Selenium and Nano-Selenium Biofortification for Human Health: Opportunities and Challenges

Hassan El-Ramady 1, Salah E.-D. Faizy 1, Neama Abdalla 2, Hussein Taha 2, Éva Domokos-Szabolcsy 3, Miklós Fari 3, Tamer Elsakhawy 4*, Alaa El-Dein Omara 4, Tarek Shalaby 5,6, Yousry Bayoumi 5, Said Shehata 7, Christoph-Martin Geilfus 8 and Eric C. Brevik 9,*

1 Soil and Water Department, Faculty of Agriculture, Kafrelsheikh University, Kafr El-Sheikh 33516, Egypt; hassan.elramady@agr.kfs.edu.eg (H.E.-R.); salahfaizy@rocketmail.com (S.E.-D.F.)
2 Plant Biotechnology Department, Genetic Engineering Division, National Research Center, Cairo 12622, Egypt; neama_ncr@yahoo.com (N.A.); hussein.taha2@hotmail.com (H.T.)
3 Agricultural Botany, Crop Physiology and Biotechnology Department, Debrecen University, Böszörményi u. 138., H-4032 Debrecen, Hungary; domokosszabolcsy@gmail.com (E.D.-S.); fari@agr.unideb.hu (M.F.)
4 Agriculture Microbiolgy Department, Soil, Water and Environment Research Institute (SWERI), Sakha Agricultural Research Station, Agriculture Research Center (ARC), Kafr El-Sheikh 33517, Egypt; drelsakhawyg@gmail.com (T.E.); alaa.omara@yahoo.com (A.E.-D.O.)
5 Horticulture Department, Faculty of Agriculture, Kafrelsheikh University, Kafr El-Sheikh 33516, Egypt; tshalaby@kfu.edu.sa (T.S.); ybayoumi2002@yahoo.com.sg (Y.B.)
6 Arid Land Agriculture Department, College of Agricultural and Food Sciences, King Faisal University, 31982 Al-Hasa, Saudi Arabia
7 Vegetable Crops Department, Faculty of Agriculture, Cairo University, Giza 12613, Egypt; said_shehata2@yahoo.com
8 Division of Controlled Environment Horticulture, Institute of Agriculture and Horticulture, Faculty of Life Science, Humboldt-Universität zu Berlin, Albrecht-Thaer-Weg 1and3, 14195 Berlin, Germany; geilfus@hu-berlin.de
9 Departments of Natural Sciences and Agriculture and Technical Studies, Dickinson State University, Dickinson, ND 58601, USA
* Correspondence: Eric.Brevik@dickinsonstate.edu

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Abstract: Selenium is an essential micronutrient required for the health of humans and lower plants, but its importance for higher plants is still being investigated. The biological functions of Se related to human health revolve around its presence in 25 known selenoproteins (e.g., selenocysteine or the 21st amino acid). Humans may receive their required Se through plant uptake of soil Se, foods enriched in Se, or Se dietary supplements. Selenium nanoparticles (Se-NPs) have been applied to biofortified foods and feeds. Due to low toxicity and high efficiency, Se-NPs are used in applications such as cancer therapy and nano-medicines. Selenium and nano-selenium may be able to support and enhance the productivity of cultivated plants and animals under stressful conditions because they are antimicrobial and anti-carcinogenic agents, with antioxidant capacity and immune-modulatory efficacy. Thus, nano-selenium could be inserted in the feeds of fish and livestock to improvise stress resilience and productivity. This review offers new insights in Se and Se-NPs biofortification for edible plants and farm animals under stressful environments. Further, extensive research on Se-NPs is required to identify possible adverse effects on humans and their cytotoxicity.

Keywords: human disease; cereal crops; vegetable crops; hyper-accumulators; biofortified crops
1. Introduction

The discovery of selenium in 1817 triggered a huge amount of innovative scientific inquiry into human health. Selenium is an essential micronutrient for humans and animals as well as some lower plants, but it still needs more investigation to establish whether or not it is essential for higher plants [1,2]. Selenium (Se) plays a vital role in the metabolism of humans, animals, and many prokaryotes as well as some algae [1]. This micronutrient is the only metalloid that is incorporated into specific proteins, called “selenoproteins”, and genetically encoded as well as forming a constitutive part of selenocysteine (SeCys), “the 21st amino acid” [3]. In total, 25 selenoproteins have been identified in the human proteome and are often oxido-reductases, including SeCys as a catalytic residue [4,5]. These selenoproteins mainly have wide redox functions that are vital for regulating human immunity [6], mediating thyroid disorders [7], and for the health of the reproductive system [1,3,8,9]. The essential role of selenium in human health has been confirmed by several researchers [10–16]. A major distinguishing feature of Se is the narrow margin between Se-deficiency (<40 µg day$^{-1}$) and toxicity (>400 µg day$^{-1}$) [17]. The recommended daily dose for adults is 55 µg day$^{-1}$ in the USA and 55 to 70 µg day$^{-1}$ in Europe [18]. Selenium is called the “the essential poison” and characterized as “the double-edged sword” due to its biological effects under deficiency and toxicity [13].

Selenium and nano-selenium (nano-Se) or (Se-NPs) have been used in the maintenance of human health [19]. They can be applied in biomedical and drug delivery [20] dietary supplements, therapeutic agents [18], and nano-medicine applications [21]. The antimicrobial and anticancer properties of both Se and Se-NPs have been confirmed [19,22]. The biofortification of edible foods [23,24] and feeds [25,26] with Se and Se-NPs is an important approach to support human and livestock health.

The primary natural source of Se in foods is crop uptake from soil [13,27]. There are wide geographic variations in the Se content of soils, meaning some regions face Se deficiencies while others have Se toxicity issues based on the Se content in their crops, with both situations having negative impacts on human health [28]. Crops grown in Se deficient soils can be biofortified, including the use of both soil-based and foliar fertilizers to correct the deficiency [27]. Food crops that are commonly biofortified include cereals [29], leafy vegetables like spinach [30] and lettuce [31], and fruits like strawberry [24,32,33] and pomegranate [23]. Due to their lower toxicity, strong capacity to scavenge free radicals, higher bioavailability, and stimulation effect, Se-NPs have been recently used in the production of plants [23,24,34–36], fish [37–40], livestock [41], and poultry [42–48].

Therefore, this review explored available information on the use of Se and Se-nanoparticles in biofortification. The use of selenium and nano-selenium to promote human health is discussed, including the biofortification of crops through soil and other amendments. We also investigated the role of Se and nano-Se to support crops under stress.

2. Selenium and Nano Selenium: General Information

Although Selenium and its nanoparticles share some common and general properties, they important differences based on their unique chemical, physical, and biological properties (Table 1). For example, bulk elemental Se is not water soluble, but Se-NPs are partially water soluble (Figure 1). The behavior and biological features of Se and Se-NPs in the nutrition of higher plants and humans may differ. The role of Se in human nutrition has been confirmed, whereas the biological effects, recommended daily intake and toxicity/deficiency levels of Se-NPs still need more investigations [3,8,10,11,19,49]. Indications of the general role of Se-NPs on human nutrition have been distinguished through studies on fertilization of crops [50–53], poultry [42–44,46–48,54], and human health [18,19,21,55–57].
Figure 1. An overview of selenium and its transformations in the soil environment. Different pathways for the fate and transformation of Se and its forms in the environment can be distinguished, including selenate, selenite, and elemental nano-Se.

There are many studies on Se and Se-NPs concerning their potential impact on human health, but the situation is different for higher plants, where much effort is still needed. Uptake from the soil and translocation as well as transformation of Se-NPs in higher plants needs more research. Will these nanoparticles be transformed into toxic forms? What will happen if Se nanoparticles are added or co-applied with another nanoparticle? What are the conditions that control Se-NPs transformations in the rhizosphere? What are the expected ecotoxicological effects of applied Se-NPs in the rhizosphere? At present, there are limited studies of the role of Se-NPs in plant nutrition [23,24,58–60], but the biogeochemistry of Se and Se-NPs in agroecosystems and their speciation in cultivated plants are important issues in terms of biofortification of crops for human health [13,61].

Major questions exist regarding Se and Se-NPs biofortification. Do biological Se-NPs have the ability to replace mineral Se-fertilizer in the framework of sustainable agriculture [62,63]? Will it be possible to find standard levels for deficiency and toxicity of Se-NPs as has been done for Se for humans, animals and higher plants? It is important to understand the different forms of Se, including inorganic (i.e., selenate, selenite, selenide, and elemental nano-Se) and organic (i.e., selenomethionine and selenocysteine), as these are important for Se behavior, especially in soil environments (Figure 1). These forms might control Se availability for plant uptake with contributions to the biofortification process [64–66].
Selenium as a contaminant for health in treated plants [60].

| Table 1. The biological features of selenium and nano-selenium and the possible roles in plant and human nutrition. |
|---------------------------------------------------------------|
| Comparison Item | Selenium (Se) | Selenium Nanoparticles (Se-NPs) |
| Plant Nutrition | | |
| Essentiality | NOT yet confirmed, but it is a beneficial nutrient at low concentrations [1] | NOT yet confirmed, but may have a positive impact on levels of bio-compounds beneficial for human health in treated plants [60] |
| Main uptake form | Selenate (SeO₄²⁻) through sulfate transporter (e.g., SULTR1;1 and SULTR1;2), selenite (SeO₃⁻) via phosphate transport (like OsPT2), and silicon transporter (OsNIF2;1) in roots [67] | Unclear (may be through a passive diffusion process), Se-NPs are soluble, highly stable, have low toxicity, and high bioavailability [23] |
| Converted form after uptake | Uptake is only by roots, both selenate and selenite will be converted into organic forms like SeCys, SeMet, and MeSeCys [68]. SeMet and MeSeCys are the most dominant species in Se-enriched plants | There is bioavailability of Se-NPs in plants, Se-NPs uptake could occur by roots, then transforms into organic Se compounds like SeCys, SeMet, and MeSeCys, with dominance of SeMet [68] |
| Translocation from roots to shoots | Chemical Se-NPs and selenite have similar translocation of Se from roots to shoots during the longer exposure period (72 h), whereas biological Se-NPs rarely translocate to shoots [68] | A few Se-NPs may transport from roots to shoots due to their rapid assimilation into selenite and organic forms [68] |
| Main functions in plant | Selenium may increase plant growth and biomass; protect plants from abiotic/biotic stresses; deter herbivores via volatile Se (dimethyl selenide) [69] | Se-NPs (especially 5–200 nm), increase activities of some enzymes like GSH-Px, TrxR, and GST could scavenge free radicals, have excellent bio-availability, low toxicity, and high biological activity in plants [23] |
| Toxicity level | For agricultural crops < 50 mg Se kg⁻¹ [23], for most angiosperm species > 10–100 mg Se kg⁻¹ DM [70] | About 100 mg kg⁻¹ is not toxic for most cultivated crops [71], 275 mg L⁻¹ is the toxic level for sorghum [34] |
| Deficiency level | Se content (µg kg⁻¹) < 20 for severely deficient areas and 30–50 for deficient areas [72] | NOT yet reported |
| Selenium as a contaminant for plants | At concentrations > 10 mg kg⁻¹ soil, Se may cause oxidative stress for plants [73] | Few publications addressed Se-NPs as a contaminant [74]. Se-NPs can remove Hg in soil [69] |
| Human Nutrition | | |
| Essentiality and absorption | Confirmed forms of soluble selenium are mainly absorbed in lower part of the small intestine [18] | May be essential. Se-NPs may absorb and be metabolized in the gastrointestinal tract [18] |
| Main dietary sources | Cereals or grains, poultry, breads, fish, eggs, meat, nuts, and broccoli [10,25] | Se-NPs could be used as dietary supplementation due to their therapeutic properties, such as being an anti-carcinogen [18] |
| Main applications or uses | Biomedical and drug delivery [20], biofortification of edible crops, and animals for human health [76] | Therapeutic or nanomedicine applications [21,56] |
| Main Se-forms for human intake | Se-methionine, Se-cysteine, and Se-methyl-selenocysteine [77] | Se-NPs in biological or chemical form could be used in nutritional supplements [18] or to combat cancer [57] |
| Main components in humans | Selenoproteins or the 21st proteinogenic amino acid selenocysteine, e.g., glutathione peroxidases [16] | NOT yet established |
| Main functions in humans | Regulates the immune system, mediates thyroid disorders and the health of the human reproductive system [1,8] | Se-NPs may have higher antioxidative capacity compared to other Se-forms (inorganic or organic) and be a more effective therapeutic agent against MeHg neurotoxicity than other forms of Se [78] |
| Toxicity level | The upper intake level may be more than 400 µg day⁻¹ [53], mortality results from 1 to 100 mg Se kg⁻¹ body weight [79] | NOT yet established |
| Toxicity symptoms | The symptoms of mild selenium (excessive dietary Se intakes) in humans include cracking of nails, hair loss, and dermatitis, while severe selenium may cause renal failure, acute respiratory distress, and myocardial infarction [70] | NOT yet established. Se-NPs have a lower toxicity compared to other forms of Se like selenite or selenomethionine [18] |
| Deficiency level | Less than 40 µg day⁻¹ or less than 11 µg day⁻¹ like in the Keshan region, China causes Keshan disease [53] | NOT yet established. Se-NPs are higher in bioavailability efficacy compared to other Se-forms [18] |
| Deficiency symptoms | Se deficiency may cause several diseases like cardiovascular disease, male infertility, weakened immune system, hypothyroidism, cognitive decline and increased incidence of various cancers [70,80] | NOT yet established |
| Recommended daily intake | About 55 µg day⁻¹ based on USDA [1] | NOT yet established |
| Dietary Reference Intake (DRI) | 100 µg Se day⁻¹ [77] | NOT yet established |

Abbreviations: selenocysteine: SeCys; Se-methyl-selenocysteine: MeSeCys; seleno-methionine: SeMet; glutathione peroxidase: GSH-Px; thioredoxin reductase: TrxR; glutathione S-transferase: GST; DM: dry matter.
The biofortification of cultivated crops using nano-Se may be an important strategy [30] that could be adapted to minimize environmental problems, in particular problems that resulted from the over-use of mineral fertilizers. This is particularly true because Se is rare in the Earth’s crust. Nano-Se and Se biofortified edible crops still need more research from different points of view, such as environmental, economic, human health, and animal health perspectives [81–83]. Nano-Se has the potential to protect animals against oxidative stress [84], ameliorate heavy metal stress [85], or function as an effective cancer therapy [86]. The use of nano-Se or Se to support cultivated plants under different stresses is an important strategy due to the ameliorative effects of Se and nano-Se in enhancing the productivity of cultivated crops under harsh conditions such as heat stress [34], nitrate stress [87], pathogen (like Alternaria solani) stress [59], NaCl stress [60], and soil salinity stress [24].

