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Nanotechnology-enabled biofortification strategies for micronutrients enrichment of food crops: Current understanding and future scope

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ABSTRACT

Nutrient deficiency in food crops severely compromises human health, particularly in under privileged communities. Globally, billions of people, particularly in developing nations, have limited access to nutritional supplements and fortified foods, subsequently suffering from micronutrient deficiency leading to a range of health issues. The green revolution enhanced crop production and provided food to billions of people but often falls short with respect to the nutritional quality of that food. Plants may assimilate nutrients from synthetic chemical fertilizers, but this approach generally has low nutrient delivery and use efficiency. Further, the overexposure of chemical fertilizers may increase the risk of neoplastic diseases, render food crops unfit for consumption and cause environmental degradation. Therefore, to address these challenges, more research is needed for sustainable crop yield and quality enhancement with minimum use of chemical fertilizers. Complex nutritional disorders and 'hidden hunger' can be addressed through biofortification of food crops. Nanotechnology may help to improve food quality via biofortification as plants may readily acquire nanoparticle-based nutrients. Nanofertilizers are target specific, possess controlled release, and can be retained for relatively long time periods, thus prevent leaching or run-off from soil. This review evaluates the recent literature on the development and use of nanofertilizers, their effects on the environment, and benefits to food quality. Further, the review highlights the potential of nanomaterials on plant genetics in biofortification, as well as issues of affordability, sustainability, and toxicity.

1. Introduction

Micronutrient deficiency or 'hidden hunger' is a serious concern in developing countries, including Sub-Saharan Africa and Southeast Asia. A lack of micronutrients, such as vitamins (vitamin A, B_9) and minerals such as iron (Fe), zinc (Zn), iodide (I) in the diet impacts human health negatively, including reduced growth, dementia, perinatal complications, and increased mortality (Bailey et al., 2015; Bailey et al., 2011; de Benoist et al., 2008). Iron deficiency is the most common disorder, with 24.8% of the global population (~1.6 billion) suffering from Fe deficiency and related diseases (McLean et al., 2009). The suggested daily Fe intake ranges from 8–18 mg/day depending on age, gender, weight, and is 27 mg/day for pregnant women. Half of reported anaemia cases are due to Fe deficiency, referred to as iron deficiency anaemia (IDA) (Russell et al., 2001). IDA is a very common health issue in women due to increased blood loss during the menstruation cycle and parturition. Vitamin A deficiency leads to night blindness, xerophthalmia, and corneal ulcerations (Gilbert, 2013). The World Health Or-

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ganization (WHO) reported that during pregnancy, vitamin A deficiency is very common in underdeveloped countries, affecting a significant fraction of the global population (10 to 20%), and can lead to child blindness (250–500 million) (McLean et al., 2009). Iodine is crucial for thyroid hormone synthesis. Globally, ~2 billion people have iodine deficiency causing hypothyroidism; iodine intake below 10–20 μg/day can cause goitre diseases (Andersson et al., 2012; Trumbo et al., 2001). Zn deficiency in developing nations is one of the most prominent cause of morbidity, affecting 17.3 % of the world's population and causing diarrhoea, poor growth, weak immunity and increased risk of respiratory problems (Caulfield and Black, 2004; de Benoist et al., 2007; Gibson, 2012; Wessells and Brown, 2012). Therefore, if consumed food is to meet optimum nutritional requirements for a healthy human, it must be enriched with essential micronutrients to reduce hidden hunger. Biofortification of food crops with essential micronutrients is a vital tool to mitigate malnutrition and promote global human health.

Biofortification increases micronutrient content in staple food crops and can be achieved by a number of different strategies such as agronomic biofortification, selective breeding, and genetic manipulation (Khush et al., 2012; Ottaway, 2008). The production of biofortified crops is an economical and a one-time investment providing sustainable benefits to farmers. Agronomic biofortification involves fertilization of food crops with micronutrients through physical application either directly to the soil, as foliar spray, by seed priming or by immersing seedlings into fertilizer solutions (Dimkpa and Bindraban, 2016; Rajendra, 2009). The nutritional status of rice, wheat, maize, barley, and sorghum has been improved by enhancing the content of Zn, Fe, selenium (Se) in edible tissues via agronomic biofortification (Fahad et al., 2015; Giacosa et al., 2014; Guo et al., 2016; Ram et al., 2016; Ramzani et al., 2016). The main pitfall of mineral fertilizer application is the need for repeated amendment, more labour and resource intensive, leading to potential secondary environmental damage (Bilski et al., 2012; Collard and Mackill, 2008).

Different plant breeding practices and biotechnological approaches such as marker assisted selection (MAS) can also be used to produce desired micronutrient-enriched plants (Mayer et al., 2008; Stein et al., 2007). Backcross breeding programs generated Zn biofortified wheat varieties; *i.e.* 'Zinc Shakti', 'Zincol-2016', WB-02 and HPBW-01 (Singh and Velu, 2017). Plant growth promoting (PGP) microbes (Khan et al., 2019a, 2019b; Singh et al., 2018a, 2018b, 2018c) may also improve micronutrient availability in soil and bioavailability in food crops through the production of chelating agents such as mugineic acid and siderophores. For example, the inoculation of arbuscular mycorrhizae improved micronutrient (mainly Zn) availability in soil (Balakrishnan and Subramanian, 2012).

Biofortification can also be achieved by advanced tools such as genetic engineering to generate transgenic crops through direct transfer of genes and by genome editing which precisely modifies the target genes to create desired genotypes. This strategy optimizes the accumulation of nutrients in edible tissues without negatively affecting other developmental and physiological characteristics of economically important crops (Vanderschuren et al., 2013). Transgenic rice (*Oryza sativa* L.) produced with high Fe and Zn can provide 30% of the estimated average requirement (EAR) for both nutrients (Trijatmiko et al., 2016). Recently, CRISPR-Cas9 was used for the biofortification of β-carotene in rice endosperm. The endosperm of the edited rice line was found to contain 7.9 μg/g β-carotene, similar to Golden Rice 2, and is capable of supplying more than 50% of EAR for vitamin A (Dong et al., 2020; Paine et al., 2005). However, the expensive nature of this approach and the widespread unease toward genetically modified crops significantly limit its practical use. Importantly, nanotechnology has the potential to revolutionize agricultural systems by providing safe, easy, and effective delivery of agrochemicals and may be used for the biofortification of food crops (Dimkpa and Bindraban, 2016). This article critically reviews recent progress in nanotechnology-based biofortification of staple crops. Further, the application of nanomaterials, their fate, and impacts on agroecosystems is discussed.

2. Biofortification through Nanotechnology-Based Approaches

Nanotechnology exploits the nanoscale (< 100 nm) properties of a material. Nanoparticles have many unique properties, including high surface area to volume ratio and tuneable dissolution profiles (Boverhof et al., 2015; Khan et al., 2019a, 2019b). Nanotechnology has great potential in precision agriculture to improve the quantity and quality of staple crops via biofortification (Clemens, 2014; Datta and Vitolins, 2016; Sharma et al., 2017; Xiong et al., 2017). Foliar spray or soil application of nanoparticles can increase growth, crop production (shoot, root and yield) and in planta micronutrient levels (Buzea et al., 2007; Deepa and Ganesan, 2015; Sharma et al., 2014). Nutrient availability can be responsively managed with nanoparticle-assisted controlled release, simultaneously mitigating leaching, and fostering the effective accumulation of nutrients in edible tissues.

However, cell always maintain a reduced intracellular homeostasis under standard physiological conditions, any oxidising agent such as oxide NPs encountering cell can imbalance its equilibrated state. There are many *in vitro* models explaining nanoparticle toxicity via production of reactive oxygen species (ROS) (Meng et al., 2009). Therefore, a model based on their mechanism of actions have been proposedto precisely predict the reducing ability of NPs causing oxidative stress (Burello and Worth, 2011a, 2011b). This model measure the band energies of NPs and compare it with the redox potential of the biological reactions of cell to justify its potential to cause oxidative stress. This model was executed on high-throughput screening (HTS) platform to predict the toxicity profile of oxide NPs at cellular level encouraging the designing of safer nanomaterial that maintain the homeostasis and equilibrium in redox reactions of a cell. All this can be achieved by modifying some specific properties of nanomaterials such as size and biocompatible coating while preserving its functionality and still if these approaches fails to produce a safer nanomaterial, researchers must be confronted with the innovative idea of making a next generation nanomaterial. Therefore, HTS approaches would be a potential source to conveniently profile nanomaterial for its structural properties, functionality, and toxicity to make it a "Safe-by-Design" nanomaterial, which cause no hazards to environment (Burello and Worth, 2015).

