPs/Cu NPs have attracted increasing attention as one of the most important MNPs due to their beneficial properties for plants in terms of defense, growth, and nutrition (Eid et al., 2023). The use of CuO NPs in agriculture reduces chemical emissions, nutrient losses, increases crop yield, and productivity, and its effect varies with applied concentrations, physicochemical properties, and plant species (Aqeel et al., 2022). The use of CuO NPs as abiotic stimuli can be a useful strategy to increase phytochemical productivity in plant biotechnology (Chung et al., 2018). Cu-based NPs seem to have the potential to replace traditional bulk Cu materials and reduce Cu concentrations in the ecosystem (Borgatta et al., 2018). Ji et al. reported (2022) that the optimum concentration of Cu NPs of 10 mg/kg increased the uptake of some macronutrients and micronutrients in *Medicago polymorpha L*. compared with untreated plants. Thus, it enhances plant nutrition without disturbing soil texture and may vary depending on factors such as concentration and duration of exposure. It was reported in a study that CuO NPs controlled the growth of bacterial blight caused by *Xanthomonas axonopodis pv* (Mondal & Mani, 2012). In addition, since CuO NPs are inorganic, they are used in many industries due to their environmentally sustainable properties and high economic benefits compared with their organic counterparts (Dankovich & Smith, 2014; Shahane & Kumar, 2022).

3.7.6.2 Risk and environmental impact assessment

a) Reduced yield: CuO in food plants can reduce crop yield. Accumulation of CuO in plant tissues may lead to reduced productivity (Rawat et al., 2018).

b) Human health risks: When humans use plants containing CuO, there is a potential risk of human exposure to these nanomaterials. Understanding the transport and toxicity of CuO NPs in plants is crucial for risk assessment (Letchumanan et al., 2021).

c) Long-term accumulation: Repeated application of biosolids (containing CuO NPs) to soil or the use of nanoagricultural methods can lead to long-term accumulation of CuO NPs in plants, with subsequent widespread risks (Burachevskaya et al., 2021).

3.8 Future Research Directions

3.8.1 Nanoparticles on medicinal plants

Environmental implications of Cu-based metal and metal oxide nanoparticles clearly have the potential to induce oxidative DNA damage in plants (Gowtham et al., 2024). Plants show varying degrees of tolerance (formation and accumulation of DNA damage) to CuO NPs exposure, depending on the species (Kacziba et al., 2023), but all species show concentration-dependent growth inhibition induced by CuO NPs for the range of concentrations tested (Rao & Shekhawat, 2016). Wang et al. suggested that the ability of CuO NPs to induce oxidative DNA damage is an important toxicological endpoint that should be investigated in future studies (Wang et al., 2016). In particular, the ability of CuO NPs to induce DNA damage in plants grown in different soil types and plant species should be studied (Tripathi et al., 2024). The effect of low concentrations of nanoparticles for long periods, and the biochemical mechanisms underlying interspecific variability in plants in their ability to produce this damage, are other important research topics (Rajput, Minkina, Sushkova, et al., 2020). It is likely that the accumulation of mutagenic DNA damage in various drug-resistant strains could have profound generational effects on plant viability (Ma et al., 2018; Zigau et al., 2024). Moreover, a study by Nie et al. (2020) reported that CuO NPs cause phytotoxicity through physical damage and biochemical disruption of the cell wall, leading to loosening of the connections between cellulose microfibrils in the cell wall and disruption of cell adhesion in Arabidopsis. These findings contribute to a better understanding of the negative effects of CuO NPs on plant cellwalls.

3.8.2 Importance of long-term impacts on plant health and the ecosystem

Reports on consumer nanotechnology-based products and online databases indicate that more than 600 products and 2870 products contain NPs, respectively (Vignesh et al., 2024). Engineered nanoparticles can enter the environment through various routes and accumulate in the environment, causing high contamination in various environmental matrices in the atmosphere (Duhan et al., 2017). In agricultural soils, especially when amended with sewage sludge from wastewater treatment plants, in drainage water from agricultural fields that flows into rivers, lakes, and streams (Brar et al., 2010). Studies have shown that CuO may cause damage to the embryogenesis process in fish through non-point source contamination (Zhang et al., 2018). Studies show that the increasing number of nanoproducts and their use leads to increased release and accumulation of engineered nanoparticles in the environment, including soil. At the same time, soil provides essential nutrition for food crops, which can act as a reservoir for Cu NPs (Kusiak et al., 2022). Stamou & Antizar-Ladislao (2016) showed in a life cycle assessment (LCA) study that the impacts of nanoparticle-contaminated compost on human health endpoints and ecosystems are enhanced by the presence of NPs. Their accumulation in agricultural soils can also negatively affect the environment and soil microbial health (Fernández-Triana et al., 2024). This accumulation may occur in the original form of NPs or in the form of metal ions. This can vary according to the physicochemical properties. To this end, the accumulation of Cu NPs can alter plant physiological processes and affect the integrity of cellular and subcellular organelle organizations, modifying proteins, lipids, and nucleic acids by generating hydroxyl radicals (Rajput, Minkina, Mazarji, et al., 2020). Such a change in the physical properties of the membrane subsequently leads to the stimulation of an internal signaling cascade that disrupts the cells (Hussain et al., 2014; Khanna et al., 2021). The NPs then dissolve to release cell-permeable ions (which are toxic in nature) through toxic pathways on the cell surface.

3.9 Summary of key findings on the toxicity effects of CuO-based NPs on medicinal plants

CuO produces reactive oxygen species (ROS) that cause oxidative stress (Manceau et al., 2008). The toxicity of CuO NPs to medicinal plants depends on the concentration used, soil type, climatic conditions, and plant species sensitivity (Fedorenko et al., 2021). In a study, it was found that higher concentrations of Cu reduced root and hypocotyl elongation, germination, and chlorophyll and carotenoid concentrations in *E. haichowensis* (Lou et al., 2004). CuO may inhibit plant growth by disrupting cellular processes, affecting nutrient uptake, and altering hormonal balance. Kováčik et al. (2008) showed that total chlorophyll and leaf water content decreased when Cu was applied at higher concentrations. CuO NPs also affect plant growth by reducing germination rate and altering photosynthetic processes.

3.9.1 Implications for sustainable agriculture and plant health

CuO is an essential micronutrient that plays a role in carbon fixation and nitrogen metabolism, as well as in lignin biosynthesis, which not only strengthens cell walls but also prevents wilting (Malhi, 2009). The use of NPs as nanofertilizers has a positive effect on plant growth, development, and interaction with soil microflora, and this effect depends on the chemical composition of the NPs, the applied concentration, environmental conditions (e.g., pH, temperature, humidity, EC, and soil type), and also on the plant species (Achari & Kowshik, 2018). The behavior and environmental fate of MNPs have a clear impact on the quantity of MNPs, considering their adsorption, accumulation, stability, aggregation, and mobility in different environments. This increases the potential for environmental and human exposure to these particles (Gao et al., 2013). Water is known to be an important factor in the transport and fate of MNPs, which can enter aquatic environments along with chemicals used in landfill leachate, road runoff, sewage, etc (Bernhardt et al., 2010). In terrestrial ecosystems, soil–microbiota and plants are among the main environmental receptors of nanoparticles. In particular, soil microbial biomass acts as a reservoir of nutrients and is a sensitive indicator of microbial changes in the soil (Atlas, 1984). Therefore, it is not surprising that the conservation of soil–microbial biomass and diversity is one of the main challenges for sustainable resource use (Torsvik & Øvreås, 2002).

4. Conclusion

In general, this study Copper oxide nanoparticles in medicinal plant protection products: A review of soil ecotoxicology and threats to human health, and the conclusion are as follows:

1. Although the use of CuO NPs can increase the productivity of medicinal plants, their bioaccumulation, exposure time, and unique properties may lead to a wide range of adverse effects in humans.

2. Exposure of medicinal plants to different concentrations of CuO NPs initiates some stress strategies to reduce physiological and biochemical responses in cells. This study showed that the accumulation of CuO NPs in medicinal plant tissues varies based on the plant species and the concentration used.

3. The environmental fate of CuO NPs must be precisely determined, and criteria for sustainable applications in different plants should be established. In addition, the impact of NPs on humans and the identification of acceptable limits are also essential.

4. However, various detoxification mechanisms are involved in the uptake, transport and storage of CuO NPs in plants, which vary depending on the sources of contamination and the routes of exposure. Unfortunately, these mechanisms have not yet been fully investigated because they are not well understood, so further study is needed in this area.

5. The size and shapes of nanoparticles can be predicted by considering the preparation factors, reaction conditions, materials used and their concentration. The efficiency and practical application of nanofertilizers in agriculture strongly depend on their physical properties, including size, charge, shape, surface-to-volume ratio, crystal structure and density.

Therefore, understanding their benefits requires continued innovation and more interdisciplinary research is still needed to achieve the size, morphology, quality, and real cost of production, product type and its structural specifications. Therefore, by tuning their physical properties and addressing formulation challenges, their full potential can be exploited and create more sustainable and efficient agricultural systems. As a result, it will improve food security and contribute to environmental sustainability.

Statements and Declarations

Data availability

No data was used for the research described in the article.

Conflicts of interest

The authors of this paper declared no conflict of interest regarding the authorship or publication of this paper.

Author contribution

A. Pirmoghani: Writing original draft, Supervision, Formal analysis, D. Sheykhi Sanandaji: Writing original draft; H. Salehzadeh: Validation, Writing– Review & Editing; H. J. Choi: Writing– Review & Editing; B. Shahmoradi: Conceptualization, Writing– Review & Editing,

AI Use Declaration

During the preparation of this work, the author(s) used ChatGPT to improve some sentences. The authors have thoroughly reviewed and revised the content as necessary and assumed full responsibility for the final manuscript.

References

Abbasi Khalaki, M., Moameri, M., Asgari Lajayer, B., & Astatkie, T. (2021). Influence of nano-priming on seed germination and plant growth of forage and medicinal plants. *Plant growth regulation*, *93*(1), 13-28. DOI: 10.1007/s10725-020-00670-9.

Abbasifar, A., Shahrabadi, F., & ValizadehKaji, B. (2020). Effects of green synthesized zinc and copper nano-fertilizers on the morphological and biochemical attributes of basil plant. *Journal of Plant Nutrition*, *43*(8), 1104-1118. DOI: 10.1080/01904167.2020.1724305.

Abdallah, Y., Ogunyemi, S. O., Abdelazez, A., Zhang, M., Hong, X., Ibrahim, E., Hossain, A., Fouad, H., Li, B., & Chen, J. (2019). The green synthesis of MgO nano-flowers using Rosmarinus officinalis L.(Rosemary) and the antibacterial activities against Xanthomonas oryzae pv. oryzae. *BioMed Research International*, *2019*(1), 5620989. DOI: 10.1155/2019/5620989.

Abdelkader, M., Geioushy, R. A., Fouad, O. A., & Khaled, A. G. (2022). Investigation the activities of photosynthetic pigments, antioxidant enzymes and inducing genotoxicity of cucumber seedling exposed to copper oxides nanoparticles stress. *Scientia Horticulturae*, *305*, 111364. DOI: 10.1016/j.scienta.2022.111364.

Achari, G. A., & Kowshik, M. (2018). Recent developments on nanotechnology in agriculture: plant mineral nutrition, health, and interactions with soil microflora. *Journal of Agricultural and Food Chemistry*, *66*(33), 8647-8661. DOI: 10.1021/acs.jafc.8b00691.