3. Biofortification of Selenium and Nano-Selenium for Human Health

Realization of the relationship between Se as a nutrient and human health started with the discovery of the essentiality of this micronutrient in 1817. Many studies have confirmed that Se is essential for human health due to its role in preventing many chronic diseases such as cancer, neurodegenerative diseases, and cardiovascular disease as an essential component of more than 25 enzymes in humans [53]. The level of Se or nano-Se can be increased in foods through the biofortification approach [29,36,52,88–92]. Products from farm animals can also be enriched with Se [41,45,93]. The biofortification of cereal crops including wheat, rice and maize as well as some main vegetable crops including tomato, potato and lettuce will be reviewed in this section.

3.1. Biofortification of Cereal Crops: Wheat, Rice and Maize

The biofortification process is a method in which selected nutrients (e.g., Ca, Cu, Fe, I, Se, and Zn) or nutritional materials are inserted into the food chain [94]. These materials might include folate [95–97], riboflavin [98,99], lysine [100–102], and pro-vitamin A [103]. This can be achieved using the agronomic approach, traditional breeding, and transgenic approaches to reduce nutrient deficiencies for humans [104,105]. The most important nutrients that have been investigated in several biofortification studies include calcium [106], iron [92,107], copper [108], zinc [109–111], iodine [29,92], potassium [112], and selenium [66,113]. The use of Se fertilizers is one of the most common methods for Se-biofortification of several crops [105], such as rice [113–115], maize [116,117], wheat [92,111,118], cowpea [119], potato [85,120], carrot [90,121], turnip [122,123], shallot [124], beans [125], lettuce [91,126], basil [127], strawberry [32,33], and apple [128,129]. Edible plants that have been biofortified with Se [105] or livestock fed selenium-enriched alfalfa [25,130] are used to support human health as reported by the Finnish experience in biofortification with Se through fertilizers. This Finnish experience started in 1984, when the Finnish authorities decided to improve the Se content of foods and feeds by applying synthetic fertilizers containing Na$_2$SeO$_4$. The applied doses of Se to soil reached 10 mg ha$^{-1}$ in 2012 with an optimal level of 70–80 µg in the daily Se intake of the Finnish people.

Malnutrition and micronutrient deficiencies have become a global issue and improving the nutrition of millions of people around the world may be achieved using staple crops and appropriate agronomic practices [105,131]. In the past biofortification mainly involved the main cereal crops (e.g., rice, maize, and wheat) and then moved to include pulse crops as well as some animal-based foods such as milk and cheese [132], meat [133], and eggs [134]. The Se-biofortification of cereal crops depends on Se forms, method of application, the efficacy of Se-fertilizers [118], the time of application, and plant growth stage [83,135]. It also depends on soil properties, in particular soil pH, salinity content, redox potential, organic matter content, and the soil microbial community [13,69,116,136–139]. The Se-biofortification of cereal crops including wheat, rice, and maize could be evaluated under different applied Se-forms and different growth conditions (Table 2). A review of the literature led to the following conclusions:

1. The main Se-forms applied to cereal crops for biofortification include selenate, selenite, selenomethionine (SeMet), methio-seleno-cysteine (MeSeCys), and nano-Se.
2. The recommended Se-dose for biofortification of cereal crops mainly depends on the plant species and its variety or cultivar, the application method (seed coating and priming, foliar, or soil application), the growth media (e.g., soil, hydroponics, artificial growth media), the growth conditions (open field, controlled greenhouse, or in vitro experiment), the Se-form (inorganic, organic, or nano form), nano-Se characterization (the method of preparing, the size and color of nanoparticles), the background Se content in the soil, and the agricultural management practices [69,85].

3. For wheat crops, the recommended Se-dose under field experiments was 21 g Se ha\(^{-1}\) as a foliar application [89], while an applied dose of up 120 g Se ha\(^{-1}\) did not cause any visible phytotoxicity symptoms [140]. Under pot experiments, an applied Se-dose of 2.5 mg Se kg\(^{-1}\) soil was a suitable dose for Se-fortification of grain wheat [136].

4. For rice crops, Se-foliar fertilization up to 100 g Se ha\(^{-1}\) as sodium selenite produces safe and high converting levels of Se into general rice proteins under field experiments when there was an initial low total soil Se content up to 0.1 mg Se kg\(^{-1}\) soil [141]. The best method to fortify the rice plants was to use 6 mg Se L\(^{-1}\) under NaCl stress as a combination of foliar spraying and seed priming [73]. The recommended applied Se-dose for the growth of rice clearly depends on the growth stage (the seedling, tillering, booting, full heading, and mature stage). Foliar application of sodium selenite (10 mg L\(^{-1}\)) at the booting and full heading stages enhanced the accumulation of SeMet, confirming that the previous Se rate is the ideal level for Se-biofortification of rice [115].

5. For maize crops, biofortification with Se could be achieved under field conditions through a fertigation system at an application rate of 100–200 g of Se ha\(^{-1}\) as sodium selenite. The applied Se might enhance the nutraceutical value and antioxidant content of maize grains without any leaching of Se into groundwater [142,143]. Ngigi et al. [125] reported that the Se biofortification level (0.3 mg kg\(^{-1}\)) could be achieved in three field locations in Kenya using a foliar Se-dose of 20 g ha\(^{-1}\) as sodium selenite, whereas Wang et al. [64] indicated that the Se-level may be up to 30 g Se ha\(^{-1}\) in China.

### Table 2.
Selenium biofortification results of some selected cereal crops (wheat, rice, and maize) under different growth conditions.

| Plant Cultivar | Selenium Forms and Added Rate | Experimental Conditions and Se-Biofortified Dose |
|---------------|-------------------------------|-----------------------------------------------|
| **I. Wheat plants (Triticum aestivum L.)** | | |
| Variety BRS 264 (Brazil, [89]) | Foliar application of sodium selenate doses: 12, 21, 38, 68 and 120 g ha\(^{-1}\) at vegetative growth and grain filling stage | Field experiment used soil (pH 5.1; clayey, total Se < 0.018 mg kg\(^{-1}\)), the dose 21 g of Se ha\(^{-1}\) showed the highest grain Se absorption efficiency and highest grain yield |
| **Cultivar: Gazul during the period from 2001–2011 (Spain, [77])** | Survey of the total mean Se in soil (159 µg Se kg\(^{-1}\)) and mean Se in harvested grain (41.3–18.4 µg Se kg\(^{-1}\)) | Field experiment used soil (pH 7.7, clay 70%), accumulation of Se in grain was directly related to N-accumulation in wheat |
| 12 Brazilian cultivars (Brazil, [83]) | Sodium selenate, i.e., Na\(_2\)SeO\(_4\) added at 13 µM L\(^{-1}\) Se | Pot experiment seeds were sown for 132 days, the dosage (13 µM L\(^{-1}\) Se) improved the nutritional value and sulfur content of different cultivars of wheat |
| Seeds of winter wheat: Xiaoyan No. 22 (China, [136]) | Separate treatments of sodium selenite and selenate: 0.5, 1, 2.5, 5, and 10 mg Se kg\(^{-1}\) | Pots filled with soil (SiO\(_2\) 57.8%; pH 7.75 and the total Se 0.078 mg kg\(^{-1}\)), a dose of 2.5 mg Se kg\(^{-1}\) soil was suitable for fortification |
| Four Italian durum wheat varieties (Italy, [140]) | Foliar-Se applied at rates of 1, 5, 10, 15, 20, 25, 30, 50, 100, and 120 g Se ha\(^{-1}\) as sodium selenate, Se applied at early stem elongation and at the booting stage | Field experiment, soil pH 7.8, the background total Se-content was 0.130 mg kg\(^{-1}\) soil, no visible phytotoxicity symptoms were observed even at 120 g Se ha\(^{-1}\), which may be the best for fortification of wheat |
| Variety: Seher 2006 (Pakistan, [144]) | Two doses at 300 µM sodium selenate (3 mg Se kg\(^{-1}\) of soil) was given to the plants, which were harvested after 18 weeks | Natural field soil in pots, two Se- doses were given to plants: one-week post-germination and at the reproductive phase, wheat could be fortified at lower Se levels like in this study |
Table 2. Cont.

| Plant Cultivar (Country, Reference) | Selenium Forms and Added Rate | Experimental Conditions and Se-Biofortified Dose |
|------------------------------------|-------------------------------|-----------------------------------------------|
| **II. Rice plants (Oryza sativa L.)** |                               |                                               |
| Cultivar: Xiushiai 134 (China, [83]) | In hydroponics, foliar and root dressing using selenite, selenate and MeSeCys, soil culture using foliar method (100 µM Se) | Plastic containers used in 2 different experiments, i.e., soil culture and hydroponics, root dressing of selenite caused highest accumulation of organic Se compounds, which are desirable for human health |
| Rice seeds of Xinongyou No. 1 (China, [78]) | Se was added at 50 µg L⁻¹ as Na₂SeO₃·5H₂O after 15 days, Se added to rice seedlings and harvested after 48 h | Pot experiment using a nutrient solution, low added phosphorus (1.5 mM L⁻¹) may promote Se content in rice grains |
| Se-free white rice lines (China, [115]) | Foliar sodium selenite at a rate of 10 mg L⁻¹ at booting and full heading stage of Se-free white rice | Pot experiment filled with soil (total Se: 0.35 mg kg⁻¹ DW), foliar sodium selenite fertilizer enhanced the accumulation of SeMet confirming that the utilized Se rate was effective for Se-biofortification |
| Cultivar: Nipponbare; GSOR-100 (Belgium, [73]) | Exogenous applied Na₂SeO₃ as foliar (2, 4, 6, 8, 10, and 12 mg l⁻¹), seed priming (6 mg l⁻¹) and combination of seed priming and foliar spraying | Seedlings sown in PVC tubes that contained 100 g sand and polymer mixture, combination of foliar spray and seed priming was the best method to fortify the rice plants (at 6 mg l⁻¹) under NaCl stress |
| Cultivar: Selenio (Milano, Italy, [114]) | Sodium selenite and selenate solutions at 15, 45, 135, and 405 mg Se L⁻¹ harvested 10 days after sowing | Grains sown in plastic trays and incubated in a growth chamber, sprouts fortified by 45 mg Se L⁻¹ contained high Se and phenolic acid yield |
| Two cultivars: | Soil mixture with selenite at 0.5, 1, and 5 mg Se kg⁻¹ soil, plants harvested and grains were collected for analysis | Pot experiment filled with soil, total plant Se was 0.45 mg kg⁻¹ DW, pH 5.40, the highest content of SeMet was recorded for 5 mg kg⁻¹ in rice grains |
| Cultivar: Nongda 108 (China, [147]) | A total of 0.5 mg kg⁻¹ DW soil selenite applied to the soil at different growth stages of rice (i.e., seedling, tillering, booting and mature stages) | Field experiment, total soil Se content was 0.1 mg kg⁻¹ of soil, Se-foliar fertilization up to 100 g Se ha⁻¹ produced a safe and high conversion of Se into general rice proteins |
| Brown rice, cultivar: Suxiangjing 1 (China, [33]) | A total of 0.5 mg kg⁻¹ DW soil selenite applied to the soil at different growth stages of rice (i.e., seedling, tillering, booting and mature stages) | Pot experiments contained two separate soils: neutral (0.30 mg Se kg⁻¹), pH 7.41 and acidic soil (0.37 mg Se kg⁻¹, pH 5.02), the highest concentration of Se in rice was found during the booting stage, SeMet was predominant (90% organics species) in rice |