Engineered nanoparticles with desired structure and physicochemical properties can be a safer alternative to facilitate biofortification of food crops (Elemike et al., 2019). Nanoparticles are synthesized via bottom-up and top-down approaches. Bottom-up approaches involve chemical and biological methods, including photochemical, sonochemical, vapor deposition, microwave, sol-gel, electrochemical deposition, spray/laser pyrolysis, and atomic and molecular condensation strategies. Conversely, top down approaches involve physical methods, such as sputtering, chemical etching, mechanical/ball milling, and photolithography (Arole and Munde, 2014) (Fig. 1). The biosynthesis of nanomaterials involves microbial or plant-assisted strategies. Here, plant or microbial extracts reduce elements and/or oxides or ionic/salt forms to nanoscale materials (Mateus et al., 2021). Microorganism-mediated methods use algae, fungi, actinomycetes, and bacteria, whereas the plant assisted methods use tissues such as fruit, sap, stem, bark, root, leaf and agricultural waste (Malik et al., 2014). Plant-assisted methods also exploit phytochemicals (carbohydrates, proteins, terpenoids, phenolics, flavonoids, amino acids, and saponins) for nanoparticle preparation. Phytochemicals may also act as stabilizing or capping agents for resultant nanoparticles. Plant-assisted green approaches for nanoparticle synthesis are sustainable, cost effective, efficient, fast, and less toxic. However, biosynthetic approaches have certain limitations, with batch-to-batch variability in properties being the major shortcoming (Baig et al., 2021; Singh et al., 2018a).

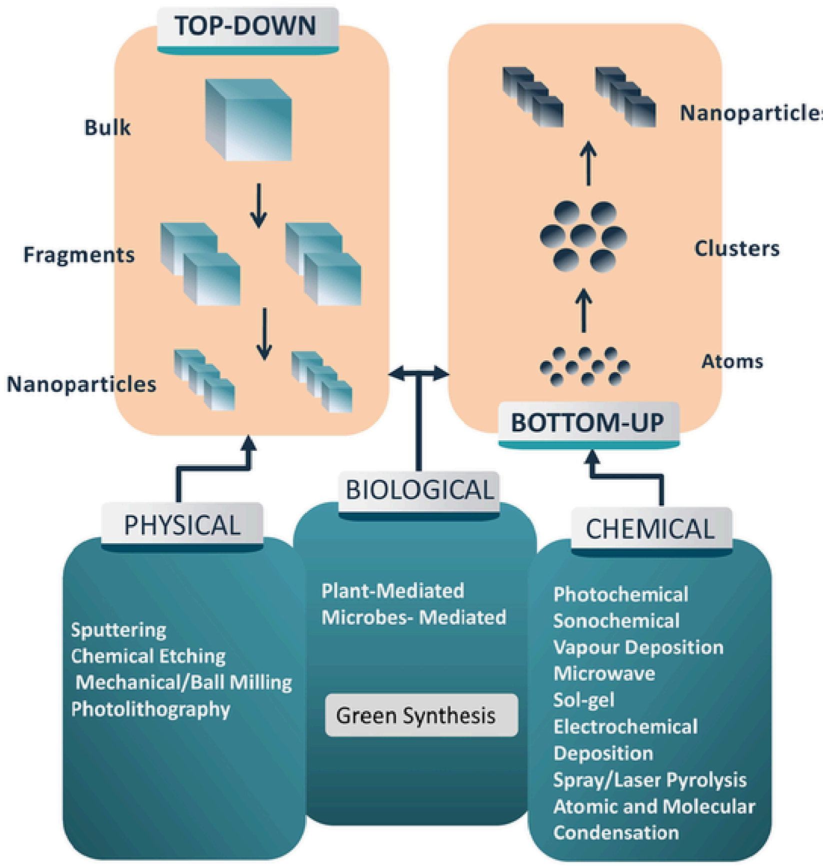

Fig. 1. The schematic representation describes the fabrication of nanoparticles emphasizing on Top-Down approach that includes physical methods and Bottom-Up approach that includes chemical methods whereas biological methods aiming green synthesis are included under both approaches.

Nanotechnology exploits the nanoscale chemistry of plants and materials for sustainable nutrient delivery (Prasad et al., 2017). Nanoparticles are promising materials for slow and controlled release of micronutrients for plant growth and production (Kabiri et al., 2017; Park et al., 2020), and as such, nanofertilizers may also be used to address micronutrient deficiency (Dimkpa and Bindraban, 2018; Pestovsky and Martínez-Antonio, 2017; Suppan, 2017). Nanofertilizers, in comparison to conventional agrochemicals, are more efficient in terms of nutrient delivery and hence, can be produced and applied in lesser amounts. Nanomaterials promote crop resilience, aid in agrochemical uptake, reduce their loss via volatilization, and increase efficiency in a sustainable fashion. Overall, nanotechnology-based approaches may significantly decrease the environmental footprint of agricultural practices.

The performance and efficiency of nanofertilizers can be further increased through the use of nanoclays, zeolites, and encapsulation to improve soil fertility, plant growth, and micronutrient levels (Polat et al., 2004). The most commonly investigated nanofertilizers for food crop biofortification are Zn, Fe, Cu, and Se (Prasad et al., 2017). Importantly, the efficacy of nanofertilizers towards plant growth depends on crop species and the physiochemical properties of nanomaterials (concentration, size, shape, and composition), as well as growth conditions and other environmental variables (Fig. 2).

2.1. Zinc

Approximately one third of the global population consumes Zn deficient food (Caulfield and Black, 2004). Zinc is a primary micronutrient in enzymes and critical for hormonal regulation of carbohydrate metabolism. It is absorbed as zinc gluconate in the human body. Deficiency of Zn in soil results in low Zn absorption by plants (Biesalski, 2013; Guilbert, 2003). The sources of Zn include zinc oxide (ZnO) and Zn sulfates. ZnO nanoparticles are known to be efficiently absorbed, accumulated, and metabolized in plants due to their high surface area to volume ration and less volatilization to address Zn deficiency (Milani et al., 2015) (Fig. 2). It has been reported that foliar application of ZnO NPs increases Zn concentration (82%) in maize (*Zea mays* L.) as compared to a conventional Zn fertilizer such as zinc sulphate ($ZnSO_4$) (Umar et al., 2020). Interestingly, foliar application of ZnO nanoparticles at 100 ppm facilitated greater Zn accumulation (35.96 ppm) in maize grains than did the same material at 400 ppm (31.05 ppm) (Subbaiah et al., 2016). Wheat (*Triticum aestivum* L.) germinated in ZnO NPs amended soil (50-1000 mgL^{-1}) showed maximum grain yield and enhanced Zn content. The concentration of Zn in grains increased by 3.3 times and 2.4 times for ZnO NPs and $ZnSO_4$ at 1000 mg kg^{-1} , respectively (Du et al., 2019). A foliar application of ZnO nanoparticles in wheat significantly enhanced grain Zn content, increased grain yield, facilitated plant growth, as well as increased the catalase and peroxidase antioxidant enzyme activities for removing reactive oxygen species (ROS) (Munir et al., 2018; Read et al., 2020; Sun et al., 2020a, 2020b). In a comparative study, foliar spray of Zn complexed chitosan nanoparticles (Zn-CNP) enhanced Zn content in grain by 36%, similar to the level achieved with conventional $ZnSO_4$ that was added at 10-fold greater concentration (Dapkekar et al., 2018).