Adams, J., Wright, M., Wagner, H., Valiente, J., Britt, D., & Anderson, A. (2017). Cu from dissolution of CuO nanoparticles signals changes in root morphology. *Plant Physiology and Biochemistry*, *110*, 108-117. DOI: 10.1016/j.plaphy.2016.08.005.

Ahmad, A., Khan, M., Osman, S. M., Haassan, A. M., Javed, M. H., Ahmad, A., Rauf, A., & Luque, R. (2024). Benign-by-design plant extract-mediated preparation of copper oxide nanoparticles for environmentally related applications. *Environmental Research*, *247*, 118048. DOI: 10.1016/j.envres.2023.118048.

Ahmed, M., & Omran, Z. (2024). EFFECT OF CuO NANOPARTICLES ON SEED GERMINATION AND SEEDLING GROWTH IN ECHINACEA PURPUREA IN VITRO. *Iraqi Journal of Agricultural Sciences*, *55*(Special), 34-42. DOI: 10.36103/ijas.v55iSpecial.1883.

Ahmed, T. S. (2023). Effect of Spraying with Some Plant Extracts and Copper Oxide Nanoparticles and their Interactions in Vegetative Growth, Mineral Content and Volatile Oils of Basil Plant Ocimum basilicum L. IOP Conference Series: Earth and Environmental Science, DOI: 10.1088/1755-1315/1213/1/012068.

Akintelu, S. A., Folorunso, A. S., Folorunso, F. A., & Oyebamiji, A. K. (2020). Green synthesis of copper oxide nanoparticles for biomedical application and environmental remediation. *Heliyon*, *6*(7). DOI: 10.1016/j.heliyon.2020.e04508.

Al-Ghabban, A., & Eldiasty, J. (2022). Green Synthesis of Copper Oxide Nanoparticle by Using Achillea fragrantissima and Nigella sativa Extracts and Their Effects as Larvicidal, Molluscicidal and Antimicrobial Agents. *Egyptian Academic Journal of Biological Sciences, E. Medical Entomology & Parasitology*, *14*(2), 127-148. DOI: 10.21608/EAJBSE.2022.270408.

Alangari, A., Aboul-Soud, M. A., Alqahtani, M. S., Shahid, M., Syed, R., Lakshmipathy, R., Modigunta, J. K. R., Jaiswal, H., & Verma, M. (2024). Green synthesis of copper oxide nanoparticles using genus Inula and evaluation of biological therapeutics and environmental applications. *Nanotechnology Reviews*, *13*(1), 20240039. DOI: 10.1515/ntrev-2024-0039.

Alengebawy, A., Abdelkhalek, S. T., Qureshi, S. R., & Wang, M.-Q. (2021). Heavy metals and pesticides toxicity in agricultural soil and plants: Ecological risks and human health implications. *Toxics*, *9*(3), 42. DOI: 10.3390/toxics9030042.

Alhalili, Z. (2022). Green synthesis of copper oxide nanoparticles CuO NPs from Eucalyptus Globoulus leaf extract: Adsorption and design of experiments. *Arabian Journal of Chemistry*, *15*(5), 103739. DOI: 10.1016/j.arabjc.2022.103739.

Ali, K., Sajid, M., Bakar, S. A., Younus, A., Ali, H., & Rashid, M. Z. (2024). Synthesis of copper oxide (CuO) via coprecipitation method: Tailoring structural and optical properties of CuO nanoparticles for optoelectronic device applications. *Hybrid Advances*, *6*, 100250. DOI: 10.1016/j.hybadv.2024.100250.

Amaliyah, S., Pangesti, D. P., Masruri, M., Sabarudin, A., & Sumitro, S. B. (2020). Green synthesis and characterization of copper nanoparticles using Piper retrofractum Vahl extract as bioreductor and capping agent. *Heliyon*, *6*(8). DOI: 10.1016/j.heliyon.2020.e04636.

Amin, N., & Aziz, K. (2025). Copper oxide-based nanoparticles in agro-nanotechnology: advances and applications for sustainable farming. *Agriculture & Food Security*, *14*(1), 7. DOI: 10.1186/s40066-025-00530-7.

Antonio-Pérez, A., Durán-Armenta, L. F., Pérez-Loredo, M. G., & Torres-Huerta, A. L. (2023). Biosynthesis of copper nanoparticles with medicinal plants extracts: From extraction methods to applications. *Micromachines*, *14*(10), 1882. DOI: 10.3390/mi14101882.

Applequist, W. L., Brinckmann, J. A., Cunningham, A. B., Hart, R. E., Heinrich, M., Katerere, D. R., & Van Andel, T. (2020). Scientists' warning on climate change and medicinal plants. *Planta medica*, *86*(01), 10-18. DOI: 10.1055/a-1041-3406.

Aqeel, U., Aftab, T., Khan, M. M. A., Naeem, M., & Khan, M. N. (2022). A comprehensive review of impacts of diverse nanoparticles on growth, development and physiological adjustments in plants under changing environment. *Chemosphere*, *291*, 132672. DOI: 10.1016/j.chemosphere.2021.132672.

Araya-Castro, K., Chao, T.-C., Durán-Vinet, B., Cisternas, C., Ciudad, G., & Rubilar, O. (2020). Green synthesis of copper oxide nanoparticles using protein fractions from an aqueous extract of brown algae Macrocystis pyrifera. *Processes*, *9*(1), 78. DOI: 10.3390/pr9010078.

Asemani, M., & Anarjan, N. (2019). Green synthesis of copper oxide nanoparticles using Juglans regia leaf extract and assessment of their physico-chemical and biological properties. *Green Processing and Synthesis*, *8*(1), 557-567. DOI: 10.1515/gps-2019-0025.

Atha, D. H., Wang, H., Petersen, E. J., Cleveland, D., Holbrook, R. D., Jaruga, P., Dizdaroglu, M., Xing, B., & Nelson, B. C. (2012). Copper oxide nanoparticle mediated DNA damage in terrestrial plant models. *Environmental science & technology*, *46*(3), 1819-1827. DOI: 10.1021/es202660k.

Atlas, R. M. (1984). Use of microbial diversity measurements to assess environmental stress. *Current perspectives in microbial ecology*, 540-545.

Auffan, M., Rose, J., Bottero, J.-Y., Lowry, G. V., Jolivet, J.-P., & Wiesner, M. R. (2009). Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective. *Nature nanotechnology*, *4*(10), 634-641. DOI: 10.1038/nnano.2009.242.

Bambharoliya, K. S., Bhatt, B., Salvi, P., Bhatt, M. D., Arora, S., & Bhatt, D. (2025). Green and Chemical Synthesis of Copper Oxide Nanoparticles for Antifungal Protection and Plant Growth Enhancement of Chickpea via Nanopriming. *Journal of Agricultural and Food Chemistry*. DOI: 10.1021/acs.jafc.5c03300.

Bansal, S. A., Khanna, V., Singh, A. P., & Kumar, S. (2022). Small percentage reinforcement of carbon nanotubes (CNTs) in epoxy (bisphenol-A) for enhanced mechanical performance. *Materials Today: Proceedings*, *61*, 275-279. DOI: 10.1016/j.matpr.2021.09.225.

Bernhardt, E. S., Colman, B. P., Hochella, M. F., Cardinale, B. J., Nisbet, R. M., Richardson, C. J., & Yin, L. (2010). An ecological perspective on nanomaterial impacts in the environment. *Journal of environmental quality*, *39*(6), 1954-1965. DOI: 10.2134/jeq2009.0479.

Betancourt-Galindo, R., Reyes-Rodriguez, P., Puente-Urbina, B., Avila-Orta, C., Rodríguez-Fernández, O., Cadenas-Pliego, G., Lira-Saldivar, R., & García-Cerda, L. (2014). Synthesis of copper nanoparticles by thermal decomposition and their antimicrobial properties. *Journal of Nanomaterials*, *2014*(1), 980545. DOI: 10.1155/2014/980545.

Bhat, B. A., Islam, S. T., Ali, A., Sheikh, B. A., Tariq, L., Islam, S. U., & Hassan Dar, T. U. (2020). Role of micronutrients in secondary metabolism of plants. In *Plant micronutrients: deficiency and toxicity management* (pp. 311-329). Springer. DOI: 10.1007/978-3-030-49856-6_13.

Borgatta, J., Ma, C., Hudson-Smith, N., Elmer, W., Plaza Perez, C. D., De La Torre-Roche, R., Zuverza-Mena, N., Haynes, C. L., White, J. C., & Hamers, R. J. (2018). Copper based nanomaterials suppress root fungal disease in watermelon (Citrullus lanatus): role of particle morphology, composition and dissolution behavior. *ACS Sustainable Chemistry & Engineering*, *6*(11), 14847-14856. DOI: 10.1021/acssuschemeng.8b03379.

Borkow, G., & Gabbay, J. (2009). Copper, an ancient remedy returning to fight microbial, fungal and viral infections. *Current Chemical Biology*, *3*(3), 272-278. DOI: 10.2174/187231309789054887.

Brar, S. K., Verma, M., Tyagi, R., & Surampalli, R. (2010). Engineered nanoparticles in wastewater and wastewater sludge–evidence and impacts. *Waste management*, *30*(3), 504-520. DOI: 10.1016/j.wasman.2009.10.012.

Brunner, T. J., Wick, P., Manser, P., Spohn, P., Grass, R. N., Limbach, L. K., Bruinink, A., & Stark, W. J. (2006). In vitro cytotoxicity of oxide nanoparticles: comparison to asbestos, silica, and the effect of particle solubility. *Environmental science & technology*, *40*(14), 4374-4381. DOI: 10.1021/es052069i.

Burachevskaya, M., Minkina, T., Mandzhieva, S., Bauer, T., Nevidomskaya, D., Shuvaeva, V., Sushkova, S., Kizilkaya, R., Gülser, C., & Rajput, V. (2021). Transformation of copper oxide and copper oxide nanoparticles in the soil and their accumulation by Hordeum sativum. *Environmental Geochemistry and Health*, *43*(4), 1655-1672. DOI: 10.1007/s10653-021-00857-7.

Canaparo, R., Foglietta, F., Limongi, T., & Serpe, L. (2020). Biomedical applications of reactive oxygen species generation by metal nanoparticles. *Materials*, *14*(1), 53. DOI: 10.3390/ma14010053.

Carlson, C., Hussain, S. M., Schrand, A. M., K. Braydich-Stolle, L., Hess, K. L., Jones, R. L., & Schlager, J. J. (2008). Unique cellular interaction of silver nanoparticles: size-dependent generation of reactive oxygen species. *The journal of physical chemistry B*, *112*(43), 13608-13619. DOI: 10.1021/jp712087m.

Cavallo, D., Chiarella, P., Fresegna, A. M., Ciervo, A., Del Frate, V., & Ursini, C. L. (2023). Metal Oxide Nanoparticles and Graphene-Based Nanomaterials: Genotoxic, Oxidative, and Epigenetic Effects. *Impact of Engineered Nanomaterials in Genomics and Epigenomics*, 99-143. DOI: 10.1002/9781119896258.ch5.