III. Maize plants (Zea mays L.)

| Maize: | Applied-Se through fertigation at a rate of 200 g of Se ha⁻¹ as sodium selenite under high and low water regimes | Field experiment, soil total Se content was 0.25 mg kg⁻¹ soil, Se-fortified maize enhanced nutraceutical value and antioxidant content of grains |
| Maize: | Se was applied as Na₂SeO₃ through fertigation at a rate of 100 µg ha⁻¹ twice under low and high irrigation regimes | Field experiment, total soil Se content was 0.183 mg kg⁻¹ soil, soil Se did not leach into groundwater but was lost over time through volatilization process |
| Varieties: KH 600-15A, KH 500-33A and K132 (Kenya, [125]) | Soil and foliar Se-fertilizer applied at 5, 10, and 20 g Se ha⁻¹ as sodium selenate, the mean of total Se was 0.345 mg kg⁻¹ for all locations | Field experiments were carried out at three locations (Mbuyu, Mbeu and Kiaga), the Se level of biofortification (0.3 mg kg⁻¹) was achieved in Kiaga and Mbeu using a foliar Se-dose of 20 g ha⁻¹ |
| Cultivar: Agaiti-2002 (Pakistan, [146]) | Foliar sprayed with sodium selenate (20 and 40 mg L⁻¹) under NaCl salt stress (EC = 12 dS m⁻¹) at both reproductive and vegetative stages | Pot filled with washed river sand, plants harvested 10 days after foliar spraying, foliar Se level of 20 mg L⁻¹ was more effective at inducing salt tolerance in maize plants |
| Cultivar: Nongda 108 (China, [147]) | Added Se at 1, 5, and 25 µM Na₂SeO₃, 15 days after treatments, antioxidant capacity, and biomass determined | Pots filled with vermiculite, induced salinity stress (NaCl 100 mM), application of 5 µM Se may alleviate the adverse effects of salt stress |
| Variety: Luyuan 502 (China, [64]) | Foliar applied 30 g Se ha⁻¹ in multiple forms: sodium selenate, seleno-methionine, and chemical nano-Se | Field experiment, soil total Se 0.46 mg kg⁻¹, pH 7.82, residual effect of Se applied on wheat was studied on maize in the following year |

3.2. Biofortification of Vegetable Crops: Tomato, Potato and Lettuce

Vegetables are a major source of nutrients and phytochemicals that support human health and nutritional sustainability [148]. Vegetables routinely grown for human consumption include allium, cruciferous, legumes, yellow-orange-red, and leafy green vegetables [149]. These vegetables are important in biofortification programs due to their importance for human health and short growth period (Table 3). Several vegetable crops have already been used in biofortification programs, including
vegetables enriched in Se such as tomato [150,151], potato [85,94,120], lettuce [91,126,152], onion [153], garlic [154,155], cabbage [139], carrot, broccoli [156,157], asparagus [158], radish [66,159,160], and spinach [30,158].

Table 3. Some selected vegetable crops (tomato, potato, and lettuce) that have been investigated for selenium biofortification.

| Plant Cultivar (Country, Reference) | Selenium Forms and Added Rate | Experimental Conditions and Se-Biofortified Dose |
|-------------------------------------|------------------------------|-------------------------------------------------|
| **I. Tomato plants** (*Solanum lycopersicum L.*) | | |
| Tomato seeds from Yangling Longkind Hollandings Co., Ltd. (China, [169]) | 45 days after transplanting: Se added as Na₂SeO₃ and/or Na₂SeO₄ at 0.01, 0.05, 0.1, 0.5, and 1 mg Se L⁻¹ for 7 days exposure | Under hydroponic culture, Se concentration at 0.05 mg L⁻¹ with both selenite and selenate as Se sources was the optimum for tomato fruit Se content |
| Cultivar: Red Bunch (Italy, [151]) | Sodium selenate added into the nutrient solution at a rate of 1 and 1.5 mg Se L⁻¹, 14 days after transplanting | In greenhouse seedlings were transferred into rock wool blocks under drip irrigation, fruit quality and fruit shelf life performance during postharvest and storage were improved using 1.5 mg Se L⁻¹ |
| Seeds of cultivar Micro-Tom and genotype high pigment-1 (Brazil, [161]) | At 3-weeks old, 50 µM Na₂SeO₃ applied, the exposure of seedlings was for 74 days | Cultivated in boxes containing a mixture of pot mix and vermiculite (1:1 by volume); Se may restrict Cd uptake (0.5 mM CdCl₂) improving fruit quality |
| Cultivar: Provence (China [150,162,163]) | A foliar spray applied at 1 mg Se L⁻¹ as sodium selenate 4 weeks after transplanting | In a greenhouse, sandy soil (49% sand, soil pH 6.5), harvested at pink stage from Se treated, Se (1 mg Se L⁻¹) may delay ripening, improve fruit nutritional quality |
| **II. Potato plants** (*Solanum tuberosum L.*) | | |
| Cultivar: E-potato 10 (China, [85]) | Applied Se through foliar spraying at 100 g ha⁻¹ as sodium selenate and selenite, plants harvested after 92–95 days | Field experiment, two locations, total Se: 0.26 and 0.35 mg kg⁻¹ soil, applied at three growth stages, selenate applied at the tuber bulking stage of potato had the highest tuber Se-content |
| Cultivar: Sante (Pennsylvania, USA, [164]) | One week after planting, seedlings treated with 9 µM Se as sodium selenate and harvested after 55 days | Pots in growth chamber filled with fine acid-washed sand, pots treated by adding Cd (40 µM) and/or As (40 µM), Se may reduce Cd and As toxicity |
| Cultivar: Agata (Brazil, [94]) | Selenium was applied together with planting fertilization using 0.75, 1.5, 3, and 5 mg kg⁻¹ as sodium selenate and selenite | Pots filled with tropical soil (pH 4.8; clay 71%; total Se content 0.065 mg kg⁻¹), selenate at low dose (0.75 mg kg⁻¹) was the most efficient source for potato biofortification under tropical conditions |
| Cultivar: Vineta (Poland, [120]) | Applied Se as Na₂SeO₃ at 0.5 mg Se L⁻¹ (i.e., 6.3 µM Se), in the presence of 5 mg I L⁻¹, and 0.1, 1 and 10 mg L⁻¹ salicylic acid | NFT hydroponic system, applied iodine + Se (0.5 mg Se L⁻¹) and also salicylic acid may increase N and K in tubers but decrease Mn and Zn content in roots |
| **III. Lettuce plants** (*Lactuca sativa L.*) | | |
| Lettuce var. crispa cv Veneza Roxa (Brazil, [126]) | Added selenate- and selenite (25 and 40 µmol L⁻¹ Se), plants harvested after 28 days from cultivation | In hydroponic system, the Se-bioavailability was higher for selenite (40 µmol L⁻¹ Se) compared with selenate due to its fast bio-transformation into organic forms in plant cells |
| Six different varieties (Poland, [91]) | Seedlings fortified with Na₂SeO₃ at 0.5 mg Se L⁻¹, with and without 5 mg I L⁻¹. | In greenhouse, seeds sown into mineral wool plugs, seedlings placed into the NFT hydroponic method, salicylic acid improved bio-fortification efficiency using Se and I |
| Seeds of lettuce (Rijk Zwaan, the Netherlands, [165]) | Applied Se at 0.1, 0.5, 5, 10, and 50 µmol L⁻¹ as Na₂SeO₃ for 30 days | Hydroponic system, the 0.5 µmol L⁻¹ Se may be used to reduce nitrate content in leaves with increasing lettuce yield, inducing assimilation of NO₃⁻ |
| Cultivar: Veneza Roxa (Italy, [166]) | 10, 25, and 40 µmol Se L⁻¹ as sodium selenate or selenite added to solution, harvested after 28 days | Hydroponic system with pH adjusted between 5.5–6.5 daily, Se accumulation in lettuce leaves was highest in the case of selenate (bioaccessibility 70%), Selenate enriched lettuce was more favorable at lowest fortification level (10 µmol Se L⁻¹) |
| Hungarian cultivar: Susana (Egypt, [152]) | Soil and foliar applied Se at 50, 75, and 100 mg kg⁻¹ in the form HNaO₃Se | Field experiment, salt-affected soil (pH 8.65; EC: 4.49 dS m⁻¹; clay: 53.3%; total Se content: 0.050 mg kg⁻¹), foliar application of 100 mg kg⁻¹ is the best treatment under this salinity stress |
| Variety: capitata (Poland, [91]) | Selenium fortified seedlings at 0.5 mg Se L⁻¹ as Na₂SeO₃, with and without 5 mg I L⁻¹ | NFT or dry hydroponic method, salicylic acid applied at 0.1 mg L⁻¹ may increase the leaf content of selenomethionine under enrichment with I and Se |

Abbreviation: NFT (nutrient film technique).
For tomato crops, the Se-biofortification program may differ depending on the growth media. A Se concentration of 0.05 mg L\(^{-1}\) with selenite and selenite as dual Se sources may be optimum for tomato fruits grown under the hydroponic technique [69], but under drip irrigation this dose may be up 1.5 mg Se L\(^{-1}\) [151]. For potato crops, foliar applied Se at 100 g ha\(^{-1}\) at the tuber bulking stage led to the highest tuber Se-content [85], whereas a low Se dose (0.75 mg kg\(^{-1}\) as selenate) for pots filled with tropical soil (pH 4.8; clay 71%; total Se content 0.065 mg kg\(^{-1}\)) was the most efficient source for potato biofortification under tropical conditions [94]. The hydroponic system is a common technique for producing lettuce under greenhouse conditions and the Se-bioavailability in a hydroponic system was higher for selenite (40 \(\mu\)mol L\(^{-1}\) Se) compared with selenate due to its fast bio-transformation into organic forms in plant cells [126]. Under field conditions, a foliar rate of 100 mg kg\(^{-1}\) may be the proper Se dose for lettuce biofortification in salt-affected soils (pH: 8.65; EC: 4.49 dS m\(^{-1}\); [152]).

4. Interaction of Selenium and Nano-Selenium with Environmental Conditions

Plant growth and development are mainly controlled by environmental conditions (e.g., water, nutrients, air, light, etc.). These conditions include both normal and stressful environments (i.e., biotic and abiotic stresses). Plants have the ability to alleviate these stresses using exogenous and endogenous anti-stressors or tools (through their defense system) such as plant growth-promoting rhizobacteria [167], silicon [168–170], nanoparticles of selenium, or silicon [171] and selenium [2]. Several studies have confirmed the identified role of Se in promoting cultivated plant growth under a variety of stresses [24,83,86,172,173]. There is a growing body of literature that shows the potential of Se-nanoparticles to promote plant growth under different conditions (Table 4), but this still needs more investigation, particularly under stressful conditions. Comparing the potential of Se-NPs as revealed in human and animal studies with plant investigations, much more progress has been achieved in the human and animal fields.

It is well documented that biological nano-Se has desirable characteristics such as high biosafety and bioactivity properties, low toxicity, high solubility, and high mobility due to their large surface area to volume ratio compared with soluble inorganic Se salts, mainly selenite and selenite [24,34]. The uptake of Se-NPs by plants primarily depends on the synthesis method (bio-synthesis or chemo-synthesis) and the size of the nanoparticles [141].

Table 4. The role of selenium-nanoparticles (Se-NPs) in the growth of selected plants under different growth conditions.

| Plant Cultivar (Country, Reference) | Se-Nanoparticles and Added Rate | Experimental Conditions and Se-Biofortified Dose |
|-----------------------------------|--------------------------------|-----------------------------------------------|
| Groundnut: Arachis hypogaea L. three cultivars: NC, Gregory and Giza 6 (Egypt, [35]) | Foliar applied Se-NPs (10–30 nm) at 20 and 40 mg kg\(^{-1}\) during vegetative stage, plants harvested 45 days after planting | Pot experiment with sandy soil (pH 8.2), Se-NPs may act as stimulator and/or stressor, enhanced the antioxidant defense systems under sandy soil conditions at 20 mg kg\(^{-1}\). |
| Tomato (Solanum lycopersicum L.), type saladette El Cid F1 from Harris Moran, Davis, CA, USA (Mexico, [58]) | Foliar applied Se-NPs (2–20 nm) at 1, 10, and 20 mg L\(^{-1}\) in combination with Cu-NPs (40 nm) at 10, 50 and 250 mg L\(^{-1}\), harvested fruits at light red stage 102 days after transplanting | Under multi-tunnel greenhouse, bags filled with potting mix (1:1 (v/v) peat moss and perlite), Se-NPs (10 mg L\(^{-1}\)) alone recorded the highest yield (increase up to 21%). Combination with Cu-NPs (50 mg L\(^{-1}\)) improved antioxidant system and fruit quality (vitamin C, flavonoids, firmness and glutathione). |
| Tomato (Solanum lycopersicum L.), type saladette El Cid F1 from Harris Moran, Davis, CA, USA (Mexico, [58]) | Foliar applied Se-NPs (2–20 nm) at 10 and 50 mg L\(^{-1}\), harvested fruits at light red stage | In multi-tunnel greenhouse, bags filled with potting mix (1:1 (v/v) peat moss and perlite), Se-NPs (20 mg L\(^{-1}\)) may enhance non-enzymatic antioxidants under stress from the fungal pathogen (Alternaria solani), Cu-NPs may also enhance this effect. |
| Tomato (Solanum lycopersicum L.), type saladette El Cid F1 (Mexico, [60]) | Se-NPs (2–20 nm) added at 1, 5, 10, and 20 mg L\(^{-1}\) every two weeks, harvested fruits at light red stage | In multi-tunnel greenhouse, polyethylene bags filled with potting mix (1:1 (v/v) peat moss and perlite), Se-NPs (20 mg L\(^{-1}\)) increased antioxidant compounds (lycopene, flavonoids, β-carotene and phenols) in fruits and fruit quality under salt stress (50 mM NaCl). |
| Pomegranate: Punica granatum, cv. Malase Saeveh, trees 10 years old (Iran, [23]) | Foliar applied sodium selenite and Se-NPs (10–45 nm) on the upper surface of leaves at 1 or 2 \(\mu\)M for both Se forms | In field experiment, soil (sand 58%, pH 7.8), trees were sprayed twice one week before the first full bloom, Se (1 \(\mu\)M) and Se-NPs (2 \(\mu\)M) promoted maturity index and quality of fruits. |
5. Selenium and Nano-Selenium Reduce the Toxicity of As, Cd, and Hg

Selenium has long been of great interest in a wide range of fields including the medical, pharmaceutical, agricultural, and industrial sectors. Recently, a considerable literature has developed around the potential of Se and Se-NPs to help humans and animals deal with environmental stresses, but much less research has been done regarding Se, Se-NPs, and environmental stress in plants [175]. Plant related soil and environmental stresses include salinity, drought, waterlogging, heat, and heavy metal stress, which represent serious constraints for global crop productivity [109]. Heavy metals and potential toxic trace metals that may exist in soil include arsenic (As), cadmium (Cd), chromium (Cr), mercury (Hg), lead (Pb), and selenium, which can be introduced into the soil through human activities such as mining [176], industrialization [177], urbanization [33], and agricultural practices [178,179]. These metals can also naturally occur in soils at levels that may cause problems [28,105].