Soil application of urea coated ZnO nanoparticles (≤2.17 $mgkg^{-1}$) increased Zn uptake by 24% and enhanced wheat grain yield by 51% (Dimkpa et al., 2020a). ZnO nanoparticle application (foliar, soil or by seed priming) enhanced Zn concentration in the grain (40-190%) relative to conventional fertilizer. Further, the protein content was increased and cadmium (Cd) levels decreased in the treated plants (Hussain et al., 2018; Rizwan et al., 2019; Sheoran et al., 2021). Soil application of ZnO NPs at 25 and 100 mg Zn kg^{-1} enhanced nitrogen (N), phosphorus (P), and potassium (K) content in rice (*O. sativa*), with sub-

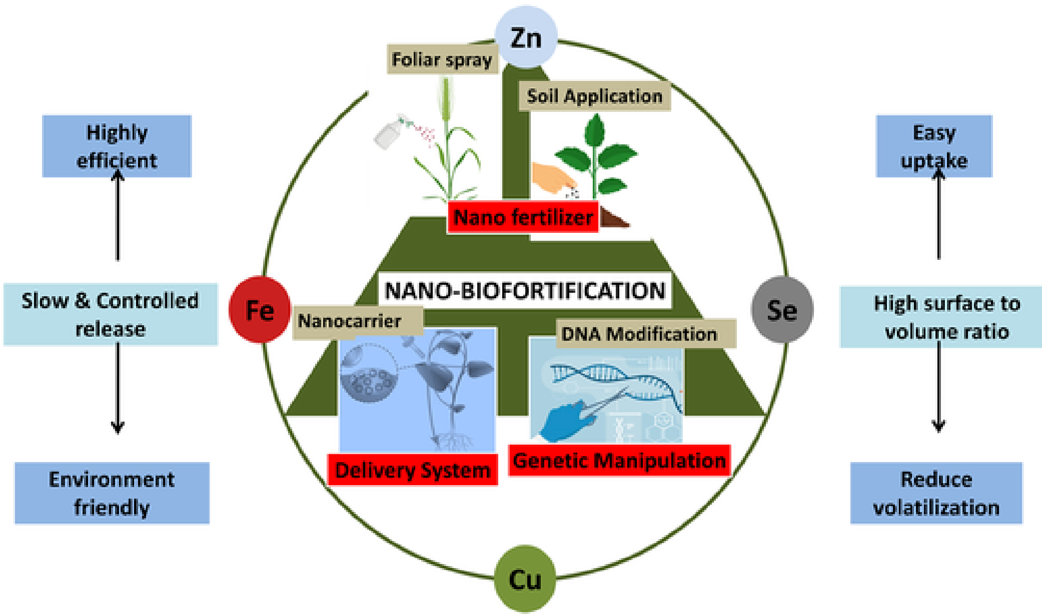

Fig. 2. The illustration shows the foliar and soil application strategies of Zn, Fe, Cu, Se nanoparticles along with their properties and implementation approaches for biofortification of food crops.

sequent increases in total biomass (6.8–7.6%) and yield. In comparison with conventional fertilization, ZnO NPs elevated Zn content (13.5–39.4%) in brown rice (*O. sativa*) without affecting plant health (Yang et al., 2021). Seed priming of rice with 20 mgL^{-1} of ZnO NPs significantly enhanced Zn acquisition in seeds and increased total soluble sugars and improved antioxidant activities (Sharma et al., 2021). Foliar application ZnO NPs (10-40 ppm) on common bean (*Phaseolus vulgaris* L.) significantly increased Zn content (20.6 ppm) in the seed and enhanced the levels of essential amino acids (Salama et al., 2019). It has been reported that soil application of ZnO NPs (5 mg kg^{-1}) enhances Zn concentration in the grain by 94 % in sorghum (*Sorghum bicolor* (L.) Moench) and in finger millet (*Eleusine coracana* (L.) Gaertn. ssp. *Coracana*), seed priming with ZnO NPs (5 ppm) increases zinc content of grain by 13.96% in comparison to control plants (Dimkpa et al., 2019; Kumar et al., 2021). Importantly, ZnO NPs did not cause toxicity or nanoscale-specific risks. Elshayb *et al* reported that foliar application of 20-60 mgL^{-1} ZnO NPs enhanced Zn concentration from 17.7 to 50% in rice grains. Also, nutrients (N, K, and Zn) uptake was significantly enhanced by mixed foliar application of basal ZnSO4 and ZnO NP as compared to $ZnSO_4$ treated control plants (Elshayb et al., 2021). As such, nanoscale ZnO has significant potential for use as a fertilizer to increase grain Zn content as a biofortification strategy (Ivanov et al., 2021) (Table 1).

2.2. Iron

Iron (Fe) in soil may be present as magnetite (Fe_3O_4), hematite (α-Fe_2O_3), or maghemite (γ-Fe_2O_3). Fe may be difficult for plants to absorb due to common transformation reactions into unavailable forms in soil. Sufficient Fe increases seed germination, root growth, and enhances chlorophyll content in plants. Therefore, conventional chelated Fe fertilizers are used to alleviate Fe deficiency. However, in comparison to bulk iron oxide, γ-Fe_2O_3 nanoparticles more effectively translocate from roots to other parts of the plants because of their low volatilization and nanosize (Alidoust and Isoda, 2013) (Fig. 2). Seed priming with 25 ppm of iron oxide nanoparticles significantly increased Fe content in the grain (45.7%) of IITR26 and in WL711 (26.8%) wheat (*T. aestivum)* genotypes in comparison to untreated seeds (Sundaria et al., 2019). It has also been reported that foliar application of 1 mM and 10 mM iron oxide nanoparticles enhanced Fe content in wheat leaves (70-75%) as compared to Fe-EDTA (Zimbovskaya et al., 2020). The priming of wheat seed with Fe nanoparticles (5-20 mgL^{-1}) significantly increased the nutrients content in grain (20-121%) (Rizwan et al., 2019). Similarly, soil application of FeO NPs (25-100 $mgkg^{-1}$) enhanced Fe uptake by wheat (*T. aestivum*), as well as the concentration of N (33%), P (35%) and K (32.7%), and reduced Cd uptake by 72.5% (Manzoor et al., 2021). Fe_2O_3 nanoparticles (50 and 500 $mgkg^{-1}$) applied in soil not only increased wheat Fe content and biomass but also improved the content of amino acids, including cysteine and tyrosine (Wang et al., 2019). A comparative study by El-Desouky *et al* revealed that soil application of 100 $mgKg^{-1}$ Nano Fe_2O_3 significantly increased tomato (*Solanum lycopersicum* L.) yield by 11% compared to conventional, $FeCl_3.6H_2O$ and chelated Fe. Also, NP treated tomato produce had enhanced fruit diameter (4.3 cm), fruit numbers/plant (34 fruits), total fruit weight/plant (14 Kg) as compared to control plants (El-Desouky et al., 2021) . Further, in a comparative study on the application of Fe-nano-chelated (Fe-N), Fe-chelated (Fe-C) and Fe-siderophore (Fe-S), foliar application of 0.5-1 g L^{-1} of nanoscale chelated Fe on cumin (*Cuminum cyminum* L.) significantly increased Fe concentration in seeds, and enhanced plant growth and yield (Sabet and Mortazaeinezhad, 2018). Similarly, priming of finger millet (*E. coracana*) seeds with 100 ppm Fe_3O_4 nanoparticles increased grain Fe content by 12.3% in comparison to $FeSO_4.7H_2O$ (Kumar et al., 2021). Guha et al. also showed that seed priming of rice with 20 mgL^{-1} of nano-scale zero valent iron (nZVI) not only enhanced grain nutrient content, but also increased photosynthetic efficiency, yield, and accumulation of photo-assimilates (starch, soluble sugar, protein, lipid, phenol, riboflavin, thiamine, and ascorbic acid) in the grains (Guha et al., 2021). In addition, nZVI can be utilized commercially as a 'pro-fertilizer' for seed treatment. Amendment with nZVI has been shown to increase plant growth and yield with minimal impact on the soil ecosystem (Guha et al., 2021). It has also been reported that biosynthesized orthorhombic Fe–oxalate capped-Fe-oxide (Fe_3O_4) nanomaterials significantly increased the enzymatic activity of soil and alleviated iron deficiency in tomato (*S. lycopersicum*) as compared to the application of $FeSO_4$ and Fe-EDTA. The ability to modulate tuneable release at the nanoscale makes these nanoscale materials particularly useful as a sustainable source of Fe for plants (Das et al., 2016) (Table 2). Afzal *et al* studied that Nano-priming of rice seeds (*O. sativa*) with 20 and 40 mgL^{-1} FeO NPs capped with phytochemicals showed significant increase in Fe content in rice seeds and also showed enhanced seedling

Table 1
Effect of different concentrations and types of zinc nanoparticles for micronutrient enrichment in different food crops.