Chang, M., Liu, Y., Xu, M., Li, H., & Li, S. W. (2024). Particle morphology and soil properties affect the retention of copper oxide nanoparticles in agricultural soils. *Environmental Geochemistry and Health*, *46*(8), 281. DOI: 10.1007/s10653-024-02057-5.

Chen, Z., Meng, H., Xing, G., Chen, C., Zhao, Y., Jia, G., Wang, T., Yuan, H., Ye, C., & Zhao, F. (2006). Acute toxicological effects of copper nanoparticles in vivo. *Toxicology letters*, *163*(2), 109-120. DOI: 10.1016/j.toxlet.2005.10.003.

Chung, I.-M., Rekha, K., Rajakumar, G., & Thiruvengadam, M. (2018). Production of bioactive compounds and gene expression alterations in hairy root cultures of chinese cabbage elicited by copper oxide nanoparticles. *Plant Cell, Tissue and Organ Culture (PCTOC)*, *134*(1), 95-106. DOI: 10.1007/s11240-018-1402-0.

Cifuentes, Z., Custardoy, L., de la Fuente, J. M., Marquina, C., Ibarra, M. R., Rubiales, D., & Pérez-de-Luque, A. (2010). Absorption and translocation to the aerial part of magnetic carbon-coated nanoparticles through the root of different crop plants. *Journal of Nanobiotechnology*, *8*(1), 26. DOI: 10.1186/1477-3155-8-26.

Croteau, M.-N., Misra, S. K., Luoma, S. N., & Valsami-Jones, E. (2014). Bioaccumulation and toxicity of CuO nanoparticles by a freshwater invertebrate after waterborne and dietborne exposures. *Environmental science & technology*, *48*(18), 10929-10937. DOI: 10.1021/es5018703.

Da Costa, M., & Sharma, P. (2016). Effect of copper oxide nanoparticles on growth, morphology, photosynthesis, and antioxidant response in Oryza sativa. *Photosynthetica*, *54*(1), 110-119. DOI: 10.1007/s11099-015-0167-5.

Daimari, J., & Deka, A. K. (2024). Anticancer, antimicrobial and antioxidant activity of CuO–ZnO bimetallic nanoparticles: green synthesised from Eryngium foetidum leaf extract. *Scientific reports*, *14*(1), 19506. DOI: 10.1038/s41598-024-69847-w.

Dankovich, T. A., & Smith, J. A. (2014). Incorporation of copper nanoparticles into paper for point-of-use water purification. *Water research*, *63*, 245-251. DOI: 10.1016/j.watres.2014.06.022.

DeAlba-Montero, I., Guajardo-Pacheco, J., Morales-Sánchez, E., Araujo-Martínez, R., Loredo-Becerra, G., Martínez-Castañón, G.-A., Ruiz, F., & Compeán Jasso, M. (2017). Antimicrobial properties of copper nanoparticles and amino acid chelated copper nanoparticles produced by using a soya extract. *Bioinorganic chemistry and applications*, *2017*(1), 1064918. DOI: 10.1155/2017/1064918.

Deka, P., Borah, B. J., Saikia, H., & Bharali, P. (2019). Cu-based nanoparticles as emerging environmental catalysts. *The Chemical Record*, *19*(2-3), 462-473. DOI: 10.1002/tcr.201800055.

Deline, A. R., Frank, B. P., Smith, C. L., Sigmon, L. R., Wallace, A. N., Gallagher, M. J., Goodwin Jr, D. G., Durkin, D. P., & Fairbrother, D. H. (2020). Influence of oxygen-containing functional groups on the environmental properties, transformations, and toxicity of carbon nanotubes. *Chemical reviews*, *120*(20), 11651-11697. DOI: 10.1021/acs.chemrev.0c00351.

Dev, A., Srivastava, A. K., & Karmakar, S. (2017). Uptake and toxicity of nanomaterials in plants. *Nanoscience in Food and Agriculture 5*, 169-204. DOI: 10.1007/978-3-319-58496-6_7.

Dietz, K.-J., & Herth, S. (2011). Plant nanotoxicology. *Trends in plant science*, *16*(11), 582-589. DOI: 10.1016/j.tplants.2011.08.003.

Doherty, G. J., & McMahon, H. T. (2009). Mechanisms of endocytosis. *Annual review of biochemistry*, *78*(1), 857-902. DOI: 10.1146/annurev.biochem.78.081307.110540.

Dorjee, L., Gogoi, R., Kamil, D., Kumar, R., Mondal, T. K., Pattanayak, S., & Gurung, B. (2023). Essential oil-grafted copper nanoparticles as a potential next-generation fungicide for holistic disease management in maize. *Frontiers in Microbiology*, *14*, 1204512. DOI: 10.3389/fmicb.2023.1204512.

Duhan, J. S., Kumar, R., Kumar, N., Kaur, P., Nehra, K., & Duhan, S. (2017). Nanotechnology: The new perspective in precision agriculture. *Biotechnology reports*, *15*, 11-23. DOI: 10.1016/j.btre.2017.03.002.

Eid, A. M., Fouda, A., Hassan, S. E.-D., Hamza, M. F., Alharbi, N. K., Elkelish, A., Alharthi, A., & Salem, W. M. (2023). Plant-based copper oxide nanoparticles; biosynthesis, characterization, antibacterial activity, tanning wastewater treatment, and heavy metals sorption. *Catalysts*, *13*(2), DOI: 348. 10.3390/catal13020348.

Elbanna, H. M., Ahmed, O. K., Fayed, S. A.-K., Hammam, K. A.-M., & Yousef, R. S. (2024). Enhancing french basil growth through synergistic Foliar treatment with copper nanoparticles and Spirulina sp. *BMC Plant Biology*, *24*(1), 512. DOI: 10.1186/s12870-024-05153-x.

Elsayed, A. A., Ahmed, E.-G., Taha, Z. K., Farag, H. M., Hussein, M. S., & AbouAitah, K. (2022). Hydroxyapatite nanoparticles as novel nano-fertilizer for production of rosemary plants. *Scientia Horticulturae*, *295*, 110851. DOI: 10.1016/j.scienta.2021.110851.

Ermini, M. L., Summa, M., Zamborlin, A., Frusca, V., Mapanao, A. K., Mugnaioli, E., Bertorelli, R., & Voliani, V. (2023). Copper nano-architecture topical cream for the accelerated recovery of burnt skin. *Nanoscale Advances*, *5*(4), 1212-1219. DOI: 10.1039/d2na00786j.

Faraz, A., Faizan, M., D. Rajput, V., Minkina, T., Hayat, S., Faisal, M., Alatar, A. A., & Abdel-Salam, E. M. (2023). CuO nanoparticle-mediated seed priming improves physio-biochemical and enzymatic activities of Brassica juncea. *Plants*, *12*(4), 803. DOI: 10.3390/plants12040803.

Faraz, A., Faizan, M., Hayat, S., & Alam, P. (2022). Foliar application of copper oxide nanoparticles increases the photosynthetic efficiency and antioxidant activity in Brassica juncea. *Journal of Food Quality*, *2022*(1), 5535100. DOI: 10.1155/2022/5535100.

Farré, M., Sanchís, J., & Barceló, D. (2011). Analysis and assessment of the occurrence, the fate and the behavior of nanomaterials in the environment. *TrAC Trends in Analytical Chemistry*, *30*(3), 517-527. DOI: 10.1016/j.trac.2010.11.014.

Fedorenko, A. G., Minkina, T. M., Chernikova, N. P., Fedorenko, G. M., Mandzhieva, S. S., Rajput, V. D., Burachevskaya, M. V., Chaplygin, V. A., Bauer, T. V., & Sushkova, S. N. (2021). The toxic effect of CuO of different dispersion degrees on the structure and ultrastructure of spring barley cells (Hordeum sativum distichum). *Environmental Geochemistry and Health*, *43*(4), 1673-1687. DOI: 10.1007/s10653-020-00530-5.

Feigl, G. (2023). The impact of copper oxide nanoparticles on plant growth: a comprehensive review. *Journal of Plant Interactions*, *18*(1), 2243098. DOI: 10.1080/17429145.2023.2243098.

Feng, G., Xiong, Y.-J., Wei, H.-Y., Li, Y., & Mao, L.-F. (2023). Endemic medicinal plant distribution correlated with stable climate, precipitation, and cultural diversity. *Plant Diversity*, *45*(4), 479-484. DOI: 10.1016/j.pld.2022.09.007.

Fernández-Triana, I., Rubilar, O., Parada, J., Fincheira, P., Benavides-Mendoza, A., Durán, P., Fernández-Baldo, M., Seabra, A., & Tortella, G. (2024). Metal nanoparticles and pesticides under global climate change: Assessing the combined effects of multiple abiotic stressors on soil microbial ecosystems. *Science of The Total Environment*, *942*, 173494. DOI: 10.1016/j.scitotenv.2024.173494.

Fouda, A., Hassan, S. E.-D., Eid, A. M., Awad, M. A., Althumayri, K., Badr, N. F., & Hamza, M. F. (2022). Endophytic bacterial strain, Brevibacillus brevis-mediated green synthesis of copper oxide nanoparticles, characterization, antifungal, in vitro cytotoxicity, and larvicidal activity. *Green Processing and Synthesis*, *11*(1), 931-950. DOI: 10.1515/gps-2022-0080.

Gabal, E., Ramadan, M. M., Alghuthaymi, M. A., & Abd-Elsalam, K. A. (2018). Copper nanostructures applications in plant protection. In *Nanobiotechnology applications in plant protection* (pp. 63-86). Springer. DOI: 10.1007/978-3-319-91161-8_3

Galhardi, C. M., Diniz, Y. S., Faine, L. A., Rodrigues, H. G., Burneiko, R. C., Ribas, B. O., & Novelli, E. L. (2004). Toxicity of copper intake: lipid profile, oxidative stress and susceptibility to renal dysfunction. *Food and chemical toxicology*, *42*(12), 2053-2060. DOI: 10.1016/j.fct.2004.07.020.

Gao, M., Chang, J., Wang, Z., Zhang, H., & Wang, T. (2023). Advances in transport and toxicity of nanoparticles in plants. *Journal of Nanobiotechnology*, *21*(1), 75. DOI: 10.1186/s12951-023-01830-5.

Gao, Y., Luo, Z., He, N., & Wang, M. K. (2013). Metallic nanoparticle production and consumption in China between 2000 and 2010 and associative aquatic environmental risk assessment. *Journal of nanoparticle research*, *15*(6), 1681. DOI: 10.1007/s11051-013-1681-7.

García-Mayagoitia, S., Torres-Gómez, A. P., Pérez-Hernández, H., Patra, J. K., & Fernández-Luqueño, F. (2023). Collateral effects of nanopollution on human and environmental health. In *Agricultural and environmental nanotechnology: Novel technologies and their ecological impact* (pp. 619-645). Springer. DOI: 10.1007/978-981-19-5454-2_23.

Gawande, M. B., Goswami, A., Felpin, F.-X., Asefa, T., Huang, X., Silva, R., Zou, X., Zboril, R., & Varma, R. S. (2016). Cu and Cu-based nanoparticles: synthesis and applications in catalysis. *Chemical reviews*, *116*(6), 3722-3811. DOI: 10.1021/acs.chemrev.5b00482.

Geremew, A., Palmer, L., Johnson, A., Reeves, S., Brooks, N., & Carson, L. (2024). Multi-functional copper oxide nanoparticles synthesized using Lagerstroemia indica leaf extracts and their applications. *Heliyon*, *10*(9). DOI: 10.1016/j.heliyon.2024.e30178.