Several investigations suggest that Se can play an important role for plants growing under stressful conditions, although further work on Se is required to confirm its essentiality for higher plants. Many studies conducted on Se and its potential in higher plants have investigated its uptake, translocation, metabolism, and toxicity [17,160,180,181]. Biofortification studies with Se and Se-NPs are considered promising because Se is essential for human and animal health [53]. Selenium biofortification and phytoremediation are at the same level of importance from the environmental protection point of view [81]. Based on the work done to date, some general comments can be made concerning the role of Se and nano-Se in higher plants under different stresses:

1. The ameliorative role of Se when plants are stressed by soil heavy metal content has been investigated in several studies, including how Se protects plants against heavy metal stress, whereas there is little work investigating the use of Se-NPs in this context [34,78].

2. Selenium has already been investigated by many researchers as a way to ameliorate As stress on rice plants [2,92,182–191]. These studies primed rice seed with Se during germination under As-stress. The ameliorative role of Se under As-oxidative stress occurred through the modulation of thiol (R-SH) and antioxidant enzymes in rice or Se-modulating the level of phenolics and nutrients alleviating the toxicity of arsenic in the rice plants.

3. The most important studies investigating Se and its role under Cd stress on rice plants include the application of Se to mitigate Cd accumulation in high-Cd-contaminated soils [192], the behavior of Se at different planting times [115], the effects of Se-forms and application methods on modulation...
of rice growth [83], how Se reduces the uptake and translocation of Cd from contaminated soils [193], and reducing oxidative stress induced by Cd [33,194–198].

4. Selenium has been shown to moderate the impacts of mercury (Hg) stress on cultivated rice [78,138,199–201]. Chapman et al. [202] studied how native plants in a mined field were able to grow under Hg and As soil pollution as well as how selenium promoted the growth of the plant seedlings by decreasing Hg and As bioaccumulation in these plants. Selenium also has the ability to decrease rice plant uptake of methylmercury in Hg-contaminated soils while increasing the uptake of other nutrient elements [78].

5. Selenium can alleviate chromium (Cr) stress in many crops by regulating the Cr uptake. Research into this relationship has included Chinese cabbage [203], pak choi (Brassica campestris L. ssp. Chinensis Makino) [204], and mitigating Cr-toxicity in Brassica napus L. [205], Brassica juncea seedlings [206], and cabbage (Brassica campestris L. ssp. Pekinensis) [207].

6. Studies have demonstrated the mitigation of lead (Pb) toxicity by Se-application in ginger (Zingiber officinale Roscoe.) [208] and oilseed rape (Brassica napus L.) plants [209].

7. Selenium nanoparticles are also thought to behave like Se in protecting cultivated plants under heavy metals stress but only a few studies have been published. Investigations that have been conducted regarding Se-NPs and stressful environments include the role of Se-NPs in enhancing the growth of some cultivated plants under stress such as sorghum under high temperature stress [34], strawberry under salinity stress [24] and rice under Cd and Pb toxicity [171].

6. Are Selenium and Nano-Selenium Emerging Pollutants?

With widespread interest in Se biofortification, it is possible that the environment (i.e., soil, water, air, and plants) might become contaminated with Se due to extensive Se applications, which in turn could create a risk for human health [28,210] (Figure 2). The main anthropogenic sources of Se-pollution include agricultural and industrial activities [211–213]. The most serious problem resulting from Se-pollution is contamination of drinking water sources; hence, remediation requires effective techniques to remove Se from natural waters [214,215]. Environmental Se-contamination may be bio-remediated using proper microbial adaptations like alkylation [216] or Se-transformation, bioavailability, mobility and volatilization into the atmosphere [15].

In addition to anthropogenic Se contamination problems, soils that are naturally high in Se content (seleniferous soils) are found in several places worldwide such as Punjab, India [217–219], Pine Ridge, Fort Collins, Colorado, USA [220], Western Colorado, USA [221], Enshi in China [222,223], Saskatchewan in Canada, Queensland in Australia, Irapuato in Mexico, the State of Boyaca in Colombia, and the Deog-Pyoung area in Korea [224]. Therefore, to address both anthropogenic and natural Se problems in soil, there is an urgent need to study Se-biofortification and phytoremediation through hyper-accumulating plants, which have the ability to uptake huge amounts of Se from soils and transfer it into the atmosphere by volatilization [67]. The agronomic Se biofortification of edible plants, pasture and forage crops should be improved through judicious biofortification programs without excessive applications or applications of Se in places that do not experience Se deficiency in the soil. Over-biofortification of products with selenium should be avoided, even in areas with Se-deficiencies, to prevent the build-up of Se to toxic levels in food and related products.

Further investigations are needed to monitor the behavior of Se-NPs in different environments including agricultural soils, waters, and farm animals. Se-NPs have already been used in the remediation of soils and waters that were contaminated with heavy metals like mercury [225–227]. This work confirmed that soils and groundwater contaminated with elemental mercury could be remediated via biogenic Se-NPs based on mechanisms like the immobilization of elemental mercury [226,227], applied hetero-aggregation of soil particulate organic matter [225], applied biofilm-coated quartz sand [228], and applied goethite colloids [138] in the presence of Se-NPs [64].
Selenium is an essential micronutrient for the nutrition of humans, animals, and lower plants, but whether or not it is essential for higher plants has yet to be confirmed. Nano-selenium is one of the most potentially useful Se-forms and has fascinating properties that lead to its use in nanomedicine applications, drug delivery, therapeutic applications, biomedical applications, and cancer prevention. Several places worldwide have a Se-deficiency problem due to low Se soils and should implement programs that guarantee safe and proper Se-supplementation levels for human health. The biofortification approach has shown particular promise for dietary supplementation of Se so that humans and/or animals have Se present in the right form, place, dose, and time. Due to the changing world and environmental stressors, there is an urgent need to document how and when Se helps plants and animals overcome stresses, including the identification of suitable Se and Se-NP fertilizers, application timing, and application rates. Several studies have demonstrated the ameliorative effects of Se and nano-Se on plants and farm animals under stress, but the use of Se-NPs in biofortification programs still needs more research. Despite all the documented benefits of Se, the difference between Se deficiency and Se toxicity is very small. We also need to understand the possible adverse effects and cytotoxicity of these Se-NPs on humans and effects on crops. It is also important to understand Se and Se-NP accumulation, transformation, and transport through soil. Due to the intensive use of Se and its forms in many fields, Se and nano-Se have become potential emerging pollutants in agroecosystems. This issue has increasingly been recognized as a potentially serious, worldwide public health concern.

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References

1. Pilon-Smits, E.A.H. On the Ecology of Selenium Accumulation in Plants. *Plants* 2019, 8, 197. [CrossRef] [PubMed]
2. Pokhrel, G.R.; Wang, K.T.; Zhuang, H.; Wu, Y.; Chen, W.; Lan, Y.; Zhu, X.; Li, Z.; Fu, F.F.; Yang, G. Effect of selenium in soil on the toxicity and uptake of arsenic in rice plant. *Chemosphere* 2020, 239, 124712. [CrossRef]
3. Roman, M.; Jitaru, P.; Barbante, C. Selenium biochemistry and its role for human health. *Metallomics* 2014, 6, 25–54. [CrossRef] [PubMed]
4. Baclaocos, J.; Santesmasses, D.; Mariotti, M.; Bierla, K.; Vetick, M.B.; Lynch, S.; McAllen, R.; Mackrill, J.J.; Loughran, G.; Guigó, R.; et al. Processive recoding and metazoan evolution of selenoprotein P: Up to 132 UGAs in Molluscs. *J. Mol. Biol.* 2019, 431, 4381–4407. [CrossRef] [PubMed]
5. Shu, N.; Cheng, Q.; Arnér, E.S.J.; Davies, M.J. Inhibition and crosslinking of the selenoprotein thioredoxin reductase-1 by p-benzoquinone. *Redox Biol.* 2020, 28, 101335. [CrossRef] [PubMed]
6. Avery, J.C.; Hoffmann, P.R. Selenium, Selenoproteins, and Immunity. *Nutrients* 2018, 10, 1203. [CrossRef]
7. Santos, L.R.; Neves, C.; Melo, M.; Soares, P. Selenium and selenoproteins in immune mediated thyroid disorders. *Diagnostics* 2018, 8, 70. [CrossRef]
8. Rayman, M.P. Selenium and human health. *Lancet* 2012, 379, 1256–1268. [CrossRef]
9. Qazi, I.H.; Angel, C.; Yang, H.; Zoidis, E.; Pan, B.; Wu, Z.; Ming, Z.; Zeng, C.J.; Meng, Q.; Han, H.; et al. Role of selenium and selenoproteins in male reproductive function: A review of past and present evidences. *Antioxidants* 2019, 8, 268. [CrossRef]
10. Schomburg, L. Dietary selenium and human health. *Nutrients* 2016, 9, 22. [CrossRef]
11. Vinceti, M.; Filippini, T.; Cilloni, S.; Bargellini, A.; Vergoni, A.V.; Tsatsakis, A.; Ferrante, M. Health risk assessment of environmental selenium: Emerging evidence and challenges: Review. *Mol. Med. Rep.* 2017, 15, 3323–3335. [CrossRef] [PubMed]
12. Brigelius-Flohé, R. Selenium in human health and disease: An overview. In *Selenium: Its Molecular and Integrative Toxicology*; Michalke, B., Ed.; Springer International Publishing AG: Cham, Switzerland, 2018; pp. 3–26. [CrossRef]
13. Shahid, M.; Niazi, N.K.; Khalid, S.; Murtaza, B.; Bibi, I.; Rashid, M.I. A critical review of selenium biogeochemical behavior in soil-plant system with an inference to human health. *Environ. Pollut.* 2018, 234, 915–934. [CrossRef] [PubMed]
14. Ibrahim, S.A.Z.; Kerkadi, A.; Agouni, A. Selenium and health: An update on the situation in the Middle East and North Africa. *Nutrients* 2019, 11, 1457. [CrossRef] [PubMed]
15. Ullah, H.; Liu, G.; Yousaf, B.; Ali, M.U.; Irshad, S.; Abbas, Q.; Ahmad, R. A comprehensive review on environmental transformation of selenium: Recent advances and research perspectives. *Environ. Geochem. Health* 2019, 41, 1003–1035. [CrossRef]
16. Schomburg, L.; Ortho-Melander, M.; Struck, J.; Bergmann, A.; Melander, O. Selenoprotein-P deficiency predicts cardiovascular disease and death. *Nutrients* 2019, 11, 1852. [CrossRef]
17. Gupta, M.; Gupta, S. An Overview of Selenium Uptake, Metabolism, and Toxicity in Plants. *Front. Plant Sci.* 2017, 7, 2074. [CrossRef]
18. Skalickova, S.; Milosavljevic, V.; Cihalova, K.; Horky, P.; Richtera, L.; Adam, V. Selenium nanoparticles as a nutritional supplement. *Nutrition* 2017, 33, 83–90. [CrossRef]
19. Tan, H.W.; Mo, H.Y.; Lau, A.T.Y.; Xu, Y.M. Selenium species: Current status and potentials in cancer prevention and therapy. *Int. J. Mol. Sci.* 2019, 20, 75. [CrossRef]
20. Guan, B.; Yan, R.; Li, R.; Zhang, X. Selenium as a pleiotropic agent for medical discovery and drug delivery. *Int. J. Nanomed.* 2018, 13, 7473–7490. [CrossRef]
21. Lopes, G.; Hosnedlova, B.; Kepinska, M.; Skalickova, S.; Fernandez, C.; Ruttkay-Nedecky, B.; Peng, Q.; Baron, M.; Melcova, M.; Opatrilova, R.; Zidkova, J.; et al. Nano-selenium and its nanomedicine applications: A critical review. *Int. J. Nanomed.* **2018**, *13*, 2107–2128. [CrossRef]

22. Kamal, A.; Nazari, V.M.; Yaseen, M.; Iqbal, M.A.; Ahamed, M.B.K.; Majid, A.S.A.; Bhatti, H.N. Green synthesis of selenium-N-heterocyclic carbene compounds. Evaluation of antimicrobial and anticancer potential. *Bioorg. Chem.* **2019**, *90*, 103042. [CrossRef] [PubMed]

23. Zahedi, S.M.; Hosseini, M.S.; Meybodi, N.; da Silva, J.A.T. Foliar application of selenium and nano-selenium affects pomegranate (*Punica granatum* cv. Malase Saveh) fruit yield and quality. *S. Afr. J. Bot.* **2019**, *124*, 350–358. [CrossRef]