Target Crop	Concentration	Nanoparticles type	Micronutrient enrichment	Other positive effects	Application method	References
Wheat (*Triticum aestivum* L.)	50-1000 mgL^{-1}	ZnO	Increased Zn content in grains	Increased germination rate and yield by 56%	Soil	(Du et al., 2019)
Wheat (*Triticum aestivum* L.)	75 and 750 mgL^{-1}	ZnO	Increased grain Zn concentration	Increased grain yield	Foliar	(Doolette et al., 2020)
Wheat (*Triticum aestivum* L.)	0.96 kg ha^{-1}	ZnO	Zn concentrations increased by approx. 30 fold in grain endosperm	Enhanced activity of catalase and peroxidase enzymes	Foliar	(Sun et al., 2020)
Wheat (*Triticum aestivum* L.)	2 mgL^{-1}	ZnO	Grain Zn content increased from 27-35 $mgKg^{-1}$	Enhanced grain Zn content	Foliar	(Zhang et al., 2017)
Wheat (*Triticum aestivum* L.)	≤2.17 $mgKg^{-1}$	Urea coated ZnO	Zn uptake increased by 24% with coated urea and or 8% with uncoated ZnO NPs	Yield enhanced by 51 or 39%, with ZnO-NP-coated or uncoated urea.	Soil	(Dimkpa et al., 2020a)
Wheat (*Triticum aestivum* L.)	1.7 $mgKg^{-1}$	ZnO	Grain Zn concentration increased by 29%	-	Soil	(Dimkpa et al., 2020b)
Wheat (*Triticum aestivum* L.)	25-100 mgL^{-1}	ZnO	Increased the grain Zn content by 33-105% approx..	Decreased Cd uptake with increased dose of ZnO NPs	Seed priming	(Rizwan et al., 2019)
Wheat (*Triticum aestivum* L.)	40-120 mgL^{-1}	ZnO	Enhanced absorption of Zn NPs	Enhanced yield and protein content (39.24%)	Foliar	(Sheoran et al., 2021)
Wheat (*Triticum aestivum* L.)	25-100 $mgKg^{-1}$	ZnO	40-180% Zn enhancement in grains by foliar spray and 190% by soil application	16-78% decrease in Cd uptake in grains	Foliar and soil	(Hussain et al., 2018)
Wheat (*Triticum aestivum* L.)	25-100 mgL^{-1}	ZnO	Grains Zn content increased by 8-64%	Enhanced plant growth and grain yield by 185%	Seed priming	(Munir et al., 2018)
Wheat (*Triticum aestivum* L.)	20 mgg^{-1}	Zn complexed chitosan NPs	27 and 42% increase in grain Zn content	Increased plant growth and yield	Foliar	(Deshpande et al., 2017)
Rice (*Oryza sativa* L.)	20 mgL^{-1}	ZnO	Enhanced Zn acquisition in seeds	Enhancement in total soluble sugar and antioxidants activity	Seeds	(Sharma et al., 2021)
Rice (*Oryza sativa* L.)	25 and 100 $mgKg^{-1}$	ZnO	Increased Zn concentration by 13.5–39.4%,	Enhanced NPK content and total biomass (6.8-7.6%)	Soil	(Yang et al., 2021)
Maize (*Zea mays* L.)	2%	ZnO	Grain Zn concentration increased by 82%	Enhanced maize growth and yield by 51and 61% by foliar and soil application	Foliar, Soil	(Umar et al., 2020)
Maize (*Zea mays* L.)	50-2000 mgL^{-1}	ZnO	37% increase in grain Zn content	Maize yield enhanced by 42%	Foliar	(Subbaiah et al., 2016)
Common bean (*Phaseolus vulgaris* L.)	10-40 mgL^{-1}	ZnO	Increase in seed Zn and Fe content	Enhanced level of essential amino acids	Foliar	(Salama et al., 2019)
Sorghum (*Sorghum bicolor* (L.) Moench)	5 $mgKg^{-1}$	ZnO	94% increase in grain Zn content	Improved N,P and Zn content	Soil	(Dimkpa et al., 2019)
Finger millet (*Eleusine coracana* (L.) Gaertn. ssp. *Coracana*)	5 mgL^{-1}	ZnO	Grain Zn concentration increased by 13.96 %	-	Seed priming	(Kumar et al., 2021)

Table 2
Effect of different concentrations and types of iron nanoparticles for micronutrient enrichment in different food crops.

Target Crop	Concentration	Nanoparticles type	Micronutrient enrichment	Other positive effects	Application method	References
Wheat (*Triticum aestivum* L.)	25-100 $mgKg^{-1}$	FeO	Enhanced Fe uptake	Enhanced NPK concentrations and reduced Cd uptake by 72.5%	Soil	(Manzoor et al., 2021)
Wheat (*Triticum aestivum* L.)	500 mgL^{-1}	Fe_2O_3	Enhanced Fe uptake	Increased chla, chlb and carotenoid amount	Hydroponics	(Al-Amri et al., 2020)
Wheat (*Triticum aestivum* L.)	5-20 mgL^{-1}	Fe	Increased Fe content in grains by 20-121%	Decreased Cd accumulation in root (56%), shoot (54%) and grains (84%)	Seed priming	(Rizwan et al., 2019)
Wheat (*Triticum aestivum* L.)	50 and 500 $mgKg^{-1}$	Fe_2O_3	Increased Fe content	Increased amount of Cysteine and tyrosine amino acids along with enhanced biomass	Soil	(Wang et al., 2019)
Wheat (*Triticum aestivum* L.)	0.08986 and 0.8986 gL^{-1}	iron hydroxide NPs	70-75% increase in Fe content	-	Foliar	(Zimbovskaya et al., 2020)
Wheat (*Triticum aestivum* L.)	25-600 mgL^{-1}	FeO	Grain Fe content increased by 26.8 and 45.7%	Increase in seed germination and shoot length	Seed priming	(Sundaria et al., 2019)
Cumin (*Cuminum cyminum* L.)	0.5-1 gL^{-1}	Nano chelated Fe	Increased Fe concentration in seed	Enhanced growth and yield	Foliar	(Sabet and Mortazaeinezhad, 2018)
Finger millet (*Eleusine coracana* (L.) Gaertn. ssp. *Coracana*)	100 mgL^{-1}	Fe_3O_4	Grain Fe content increased by 12.26%	-	Seed priming	(Kumar et al., 2021)

vigour, increased germination and antioxidant enzyme activity as compared to ferrous sulphate ($FeSO_4$) priming and hydro-primed control (Afzal et al., 2021).

These studies clearly show that seed priming with iron oxide nanoparticles represents an innovative and sustainable approach for iron loading and for the successful biofortification of food crops (De La Torre-Roche et al., 2020; Guha et al., 2021; Sundaria et al., 2019).

2.3. Copper

Copper oxide nanoparticles (CuO NPs) are used as fertilizers, plant growth regulators, and as additives for soil remediation (Xiong et al., 2017) (Fig. 2). Both foliar and soil applications of CuO nanoparticles have been shown to increase Cu content in food crops as compared to unamended controls. However, the copper absorption rate and quantity depends on plant species, soil characteristics, and a range of environmental factors. Pestovsky et al revealed that 0.3 mgL^{-1} Cu^{2+} released from 1000 mgL^{-1} of copper nanoparticles increased plant growth. Importantly, the nanoparticles exerted no phytotoxicity to Mung Bean (*Vigna radiata* (L.) R.Wilczek) and wheat (*T. aestivum*) seedlings (Pestovsky and Martínez-Antonio, 2017). Foliar application of Cu nanoparticles (10-250 mgL^{-1}) on tomato (*S. lycopersicum*) not only enhanced vitamin C content (36 %) but also increased β-carotenoid levels (Hernández-Hernández et al., 2019). Tamez et al. observed that Cu nanoparticles applied in soil (40-60 mg kg^{-1}) increased the Fe and Cu content in sugarcane (*Saccharum officinarum* L.) by 73% and 74.5%, respectively (Tamez et al., 2019). Wang et al. showed that soil application of CuO nanoparticles (75-600 mg kg^{-1}) enhanced leaf allicin content by 56-187% in onion (*Allium fitulosum* L.), and also increased Cu, Ca, and Mg content in the bulbs (Wang et al., 2020a, 2020b). CuO nanoparticles applied to soil (50-500 mgkg^{-1}) significantly increased Cu accumulation in the roots, leaf, stem, and seed of soybean (*Glycine max* L., Merr.); soybean seeds contained 1.8 times greater Cu than other tissues of the soybean plant (Yusefi-Tanha et al., 2020). In a comparative study, Marmiroli et al also reported that soil application of nano-CuO (100 mg Kg^{-1}), bulk CuO (100 mg Kg^{-1}), and $CuSO_4$ (320 mg Kg^{-1}) at different stages of germination to flowering in zucchini (*Cucurbita pepo* L.), had no significant impact on its biomass (fresh weight). Whereas inductively coupled plasma mass spectrometry (ICP−MS) results of flower revealed that the Cu content was significantly increased by 43% and 30 % upon treatment of CuO NPs and bulk material as compared with untreated control, respectively. A total of 21.1 % genes were up regulated and 12.5 % genes were downregulated on treatment with CuO NPs when compared to the other bulk and salt treatments. Also, RNA-seq analyses of vegetative and reproductive tissues of zucchini plant, revealed that expression of ZAT12 a transcription factor having a key role in abiotic stress response involved in the ROS signalling pathway and ORF31 a chloroplastic electron carrier involved in photosynthesis was strongly upregulated on exposure of CuO NPs as compared with bulk and salt forms. Hence, this investigation revealed that treatment of CuO NPs trigger a "nanoscale-specific" response on zucchini plant by which chloroplast and mitochondrial function are modulated (Marmiroli et al., 2021).