Gomes, D. G., Pieretti, J. C., Lange, C. N., Santana, B. d. M., Batista, B. L., Parreira, P. S. r., Zucareli, C., Seabra, A. B., & Oliveira, H. C. (2024). Seed Nanopriming with Green-Synthesized Cu-Based Nanoparticles for Maize Plants with Improved Tolerance to Hydric Stress. *ACS Applied Nano Materials*, *7*(17), 20058-20070. DOI: 10.1021/acsanm.4c02607.

Gomes, D. G., Pieretti, J. C., Lourenço, I. M., Oliveira, H. C., & Seabra, A. B. (2022). Copper-based nanoparticles for pesticide effects. In *Inorganic nanopesticides and nanofertilizers: A view from the mechanisms of action to field applications* (pp. 187-212). Springer. DOI: 10.1007/978-3-030-94155-0_6.

Gosens, I., Costa, P. M., Olsson, M., Stone, V., Costa, A. L., Brunelli, A., Badetti, E., Bonetto, A., Bokkers, B. G., & de Jong, W. H. (2021). Pulmonary toxicity and gene expression changes after short-term inhalation exposure to surface-modified copper oxide nanoparticles. *NanoImpact*, *22*, 100313. DOI: 10.1016/j.impact.2021.100313.

Govindaraju, K., Basha, S. K., Kumar, V. G., & Singaravelu, G. (2008). Silver, gold and bimetallic nanoparticles production using single-cell protein (Spirulina platensis) Geitler. *Journal of Materials Science*, *43*(15), 5115-5122. DOI: 10.1007/s10853-008-2745-4.

Gowtham, H., Shilpa, N., Singh, S. B., Aiyaz, M., Abhilash, M., Nataraj, K., Amruthesh, K., Ansari, M. A., Alomary, M. N., & Murali, M. (2024). Toxicological effects of nanoparticles in plants: Mechanisms involved at morphological, physiological, biochemical and molecular levels. *Plant Physiology and Biochemistry*, *210*, 108604. DOI: 10.1016/j.plaphy.2024.108604.

Grigore, M. E., Biscu, E. R., Holban, A. M., Gestal, M. C., & Grumezescu, A. M. (2016). Methods of synthesis, properties and biomedical applications of CuO nanoparticles. *Pharmaceuticals*, *9*(4), DOI: 75. 10.3390/ph9040075.

Gunalan, S., Sivaraj, R., & Venckatesh, R. (2012). Aloe barbadensis Miller mediated green synthesis of mono-disperse copper oxide nanoparticles: optical properties. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *97*, 1140-1144. DOI: 10.1016/j.saa.2012.07.096.

Hamdy, E., El-Gendi, H., Al-Askar, A., El-Far, A., Kowalczewski, P., Behiry, S., & Abdelkhalek, A. (2024). Copper oxide nanoparticles-mediated Heliotropium bacciferum leaf extract: antifungal activity and molecular docking assays against strawberry pathogens. *Open Chemistry*, *22*(1), 20240028. DOI: 10.1515/chem-2024-0028.

Helmlinger, J., Sengstock, C., Groß-Heitfeld, C., Mayer, C., Schildhauer, T. A., Köller, M., & Epple, M. (2016). Silver nanoparticles with different size and shape: equal cytotoxicity, but different antibacterial effects. *RSC advances*, *6*(22), 18490-18501. DOI: 10.1039/c5ra27836h.

Hong, J., Wang, C., Wagner, D. C., Gardea-Torresdey, J. L., He, F., & Rico, C. M. (2021). Foliar application of nanoparticles: mechanisms of absorption, transfer, and multiple impacts. *Environmental Science: Nano*, *8*(5), 1196-1210. DOI: 10.1039/D0EN01129K.

Hu, P., An, J., Faulkner, M. M., Wu, H., Li, Z., Tian, X., & Giraldo, J. P. (2020). Nanoparticle charge and size control foliar delivery efficiency to plant cells and organelles. *ACS nano*, *14*(7), 7970-7986. DOI: 10.1021/acsnano.9b09178.

Huang, G., Zuverza-Mena, N., White, J. C., Hu, H., Xing, B., & Dhankher, O. P. (2022). Simultaneous exposure of wheat (Triticum aestivum L.) to CuO and S nanoparticles alleviates toxicity by reducing Cu accumulation and modulating antioxidant response. *Science of The Total Environment*, *839*, 156285. DOI: 10.1016/j.scitotenv.2022.156285.

Huang, Y., Bai, X., Li, C., Kang, M. e., Weng, Y., & Gong, D. (2022). Modulation mechanism of phytotoxicity on Ipomoea aquatica Forssk. by surface coating-modified copper oxide nanoparticles and its health risk assessment. *Environmental Pollution*, *314*, 120288. DOI: 10.1016/j.envpol.2022.120288.

Hussain, S., Garantziotis, S., Rodrigues-Lima, F., Dupret, J.-M., Baeza-Squiban, A., & Boland, S. (2014). Intracellular signal modulation by nanomaterials. *Nanomaterial: Impacts on Cell Biology and Medicine*, 111-134. DOI: 10.1007/978-94-017-8739-0_7.

Ibraheem, I., Abd-Elaziz, B., Saad, W., & Fathy, W. (2016). Green biosynthesis of silver nanoparticles using marine Red Algae Acanthophora specifera and its antimicrobial activity. *J Nanomed Nanotechnol*, *7*(409), 1-4. DOI: 10.4172/2157-7439.1000409.

Idrees, S., Abbasi, B. A., Iqbal, J., & Kazi, M. (2025). Euphorbia serpens extracts mediated synthesis of copper oxide nanoparticles and their biological applications. *Heliyon*, *11*(1). DOI: 10.1016/j.heliyon.2024.e41397.

Iranbakhsh, A., Oraghi Ardebili, Z., & Oraghi Ardebili, N. (2021). Synthesis and characterization of zinc oxide nanoparticles and their impact on plants. In *Plant responses to nanomaterials: recent interventions, and physiological and biochemical responses* (pp. 33-93). Springer. DOI: 10.1007/978-3-030-36740-4_3.

Jain, M., Yadav, M., & Chaudhry, S. (2021). Copper oxide nanoparticles for the removal of divalent nickel ions from aqueous solution. *Toxin Reviews*, *40*(4), 872-885. DOI: 10.1080/15569543.2020.1799407.

Jampilek, J., & Králová, K. (2015). Application of nanotechnology in agriculture and food industry, its prospects and risks. *Ecological Chemistry and Engineering*, *22*(3), 321. DOI: 10.1515/eces-2015-0018.

Jampílek, J., & Kráľová, K. (2019). Impact of nanoparticles on photosynthesizing organisms and their use in hybrid structures with some components of photosynthetic apparatus. In *Plant Nanobionics: Volume 1, Advances in the Understanding of Nanomaterials Research and Applications* (pp. 255-332). Springer. DOI: 10.1007/978-3-030-12496-0_11.

Javed, R., Mohamed, A., Yücesan, B., Gürel, E., Kausar, R., & Zia, M. (2017). CuO nanoparticles significantly influence in vitro culture, steviol glycosides, and antioxidant activities of Stevia rebaudiana Bertoni. *Plant Cell, Tissue and Organ Culture (PCTOC)*, *131*(3), 611-620. DOI: 10.1007/s11240-017-1312-6.

Jayarambabu, N., Akshaykranth, A., Rao, T. V., Rao, K. V., & Kumar, R. R. (2020). Green synthesis of Cu nanoparticles using Curcuma longa extract and their application in antimicrobial activity. *Materials Letters*, *259*, 126813. DOI: 10.1016/j.matlet.2019.126813.

Jeevanandam, J., Barhoum, A., Chan, Y. S., Dufresne, A., & Danquah, M. K. (2018). Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. *Beilstein journal of nanotechnology*, *9*(1), 1050-1074. DOI: 10.3762/bjnano.9.98.

Ji, H., Guo, Z., Wang, G., Wang, X., & Liu, H. (2022). Effect of ZnO and CuO nanoparticles on the growth, nutrient absorption, and potential health risk of the seasonal vegetable Medicago polymorpha L. *PeerJ*, *10*, e14038. DOI: 10.7717/peerj.14038.

Jośko, I., Dobrzyńska, J., Dobrowolski, R., Kusiak, M., & Terpiłowski, K. (2020). The effect of pH and ageing on the fate of CuO and ZnO nanoparticles in soils. *Science of The Total Environment*, *721*, 137771. DOI: 10.1016/j.scitotenv.2020.137771.

Ju, Y., Li, X., Ju, L., Feng, H., Tan, F., Cui, Y., Yang, Y., Wang, X., Cao, J., & Qiao, P. (2022). Nanoparticles in the

Earth surface systems and their effects on the environment and resource. *Gondwana Research*, *110*, 370-392. DOI: 10.1016/j.gr.2022.02.012.

Kacziba, B., Szierer, Á., Mészáros, E., Rónavári, A., Kónya, Z., & Feigl, G. (2023). Exploration the homeostasis of signaling molecules in monocotyledonous crops with different CuO nanoparticle tolerance. *Plant Stress*, *7*, 100145. DOI: 10.1016/j.stress.2023.100145.

Karlsson, H. L., Gustafsson, J., Cronholm, P., & Möller, L. (2009). Size-dependent toxicity of metal oxide particles—a comparison between nano-and micrometer size. *Toxicology letters*, *188*(2), 112-118. DOI: 10.1016/j.toxlet.2009.03.014.

Kavitha, K., Paul, J. A. J., Kumar, P., Archana, J., Begam, H. F., Karmegam, N., & Biruntha, M. (2022). Impact of biosynthesized CuO nanoparticles on seed germination and cyto-physiological responses of Trigonella foenum-graecum and Vigna radiata. *Materials Letters*, *313*, 131756. DOI: 10.1016/j.matlet.2022.131756.

Keller, A. A., Adeleye, A. S., Conway, J. R., Garner, K. L., Zhao, L., Cherr, G. N., Hong, J., Gardea-Torresdey, J. L., Godwin, H. A., & Hanna, S. (2017). Comparative environmental fate and toxicity of copper nanomaterials. *NanoImpact*, *7*, 28-40. DOI: 10.1016/j.impact.2017.05.003.

Keller, A. A., McFerran, S., Lazareva, A., & Suh, S. (2013). Global life cycle releases of engineered nanomaterials. *Journal of nanoparticle research*, *15*(6), 1692. DOI: 10.1007/s11051-013-1692-4.

Khan, M. R., Siddiqui, Z. A., & Fang, X. (2022). Potential of metal and metal oxide nanoparticles in plant disease diagnostics and management: Recent advances and challenges. *Chemosphere*, *297*, 134114. DOI: 10.1016/j.chemosphere.2022.134114.

Khanna, K., Kohli, S. K., Handa, N., Kaur, H., Ohri, P., Bhardwaj, R., Yousaf, B., Rinklebe, J., & Ahmad, P. (2021). Enthralling the impact of engineered nanoparticles on soil microbiome: A concentric approach towards environmental risks and cogitation. *Ecotoxicology and Environmental Safety*, *222*, 112459. DOI: 10.1016/j.ecoenv.2021.112459.