24. Zahedi, S.M.; Abdelrahman, M.; Hosseini, M.S.; Hoveizeh, N.F.; Tran, L.P. Alleviation of the effect of salinity on growth and yield of strawberry by foliar spray of selenium-nanoparticles. *Environ. Pollut.* **2019**, *253*, 246–258. [CrossRef] [PubMed]

25. Hall, J.A.; Isaiah, A.; Estill, C.T.; Pirelli, G.J.; Suchodolski, J.S. Weaned beef calves fed selenium-biofortified diet gained more weight than those fed selenium supplement. *Biotechnol. Rep.* **2019**, *9*, 149–160. [CrossRef]

26. Saleh, A.A.; Ebeid, T.A. Feeding sodium selenite and nano-selenium stimulates growth and oxidation resistance in broilers. *S. Afr. J. Anim. Sci.* **2019**, *49*. [CrossRef]

27. Lopes, G.; Ávila, F.W.; Guilerme, L.R.G. Selenium behavior in the soil environment and its implication for human health. *Ciência Agrotecnologia* **2017**, *41*, 605–615. [CrossRef]

28. Steffan, J.J.; Brevik, E.C.; Burgess, L.C.; Cerdà, A. The effect of soil on human health: An overview. *Eur. J. Soil Sci.* **2018**, *69*, 159–171. [CrossRef]

29. Lyons, G. Biofortification of cereals with foliar selenium and iodine could reduce hypothyroidism. *Front. Plant Sci.* **2018**, *9*, 730. [CrossRef]

30. Golubkina, N.A.; Koshelev, O.V.; Krivenkova, L.V.; Dobrutskaya, H.G.; Nadezhkin, S.; Caruso, G. Intersexual differences in plant growth, yield, mineral composition and antioxidants of spinach (*Spinacia oleracea* L.) as affected by selenium form. *Sci. Hortic.* **2017**, *225*, 350–358. [CrossRef]

31. Leija-Martínez, P.; Benavides-Mendoza, A.; La Fuente, M.C.; Robledo-Olivo, A.; Ortega-Ortiz, H.; Sandoval-Rangel, A.; González-Morales, S. Lettuce biofortification with selenium in chitosan-polyacrylic acid complexes. *Agronomy* **2018**, *8*, 275. [CrossRef]

32. Mimmo, T.; Tiziani, R.; Valentiniuzzi, F.; Lucini, L.; Nicoletto, C.; Sambo, P.; Scampicchio, M.; Pii, Y.; Cesco, S. Selenium biofortification in *Fragaria* × *ananassa*: Implications on strawberry fruits quality, content of bioactive health beneficial compounds and metabolomic profile. *Front. Plant Sci.* **2017**, *8*, 1887. [CrossRef] [PubMed]

33. Huang, C.; Qin, N.; Sun, L.; Yu, M.; Hu, W.; Qi, Z. Selenium Improves Physiological Parameters and Alleviates Oxidative Stress in Strawberry Seedlings under Low-Temperature Stress. *Int. J. Mol. Sci.* **2018**, *19*, 1913. [CrossRef] [PubMed]

34. Djanaguiraman, M.; Belliraj, N.; Bossmann, S.H.; Vara Prasad, P.V. High-Temperature stress alleviation by selenium nanoparticle treatment in grain sorghum. *ACS Omega* **2018**, *3*, 2479–2491. [CrossRef] [PubMed]

35. Hussein, H.A.; Darwesh, O.M.; Mekki, B.B. Environmentally friendly nano-selenium to improve antioxidant system and growth of groundnut cultivars under sandy soil conditions. *Biocatal. Agric. Biotechnol.* **2019**, *18*, 101080. [CrossRef]

36. Hussein, H.A.; Darwesh, O.M.; Mekki, B.B.; El-Hallouty, S.M. Evaluation of cytotoxicity, biochemical profile and yield components of groundnut plants treated with nano-selenium. *Biotechnol. Rep.* **2019**, *24*, e00377. [CrossRef]

37. Kumar, N.; Krishnani, K.K.; Gupta, S.K.; Singh, N.P. Selenium nanoparticles enhanced thermal tolerance and maintain cellular stress protection of *Pangasius hypophthalmus* reared under lead and high temperature. *Respir. Physiol. Neurobiol.* **2017**, *246*, 107–116. [CrossRef]

38. Kumar, N.; Krishnani, K.K.; Singh, N.P. Comparative study of selenium and selenium nanoparticles with reference to acute toxicity, biochemical attributes, and histopathological response in fish. *Environ. Sci. Pollut. Res. Int.* **2018**, *25*, 8914–8927. [CrossRef]

39. Kumar, N.; Krishnani, K.K.; Gupta, S.K.; Sharma, R.; Baitha, R.; Singh, D.K.; Singh, N.P. Immuno-protective role of biologically synthesized dietary selenium nanoparticles against multiple stressors in *Pangasinoson hypophthalmus*. *Fish Shellfish Immunol.* **2018**, *78*, 289–298. [CrossRef]
40. Kumar, N.; Brahmacari, R.K.; Bhushan, S.; Thorat, S.T.; Kumar, P.; Chandan, N.K.; Kumar, M.; Singh, N.P. Synergistic effect of dietary selenium nanoparticles and riboflavin on the enhanced thermal efficiency of fish against multiple stress factors. *J. Therm. Biol.* 2019, 85, 102417. [CrossRef]

41. Sarkar, B.; Bhattacharjee, S.; Daware, A.; Tribedi, P.; Krishnani, K.K.; Minhas, P.S. Selenium nanoparticles for stress-resilient fish and livestock. *Nanoscale Res. Lett.* 2015, 10, 371. [CrossRef]

42. Gulyas, G.; Csosz, E.; Prokisch, J.; Javor, A.; Mezes, M.; Erdelyi, M.; Balogh, K.; Janaky, T.; Szabo, Z.; Simon, A.; et al. Effect of nano-sized, elemental selenium supplement on the proteome of chicken liver. *J. Anim. Physiol. Anim. Nutr.* 2017, 101, 502–510. [CrossRef] [PubMed]

43. Xueting, L.; Rehman, M.U.; Zhang, H.; Tian, X.; Wu, X.; Shixue, M.K.; Zhou, D. Protective effects of nano-elemental selenium against hexavalent chromium-induced apoptosis in broiler liver. *Environ. Sci. Pollut. Res. Int.* 2018, 25, 15609–15615. [CrossRef] [PubMed]

44. Xueting, L.; Rehman, M.U.; Zhang, H.; Tian, X.; Wu, X.; Shixue, M.K.; Zhou, D. Protective effects of Nano-elemental selenium against chromium-vi-induced oxidative stress in broiler liver. *J. Biol. Regul. Homeost. Agents.* 2018, 32, 47–54. [PubMed]

45. Bakhshalinejad, R.; Hassanabadi, A.; Swick, R.A. Dietary sources and levels of selenium supplements affect growth performance, carcass yield, meat quality and tissue selenium deposition in broilers. *Anim. Nutr.* 2019, 5, 256–263. [PubMed]

46. Jalali, S.S.; Talebi, J.; Allymehr, M.; Soleimanzadeh, A.; Razi, M. Effects of nano-selenium on mRNA expression of markers for spermatogonial stem cells in the testis of broiler breeder males. *Vet. Res. Forum.* 2019, 10, 139–144. [CrossRef]

47. Lee, J.; Hosseindoust, A.; Kim, M.; Kim, K.; Choi, Y.; Lee, S.; Cho, H.; Kang, W.S.; Chae, B. Biological evaluation of hot-melt extruded nano-selenium and the role of selenium on the expression profiles of selenium-dependent antioxidant enzymes in chickens. *Biol. Trace Elem. Res.* 2019, 194, 536–544. [CrossRef]

48. Meng, T.; Liu, Y.L.; Xie, C.Y.; Zhang, B.; Huang, Q.Y.; Zhang, Y.W.; Yao, Y.; Huang, R.; Wu, X. Effects of different selenium sources on laying performance, egg selenium concentration, and antioxidant capacity in laying hens. *Biol. Trace Elem. Res.* 2019, 189, 548–555. [CrossRef] [PubMed]

49. Dinh, Q.T.; Cui, Z.; Huang, J.; Tran, T.A.T.; Wang, D.; Yang, W.; Zhou, F.; Wang, M.; Yu, D.; Liang, D. Selenium distribution in the Chinese environment and its relationship with human health: A review. *Environ. Int.* 2018, 112, 294–309. [CrossRef]

50. Alfthan, G.; Eurola, M.; Ekholm, P.; Venäläinen, E.R.; Root, T.; Korkalainen, K.; Hartikainen, H.; Salminen, P.; Hietaniemi, V.; Aspila, P.; et al. Effects of nationwide addition of selenium to fertilizers on foods, and animal and human health in Finland: From deficiency to optimal selenium status of the population. *J. Trace Elem. Med. Biol.* 2015, 31, 142–147. [CrossRef]

51. Malagoli, M.; Schiavon, M.; dall’Acqua, S.; Pilon-Smits, E.A.H. Effects of selenium biofortification on crop nutritional quality. *Front. Plant Sci.* 2015, 6, 280. [CrossRef] [PubMed]

52. Puccinelli, M.; Malorgio, F.; Pezzarossa, B. Selenium enrichment of horticultural crops. *Molecules* 2017, 22, 933. [CrossRef] [PubMed]

53. Newman, R.; Waterland, N.; Moon, Y.; Tou, J.C. Selenium biofortification of agricultural crops and effects on plant nutrients and bioactive compounds important for human health and disease prevention—A review. *Plant Foods Hum. Nutr.* 2019, 74, 449–460. [CrossRef] [PubMed]

54. Bakhshalinejad, R.; Kakhki, R.A.M.; Zoidis, E.E. Effects of different selenium sources on laying performance, egg selenium concentration, and antioxidant capacity in laying hens. *Biol. Trace Elem. Res.* 2019, 194, 536–544. [CrossRef]

55. Maiyo, F.; Singh, M. Selenium nanoparticles: Potential in cancer gene and drug delivery. *Nanomedicine* 2017, 12, 1075–1089. [CrossRef] [PubMed]

56. Khurana, A.; Tekula, S.; Saifi, M.A.; Venkatesh, P.; Godugu, C. Therapeutic applications of selenium nanoparticles. *Biomol. Pharmacother.* 2019, 111, 802–812. [CrossRef]

57. Vahidi, H.; Barabadi, H.; Saravanan, M. Emerging selenium nanoparticles to combat cancer: A systematic review. *J. Clust. Sci.* 2020, 31, 301–309. [CrossRef]

58. Hernández-Hernández, H.; Quiterio-Gutiérrez, T.; Cadenas-Pliego, G.; Ortega-Ortiz, H.; Hernández-Fuentes, A.D.; de la Fuente, M.C.; Valdés-Reyna, J.; Juárez-Maldonado, A. Impact of selenium and copper nanoparticles on yield, antioxidant system, and fruit quality of tomato plants. *Plants* 2019, 8, 355. [CrossRef]
59. Quiterio-Gutiérrez, T.; Ortega-Ortiz, H.; Cadenas-Pliego, G.; Hernández-Fuentes, A.D.; Sandoval-Rangel, A.; Benavides-Mendoza, A.; la Fuente, M.; Juárez-Maldonado, A. The application of selenium and copper nanoparticles modifies the biochemical responses of tomato plants under stress by Alternaria solani. Int. J. Mol. Sci. 2019, 20, 1950. [CrossRef]

60. Morales-Espinoza, M.C.; Cadenas-Pliego, G.; Pérez-Alvarez, M.; Hernández-Fuentes, A.D.; de la Fuente, M.C.; Benavides-Mendoza, A.; Valdés-Reyna, J.; Juárez-Maldonado, A. Se nanoparticles induce changes in the growth, antioxidant responses, and fruit quality of tomato developed under NaCl stress. Molecules 2019, 24, 3030. [CrossRef]

61. El-Ramady, H.R.; Domokos-Szabolcsy, É.; Abdalla, N.A.; Alshaal, T.A.; Shalaby, T.A.; Sztrik, A.; Prokisch, J.; Fári, M. Selenium and nano-selenium in agroecosystems. Environ. Chem. Lett. 2014, 12, 495–510. [CrossRef]

62. El-Ramady, H.; Abdalla, N.; Alshaal, T.; El-Henawy, A.; Elmahrouk, M.; Bayoumi, Y.; Shalaby, T.; Amer, M.; Shalaby, T.A.; Sztrik, A.; Prokisch, J.; Fári, M.; et al. Plant nano-nutrition: Perspectives and challenges. In Nanotechnology, Food Security and Water Treatment; Gothandam, K.M., Ranjan, S., Dasgupta, N., Ramalingam, C., Lichtfouse, E., Eds.; Springer International Publishing AG: Cham, Switzerland, 2018; pp. 129–161. [CrossRef]

63. Sharma, D.; Dhuriya, Y.K.; Dhuriya, Y.K.; Sharma, J.; Gupta, M. Nanoelements: An agricultural paradigm for targeted plant nutrition therapeutic approach. In Nanotechnology for Agriculture: Crop Production & Protection; Panpatte, D.G., Jhala, Y.K., Eds.; Springer International Publishing AG: Cham, Switzerland, 2019; pp. 73–83. [CrossRef]

64. Hu, T.; Liang, Y.; Zhao, G.; Wu, W.; Li, H.; Guo, Y. Selenium Biofortification and Antioxidant Activity in Cordyceps militaris Supplied with Selenate, Selenite, or Selenomethionine. Biol. Trace Elem. Res. 2019, 187, 553–561. [CrossRef] [PubMed]