Several recent studies highlighted the importance of Cu nutrient status in plants for controlling diseases in crop. For example, In a greenhouse study, Borgatta et al. reported that application of $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets at 10 mg/L significantly repressed root fungal disease by 58% caused by *Fusarium oxysporum* f. sp. *niveum* in watermelon (*Citrullus lanatus* (Thunb.) Mansf.), whereas only significant effects was observed on disease application of 1000 mg/L CuO NP. Similarly, field studies showed significant decrease in root fungal disease by 39.2% on application of, $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets, whereas only 29.9 % decrease was observed on application of CuO NP (Borgatta et al., 2018). Foliar amendment of $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets (500 mg/L; 1-2 mL dose) to seedlings of tomato (*S. lycopersicum*) efficiently reduced *Fusarium oxysporum* f. sp. *lycopersici* disease by an average of 31%, and significantly increase plant biomass and micro and macronutrient levels compared to untreated infected controls (Ma et al., 2019). Foliar application of $Cu_3(PO_4)_2$ NS, CuO NS, and CuO NPs50-250 mg l^{-}) effectively suppress *Fusarium virguliforme* in soybean and significantly decrease soybean sudden death syndrome compared to untreated control plants (Ma et al., 2020). These studies highlighted the importance of sufficient nutrients and the potential of nanoscale platforms to more effectively deliver critical micronutrients at early stages of plant development in crop disease response. However, CuO at higher concentrations can cause phytotoxicity, reducing growth and water content (Xiong et al., 2017). This toxicity may be mediated through released Cu ions that can disrupt redox reactions in cells (Wang et al., 2019; Xiong et al., 2017).

From these studies, it is clear that CuO NPs could be effectively used for Cu biofortification in crops; however, excess Cu could also induce toxicity and thus, CuO NPs must be used carefully. A detailed list of studies on Cu nanoparticles for crop biofortification are provided in Table 3.

2.4. Selenium

Selenium (Se) is an essential element for human and animal health. More than one billion people globally are facing Se deficiency (Haug et al., 2007). Se exists as acids, oxyhalides, oxides, halides, oxyacids, selenides, selenium nucleic acid, and selenozyme in both soil and biotic systems, including plants (Skalickova et al., 2017). Se nanoparticles used as nanofertilizer have greater bioavailability due to their high surface area to volume ratio, showed enhanced antioxidant, antimicrobial, anti-cancer properties as compared to bulk Se (Hosnedlova et al., 2018) (Fig. 2). Se readily interacts with ligands and act as a heavy metal detoxifying agent as free radicals are neutralized by selenocysteine binding with glutathione peroxidase (Zoidis et al., 2018). It has been re-

Table 3
Effect of different concentrations and types of copper nanoparticles for micronutrient enrichment in different food crops.

Target Crop	Concentration	Nanoparticles type	Micronutrient enrichment	Other Positive effects	Application method	References
Wheat (*Triticum aestivum* L.)	50 and 500 mgKg^{-1}	CuO	Grain Cu concentration enhanced by 18.84%–30.45%	-	Soil	(Wang et al., 2019)
Tomato (*Solanum lycopersicum* L.)	250 mgL^{-1}	Cu	Increased content of vitamin C and β- carotenoid	Enhanced antioxidants response	Foliar	(Hernández-Fuentes et al., 2017)
Tomato (*Solanum lycopersicum* L.)	10-250 mgL^{-1}	Cu + Se NPs	Increased vitamin C content up to 36%	Enhanced antioxidants and tomato yield	Foliar	(Hernández-Hernández et al., 2019)
Onion (*Allium fistulosum* L.)	75-600 mgKg^{-1}	CuO	Increase in bulb Cu, Ca, Mg content	Enhanced leaf allicin content by 56-187%	Soil	(Wang et al., 2020a)
Soybean (*Glycine max* (L.) Merr.)	50-500 mgKg^{-1}	CuO	1.8 times high Cu content in seeds	Increased Cu accumulation in root, leaf, stem , and seed	Soil	(Yusefi-Tanha et al., 2020)
Sugarcane (*Saccharum officinarum* L.)	20-60 mgL^{-1}	Cu	Fe content increased by 73%	Increase in Copper, iron and magnesium	Soil	(Tamez et al., 2019)

ported that foliar application of Se NPs (10-160 mg/L) increased Se content of coffee grains (4.84-5.82 $mgkg^{-1}$) as compared to sodium selenite (0.116 to 4.47 mg kg^{-1}) application (Mateus et al., 2021). Shalaby et al. observed that foliar application of Se NPs (25 mgL^{-1}) on cucumber (*Cucumis sativus* L.) not only enhanced uptake of that nutrient but also increased the *in planta* concentration of N, P, K, and also increased crop yield (Shalaby et al., 2021). Se nanoparticles applied in a hydroponic solution (10 and 30 μm) significantly enhanced Se content by 6.7-20.4 fold in rice seedlings in comparison to inorganic selenium (Wang et al., 2020a, 2020b). Wang et al. also reported that foliar spray of Se NPs (25-100 μmL^{-1}) on brown rice facilitated enrichment of Se up to 218.9-1096.6 μg kg^{-1} (Wang et al., 2021a, 2021b). Therefore, Se NPs could be utilized as cost effective micronutrient for crop biofortification, as well as for the improvement in biochemical production of proteins/ amino acids, phenolics, and glucosinolates (Carvalho et al., 2003) (Table 4).

2.5. Nanoscale-chelators for biofortification

Chelators are small molecules which strongly bind to metal ions and are effective soil amendments that improve availability of metal ions by forming two or more coordinate bonds, resulting in greater bioavailability and plant uptake (Flora, 2015). Some chelators are synthetic, such as EDTA, while others can be biosynthesized, such as transferrins and phytochelators (Nurchi et al., 2016). The metal chelating exudates secreted by plant roots or microbes in the rhizosphere are known as phytochelators and include low molecular weight organic acids, siderophores, phytochelatins, phytins, and metallothioneins. Phytochelators support the transport of metals such as Fe and Zn by conjugation, leading to ready ion transport across cell barriers (Fig. 3). NPs conjugated with nano-chelators can play a significant role in micronutrient biofortification strategies (Fakharzadeh et al., 2020). Some important properties for nano-chelators include low affinity for toxic metals, high affinity for essential metals, and high lipid solubility. Nano-chelated Fe fertilizers have been reported to increase rice yield (27%) and protein content (13%) (Fakharzadeh et al., 2020). Specifically, nano-chelated Fe fertilizer increased N, P, K, Fe, and Zn levels by 46%, 43%, 41%, 25%, and 50%, respectively (Fakharzadeh et al., 2020). An optimized nano-chelating technology could significantly decrease the need for conventional chemical fertilizers and could be a sustainable strategy to biofortify crops with required or beneficial nutrients.

2.6. Nano-zeolites

Zeolites have significant potential as fertilizers for food crops. The International Agency for Research on Cancer (IARC) and the US Food and Drug Administration (FDA) have declared zeolites to be nontoxic and suitable for food and agricultural applications. Zeolites are alkali or alkaline earth alumino-silicates that encompass nearly 50 different types of minerals. Zeolites have a 3D-crystalline structure with large porosity and surface area (500-800 m^2/g) that allows very high cationic exchange. This enables retention of negatively and positively charged nutrients for extended periods of time (Guo, 2004). Zeolite nanoparticles may slowly release elements for efficient absorption by plants, effectively preventing loss from the system (Eroglu et al., 2017). Zeolites could also be a highly effective nano-fertilizer platform for enhancing

Table 4
Effect of different concentrations and types of selenium nanoparticles for micronutrient enrichment in different food crops.