Kokorekin, V., Gamayunova, A., Yanilkin, V., & Petrosyan, V. (2017). Mediated electrochemical synthesis of copper nanoparticles in solution. *Russian Chemical Bulletin*, *66*(11), 2035-2043. DOI: 10.1007/s11172-017-1978-2.

Kováčik, J., Grúz, J., Bačkor, M., Tomko, J., Strnad, M., & Repčák, M. (2008). Phenolic compounds composition and physiological attributes of Matricaria chamomilla grown in copper excess. *Environmental and experimental botany*, *62*(2), 145-152. DOI: 10.1016/j.envexpbot.2007.07.012.

Kruszewski, M., Brzoska, K., Brunborg, G., Asare, N., Dobrzyńska, M., Dušinská, M., Fjellsbø, L. M., Georgantzopoulou, A., Gromadzka-Ostrowska, J., & Gutleb, A. C. (2011). Toxicity of silver nanomaterials in higher eukaryotes. *Advances in molecular toxicology*, *5*, 179-218. DOI: 10.1016/B978-0-444-53864-2.00005-0.

Kumar, A., Kaladharan, K., & Tseng, F.-G. (2021). Nanomaterials: Surface functionalization, modification, and applications. In *Nanomaterials and Their Biomedical Applications* (pp. 405-438). Springer. DOI: 10.1007/978-981-33-6252-9_14.

Kumar, S., Kumar, S., Kaur, H., Kumar, S., Rani, D., Singh, S., Gaur, J., Misra, M., & Singh, A. (2024). Harmonizing nature's blueprint: Enhanced synthesis of CuO nanoparticles using Trigonella foenum-graecum for advanced water purification. *Interactions*, *245*(1), 80. DOI: 10.1007/s10751-024-01915-z.

Kurepa, J., Paunesku, T., Vogt, S., Arora, H., Rabatic, B. M., Lu, J., Wanzer, M. B., Woloschak, G. E., & Smalle, J. A. (2010). Uptake and distribution of ultrasmall anatase TiO2 Alizarin red S nanoconjugates in Arabidopsis thaliana. *Nano letters*, *10*(7), 2296-2302. DOI: 10.1021/nl903518f.

Kusiak, M., Oleszczuk, P., & Jośko, I. (2022). Cross-examination of engineered nanomaterials in crop production: Application and related implications. *Journal of hazardous materials*, *424*, 127374. DOI: 10.1016/j.jhazmat.2021.127374.

Labaran, A. N., Zango, Z. U., Tailor, G., Alsadig, A., Usman, F., Mukhtar, M. T., Garba, A. M., Alhathlool, R., Ibnaouf, K. H., & Aldaghri, O. A. (2024). Biosynthesis of copper nanoparticles using Alstonia scholaris leaves and its antimicrobial studies. *Scientific reports*, *14*(1), 5589. DOI: 10.1038/s41598-024-56052-y.

Lafmejani, Z. N., Jafari, A. A., Moradi, P., & Moghadam, A. L. (2018). Impact of foliar application of copper sulphate and copper nanoparticles on some morpho-physiological traits and essential oil composition of peppermint (Mentha piperita L.). *Herba Polonica*, *64*(2). DOI: 10.2478/hepo-2018-0006.

Le Van, N., Rui, Y., Cao, W., Shang, J., Liu, S., Nguyen Quang, T., & Liu, L. (2016). Toxicity and bio-effects of CuO nanoparticles on transgenic Ipt-cotton. *Journal of Plant Interactions*, *11*(1), 108-116. DOI: 10.1080/17429145.2016.1217434.

Lee, W. M., An, Y. J., Yoon, H., & Kweon, H. S. (2008). Toxicity and bioavailability of copper nanoparticles to the terrestrial plants mung bean (Phaseolus radiatus) and wheat (Triticum aestivum): plant agar test for water-insoluble nanoparticles. *Environmental toxicology and chemistry*, *27*(9), 1915-1921. DOI: 10.1897/07-481.1.

Lerner, C. A., Rutagarama, P., Ahmad, T., Sundar, I. K., Elder, A., & Rahman, I. (2016). Electronic cigarette aerosols and copper nanoparticles induce mitochondrial stress and promote DNA fragmentation in lung fibroblasts. *Biochemical and biophysical research communications*, *477*(4), 620-625. DOI: 10.1016/j.bbrc.2016.06.109.

Letchumanan, D., Sok, S. P., Ibrahim, S., Nagoor, N. H., & Arshad, N. M. (2021). Plant-based biosynthesis of copper/copper oxide nanoparticles: an update on their applications in biomedicine, mechanisms, and toxicity. *Biomolecules*, *11*(4), 564. DOI: 10.3390/biom11040564.

Liang, J., Wei, M., Wang, Q., Zhao, Z., Liu, A., Yu, Z., & Tian, Y. (2018). Sensitive electrochemical determination of hydrogen peroxide using copper nanoparticles in a polyaniline film on a glassy carbon electrode. *Analytical Letters*, *51*(4), 512-522. DOI: 10.1080/00032719.2017.1343832.

Lin, D., & Xing, B. (2008). Root uptake and phytotoxicity of ZnO nanoparticles. *Environmental science & technology*, *42*(15), 5580-5585. DOI: 10.1021/es800422x.

Liu, Y., Zhao, W., Yin, Y., Adeel, M., Shakoor, N., Li, Y., Tan, Z., Rui, Y., Zhang, Q., & Liu, J. (2022). Agricultural applications and potential risks of copper-based nanoagrochemicals in crop cultivation. *Reviews of Environmental Contamination and Toxicology*, *260*(1), 20. DOI: 10.1007/s44169-022-00022-w.

Lou, L.-q., Shen, Z.-g., & Li, X.-d. (2004). The copper tolerance mechanisms of Elsholtzia haichowensis, a plant from copper-enriched soils. *Environmental and experimental botany*, *51*(2), 111-120. DOI: 10.1016/j.envexpbot.2003.08.002.

Lubbe, A., & Verpoorte, R. (2011). Cultivation of medicinal and aromatic plants for specialty industrial materials. *Industrial crops and products*, *34*(1), 785-801. DOI: 10.1016/j.indcrop.2011.01.019.

Ma, C., White, J. C., Zhao, J., Zhao, Q., & Xing, B. (2018). Uptake of engineered nanoparticles by food crops: characterization, mechanisms, and implications. *Annual review of food science and technology*, *9*, 129-153. DOI: 10.1146/annurev-food-030117-012657.

Malhi, S. (2009). Effectiveness of seed-soaked Cu, autumn-versus spring-applied Cu, and Cu-treated P fertilizer on seed yield of wheat and residual nitrate-N for a Cu-deficient soil. *Canadian Journal of Plant Science*, *89*(6), 1017-1030. DOI: 10.4141/CJPS08189.

Manceau, A., Nagy, K. L., Marcus, M. A., Lanson, M., Geoffroy, N., Jacquet, T., & Kirpichtchikova, T. (2008). Formation of metallic copper nanoparticles at the soil− root interface. *Environmental science & technology*, *42*(5), 1766-1772. DOI: 10.1021/es072017o.

Mandal, D., Bolander, M. E., Mukhopadhyay, D., Sarkar, G., & Mukherjee, P. (2006). The use of microorganisms for the formation of metal nanoparticles and their application. *Applied microbiology and biotechnology*, *69*(5), 485-492. DOI: 10.1007/s00253-005-0179-3.

Marcelino, S., Hamdane, S., Gaspar, P. D., & Paço, A. (2023). Sustainable agricultural practices for the production of medicinal and aromatic plants: evidence and recommendations. *Sustainability*, *15*(19), 14095. DOI: 10.3390/su151914095.

Maroufpoor, N., Mousavi, M., Hatami, M., Rasoulnia, A., & Lajayer, B. A. (2019). Mechanisms involved in stimulatory and toxicity effects of nanomaterials on seed germination and early seedling growth. *Advances in phytonanotechnology*, 153-181. DOI: 10.1016/B978-0-12-815322-2.000067.

Masarovičová, E., Kráľová, K., & Kummerová, M. (2010). Principles of classification of medicinal plants as hyperaccumulators or excluders. *Acta physiologiae plantarum*, *32*(5), 823-829. DOI: 10.1007/s11738-010-0474-1.

Mavil-Guerrero, E., Vazquez-Duhalt, R., & Juarez-Moreno, K. (2024). Exploring the cytotoxicity mechanisms of copper ions and copper oxide nanoparticles in cells from the excretory system. *Chemosphere*, *347*, 140713. DOI: 10.1016/j.chemosphere.2023.140713.

Michiels, C., Raes, M., Toussaint, O., & Remacle, J. (1994). Importance of Se-glutathione peroxidase, catalase, and Cu/Zn-SOD for cell survival against oxidative stress. *Free radical Biology and medicine*, *17*(3), 235-248. DOI: 10.1016/0891-5849(94)90079-5.

Mikolay, A., Huggett, S., Tikana, L., Grass, G., Braun, J., & Nies, D. H. (2010). Survival of bacteria on metallic copper surfaces in a hospital trial. *Applied microbiology and biotechnology*, *87*(5), 1875-1879. DOI: 10.1007/s00253-010-2640-1.

Milewska-Hendel, A., Zubko, M., Stróż, D., & Kurczyńska, E. U. (2019). Effect of nanoparticles surface charge on the Arabidopsis thaliana (L.) roots development and their movement into the root cells and protoplasts. *International journal of molecular sciences*, *20*(7), 1650. DOI: 10.3390/ijms20071650.

Mitra, D., Kang, E.-T., & Neoh, K. G. (2019). Antimicrobial copper-based materials and coatings: potential multifaceted biomedical applications. *ACS applied materials & interfaces*, *12*(19), 21159-21182. DOI: 10.1021/acsami.9b17815.

Mohammad Shafiee, M., Kargar, M., & Ghashang, M. (2016). Simple synthesis of copper oxide nanoparticles in the presence of extractive Rosmarinus officinalis leaves. *Journal of Nanostructures*, *6*(1), 28-31. DOI: 10.7508/JNS.2016.01.004.

Mondal, K. K., & Mani, C. (2012). Investigation of the antibacterial properties of nanocopper against Xanthomonas axonopodis pv. punicae, the incitant of pomegranate bacterial blight. *Annals of microbiology*, *62*(2), 889-893. DOI: 10.1007/s13213-011-0382-7.

Monreal, C., DeRosa, M., Mallubhotla, S., Bindraban, P., & Dimkpa, C. (2016). Nanotechnologies for increasing the crop use efficiency of fertilizer-micronutrients. *Biology and fertility of soils*, *52*(3), 423-437. DOI: 10.1007/s00374-015-1073-5.

Moschini, E., Colombo, G., Chirico, G., Capitani, G., Dalle-Donne, I., & Mantecca, P. (2023). Biological mechanism of cell oxidative stress and death during short-term exposure to nano CuO. *Scientific reports*, *13*(1), 2326. DOI: 10.1038/s41598-023-28958-6.

Mott, D., Galkowski, J., Wang, L., Luo, J., & Zhong, C.-J. (2007). Synthesis of size-controlled and shaped copper nanoparticles. *Langmuir*, *23*(10), 5740-5745. DOI: 10.1021/la0635092.

Moumen, A., Kumarage, G. C., & Comini, E. (2022). P-type metal oxide semiconductor thin films: Synthesis and chemical sensor applications. *Sensors*, *22*(4), 1359. DOI: 10.3390/s22041359.