65. Reynolds, R.J.B.; Pilon-Smits, E.A. Plant selenium hyperaccumulation- Ecological effects and potential implications for selenium cycling and community structure. Biochim. Biophys. Acta Gen. Subj. 2018, 1862, 2372–2382. [CrossRef] [PubMed]

66. Hu, T.; Liang, Y.; Zhao, G.; Wu, W.; Li, H.; Guo, Y. Selenium Biofortification and Antioxidant Activity in Cordyceps militaris Supplied with Selenate, Selenite, or Selenomethionine. Biol. Trace Elem. Res. 2019, 187, 553–561. [CrossRef] [PubMed]

67. Schiavon, M.; Pilon-Smits, E.A. The fascinating facets of plant selenium accumulation—Biochemistry, physiology, evolution and ecology. New Phytol. 2017, 213, 1582–1596. [CrossRef] [PubMed]

68. Hu, L.; Fan, H.; Wu, D.; Wan, J.; Wang, X.; Huang, R.; Liu, W.; Shen, F. Assessing bioaccessibility of Se and I in dual biofortified radish seedlings used simulated in vitro digestion. Food Res. Int. 2019, 119, 701–708. [CrossRef]

69. Wang, Q.; Yu, Y.; Li, J.; Wan, Y.; Huang, Q.; Guo, Y.; Li, H. Effects of different forms of selenium fertilizers on Se accumulation, distribution, and residual effect in winter wheat-summer maize rotation system. J. Agric. Food Chem. 2017, 65, 1116–1123. [CrossRef] [PubMed]

70. White, P.J. Selenium accumulation by plants. Ann. Bot. 2016, 117, 217–235. [CrossRef]

71. Zsiráros, O.; Nagy, V.; Párducz, A.; Nagy, G.; Ünnap, R.; El-Ramady, H.; Prokisch, J.; Lisztes-Szabó, Z.; Fári, M.; Csajbók, J.; et al. Effects of selenate and red Se-nanoparticles on the photosynthetic apparatus of Nicotiana tabacum. Photosynth. Res. 2019, 139, 449–460. [CrossRef]

72. Kabata-Pendias, A. Trace Elements in Soils and Plants, 4th ed.; CRC Press: Boca Raton, FL, USA, 2011.

73. Subramanyam, K.; Du Laing, G.; Van Damme, E.J.M. Sodium selenate treatment using a combination of seed priming and foliar spray alleviates salinity stress in rice. Front. Plant Sci. 2019, 10, 116. [CrossRef]

74. Kim, Y.; Oh, J.-M.; Roh, Y. Microbial precipitation of Cr(III)-hydroxide and Se(0) nanoparticles during anoxic bioreduction of Cr(VI)- and Se(VI)-contaminated water. J. Nanosci. Nanotechnol. 2017, 17, 2302–2304. [CrossRef]

75. White, P.J. Selenium accumulation by plants. Ann. Bot. 2016, 117, 217–235. [CrossRef]

76. Wiesner-Reinhold, M.; Schreiner, M.; Baldermann, S.; Schwarz, D.; Hanschen, F.S.; Kipp, A.P.; Rowan, D.D.; Bentley-Hewitt, K.L.; McKenzie, M.J. Mechanisms of selenium enrichment and measurement in brassicaceous vegetables, and their application to human health. Front. Plant Sci. 2017, 8, 1365. [CrossRef] [PubMed]

77. López-Bellido, F.J.; Sanchez, V.; Rivas, I.; López-Bellido, R.J.; López-Bellido, L. Wheat grain selenium content as affected by year and tillage system in a rainfed Mediterranean Vertisol. Field Crop. Res. 2019, 233, 41–48. [CrossRef]
78. Li, Y.; Ge, Y.; Wang, R.; Zhao, J.; Jing, H.; Lin, X.; Ma, S.; Gao, Y.; Li, B.; Chen, C.; et al. Nanoelemental selenium alleviated the mercury load and promoted the formation of high-molecular-weight mercury- and selenium-containing proteins in serum samples from methylmercury-poisoned rats. Ecotoxicol. Environ. Saf. 2019, 169, 128–133. [CrossRef]

79. Hadrup, N.; Ravn-Haren, G. Acute human toxicity and mortality after selenium ingestion: A review. J. Trace Elem. Med. Biol. 2020, 58, 126435. [CrossRef] [PubMed]

80. Ren, B.; Liu, M.; Ni, J.; Tian, J. Role of selenoprotein F in protein folding and secretion: Potential involvement in human disease. Nutrients 2018, 10, 1619. [CrossRef] [PubMed]

81. Schiavon, M.; Pilon-Smits, E.A. Selenium biofortification and phytoremediation phytotechnologies: A review. J. Environ. Qual. 2017, 46, 10–19. [CrossRef] [PubMed]

82. Germ, M.; Stibilj, V.; Šircelj, H.; Jerše, A.; Krofič, A.; Golob, A.; Maršič, N.K. Biofortification of common buckwheat microgreens and seeds with different forms of selenium and iodine. J. Sci. Food Agric. 2019, 99, 4353–4362. [CrossRef]

83. Yin, H.; Qi, Z.; Li, M.; Ahammed, G.J.; Chu, X.; Zhou, J. Selenium forms and methods of application differentially modulate plant growth, photosynthesis, stress tolerance, and selenium content in speciation in Oryza sativa L. Ecotoxicol. Environ. Saf. 2019, 169, 911–917. [CrossRef]

84. Tavoosi, S.; Baghsheikhi, A.H.; Shetab-Boushehri, S.V.; Navaei-Nigjeh, M.; Sarvestani, N.N.; Karimi, M.Y.; Ranbar, A.; Ebadollahi-Natanzi, A.; Hosseini, A. Cerium and yttrium oxide nanoparticles and nano-selenium produce protective effects against H2O2-induced oxidative stress in pancreatic beta cells by modulating mitochondrial dysfunction. Pharm. Nanotechnol. 2019, 8, 63–75. [CrossRef]

85. Zhang, X.; Gan, X.E.Q.; Zhang, Q.; Ye, Y.; Cai, Y.; Han, A.; Tian, M.; Wang, Y.; Wang, C.; Su, L.; et al. Ameliorative effects of nano-selenium against NiSO4-induced apoptosis in rat testes. Toxicol. Mech. Methods 2019, 29, 467–477. [CrossRef]

86. Zhang, X.; He, C.; Yan, R.; Chen, Y.; Zhao, P.; Li, M.; Fan, T.; Yang, T.; Lu, Y.; Luo, J.; et al. HIF-1 dependent reversal of cisplatin resistance via anti-oxidative nano selenium for effective cancer therapy. Chem. Eng. J. 2020, 380, 122540. [CrossRef] [PubMed]

87. Safari, M.; Oraghi Ardebili, Z.; Iranbakhsh, A. Selenium nano-particle induced alterations in expression patterns of heat shock factor A4A (HSFA4A), and high molecular weight glutenin subunit 1Bx (Glu-1Bx) and enhanced nitrate reductase activity in wheat (Triticum aestivum L.). Acta Physiol. Plant. 2018, 40, 117. [CrossRef]

88. Boldrin, P.F.; Faquin, V.; Clemente, A.D.C.S.; de Andrade, T.; Guilherme, L.R.G. Genotypic Variation and Biofortification with Selenium in Brazilian Wheat Cultivars. J. Environ. Qual. 2018, 47, 1371–1379. [CrossRef] [PubMed]

89. Lara, T.S.; de Lima Lessa, J.H.; de Souza, K.R.D.; Corguinha, A.P.B.; Martins, F.A.D.; Lopes, G.; Guilherme, L.R.G. Selenium biofortification of wheat grain via foliar application and its effect on plant metabolism. J. Food Compos. Anal. 2019, 81, 10–18. [CrossRef]

90. Smoleń, S.; Baranski, R.; Ledwożyw-Smoleń, I.; Skoczylas, L.; Sady, W. Combined biofortification of carrot with iodine and selenium. Food Chem. 2019, 300, 125202. [CrossRef] [PubMed]

91. Smoleń, S.; Kowalska, I.; Kovačič, P.; Halka, M.; Sady, W. Biofortification of six varieties of lettuce (Lactuca sativa L.) with iodine and selenium in combination with the application of salicylic acid. Front. Plant Sci. 2019, 10, 143. [CrossRef]

92. Zou, C.; Du, Y.; Rashid, A.; Ram, H.; Savasli, E.; Pieterse, P.J.; Ortiz-Monasterio, I.; Yazici, A.; Kaur, C.; Mahmood, K.; et al. Simultaneous biofortification of wheat with zinc, iodine, selenium, and iron through foliar treatment of a micronutrient cocktail in six countries. J. Agric. Food Chem. 2019, 67, 8096–8106. [CrossRef]

93. Ramírez Bribiesca, J.E.; Casas, R.L.; Cruz Monterrosa, R.G.; Pérez, A.R. Supplementing selenium and zinc nanoparticles in ruminants for improving their bioavailability meat. In Nutrient Delivery: A volume in Nanotechnology in the Agri-Food Industry; Grumezescu, A.M., Ed.; Academic Press: Cambridge, MA, USA, 2017; pp. 713–747. [CrossRef]

94. De Oliveira, V.C.; Faquin, V.; Andrade, F.R.; Carneiro, J.P.; da Silva Júnior, E.C.; de Souza, K.R.D.; Pereira, J.; Guilherme, L.R.G. Physiological and physicochemical responses of potato to selenium biofortification in tropical soil. Potato Res. 2019, 62, 315–331. [CrossRef]
Soil Syst. 2020, 4, 57