Target Crop	Concentration	Nanoparticles type	Micronutrient enrichment	Other Positive effect	Application method	References
Rice (*Oryza sativa* L.)	0.7896 and 2.3688 gL^{-1}	Se	6.7 and 20.4 fold higher Se content in rice seedlings	-	Hydroponics	(Wang et al., 2020)
Rice (*Oryza sativa* L.)	1.974-7.896 gL^{-1}	Se	Enrichment of Se in brown rice from 218.9-1096.6 μg/kg	Decreased accumulation of Cd, Pb and increase in grain yield	Foliar	(Wang et al., 2021a)
Cucumber (*Cucumis sativus* L.)	25 mgL^{-1}	Se	Enhanced uptake of Se	Increased concentration of N,P,K, plant growth and yield	Foliar	(Shalaby et al., 2021)
Coffee (*Coffea arabica* L.)	10-160 mgL^{-1}	Se	Se content in coffee grains ranged from 4.84-5.82 mg/Kg	Enhanced antioxidants along with increase in yield by 42%	Foliar	(Mateus et al., 2021)

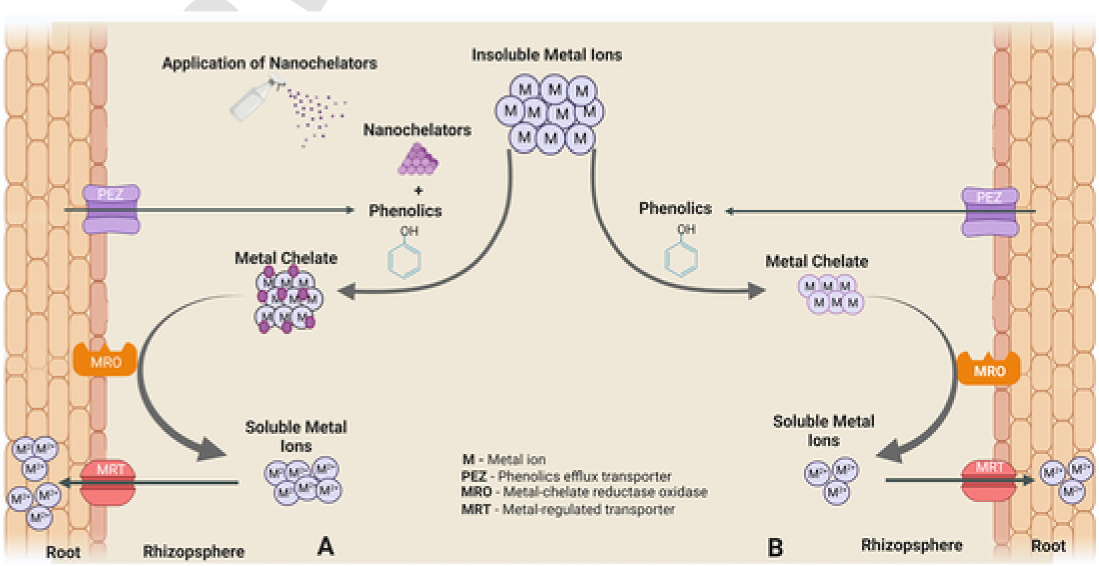

Fig. 3. An illustration of different strategies for metal ions transport in plants, A) Nanochelator-aided strategy (Strategy-I) demonstrates chelating of metal ions with nanochelators for their easy uptake through metal regulated transporters, B) Phytosiderophore-aided strategy (Strategy-II) demonstrates chelating of metal ions with phytosiderophores released by plant in deficiency conditions to facilitate easy uptake of metal ions.

seed germination and regulating soil acidity. Inorganic hydrated negative ions are trapped in the exposed surface because of interactions of polar molecules and cations. Zeolites can act as a carrier for nutrients such as N and K (Eroglu et al., 2017; Polat et al., 2004). Nanocomposites of zeolite with N, P, and K could be prepared in conjunction with other micronutrients as novel mineral fertilizers. Components of zeolite in humus have been shown to enhance crop growth and productivity (Manikandan and Subramanian, 2016; Yuvaraj and Subramanian, 2018). Customized nano-zeolites with large surface area and porosity can be designed with a significant holding capacity for specific ions; the release profile can be controlled using a top-down approach via ball milling to facilitate the delivery of essential and desired nutrients to plants (Yuvaraj and Subramanian, 2018). Therefore, the beneficial properties of cost effectiveness, high bioavailability, and non-toxicity make zeolite nanoparticles an effective choice for sustainable agricultural application. Furthermore, the application of nano zeolite-urea in soil significantly increased the nitrogen content (0.76%) in maize grains by 28% due to slow release of nutrients over an extended period of time in comparison to urea fertilized plants (0.48%). Hence, nano zeolites are a promising fertilizer and could be used to enhance plant growth and biofortification of food crops (Manikandan and Subramanian, 2016; Polat et al., 2004).

3. Mechanism of nanoparticle uptake, translocation, and accumulation in plants

The potency of NPs uptake depends on plant species, as well as particle size, chemical nature, stability and function (Rico et al., 2011).The effect of NPs size on its uptake in wheat plants has been studied; for example, Fe_2O_3 NPs of size 8-20 nm easily penetrated in the roots and translocated to the leaves (Al-Amri et al., 2020). The surface area to charge ratio and concentration of NPs are also crucial factors impacting uptake and translocation in plants. NPs with larger surface area to volume ratios can more easily penetrate the root and leaf surface (Burke et al., 2014). In soybean (*G. max*) maximum Zn (8 nm) uptake was found at 500 mgL^{-1}, whereas, a reduction in Zn uptake was observed at higher ZnO NPs concentrations i.e.1000–4000 mgL^{-1} (López-Moreno et al., 2010). The reduction in Zn uptake might be attributed to the formation of aggregates at higher concentrations, making it difficult to pass through the cell wall pores. Other studies have revealed that nano priming of seeds facilitates enhanced uptake of micronutrients, although the precise mechanisms of action are not known (Munir et al., 2018; Rizwan et al., 2019; Sundaria et al., 2019).

3.1. Foliar uptake and translocation of NPs

Foliar application of nanoparticles is perhaps the most direct way to fortify plants. Foliar uptake of NPs from the leaf surface occurs through cuticular and stomatal pathways (Lv et al., 2019). Lipophilic substances enter by diffusion in leaves via the cuticular pathway, while polar or ionic substances enter through stomatal pores (0.6–4.8 nm diameter). Therefore, NPs with size below 4.8 nm may cross through cuticular pathway. However, the uptake of NPs (with size >5nm) likely involves other pathways of foliar uptake. In the stomatal pathway, hydrophilic substances enter through stomata pores with diameter ≥40 nm. Due to small cuticular pore size, studies generally support the stomatal pathway for NPs uptake in leaves (Ali et al., 2021; Eichert and Goldbach, 2008; Schreiber, 2005; Wang et al., 2021b). After entering into the leaf apoplast, NPs translocate to grain, fruit, stem, and root via phloem (Fig. 4). The uptake of Fe_2O_3, magnesium oxide (MgO), and ZnO NPs (24-47 nm size) in watermelon (*C. lanatus*) was confirmed as penetration of NPs through the stomata (Wang et al., 2013). Further, the presence of