Naderi, A., & Amooaghaie, R. (2023). The effect of CuO nanoparticles and irrigation intervals on antioxidant responses, yield components and essential oil content in Foeniculum vulgare Mill. *Journal of Plant Process and Function*, *12*(56), 59-74.

Nagar, N., & Devra, V. (2018). Green synthesis and characterization of copper nanoparticles using Azadirachta indica leaves. *Materials Chemistry and Physics*, *213*, 44-51. DOI: 10.1016/j.matchemphys.2018.04.007.

Naika, H. R., Lingaraju, K., Manjunath, K., Kumar, D., Nagaraju, G., Suresh, D., & Nagabhushana, H. (2015). Green synthesis of CuO nanoparticles using Gloriosa superba L. extract and their antibacterial activity. *Journal of Taibah University for Science*, *9*(1), 7-12. DOI: 10.1016/j.jtusci.2014.04.006.

Nair, P. M. G., & Chung, I. M. (2015a). Changes in the growth, redox status and expression of oxidative stress related genes in chickpea (Cicer arietinum L.) in response to copper oxide nanoparticle exposure. *Journal of Plant Growth Regulation*, *34*(2), 350-361. DOI: 10.1007/s00344-014-9468-3.

Nair, P. M. G., & Chung, I. M. (2015b). Study on the correlation between copper oxide nanoparticles induced growth suppression and enhanced lignification in Indian mustard (Brassica juncea L.). *Ecotoxicology and Environmental Safety*, *113*, 302-313. DOI: 10.1016/j.ecoenv.2014.12.013.

Nair, P. M. G., & Chung, I. M. (2017). Evaluation of stress effects of copper oxide nanoparticles in Brassica napus L. seedlings. *3 Biotech*, *7*(5), 293. DOI: 10.1007/s13205-017-0929-9.

Nazir, A., Malik, K., Qamar, H., Basit, M. H., Liaqat, A., Shahid, M., Khan, M. I., Fatima, A., Irshad, A., & Sadia, H. (2020). 9. A review: Use of plant extracts and their phytochemical constituents to control antibiotic resistance in S. aureus. *Pure and Applied Biology (PAB)*, *9*(1), 720-727. DOI: 10.19045/bspab.2020.90078.

Nekoukhou, M., Fallah, S., Pokhrel, L. R., Abbasi-Surki, A., & Rostamnejadi, A. (2023). Foliar enrichment of copper oxide nanoparticles promotes biomass, photosynthetic pigments, and commercially valuable secondary metabolites and essential oils in dragonhead (Dracocephalum moldavica L.) under semi-arid conditions. *Science of The Total Environment*, *863*, 160920. DOI: 10.1016/j.scitotenv.2022.160920.

Nekoukhou, M., Fallah, S., Pokhrel, L. R., Abbasi-Surki, A., & Rostamnejadi, A. (2024). Foliar co-application of zinc oxide and copper oxide nanoparticles promotes phytochemicals and essential oil production in dragonhead (Dracocephalum moldavica). *Science of The Total Environment*, *906*, 167519. DOI: 10.1016/j.scitotenv.2023.167519.

Nekrasova, G., Ushakova, O., Ermakov, A., Uimin, M., & Byzov, I. (2011). Effects of copper (II) ions and copper oxide nanoparticles on Elodea densa Planch. *Russian Journal of Ecology*, *42*(6), 458-463. DOI: 10.1134/S1067413611060117.

Nel, A., Xia, T., Madler, L., & Li, N. (2006). Toxic potential of materials at the nanolevel. *science*, *311*(5761), 622-627. DOI: 10.1126/science.1114397.

Nguyen, N. H., Padil, V. V. T., Slaveykova, V. I., Černík, M., & Ševců, A. (2018). Green synthesis of metal and metal oxide nanoparticles and their effect on the unicellular alga Chlamydomonas reinhardtii. *Nanoscale research letters*, *13*(1), 159. DOI: 10.1186/s11671-018-2575-5.

Nie, G., Zhao, J., He, R., & Tang, Y. (2020). CuO nanoparticle exposure impairs the root tip cell walls of Arabidopsis thaliana seedlings. *Water, Air, & Soil Pollution*, *231*(7), 324. DOI: 10.1007/s11270-020-04676-x.

Nikalje, A. P. (2015). Nanotechnology and its applications in medicine. *Med chem*, *5*(2), 081-089. DOI: 10.4172/2161-0444.1000247.

Nikzamir, M., Hanifehpour, Y., Akbarzadeh, A., & Panahi, Y. (2021). Applications of dendrimers in nanomedicine and drug delivery: A review. *Journal of Inorganic and Organometallic Polymers and Materials*, *31*(6), 2246-2261. DOI: 10.1007/s10904-021-01925-2.

Nowack, B., Bornhöft, N., Ding, Y., Riediker, M., Jiménez, A. S., Sun, T., van Tongeren, M., & Wohlleben, W. (2015). The flows of engineered nanomaterials from production, use, and disposal to the environment. In *Indoor and outdoor nanoparticles: Determinants of release and exposure scenarios* (pp. 209-231). Springer. DOI: 10.1007/698_2015_402.

Nuruzzaman, M., Rahman, M. M., Liu, Y., & Naidu, R. (2016). Nanoencapsulation, nano-guard for pesticides: a new window for safe application. *Journal of Agricultural and Food Chemistry*, *64*(7), 1447-1483. DOI: 10.1021/acs.jafc.5b05214.

Ojha, N. K., Zyryanov, G. V., Majee, A., Charushin, V. N., Chupakhin, O. N., & Santra, S. (2017). Copper nanoparticles as inexpensive and efficient catalyst: A valuable contribution in organic synthesis. *Coordination Chemistry Reviews*, *353*, 1-57. DOI: 10.1016/j.ccr.2017.10.004.

Olchowik, J., Bzdyk, R. M., Studnicki, M., Bederska-Błaszczyk, M., Urban, A., & Aleksandrowicz-Trzcińska, M. (2017). The effect of silver and copper nanoparticles on the condition of english oak (Quercus robur L.) seedlings in a container nursery experiment. *Forests*, *8*(9), 310. DOI: 10.3390/f8090310.

Pandita, D. (2022). Role of nano-biotechnology in medicinal plant production. In *Environmental Challenges and Medicinal Plants: Sustainable Production Solutions under Adverse Conditions* (pp. 355-384). Springer. DOI: 10.1007/978-3-030-92050-0_15.

Paparella, S., Araújo, S. d. S., Rossi, G., Wijayasinghe, M., Carbonera, D., & Balestrazzi, A. (2015). Seed priming:

state of the art and new perspectives. *Plant cell reports*, *34*(8), 1281-1293. DOI: 10.1007/s00299-015-1784-y.

Parveen, F., Sannakki, B., Mandke, M. V., & Pathan, H. M. (2016). Copper nanoparticles: Synthesis methods and its light harvesting performance. *Solar Energy Materials and Solar Cells*, *144*, 371-382. DOI: 10.1016/j.solmat.2015.08.033.

Perreault, F., Melegari, S. P., da Costa, C. H., Rossetto, A. L. d. O. F., Popovic, R., & Matias, W. G. (2012). Genotoxic effects of copper oxide nanoparticles in Neuro 2A cell cultures. *Science of The Total Environment*, *441*, 117-124. DOI: 10.1016/j.scitotenv.2012.09.065.

Perreault, F., Samadani, M., & Dewez, D. (2014). Effect of soluble copper released from copper oxide nanoparticles solubilisation on growth and photosynthetic processes of Lemna gibba L. *Nanotoxicology*, *8*(4), 374-382. DOI: 10.3109/17435390.2013.789936.

Pirmoghani, A., Salehi, I., Moradkhani, S., Karimi, S. A., & Salehi, S. (2019). Effect of Crataegus extract supplementation on diabetes induced memory deficits and serum biochemical parameters in male rats. *IBRO reports*, *7*, 90-96. DOI: 10.1016/j.ibror.2019.10.004.

Prabu, P., & Losetty, V. (2024). Green synthesis of copper oxide nanoparticles using Macroptilium Lathyroides (L) leaf extract and their spectroscopic characterization, biological activity and photocatalytic dye degradation study. *Journal of Molecular Structure*, *1301*, 137404. DOI: 10.1016/j.molstruc.2023.137404.

Prakash, M., Nair, G., & Chung, I. M. (2014). Impact of copper oxide nanoparticles exposure on Arabidopsis thaliana growth, root system development, root lignificaion, and molecular level changes. *Environmental Science and Pollution Research*, *21*(22), 12709. DOI: 10.1007/s11356-014-3210-3.

Rahmani, F., Peymani, A., Daneshvand, E., & Biparva, P. (2016). Impact of zinc oxide and copper oxide nano-particles on physiological and molecular processes in Brassica napus L. *Indian Journal of Plant Physiology*, *21*(2), 122-128. DOI: 10.1007/s40502-016-0212-9.

Rajput, V., Minkina, T., Mazarji, M., Shende, S., Sushkova, S., Mandzhieva, S., Burachevskaya, M., Chaplygin, V., Singh, A., & Jatav, H. (2020). Accumulation of nanoparticles in the soil-plant systems and their effects on human health. *Annals of Agricultural Sciences*, *65*(2), 137-143. DOI: 10.1016/j.aoas.2020.08.001.

Rajput, V., Minkina, T., Sushkova, S., Behal, A., Maksimov, A., Blicharska, E., Ghazaryan, K., Movsesyan, H., & Barsova, N. (2020). ZnO and CuO nanoparticles: a threat to soil organisms, plants, and human health. *Environmental Geochemistry and Health*, *42*(1), 147-158. DOI: 10.1007/s10653-019-00317-3.

Rajput, V. D., Minkina, T., Fedorenko, A., Mandzhieva, S., Sushkova, S., Lysenko, V., Duplii, N., Azarov, A., & Chokheli, V. (2019). Destructive effect of copper oxide nanoparticles on ultrastructure of chloroplast, plastoglobules and starch grains in spring barley (Hordeum sativum). DOI: 10.17957/IJAB/15.0877.

Rao, S., & Shekhawat, G. S. (2016). Phytotoxicity and oxidative stress perspective of two selected nanoparticles in Brassica juncea. *3 Biotech*, *6*(2), 244. DOI: 10.1007/s13205-016-0550-3.

Rautaray, D., Ahmad, A., & Sastry, M. (2003). Biosynthesis of CaCO3 crystals of complex morphology using a fungus and an actinomycete. *Journal of the American Chemical Society*, *125*(48), 14656-14657. DOI: 10.1021/ja0374877.

Ravele, M. P., Oyewo, O. A., Ramaila, S., Mavuru, L., & Onwudiwe, D. C. (2022). Facile synthesis of copper oxide nanoparticles and their applications in the photocatalytic degradation of acyclovir. *Results in Engineering*, *14*, 100479. DOI: 10.1016/j.rineng.2022.100479.

Rawat, S., Pullagurala, V. L., Hernandez-Molina, M., Sun, Y., Niu, G., Hernandez-Viezcas, J. A., Peralta-Videa, J. R., & Gardea-Torresdey, J. L. (2018). Impacts of copper oxide nanoparticles on bell pepper (Capsicum annum L.) plants: a full life cycle study. *Environmental Science: Nano*, *5*(1), 83-95. DOI: 10.1039/C7EN00697G.