95. Strobbe, S.; Van Der Straeten, D. Folate biofortification in food crops. *Curr. Opin. Biotechnol.* 2017, 44, 202–211. [CrossRef]
96. De Lepeleire, J.; Strobbe, S.; Verstraete, J.; Blancquaert, D.; Ambach, L.; Visser, R.G.F.; Stove, C.; Van Der Straeten, D. Folate biofortification of potato by tuber-specific expression of four folate biosynthesis genes. *Mol. Plant.* 2018, 11, 175–188. [CrossRef]
97. Liang, Q.; Wang, K.; Liu, X.; Riaz, B.; Jiang, L.; Wan, X.; Ye, X.; Zhang, C. Improved folate accumulation in genetically modified maize and wheat. *J. Exp. Bot.* 2019, 70, 1539–1551. [CrossRef] [PubMed]
98. Rajendran, S.C.C.; Chamalagain, B.; Kariluto, S.; Piironen, V.; Saris, P.E.J. Biofortification of riboflavin and folate in idli batter, based on fermented cereal and pulse, by *Lactococcus lactis* N8 and *Saccharomyces boulardii* SAA655. *J. Appl. Microbiol.* 2017, 122, 1663–1671. [CrossRef] [PubMed]
99. Yépez, A.; Russo, P.; Spano, G.; Khomenko, I.; Biasioli, F.; Capozzi, V.; Aznar, R. In situ riboflavin fortification of different kefir-like cereal-based beverages using selected Andean LAB strains. *Food Microbiol.* 2019, 77, 61–68. [CrossRef] [PubMed]
100. Wong, H.W.; Liu, Q.; Sun, S.S. Biofortification of rice with lysine using endogenous histones. *Plant Mol. Biol.* 2015, 87, 235–248. [CrossRef]
101. Yang, Q.Q.; Suen, P.K.; Zhang, C.Q.; Mak, W.S.; Gu, M.H.; Liu, Q.Q.; Sun, S.S. Improved growth performance, food efficiency, and lysine availability in growing rats fed with lysine-biofortified rice. *Sci. Rep.* 2017, 7, 1389. [CrossRef]
102. Sestili, F.; Garcia-Molina, M.D.; Gambacorta, G.; Beleggia, R.; Botticella, E.; De Vita, P.; Savatin, D.V.; Masci, S.; Lafiandra, D. Provitamin A biofortification of durum wheat through a TILLING approach. *Int. J. Mol. Sci.* 2019, 20, 5703. [CrossRef]
103. Garg, M.; Sharma, N.; Sharma, S.; Kapoor, P.; Kumar, A.; Chunduri, V.; Arora, P. Biofortified crops generated by breeding, agronomy, and transgenic approaches are improving lives of millions of people around the world. *Front. Nutr.* 2018, 5, 12. [CrossRef]
104. Brevik, E.C.; Slaughter, L.; Singh, B.R.; Steffen, J.J.; Collier, D.; Barnhart, P.; Pereira, P. Soil and human health: Current status and future needs. *Air Soil Water Res.* 2020, 13, 1–23. [CrossRef]
105. D’Imperio, M.; Renna, M.; Cardinali, A.; Buttaro, D.; Serio, F.; Santamaria, P. Calcium biofortification and bioaccessibility in soilless “baby leaf” vegetable production. *Food Chem.* 2016, 213, 149–156. [CrossRef]
106. Ludwik, Y.; Slamet-Loedin, I.H. Genetic biofortification to enrich rice and wheat grain iron: From genes to product. *Front. Plant Sci.* 2019, 10, 833. [CrossRef] [PubMed]
107. Rzymski, P.; Mleczek, M.; Niedziewski, P.; Siwulski, M.; Gasecka, M. Cultivation of *Agaricus bisporus* enriched with selenium, zinc and copper. *J. Sci. Food Agric.* 2017, 97, 923–928. [CrossRef] [PubMed]
108. Zhang, C.M.; Zhao, W.Y.; Gao, A.X.; Su, T.T.; Wang, Y.K.; Zhang, Y.Q.; Zhou, X.B.; He, X.H. How could agronomic biofortification of rice be an alternative strategy with higher cost-effectiveness for human iron and zinc deficiency in China? *Food Nutr. Bull.* 2018, 39, 246–259. [CrossRef]
109. Akhtar, M.; Yousaf, S.; Sarwar, N.; Hussain, S. Zinc biofortification of cereals-role of phosphorus and other impediments in alkaline calcareous soils. *Environ. Geochem. Health* 2019, 41, 2365–2379. [CrossRef]
110. D’Amato, R.; Fontanella, M.C.; Falcinelli, B.; Beone, G.M.; Bravi, E.; Marconi, O.; Benincasa, P.; Businelli, D. Selenium Biofortification in Rice (*Oryza sativa* L.) Sprouting: Effects on Se Yield and Nutritional Traits with Focus on Phenolic Acid Profile. *J. Agric. Food Chem.* 2018, 66, 4082–4090. [CrossRef]
111. Farooq, M.U.; Tang, Z.; Zeng, R.; Liang, Y.; Zhang, Y.; Zheng, T.; Li, H.H.; Ye, X.; Jia, X.; Zhu, J.; et al. Accumulation, mobilization, and transformation of selenium in rice grain provided with foliar sodium selenite. *J. Sci. Food Agric.* 2019, 99, 2892–2900. [CrossRef]
116. Bocchini, M.; D’Amato, R.; Ciancaleoni, S.; Fontanella, M.C.; Palmerini, C.A.; Beone, G.M.; Onofri, A.; Negri, V.; Marconi, G.; Albertini, E.; et al. Soil selenium (Se) biofortification changes the physiological, biochemical and epigenetic. by inducing a higher drought tolerance. *Front. Plant Sci.* 2018, 9, 389. [CrossRef]  
117. Joy, E.J.M.; Kalimbira, A.A.; Gashu, D.; Ferguson, E.L.; Sturgess, J.; Dangour, A.D.; Bandi, L.; Chiutsi-PHIRI, G.; Bailey, E.H.; Langley-Evans, S.C.; et al. Can selenium deficiency in Malawi be alleviated through consumption of agro-biofortified maize flour? Study protocol for a randomised, double-blind, controlled trial. *Trials* 2019, 20, 795. [CrossRef] [PubMed]  
118. Ramkissoon, C.; Degryse, E.; da Silva, R.C.; Baird, R.; Young, S.D.; Bailey, E.H.; McLaughlin, M.J. Improving the efficacy of selenium fertilizers for wheat biofortification. *Sci. Rep.* 2019, 9, 19520. [CrossRef] [PubMed]  
119. Silva, V.M.; Boleta, E.H.M.; Martins, J.T.; dos Santos, F.L.M.; da Rocha Silva, A.C.; Alcock, T.D.; Wilson, L.; de Sá, M.E.; Young, S.D.; Broadway, M.R.; et al. Agronomic biofortification of cowpea with selenium: Effects of selenium and selenite applications on selenium and phytate concentrations in seeds. *J. Sci. Food Agric.* 2020, 99, 5969–5983. [CrossRef] [PubMed]  
120. Smoleń, S.; Kowalska, I.; Skoczylas, L.; Lisza-Skoczylas, M.; Grzanka, M.; Halka, M.; Sady, W. The effect of salicylic acid on biofortification with iodine and selenium and the quality of potato cultivated in the NFT system. *Sci. Hortic.* 2018, 240, 530–543. [CrossRef]  
121. Smoleń, S.; Kowalska, I.; Skoczylas, L.; Rakoczy, R.; Kopec, A.; Piatkowska, E.; Biezanowska-Kopec, R.; Koronowicz, A.; Kapusta-Duch, J. Biofortification of carrot (*Daucus carota* L.) with iodine and selenium in a field experiment. *Front. Plant Sci.* 2016, 7, 730. [CrossRef]  
122. Li, X.; Wu, Y.; Li, B.; Yang, Y. Selenium accumulation characteristics and biofortification potentiality in turnip (*Brassica rapa* var. *rapa*) supplied with selenium or selenite. *Front. Plant Sci.* 2018, 9, 2207. [CrossRef]  
123. Li, X.; Li, B.; Yang, Y. Effects of foliar selenite on the nutrient components of turnip (*Brassica rapa* var. *rapa* Linn.). *Front. Chem.* 2018, 6, 420. [CrossRef]  
124. Golubkina, N.; Zamana, S.; Seredin, T.; Poluboyarinov, P.; Sokolov, S.; Baranova, H.; Krivenkov, L.; Pietrantonio, L.; Caruso, G. Effect of selenium biofortification and beneficial microorganism inoculation on yield, quality and antioxidant properties of shallot bulbs. *Plants* 2019, 8, 102. [CrossRef]  
125. Ngigi, P.B.; Lachat, C.; Masinde, PW; Du Laing, G. Agronomic biofortification of maize and beans in Kenya through selenium fertilization. *Environ. Geochem. Health* 2019, 41, 2577–2591. [CrossRef]  
126. Do Nascimento da Silva, E.; Cadore, S. Bioavailability assessment of copper, iron, manganese, molybdenum, selenium, and zinc from selenium-enriched lettuce. *J. Food Sci. 2019, 84, 2840–2846. [CrossRef]  
127. Puccinelli, M.; Malorgio, F.; Rosellini, I.; Pezzarossa, B. Production of selenium-biofortified microgreens from selenium-enriched seeds of basil. *J. Sci. Food Agric.* 2019, 99, 5601–5605. [CrossRef] [PubMed]  
128. Wortmann, L.; Enneking, U.; Daum, D. German consumers’ attitude towards selenium-biofortified apples and acceptance of related nutrition and health claims. *Nutrients* 2018, 10, 190. [CrossRef] [PubMed]  
129. Babalar, M.; Mohebbi, S.; Zamani, Z.; Askari, M.A. Effect of foliar application with sodium selenite on selenium biofortification and fruit quality maintenance of ‘Starking Delicious’ apple during storage. *J. Sci. Food Agric.* 2019, 99, 5149–5156. [CrossRef] [PubMed]  
130. Wallace, L.G.; Bobe, G.; Vorachek, W.R.; Dolan, B.P.; Estill, C.T.; Pirelli, G.J.; Hall, J.A. Effects of feeding pregnant beef cows selenium-enriched alfalfa hay on selenium status and antibody titers in their newborn calves. *J. Anim. Sci.* 2017, 95, 2408–2420. [CrossRef]  
131. Kihara, J.; Bolo, P.; Kinyua, M.; Rurinda, J.; Piikki, K. Micronutrient deficiencies in African soils and the human nutritional nexus: Opportunities with staple crops. *Environ. Geochem. Health* 2020. [CrossRef]  
132. Witkowska, Z.; Michalak, I.; Korczyński, M.; Szołtysik, M.; Świnarska, M.; Dobrzański, Z.; Tuhy, L.; Samoraj, M.; Chojnacka, K. Biofortification of milk and cheese with microelements by dietary feed bio-preparations. *J. Food Sci. Technol.* 2015, 52, 6484–6492. [CrossRef]  
133. Mattioli, S.; Machado Duarte, J.M.; Castellini, C.; D’Amato, R.; Negri, L.; Pietrantonio, L.; Caruso, G. Effect of feeding effect on performance, carcass and meat characteristics, and estimated indexes of fatty acid metabolism. *Meat Sci.* 2018, 143, 230–236. [CrossRef]  
134. Witkowska, Z.; Świnarska, M.; Korczyński, M.; Opalirski, S.; Konkol, D.; Michalak, I.; Saeid, A.; Mironiuk, M.; Chojnacka, K. Biofortification of hens’ eggs with microelements by innovative bio-based dietary supplement. *J. Anim. Physiol. Anim. Nutr.* 2019, 103, 485–492. [CrossRef]
135. Filek, M.; Sieprawska, A.; Telk, A.; Łabanowska, M.; Kurdziel, M.; Walas, S.; Hartikainen, H. Translocation of elements and sugars in wheat genotypes at vegetative and generative stages under continuous selenium exposure. J. Sci. Food Agric. 2019, 99, 6364–6371. [CrossRef]

136. Ali, F.; Peng, Q.; Wang, D.; Cui, Z.; Huang, J.; Fu, D.; Liang, D. Effects of selenite and selenate application on distribution and transformation of selenium fractions in soil and its bioavailability for wheat (Triticum aestivum L.). Environ. Sci. Pollut. Res. Int. 2017, 24, 8315–8325. [CrossRef]

137. Liu, K.; Cai, M.; Hu, C.; Sun, X.; Cheng, Q.; Jia, W.; Yang, T.; Nie, M.; Zhao, X. Selenium (Se) reduces Sclerotinia stem rot disease incidence of oilseed rape by increasing plant Se concentration and shifting soil microbial community and functional profiles. Environ. Pollut. 2019, 254, 113051. [CrossRef] [PubMed]

138. Wang, X.; Zhang, D.; Qian, H.; Liang, Y.; Pan, X.; Gadd, G.M. Interactions between biogenic selenium nanoparticles and goethite colloids and consequence for remediation of elemental mercury contaminated groundwater. Sci. Total Environ. 2018, 613–614, 672–678. [CrossRef] [PubMed]

139. Bañuelos, G.S.; Freeman, J.; Arroyo, I. Accumulation and speciation of selenium in biofortified vegetables grown under high boron and saline field conditions. Food Chem. 2020, 5, 100073. [CrossRef] [PubMed]

140. De Vita, P.; Platani, C.; Fragasso, M.; Ficco, D.B.M.; Colecchia, S.A.; Del Nobile, M.A.; Padalino, L.; Di Gennaro, S.; Petrozza, A. Selenium-enriched durum wheat improves the nutritional profile of pasta without altering its organoleptic properties. Food Chem. 2017, 214, 374–382. [CrossRef]

141. Hu, T.; Li, H.; Li, J.; Zhao, G.; Wu, W.; Liu, L.; Wang, Q.; Guo, Y. Absorption and bio-transformation of selenium nanoparticles by wheat seedlings (Triticum aestivum L.). Front. Plant Sci. 2018, 9, 597. [CrossRef]

142. D’Amato, R.; De Feudis, M.; Guiducci, M.; Businelli, D. Zea mays L. grain: Increase in nutraceutical and antioxidant properties due to se fortification in low and high water regimes. J. Agric Food Chem. 2019, 67, 7050–7059. [CrossRef]

143. De Feudis, M.; D’Amato, R.; Businelli, D.; Guiducci, M. Fate of selenium in soil: A case study in a maize (Zea mays L.) field under two irrigation regimes and fertilized with sodium selenite. Sci. Total Environ. 2019, 659, 131–139. [CrossRef]

144. Yasin, M.; El-Mehdawi, A.F.; Pilon-Smits, E.A.; Faisal, M. Selenium-fortified wheat: Potential of microbes for biofortification of selenium and other essential nutrients. Int. J. Phytoremediat. 2015, 17, 777–786. [CrossRef]

145. Gong, R.; Ai, C.; Zhang, B.; Cheng, X. Effect of selenite on organic selenium speciation and selenium bioaccessibility in rice grains of two Se-enriched rice cultivars. Food Chem. 2018, 264, 443–448. [CrossRef]

146. Ashraf, M.A.; Akbar, A.; Parveen, A.; Rasheed, R.; Hussain, I.; Iqbal, M. Phenological application of selenium fortification induces growth, antioxidative capacity and yield of tomato (Lycopersicon esculentum Mill.) fruit during postharvest ripening. J. Sci. Food Agric. 2019, 99, 2463–2472. [CrossRef]

147. Jiang, C.; Zu, C.; Lu, D.; Zheng, Q.; Shen, J.; Wang, H.; Li, D. Effect of exogenous selenium supply on photosynthesis, Na+ accumulation and antioxidative capacity of maize (Zea mays L.) under salinity stress. Sci. Rep. 2017, 7, 42039. [CrossRef] [PubMed]

148. Finley, J.W.; Dimick, D.; Marshall, E.; Nelson, G.C.; Mein, J.R.; Gustafson, D.I. Nutritional sustainability: Aligning priorities in nutrition and public health with agricultural production. Adv. Nutr. 2017, 8, 780–788. [CrossRef] [PubMed]

149. Blekenhorst, L.C.; Sim, M.; Bondonno, C.P.; Bondonno, N.P.; Ward, N.C.; Prince, R.L.; Devine, A.; Lewis, J.R.; Hodgson, J.M. Cardiovascular Health Benefits of Specific Vegetable Types: A Narrative Review. Nutrients 2018, 10, 595. [CrossRef] [PubMed]

150. Zhu, Z.; Zhang, Y.; Liu, J.; Chen, Y.; Zhang, X. Exploring the effects of selenium treatment on the nutritional quality of tomato fruit. Food Chem. 2018, 252, 9–15. [CrossRef] [PubMed]

151. Puccinelli, M.; Malorgio, F.; Terry, L.A.; Tosetti, R.; Rosellini, I.; Pezzarossa, B. Effect of selenium enrichment on metabolism of tomato (Solanum lycopersicum) fruit during postharvest ripening. J. Sci. Food Agric. 2019, 99, 2463–2472. [CrossRef]

152. Shalaby, T.; Bayoumi, Y.; Alshaal, T.; Elhawat, N.; Sztrik, A.; El-Ramady, H. Selenium fortification induces growth, antioxidant activity, yield and nutritional quality of lettuce in salt-affected soil using foliar and soil applications. Plant Soil. 2017, 421, 245–258. [CrossRef]