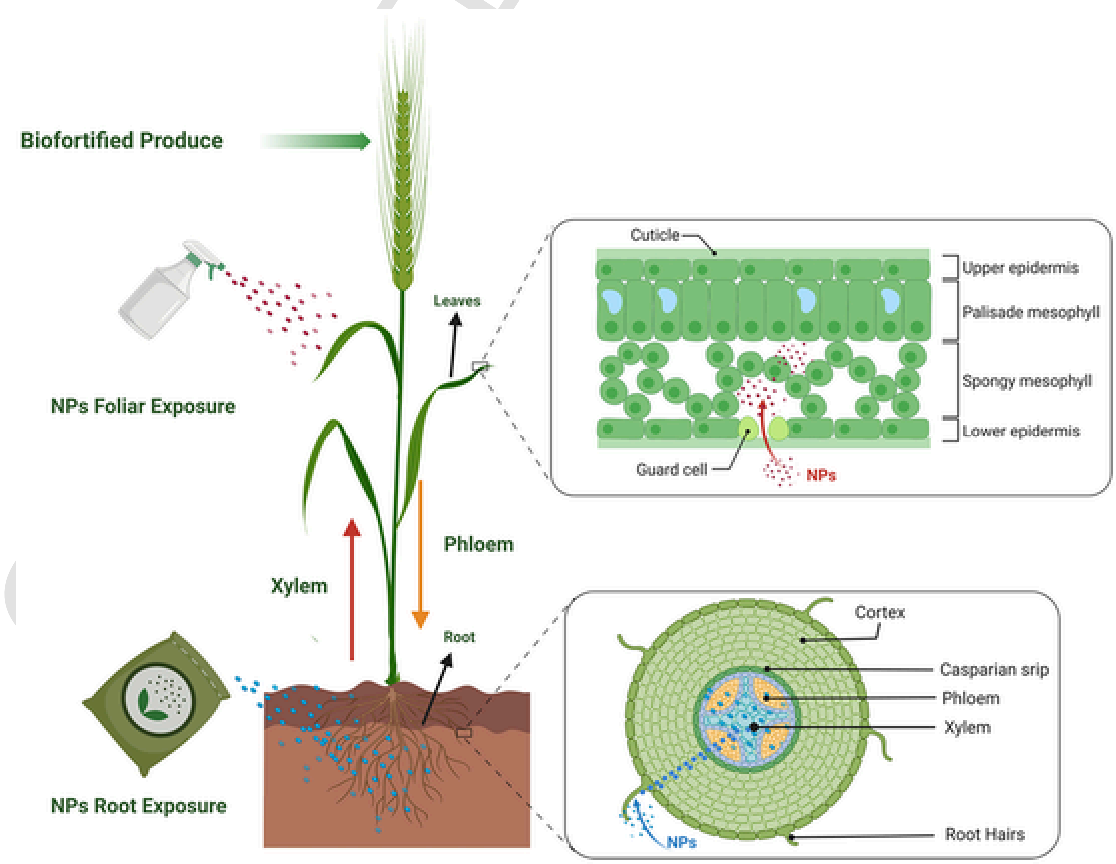

Fig. 4. The schematic representation of foliar and root uptake of nanoparticle-based fertilizers *via* stomata and root hairs, respectively and their translocation through xylem and phloem.

NPs in shoots and roots suggests their translocation to roots via phloem. Foliar uptake of ZnO NPs in coffee plants was evaluated by X–ray micro-analysis, and confirmed Zn NPs accumulation in treated leaves (~1267 $mgkg^{-1}$ dry wt.) as compared to the control plants (~53.6 $mgkg^{-1}$ dry wt.) (Rossi et al., 2019). Importantly, both cuticular and stomatal pathways remain involved in foliar uptake of Zn NPs; the significance of each pathway may vary though (Singh et al., 2018a, 2018b, 2018c). Foliar uptake and translocation of Fe_3O_4 NPs from the leaf to the stem and ultimately to the root via phloem was observed. The Fe accumulation pattern in wheat seedlings was as follows: leaves > stem > roots in (Cai et al., 2020; Lu et al., 2020). Xiong et al. showed that after foliar application of CuO NPs in cabbage and $Cu(OH)_2$ NPs in lettuce, a significant amount of Cu (97-99%) was accumulated in the leaves and only a small fraction (1-3%) translocated and accumulated in roots (Xiong et al., 2017). Another study revealed that the greatest absorption of γ-Fe_2O_3 NPs occurred via foliar application as compared to soil application (Alidoust and Isoda, 2013).

3.2. Root uptake and translocation of NPs

Most studies on nanoparticle uptake are focused on root uptake as compared to foliar exposure, in part because nanoparticles tend to persist longer in soil than on leaves. The interactions of NPs in soil and subsequent uptake and translocation of NPs in roots is more complex in comparison to foliar uptake. NPs have to cross a number of barriers, including the root cuticle, epidermis, cortex, endodermis, and casparian strip for transport to the shoots through the xylem (Fig. 4). NPs applied in the soil either directly or as nano-fertilizer will initially adhere to the root surface and then penetrate into the roots via aquaporins, ion channels, endocytosis, and carrier proteins. The movement of NPs across membranes via endocytosis is the most recognized route of uptake (Etxeberria et al., 2006; Rico et al., 2011; Schwab et al., 2016; Wong et al., 2016). Aquaporin transporters also have a role in NPs uptake; Wang et al demonstrated that inhibiting aquaporin activity decreased Se NPs influx by 60.4% in rice seedlings (Wang et al., 2020a, 2020b).

The surface of the root is primarily negatively charged due to the secretion of organic acids from the root hairs; this therefore promotes the adsorption and accumulation of positively charged NPs (Zhou et al., 2011). NPs can also directly cross the root hair cuticle due to its poor development, subsequently reaching the epidermis (Schwab et al., 2016). For further translocation of NPs, both apoplastic and symplastic pathways have been demonstrated in various reports. The apoplastic pathway involves the movement of NPs through intercellular spaces; for the symplastic pathway, NPs are translocated from cell to cell via plasmodesmata (Fig. 4). Apoplastic movement of NPs is widely accepted due to the presence of NPs in the intercellular space of root tissues in a large number of studies (Li et al., 2016; Tombuloglu et al., 2019; Wang et al., 2012; Zhu et al., 2008). Although the casparian strip acts as a barrier to apoplastic movement, NPs may enter the xylem through the root tip (where casparian strips are not developed) or via junctions in the lateral root region (where casparian strip is detached) (Lv et al., 2015; Schymura et al., 2017). For example, the accumulation of ZnO NPs in the lateral root junction and xylem of maize has been reported. Therefore, this junction is important to the apoplastic movement of NPs into the xylem (Lv et al., 2015). The uptake and translocation of CuO NPs through the xylem and phloem in maize and rice was investigated and the authors reported the presence of endosomes having CuO NPs, as well as particle accumulation in the intercellular spaces of root cells, xylem sap and leaves. Hence, CuO NPs can enter plant cells by endocytosis (followed by apoplastic pathway) and move into the xylem with subsequent transport to different parts of the plant. Further, it was found that CuO NPs biotransform (Cu^{2+} to Cu^{+}) during translocation from roots to shoots. Cu content in treated rice plants followed the order: roots > mature leaves > stem > young leaves (Peng et al., 2015). The uptake and translocation of Fe_2O_3 NPs in maize was studied using transmission electron microscopy (TEM), and apoplastic movement of Fe_2O_3 NPs from the root epidermis to endodermis was observed, although no information about translocation to other plant tissues was studied (Li et al., 2016).

In higher plants metal acquisition under deficient conditions have been well categorized into two basic strategies: Strategy I in non graminaceous plants and strategy II in graminaceous ones. Strategy I follow the metal chelates reduction at the surface of root by metal reduction oxidase (MRO), then the absorption of metal ions across the plasma membrane of root cells with the help of metal-regulated transporter gene (*MRT*) and later extrusion of protons and phenolic compounds in the rhizosphere which increases the solubility of metal ions on the surface of roots (Kobayashi and Nishizawa, 2012; Römheld and Marschner, 1986) (Fig. 3A). In contrast, strategy II includes uptake of metal by plants under metal deficiency through secretion of metal chelating phytosiderophores like mugineic acids (MA) and nicotianamine (NA) possessing strong affinity for metal ions by forming an metal-phytosiderophore soluble complex, which gets transported into the root cells of the plant (Singh and Prasanna, 2020) (Fig. 3B). Sega *et al* reported that application of citrate-capped $FePO_4$ NPs significantly increase the P level to more than double in the shoot of cucumber plant as compared to bulk-treated or negative controlled plants (Sega et al., 2020; Sega et al., 2019). Similar treatment given in maize (*Z. mays*) plants significantly increase the P level. Fe concentration also increased subsequently in root tissues of maize and cucumber on application of $FePO_4$ NPs whereas lesser increase was observed for Fe concentration in the shoot of maize plant than cucumber compared to control plants. Therefore, it has been concluded that cucumber plants (Strategy I species) uses $FePO_4$ NPs as a P source whereas maize (Strategy II species) uses $FePO_4$ NPs as a Fe source preferentially (Sega et al., 2020; Sega et al., 2019).

The mechanism of NPs uptake, translocation, and accumulation in plants are still poorly understood, in part because most studies are conducted at the seedling stage (Lv et al., 2019). Therefore, additional research to understand the mechanisms of transport of NPs in plants is critical to establish their suitability in agricultural applications. For example, NPs translocated mainly through xylem should be added to the soil, whereas NPs transported via phloem would be more amenable to foliar application (Aslani et al., 2014).