Rico, C. M., Majumdar, S., Duarte-Gardea, M., Peralta-Videa, J. R., & Gardea-Torresdey, J. L. (2011). Interaction of nanoparticles with edible plants and their possible implications in the food chain. *Journal of Agricultural and Food Chemistry*, *59*(8), 3485-3498. DOI: 10.1021/jf104517j.

Ringu, T., Das, A., Ghosh, S., & Pramanik, N. (2024). Exploring the potential of copper oxide nanoparticles (CuO NPs) for sustainable environmental bioengineering applications. *Nanotechnology for Environmental Engineering*, *9*(4), 679-707. DOI: 10.1007/s41204-024-00389-2.

Rinita, J., Jose, R., Muthupandi, S., Jothi, N. N., & Sagayaraj, P. (2023). Green synthesis and characterization of copper (II) oxide (CuO) nanospheres using natural extract from Trigonella foenum-graecum. 2ND INTERNATIONAL CONFERENCE ON MATERIALS FOR ENERGY AND ENVIRONMENT 2020, DOI: 10.1063/5.0140561.

Robertazzi, A., & Platts, J. A. (2006). Gas-phase DNA oligonucleotide structures. A QM/MM and atoms in molecules study. *The Journal of Physical Chemistry A*, *110*(11), 3992-4000. DOI: 10.1021/jp056626z.

Robinson, H., Daines, A. M., Brackovic, A., Williams, D. B. G., Sims, I. M., & Hinkley, S. F. (2024). Cu (II) complexes using acylhydrazones or cyclen for biocidal antifouling coatings. *Pure and Applied Chemistry*, *96*(4), 549-564. DOI: 10.1515/pac-2024-0203.

Roduner, E. (2006). Size matters: why nanomaterials are different. *Chemical society reviews*, *35*(7), 583-592. DOI: 10.1039/b502142c.

Roy, S., & Rhim, J.-W. (2019). Melanin-mediated synthesis of copper oxide nanoparticles and preparation of functional agar/CuO NP nanocomposite films. *Journal of Nanomaterials*, *2019*(1), 2840517. DOI: 10.1155/2019/2840517.

Rubilar, O., Rai, M., Tortella, G., Diez, M. C., Seabra, A. B., & Durán, N. (2013). Biogenic nanoparticles: copper, copper oxides, copper sulphides, complex copper nanostructures and their applications. *Biotechnology Letters*, *35*(9), 1365-1375. DOI: 10.1007/s10529-013-1239-x.

Ruiz, P., Katsumiti, A., Nieto, J. A., Bori, J., Jimeno-Romero, A., Reip, P., Arostegui, I., Orbea, A., & Cajaraville, M. P. (2015). Short-term effects on antioxidant enzymes and long-term genotoxic and carcinogenic potential of CuO nanoparticles compared to bulk CuO and ionic copper in mussels Mytilus galloprovincialis. *Marine environmental research*, *111*, 107-120. DOI: 10.1016/j.marenvres.2015.07.018.

Šalamon, I., Kráľová, K., & Masarovičová, E. (2007). Accumulation of cadmium in chamomile plants cultivated in Eastern Slovakia regions. *Acta Hort (ISHS)*, *749*, 217-222. DOI: 10.17660/ActaHortic.2007.749.26.

Salem, K. F., Abd-Ellatif, S., Abdel Razik, E.-S. S., Fadel, M. S., Elkhawas, A. E., Marzouk, E. R., Bassouny, M. A., & Ibrahim, A. A. (2023). Effect of nanomaterials on water and solutes translocation in plants. In *Nanomaterial Interactions with Plant Cellular Mechanisms and Macromolecules and Agricultural Implications* (pp. 19-47). Springer. DOI: 10.1007/978-3-031-20878-2_2.

Salvioni, L., Morelli, L., Ochoa, E., Labra, M., Fiandra, L., Palugan, L., Prosperi, D., & Colombo, M. (2021). The emerging role of nanotechnology in skincare. *Advances in colloid and interface science*, *293*, 102437. DOI: 10.1016/j.cis.2021.102437.

Sanità, G., Carrese, B., & Lamberti, A. (2020). Nanoparticle surface functionalization: how to improve biocompatibility and cellular internalization. *Frontiers in molecular biosciences*, *7*, 587012. DOI: 10.3389/fmolb.2020.587012.

Sarfraz, Z., Hussain, M., Rehman, M. A., Luqman, M., Khan, M. R., Alomayri, T., Bilal, M., & Inam-ul-Haq, M. (2024). Investigation of synergistic effects of cobalt doping on physical and dielectric properties of copper oxide nanoparticles. *Journal of Physics and Chemistry of Solids*, *193*, 112116. DOI: 10.1016/j.jpcs.2024.112116.

Senthilkumar, A., Muthuswamy, R., Nallal, U. M., Ramaiyan, S., Kannan, P., Muthupandi, S., Lakshminarayanan, S. P., Sambasivam, S., & Ayyar, M. (2024). Green synthesis of copper nanoparticles from agro-waste garlic husk. *Zeitschrift für Physikalische Chemie*, *238*(1), 75-88. DOI: 10.1515/zpch-2023-0291.

Shahane, S. P., & Kumar, A. (2022). Estimation of health risks due to copper-based nanoagrochemicals. *Environmental Science and Pollution Research*, *29*(17), 25046-25059. DOI: 10.1007/s11356-021-17308-6.

Sharafudheen, S. B., Vijayakumar, C., Rajakrishnan, R., Alfarhan, A., Arokiyaraj, S., & Bindhu, M. (2025). Biogenic synthesis of porous CuO nanoparticles: Synergistic effects in photocatalytic dye degradation and electrochemical energy storage applications. *Journal of Crystal Growth*, *649*, 127917. DOI: 10.1016/j.jcrysgro.2024.127917.

Sharma, P., Khanduja, D., & Sharma, S. (2014). Tribological and mechanical behavior of particulate aluminum matrix composites. *Journal of Reinforced Plastics and Composites*, *33*(23), 2192- DOI: 2202. 10.1177/0731684414556012.

Shi, J., Peng, C., Yang, Y., Yang, J., Zhang, H., Yuan, X., Chen, Y., & Hu, T. (2014). Phytotoxicity and accumulation of copper oxide nanoparticles to the Cu-tolerant plant Elsholtzia splendens. *Nanotoxicology*, *8*(2), 179-188. DOI: 10.3109/17435390.2013.766768.

Shirvanimoghaddam, K., Hamim, S. U., Akbari, M. K., Fakhrhoseini, S. M., Khayyam, H., Pakseresht, A. H., Ghasali, E., Zabet, M., Munir, K. S., & Jia, S. (2017). Carbon fiber reinforced metal matrix composites: Fabrication processes and properties. *Composites Part A: Applied Science and Manufacturing*, *92*, 70-96. DOI: 10.1016/j.compositesa.2016.10.032.

Shobha, G., Moses, V., & Ananda, S. (2014). Biological synthesis of copper nanoparticles and its impact. *Int. j. pharm. sci. Invent*, *3*(8), 6-28.

Siddiqi, K. S., & Husen, A. (2020). Current status of plant metabolite-based fabrication of copper/copper oxide nanoparticles and their applications: a review. *Biomaterials Research*, *24*(1), 11. DOI: 10.1186/s40824-020-00188-1.

Siddiqui, H., Qureshi, M., & Haque, F. Z. (2016). Effect of copper precursor salts: facile and sustainable synthesis of controlled shaped copper oxide nanoparticles. *Optik*, *127*(11), 4726-4730. DOI: 10.1016/j.ijleo.2016.01.118.

Singh, B. P., Chaudhary, M., Kumar, A., Singh, A. K., Gautam, Y. K., Rani, S., & Walia, R. (2020). Effect of Co and Mn doping on the morphological, optical and magnetic properties of CuO nanostructures. *Solid State Sciences*, *106*, 106296. DOI: 10.1016/j.solidstatesciences.2020.106296.

Singh, D., Sharma, A., Verma, S. K., Pandey, H., & Pandey, M. (2024). Impact of nanoparticles on plant physiology, nutrition, and toxicity: A short review. *Next Nanotechnology*, *6*, 100081. DOI: 10.1016/j.nxnano.2024.100081.

Singh, J., Kumar, V., Kim, K.-H., & Rawat, M. (2019). Biogenic synthesis of copper oxide nanoparticles using plant extract and its prodigious potential for photocatalytic degradation of dyes. *Environmental Research*, *177*, 108569. DOI: 10.1016/j.envres.2019.108569.

Singh, K., Khanna, V., Singh, S., Bansal, S. A., Chaudhary, V., & Khosla, A. (2023). Paradigm of state-of-the-art CNT reinforced copper metal matrix composites: processing, characterizations, and applications. *Journal of Materials Research and Technology*, *24*, 8572-8605. DOI: 10.1016/j.jmrt.2023.05.083.

Slikkerveer, L. J. (2006). The challenge of non-experimental validation of MAC plants: towards a multivariate model of transcultural utilization of medicinal, aromatic and cosmetic plants. *Frontis*, 1-28. DOI: 10.1007/1-4020-5449-1_1.

Sohaebuddin, S. K., Thevenot, P. T., Baker, D., Eaton, J. W., & Tang, L. (2010). Nanomaterial cytotoxicity is composition, size, and cell type dependent. *Particle and fibre toxicology*, *7*(1), 22. DOI: 10.1186/1743-8977-7-22.

Soltani, E., & Soltani, A. (2015). Meta-analysis of seed priming effects on seed germination, seedling emergence and crop yield: Iranian studies. *International Journal of Plant Production*, *9*(3), 413-432.

Sonawane, H., Shelke, D., Chambhare, M., Dixit, N., Math, S., Sen, S., Borah, S. N., Islam, N. F., Joshi, S. J., & Yousaf, B. (2022). Fungi-derived agriculturally important nanoparticles and their application in crop stress management–Prospects and environmental risks. *Environmental Research*, *212*, 113543. DOI: 10.1016/j.envres.2022.113543.

Song, X., Sun, S., Zhang, W., & Yin, Z. (2004). A method for the synthesis of spherical copper nanoparticles in the organic phase. *Journal of colloid and interface science*, *273*(2), 463-469. DOI: 10.1016/j.jcis.2004.01.019.

Stamou, I., & Antizar-Ladislao, B. (2016). A life cycle assessment of the use of compost from contaminated biodegradable municipal solid waste with silver and titanium dioxide nanoparticles. *Journal of cleaner production*, *135*, 884-891. DOI: 10.1016/j.jclepro.2016.06.150.

Surappa, M. K. (2003). Aluminium matrix composites: Challenges and opportunities. *Sadhana*, *28*(1), 319-334. DOI: 10.1007/BF02717141.

Suresh, S., Karthikeyan, S., & Jayamoorthy, K. (2016). FTIR and multivariate analysis to study the effect of bulk and nano copper oxide on peanut plant leaves. *Journal of Science: Advanced Materials and Devices*, *1*(3), 343-350. DOI: 10.1016/j.jsamd.2016.08.004.

Sutulienė, R., Brazaitytė, A., Urbutis, M., Tučkutė, S., & Duchovskis, P. (2024). Nanoparticle Effects on Ice Plant Mineral Accumulation under Different Lighting Conditions and Assessment of Hazard Quotients for Human Health. *Plants*, *13*(5), 681. DOI: 10.3390/plants13050681.

Szőllősi, R., Molnár, Á., Kondak, S., & Kolbert, Z. (2020). Dual effect of nanomaterials on germination and seedling growth: Stimulation vs. phytotoxicity. *Plants*, *9*(12), 1745. DOI: 10.3390/plants9121745.

Tariq, A., Zeng, F., Graciano, C., Ullah, A., Sadia, S., Ahmed, Z., Murtaza, G., Ismoilov, K., & Zhang, Z. (2023). Regulation of metabolites by nutrients in plants. *Plant ionomics: sensing, signaling, and regulation*, 1-18. DOI: 10.1002/9781119803041.ch1.

Thiruvengadam, M., Chi, H. Y., & Kim, S.-H. (2024). Impact of nanopollution on plant growth, photosynthesis, toxicity, and metabolism in the agricultural sector: An updated review. *Plant Physiology and Biochemistry*, *207*, 108370. DOI: 10.1016/j.plaphy.2024.108370.

Thiruvengadam, M., Chung, I.-M., Gomathi, T., Ansari, M. A., Gopiesh Khanna, V., Babu, V., & Rajakumar, G. (2019). Synthesis, characterization and pharmacological potential of green synthesized copper nanoparticles. *Bioprocess and biosystems engineering*, *42*(11), 1769-1777. DOI: 10.1007/s00449-019-02173-y.

Torsvik, V., & Øvreås, L. (2002). Microbial diversity and function in soil: from genes to ecosystems. *Current opinion in microbiology*, *5*(3), 240-245. DOI: 10.1016/S1369-5274(02)00324-7.

Tripathi, G. D., Javed, Z., & Dashora, K. (2024). Toxicity of copper oxide nanoparticles on agriculturally important soil rhizobacteria Bacillus megaterium. *Emerging Contaminants*, *10*(1), 100280. DOI: 10.1016/j.emcon.2023.100280.

V Singh, A., Patil, R., Anand, A., Milani, P., & Gade, W. (2010). Biological synthesis of copper oxide nano particles using Escherichia coli. *Current Nanoscience*, *6*(4), 365-369. DOI: 10.2174/157341310791659062.

Vaidehi, D., Bhuvaneshwari, V., Bharathi, D., & Sheetal, B. P. (2018). Antibacterial and photocatalytic activity of copper oxide nanoparticles synthesized using Solanum lycopersicum leaf extract. *Materials Research Express*, *5*(8), 085403. DOI: 10.1088/2053-1591/aad426.

Vanathi, P., Rajiv, P., & Sivaraj, R. (2016). Synthesis and characterization of Eichhornia-mediated copper oxide nanoparticles and assessing their antifungal activity against plant pathogens. *Bulletin of Materials Science*, *39*(5), 1165-1170. DOI: 10.1007/s12034-016-1276-x.

Velmurugan, G., Chohan, J. S., Babu, K., Nagaraj, M., & Velumani, A. (2024). Exploring the efficacy of biosynthesized cupric oxide nanoparticles from Jasminum sambac flower extract in wastewater treatment: Experimental investigations and potential applications. *Desalination and Water Treatment*, *319*, 100570. DOI: 10.1016/j.dwt.2024.100570.

Velsankar, K., Parvathy, G., Mohandoss, S., Kumar, R. M., & Sudhahar, S. (2022). Green synthesis and characterization of CuO nanoparticles using Panicum sumatrense grains extract for biological applications. *Applied Nanoscience*, *12*(6), 1993-2021. DOI: 10.1007/s13204-022-02441-6.

Velsankar, K., Suganya, S., Muthumari, P., Mohandoss, S., & Sudhahar, S. (2021). Ecofriendly green synthesis, characterization and biomedical applications of CuO nanoparticles synthesized using leaf extract of Capsicum frutescens. *Journal of Environmental Chemical Engineering*, *9*(5), 106299. DOI: 10.1016/j.jece.2021.106299.

Velsankar, K., Vinothini, V., Sudhahar, S., Kumar, M. K., & Mohandoss, S. (2020). Green synthesis of CuO nanoparticles via Plectranthus amboinicus leaves extract with its characterization on structural, morphological, and biological properties. *Applied Nanoscience*, *10*(10), 3953-3971. DOI: 10.1007/s13204-020-01504-w.

Viet, P. V., Nguyen, H. T., Cao, T. M., & Hieu, L. V. (2016). Fusarium antifungal activities of copper nanoparticles synthesized by a chemical reduction method. *Journal of Nanomaterials*, *2016*(1), 1957612. DOI: 10.1155/2016/1957612.

Vignesh, A., Amal, T. C., Sivalingam, R., Selvakumar, S., & Vasanth, K. (2024). Unraveling the impact of nanopollution on plant metabolism and ecosystem dynamics. *Plant Physiology and Biochemistry*, *210*, 108598. DOI: 10.1016/j.plaphy.2024.108598.

Vishveshvar, K., Aravind Krishnan, M., Haribabu, K., & Vishnuprasad, S. (2018). Green synthesis of copper oxide nanoparticles using Ixiro coccinea plant leaves and its characterization. *BioNanoScience*, *8*(2), 554-558. DOI: 10.1007/s12668-018-0508-5.

Wahab, A., Muhammad, M., Munir, A., Abdi, G., Zaman, W., Ayaz, A., Khizar, C., & Reddy, S. P. P. (2023). Role of arbuscular mycorrhizal fungi in regulating growth, enhancing productivity, and potentially influencing ecosystems under abiotic and biotic stresses. *Plants*, *12*(17), 3102. DOI: 10.3390/plants12173102.

Wang, J., Li, B., Qiu, L., Qiao, X., & Yang, H. (2022). Dendrimer-based drug delivery systems: History, challenges, and latest developments. *Journal of biological engineering*, *16*(1), 18. DOI: 10.1186/s13036-022-00298-5.

Wang, W., Liu, J., Ren, Y., Zhang, L., Xue, Y., Zhang, L., & He, J. (2020). Phytotoxicity assessment of copper oxide nanoparticles on the germination, early seedling growth, and physiological responses in Oryza sativa L. *Bulletin of Environmental Contamination and Toxicology*, *104*(6), 770-777. DOI: 10.1007/s00128-020-02850-9.

Wang, Z., Xu, L., Zhao, J., Wang, X., White, J. C., & Xing, B. (2016). CuO nanoparticle interaction with Arabidopsis thaliana: toxicity, parent-progeny transfer, and gene expression. *Environmental science & technology*, *50*(11), 6008-6016. DOI: 10.1021/acs.est.6b01017.

Watanabe, T., Misawa, S., Hiradate, S., & Osaki, M. (2008). Root mucilage enhances aluminum accumulation in Melastoma malabathricum, an aluminum accumulator. *Plant signaling & behavior*, *3*(8), 603-605. DOI: 10.4161/psb.3.8.6356.

Wei, Z., Chen, L., Thompson, D. M., & Montoya, L. D. (2014). Effect of particle size on in vitro cytotoxicity of titania and alumina nanoparticles. *Journal of Experimental Nanoscience*, *9*(6), 625-638. DOI: 10.1080/17458080.2012.683534.

Xiong, T., Zhang, T., Dumat, C., Sobanska, S., Dappe, V., Shahid, M., Xian, Y., Li, X., & Li, S. (2019). Airborne foliar transfer of particular metals in Lactuca sativa L.: translocation, phytotoxicity, and bioaccessibility. *Environmental Science and Pollution Research*, *26*(20), 20064-20078. DOI: 10.1007/s11356-018-3084-x

Yadav, R., Kumar, M., & Tomar, R. S. (2024). Cyanobacteria based nanoformulation of biogenic CuO nanoparticles for plant growth promotion of rice under hydroponics conditions. *Current Microbiology*, *81*(5), 118. DOI: 10.1007/s00284-024-03619-7.

Yeboah, S. O., Nasare, L. I., & Abunyewa, A. A. (2022). Effect of landuse on floristic composition and diversity of medicinal plants in the Guinea Savanna zone of Ghana. *Heliyon*, *8*(8). DOI: 10.1016/j.heliyon.2022.e10203.

Yruela, I. (2005). Copper in plants. *Brazilian journal of plant physiology*, *17*, 145-156. DOI: 10.1590/S1677-04202005000100012.

Yusefi-Tanha, E., Fallah, S., Rostamnejadi, A., & Pokhrel, L. R. (2020). Root system architecture, copper uptake and tissue distribution in soybean (Glycine max (L.) Merr.) grown in copper oxide nanoparticle (CuONP)-amended soil and implications for human nutrition. *Plants*, *9*(10), 1326. DOI: 10.3390/plants9101326.

Zahra, W., Rai, S. N., Birla, H., Singh, S. S., Rathore, A. S., Dilnashin, H., Keswani, C., & Singh, S. P. (2019). Economic importance of medicinal plants in Asian countries. In *Bioeconomy for sustainable development* (pp. 359-377). Springer. DOI: 10.1007/978-981-13-9431-7_19.

Zhang, Y., Zhang, R., Sun, H., Chen, Q., Yu, X., Zhang, T., Yi, M., & Liu, J.-X. (2018). Copper inhibits hatching of fish embryos via inducing reactive oxygen species and down-regulating Wnt signaling. *Aquatic Toxicology*, *205*, 156-164. DOI: 10.1016/j.aquatox.2018.10.015.

Zhao, S., Liu, Q., Qi, Y., & Duo, L. (2010). Responses of root growth and protective enzymes to copper stress in turfgrass. *Acta Biologica Cracoviensia s. Botanica*, *52*(2). DOI: 10.2478/v10182-010-0017-5.

Zhou, H., Yao, L., Jiang, X., Sumayyah, G., Tu, B., Cheng, S., Qin, X., Zhang, J., Zou, Z., & Chen, C. (2021). Pulmonary exposure to copper oxide nanoparticles leads to neurotoxicity via oxidative damage and mitochondrial dysfunction. *Neurotoxicity Research*, *39*(4), 1160-1170. DOI: 10.1007/s12640-021-00358-6.

Zhou, P., Adeel, M., Shakoor, N., Guo, M., Hao, Y., Azeem, I., Li, M., Liu, M., & Rui, Y. (2020). Application of nanoparticles alleviates heavy metals stress and promotes plant growth: An overview. *Nanomaterials*, *11*(1), 26. DOI: 10.3390/nano11010026.

Zietz, B. P., Dieter, H. H., Lakomek, M., Schneider, H., Keßler-Gaedtke, B., & Dunkelberg, H. (2003). Epidemiological investigation on chronic copper toxicity to children exposed via the public drinking water supply. *Science of The Total Environment*, *302*(1-3), 127-144. DOI: 10.1016/S0048-9697(02)00399-6.

Zigau, Z., Aliyu, B., Abubakar, U., Bello, A., Yakasai, M., & Sanusi, H. (2024). Determination of Heavy Metal Concentrations on some Selected Herbal Medicinal Preparations Marketed in Kano State, Nigeria. *UMYU*

Journal of Microbiology Research, *9*(3), 207-213. DOI: 10.47430/ujmr.2493.025.

Zoolfakar, A. S., Rani, R. A., Morfa, A. J., O'Mullane, A. P., & Kalantar-Zadeh, K. (2014). Nanostructured copper oxide semiconductors: a perspective on materials, synthesis methods and applications. *journal of materials chemistry c*, *2*(27), 5247-5270. DOI: 10.1039/C4TC00345D.