4. Fate and impact of nanomaterials on agricultural systems

Nanomaterials offer a number of innovative opportunities in sustainable agriculture. Nanotechnology based “smart” or “responsive” products offer enhanced performance as multifunctional industrial and commercial applications (Klöpffer et al., 2007). However, in certain cases, negative impacts of nanomaterials on the environment have been reported. Therefore, a comprehensive and holistic approach such as that offered by life cycle analysis (LCA) is necessary for better understanding, evaluation, analysis and use management of nanomaterials (Salieri et al., 2018). Life cycle assessment is an integrated approach to determine whether the nanomaterial manufactured is safe for the environment. LCA allows evaluation of the nanomaterial for environmental sustainability by measuring its impact on the environment and the life cycle of an organism. Hence, LCA is absolutely a benefit for the comprehensive study of the nanomaterial for improving its performance and efficacy for the environmental system. Furthermore, LCA is capable of quantifying the conversions and emission of the energy produced in a system, which ultimately acknowledges efficiency of nanomaterial for the ecosystem. It is a misconception that the nanomaterial can be handled easily as conventional material. However, due to limitation of data availability, researchers are unable to assess the transparency of nanomaterial regarding its usage, efficiency and compatibilities with the environment. This uncertainty can be countered by scaling up the nanotechnology and fate modelling of nanomaterials for their toxicity assessments and potential impact on life cycle of organisms and environment (Nizam et al., 2021).

Natural and anthropogenic nanomaterials have both positive and negative impacts on biological systems and the environment, which further depends upon dose, duration, and frequency of exposure (Hochella et al., 2019). Nanomaterials in the agricultural sector are used to enhance crop yield, biofortification, and to develop resistance against biotic and abiotic stresses. However, improper and excessive use of nanofertilizers may negatively affect the crop and perhaps the overall ecosystem. Nanomaterials can bioaccumulate in the food chain, inhibiting growth of the plant and related organisms. Nanomaterials promoting plant growth and development may cause toxicity to non-target organisms because of overproduction of ROS (He et al., 2018; Prasad et al., 2017). Nanomaterials may impact soil microbial communities through (1) direct toxic effects, (2) indirect effects while coordinating with natural organic compounds, (3) increase toxicity by interacting with co-existing organic pollutants in soil and water and (4) changing the bioavailability of nutrients and toxins. Although, the mechanism of nanomaterial toxicity for beneficial microbial communities is not completely understood, the reports highlight: (1) damage to cell membranes, (2) protein oxidation (3) genotoxicity (4) ROS production or apoptosis as observed for antimicrobial action of nanomaterials (Fiol et al., 2021; Khanna et al., 2015; Klaine et al., 2008; Paramo et al., 2020; Pérez-de-Luque, 2017). The toxicity of nanomaterials to beneficial microorganisms involved in organic carbon degradation in soil, mineralization of nutrients, and nitrogen cycling is a matter of concern. Long term exposure of nanomaterials such as Fe_2O_3, TiO_2, ZnO, CuO, carbon nanotubes (CNTs) and fullerenes have been shown to reduce microbial communities and plant growth promoting microbial consortium (mycorrhiza and rhizobacteria) in soil (Hegde et al., 2016; Judy and Bertsch, 2014; Lead et al., 2018).

Yasmeen *et al* studied that application of 25 ppm Cu and Fe NPs in soil significantly increases the proteins involved in starch degradation, glycolysis and the tricarboxylic acid cycle (TCA) of wheat. Proteome analysis of wheat seeds of Galaxy-13, Pakistan-13, and NARC-11 revealed that on treatment of Cu and Fe NPs a total of 58, 121, and 25 proteins were changed, respectively. It was also observed that Cu content was increased in wheat seeds of galaxy-13 on application of 25ppm Cu NPs whereas as a significant increase in Pakistan-13, and NARC-11 was found on application of 20ppm Cu NPs as compared to control conditions. Increased Fe content was only found in NARC-11 exposed to 35 and 40 ppm Fe NPs as compared to control plants (Yasmeen et al., 2017). Transcriptomic and metabolomic analyses of tomato (*S. lycopersicum*) plant revealed that foliar application of ZnO NPs (20 and 100 mgL^{-1}) increased the expression of genes involved in carbon and nitrogen metabolism, nutrient/element transport, and secondary metabolism which improve the levels of amino acid, sugar and antioxidants. ZnO NPs also enhanced iron (Fe) accumulation in tomato leaves by 12.2 %, and improve Fe deficiency tolerance in tomato plants (Sun et al., 2020a, 2020b). A comparative study on transcriptomic and physiological analyses of *Arabidopsis thaliana* (L.) Heynh. revealed that seedlings exposed to 20-200 mg L^{-1} ZnO nanoparticles inhibit primary root (PR) growth by 53%. Despite the stronger inhibitory effect of ZnO NPs on PR growth, upon transfer to normal conditions, plants exposed to ZnO NPs recovered from stress more rapidly than plants exposed to $ZnSO_4$. A total of 30 metal transporter genes were found to be upregulated and12 were downregulated in seedlings treated with ZnO NPs whereas only 17 were found upregulated and 4 were downregulated in seedlings treated with ZnSO4 (Wan et al., 2019). Transcriptomic, proteomics, and metabolomics study of plant treated with nanofertilizers could be the promising approaches to combat and prevent the potential hazard and toxicity of nanomaterials to the plants.

Moreover, current scientific breakthroughs have led to the abundant usage of nanoparticles in the field of agriculture to maintain proper nutrient uptake in plants. Therefore, less attention has been given for the efficient supply of nanofertilizer to crop plants, capable of releasing micronutrients while nourishing its surrounding soil without having any toxic effects. Recent studies showed that biomaterials such as polylactic acid and polyhydroxyalkanoates polymers, alginate, and chitosan act as a carrier of nanoparticles for their controlled and efficient release of which also counteract with the toxic effects of nanoparticles in the ecosystem. Ekanayake and Godakumbura (2021) conducted an experiment in which ZnO and CuO nanoparticles embedded on alginate based hydrogels were applied in soil growing tomato plants. In this study, it was observed that alginate-NP hydrogel complex facilitates controlled release of NPs in soil. In the soil, the micronutrients were continuously increasing slowly with time and the uptake of NPs was also gradually increased with time with no toxic effects in plant (Ekanayake and Godakumbura, 2021). Similarly, Leonardi and co-workers reported that a polyelectrolyte complex of chitosan-alginate nanocmposite facilitates controlled release of encapsulated CuO NPs where 80% copper was release after 22 days compared to 1 day for only CuO NPs (Leonardi et al., 2021). Also, when applied on *Fortunella margarita* Swingle seeds the nanocomposite showed increase in seed germination. Sigmon *et al* revealed that biodegradable polymer nanocomposites (PNCs) containing polyhydroxyalkanoate (PHA) and calcium phosphate nanoparticles (Ca–P–NPs) efficiently controlled the release of P during the initial stages of tomato plant growth (Sigmon et al., 2021). PHA–Ca–P PNCs significantly reduced the P loss from the soil by over 80% and increase P uptake by plant comparably to the conventional P source ($CaHPO_4$).

Since the biodegradable coating reduces environmental impact, by slowing the release of the nanofertilizer, the novel nanoformulation effectively acts as an efficient and eco-sustainable medium to regulate fertilization without dispersion in the soil. The latter property makes these materials attractive for the future design of slow-release nanofertilizers, specifically aimed at preventing their undesired accumulation in soil and plants (Leonardi et al., 2021). Therefore, future studies should focus on the development of sustainable nanomaterials for positive impacts on agriculture (Baalousha et al., 2016). Importantly, studies on nanomaterial toxicity, risk assessment, and the development of preventive measures for biological safety must be conducted on a priority basis.

5. Conclusion

Micronutrient deficiencies have a significant impact on plant and human health. Nutrient-enriched crop development through sustainable agriculture can be a key strategy for global food security. Herein, an overview of the prevalent nanomaterial-based techniques for biofortification was provided. Nanotechnology-based approaches may help achieve nutrient enriched foods, minimizing losses through leaching in soil and volatilization or by aiding in the process of genetic transformation and alteration of genes involved in uptake, translocation and accumulation of micronutrients. These approaches can effectively biofortify food crops to sustainably alleviate micronutrient deficiency in humans. Studies in the future must focus on the nanomaterial-assisted biofortification of agricultural crops under full life cycle growth conditions, as well as the effects of nanomaterials on crop yield and nutritional quality. Further, changes in physiological and biochemical characteristics of plants grown with nanomaterial treatment must be explored to understand the possible long-term benefits and consequences. In addition, diverse crops must be evaluated; both cereal crops and vegetable species should be incorporated to fully examine the potential of nanotechnology-based biofortification. Importantly, such work must focus on understanding the key mechanisms of action underlying important processes. The economic costs/benefits of nano-enabled biofortification strategies must also be thoroughly evaluated in a life cycle analysis. Currently, the utilization of nano-enabled biofortification strategies is in the preliminary stages but with the oncoming impacts of climate change and population growth, research in this area must increase to fulfil the demand for global food and nutritional security.

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Author contributions

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Declaration of Competing Interest

The authors declares no competing interests.

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