153. Castro Grijalba, A.; Martinis, E.M.; Wuilloud, R.G. Inorganic selenium speciation analysis in Allium and Brassica vegetables by ionic liquid assisted liquid-liquid microextraction with multivariate optimization. Food Chem. 2017, 219, 102–108. [CrossRef]
154. Ogra, Y.; Ogihara, Y.; Anan, Y. Comparison of the metabolism of inorganic and organic selenium species between two selenium accumulator plants, garlic and Indian mustard. *Metallomics* 2017, 9, 61–68. [CrossRef]

155. Astaneh, R.K.; Bolandnazar, S.; Nahandi, F.Z.; Oustan, S. Effects of selenium on enzymatic changes and productivity of garlic under salinity stress. *S. Afr. J. Bot.* 2019, 121, 447–455. [CrossRef]

156. Bañuelos, G.S.; Arroyo, I.; Pickering, I.J.; Yang, S.L.; Freeman, J.L. Selenium biofortification of broccoli and carrots grown in soil amended with Se-enriched hyperaccumulator *Stanleya pinnata*. *Food Chem.* 2015, 166, 603–608. [CrossRef]

157. Bañuelos, G.S.; Arroyo, I.S.; Dangi, S.R.; Zambrano, M.C. Continued Selenium Biofortification of Carrots and Broccoli Grown in Soils Once Amended with Se-enriched *S. pinnata*. *Front. Plant Sci.* 2016, 7, 1251. [CrossRef] [PubMed]

158. Conversa, G.; Lazzizera, C.; Chiaravalle, A.E.; Miedico, O.; Bonasia, A.; La Rotonda, P.; Elia, A. Selenium fern application and arbuscular mycorrhizal fungi soil inoculation enhance Se content and antioxidant properties of green asparagus (*Asparagus officinalis* L.) spears. *Sci. Hortic.* 2019, 252, 176–191. [CrossRef]

159. Da Silva, D.F.; Cipriano, P.E.; de Souza, R.R.; Júnior, M.S.; Faquin, V.; Silva, M.L.S.; Guilherme, L.R.G. Biofortification with selenium and implications in the absorption of macronutrients in *Raphanus sativus* L. *J. Food Compos. Anal.* 2020, 86, 103382. [CrossRef]

160. Da Silva, D.F.; Cipriano, P.E.; de Souza, R.R.; Júnior, M.S.; da Silva, R.F.; Faquin, V.; Silva, M.L.S.; Guilherme, L.R.G. Anatomical and physiological characteristics of *Raphanus sativus* L. submitted to different selenium sources and forms application. *Sci. Hortic.* 2020, 260, 108839. [CrossRef]

161. Lima, L.W.; Checchio, M.V.; dos Reis, A.R.; de Càssia Alves, R.; Tezzoto, T.; Gratão, P.L. Selenium restricts cadmium uptake and improve micronutrients and proline concentration in tomato fruits. *Biocatal. Agric. Biotechnol.* 2019, 18, 101057. [CrossRef]

162. Zhu, Z.; Chen, Y.L.; Zhang, X.J.; Li, M. Effect of foliar treatment of sodium selenate on postharvest decay and quality of tomato fruits. *Sci. Hortic.* 2016, 198, 304–310. [CrossRef]

163. Zhu, Z.; Chen, Y.; Shi, G.; Zhang, X. Selenium delays tomato fruit ripening by inhibiting ethylene biosynthesis and enhancing the antioxidant defense system. *Food Chem.* 2017, 219, 179–184. [CrossRef]

164. Shahid, M.A.; Balal, R.M.; Khan, N.; Zotarelli, L.; Liu, G.D.; Sarkhosh, A.; Fernández-Zapata, J.C.; Martínez-Nicolás, J.J.; García-Sanchez, F. Selenium impedes cadmium and arsenic toxicity in potato by modulating carbohydrate and nitrogen metabolism. *Ecotoxicol. Environ. Saf.* 2019, 180, 588–599. [CrossRef]

165. Lei, B.; Bian, Z.; Yang, Q.; Wang, J.; Cheng, R.; Li, K.; Liu, W.-K.; Zhang, Y.; Fang, H.; Tong, Y. The positive function of selenium supplementation on reducing nitrate accumulation in hydroponic lettuce (*Lactuca sativa* L.). *J. Integr. Agric.* 2018, 17, 837–846. [CrossRef]

166. Do Nascimento da Silva, E.; Aureli, F.; D’Amato, M.; Raggi, A.; Cadore, S.; Cubadda, F. Selenium Bioaccessibility and Speciation in Selenium-Enriched Lettuce: Investigation of the Selenocompounds Liberated after *In Vitro* Simulated Human Digestion Using Two-Dimensional HPLC-ICP-MS. *J. Agric. Food Chem.* 2017, 65, 3031–3038. [CrossRef]

167. Goswami, M.; Deka, S. Plant growth-promoting rhizobacteria—Alleviators of abiotic stresses in soil: A review. *Pedosphere.* 2020, 30, 40–61. [CrossRef] [PubMed]

168. Debona, D.; Rodrigues, F.A.; Datnoff, L.E. Silicon’s Role in Abiotic and Biotic Plant Stresses. *Annu. Rev. Phytopathol.* 2017, 55, 85–107. [CrossRef] [PubMed]

169. Etesami, H.; Jeong, B.R. Silicon (Si): Review and future prospects on the action mechanisms in alleviating biotic and abiotic stresses in plants. *Ecotoxicol. Environ. Saf.* 2018, 147, 881–896. [CrossRef] [PubMed]

170. Khan, A.; Bilal, S.; Khan, A.L.; Imran, M.; Al-Harrasi, A.; Al-Rawahi, A.; Lee, I.J. Silicon-mediated alleviation of combined salinity and cadmium stress in date palm (*Phoenix dactylifera*) L. by regulating physio-hormonal alteration. *Ecotoxicol. Environ. Saf.* 2020, 188, 109885. [CrossRef] [PubMed]

171. Hussain, B.; Lin, Q.; Hamid, Y.; Sanaullah, M.; Di, L.; Hashmi, M.L.R.; Khan, M.B.; He, Z.; Yang, X. Foliage application of selenium and silicon nanoparticles alleviates Cd and Pb toxicity in rice (*Oryza sativa* L.). *Sci. Total Environ.* 2020, 712, 136497. [CrossRef] [PubMed]

172. Kavčič, A.; Budič, B.; Vogel-Mikuš, K. The effects of selenium biofortification on mercury bioavailability and toxicity in the lettuce–slug food chain. *Food Chem. Toxicol.* 2020, 135, 110939. [CrossRef]

173. Wu, C.; Dun, Y.; Zhang, Z.; Li, M.; Wu, G. Foliage application of selenium and zinc to alleviate wheat (*Triticum aestivum* L.) cadmium toxicity and uptake from cadmium-contaminated soil. *Ecotoxicol. Environ. Saf.* 2020, 190, 110091. [CrossRef]
174. Domokos-Szabolcsy, E.; Marton, L.; Sztrik, A.; Babka, B.; Prokisch, J.; Fari, M. Accumulation of red elemental selenium nanoparticles and their biological effects in Nicotinia tabacum. *Plant Growth Regul.* **2012**, *68*, 525–531. [CrossRef]

175. Astaneh, R.K.; Bolandnazar, S.; Zaare Nahandi, F.; Oustan, S. Effect of selenium application on phenylalanine ammonia-lyase (PAL) activity, phenol leakage and total phenolic content in garlic (*Allium sativum* L.) under NaCl stress. *Inf. Process. Agric.* **2018**, *5*, 339–344. [CrossRef]

176. Teplanosyan, G.; Sahakyan, L.; Belyaeva, O.; Asmaryan, S.; Saghatelyan, A. Continuous impact of mining activities on soil heavy metals levels and human health. *Sci. Total Environ.* **2018**, *639*, 900–909. [CrossRef]

177. Jiang, Y.; Shi, L.; Guang, A.L.; Mu, Z.; Zhan, H.; Wu, Y. Contamination levels and human health risk assessment of toxic heavy metals in street dust in an industrial city in Northwest China. *Environ. Geochem. Health* **2018**, *40*, 2007–2020. [CrossRef] [PubMed]

178. Minari, G.D.; Rosalen, D.L.; da Cruz, M.C.P.; de Melo, W.J.; Alves, L.M.C.; Saran, L.M. Agricultural management of an Oxisol affects accumulation of heavy metals. *Chemosphere* **2017**, *185*, 344–350. [CrossRef] [PubMed]

179. Cai, M.; Wang, Q.S.; Wen, H.H.; Luo, J.; Wang, S. Heavy metals in agricultural soils from a typical township in Guangdong Province, China: Occurrences and spatial distribution. *Ecotoxicol. Environ. Saf.* **2019**, *168*, 184–191. [CrossRef] [PubMed]

180. De Oliveira, A.P.; Nomura, C.S.; Naozuka, J. Evaluation of selenium enrichment of adzuki bean (*Vigna angularis*) sprouts: Translocation, bioaccessibility and Se-protein speciation. *Microchem. J.* **2017**, *134*, 19–26. [CrossRef]

181. Kolbert, Z.; Molnár, Á.; Feigl, G.; Van Hoewyk, D. Plant selenium toxicity: Proteome in the crosshairs. *J. Plant Physiol.* **2019**, *232*, 291–300. [CrossRef] [PubMed]

182. Kaur, S.; Singh, D.; Singh, K. Effect of selenium application on arsenic uptake in rice (*Oryza sativa* L.). *Environ. Monit. Assess.* **2017**, *189*, 430. [CrossRef] [PubMed]

183. Moulick, D.; Ghosh, D.; Chandra Santra, S. Evaluation of effectiveness of seed priming with selenium in rice during germination under arsenic stress. *Plant Physiol. Biochem.* **2016**, *109*, 571–578. [CrossRef]

184. Chauhan, R.; Awasthi, S.; Tripathi, P.; Mishra, S.; Dwivedi, S.; Niranjan, A.; Mallick, S.; Tripathi, P.; Pande, V.; Tripathi, R.D. Selenite modulates the level of phenolics and nutrient element to alleviate the toxicity of arsenite in rice (*Oryza sativa* L.). *Ecotoxicol. Environ. Saf.* **2017**, *138*, 47–55. [CrossRef]

185. Biswas, A.; Biswas, S.; Das, A.; Roychowdhury, T. Spatial variability and competing dynamics of arsenic, selenium, iron and bioavailable phosphate from ground water and soil to paddy plant parts. *Groundw. Sustain. Dev.* **2018**, *7*, 328–335. [CrossRef]

186. Pandey, C.; Gupta, M. Selenium amelioration of arsenic toxicity in rice shows genotypic variation: A transcriptomic and biochemical analysis. *J. Plant Physiol.* **2018**, *231*, 168–181. [CrossRef]

187. Moulick, D.; Santra, S.C.; Ghosh, D. Effect of selenium induced seed priming on arsenic accumulation in rice plant and subsequent transmission in human food chain. *Ecotoxicol. Environ. Saf.* **2018**, *152*, 67–77. [CrossRef] [PubMed]

188. Singh, R.; Upadhayay, A.K.; Singh, D.P. Regulation of oxidative stress and mineral nutrient status by selenium in arsenic treated crop plant *Oryza sativa*. *Ecotoxicol. Environ. Saf.* **2018**, *148*, 105–113. [CrossRef] [PubMed]

189. Wang, Y.; Camara, A.Y.; Huang, Q.; Yu, Y.; Wang, Q.; Li, H. Arsenic uptake and accumulation in rice (*Oryza sativa* L.) with selenite fertilization and water management. *Ecotoxicol. Environ. Saf.* **2018**, *156*, 67–74. [CrossRef] [PubMed]

190. Camara, A.Y.; Wang, Y.; Yu, Y.; Wang, Q.; Li, H. Effect of selenium on uptake and translocation of arsenic in rice seedlings (*Oryza sativa* L.). *Ecotoxicol. Environ. Saf.* **2018**, *148*, 869–875. [CrossRef]

191. Camara, A.Y.; Wang, Y.; Yu, Y.; Wang, Q.; Wang, K.; Li, H. Effect of endogenous selenium on arsenic uptake and antioxidative enzymes in as-exposed rice seedlings. *Int. J. Environ. Res. Public Health* **2019**, *16*, 3350. [CrossRef] [PubMed]

192. Liu, N.; Jiang, Z.; Li, X.; Liu, H.; Li, N.; Wei, S. Mitigation of rice cadmium (Cd) accumulation by joint application of organic amendments and selenium (Se) in high-Cd-contaminated soils. *Chemosphere* **2020**, *241*, 125106. [CrossRef] [PubMed]

193. Yang, B.B.; Yang, C.; Shao, Z.Y.; Wang, H.; Zan, S.T.; Zhu, M.; Zhou, S.B.; Yang, R.Y. Selenium (Se) does not reduce cadmium ( Cd) uptake and translocation in rice (*Oryza sativa* L.) in naturally occurred Se-rich paddy fields with a high geological background of Cd. *Bull. Environ. Contam. Toxicol.* **2019**, *103*, 127–132. [CrossRef]
Soil Syst. 2020, 4, 57

194. Huang, B.; Xin, J.; Dai, H.; Zhou, W. Effects of interaction between cadmium (Cd) and selenium (Se) on grain yield and Cd and Se accumulation in a hybrid rice (Oryza sativa L.) system. J. Agric. Food Chem. 2017, 65, 9537–9546. [CrossRef]

195. Huang, G.; Ding, C.; Guo, F.; Li, X.; Zhang, T.; Wang, X. Underlying mechanisms and effects of hydrated lime and selenium application on cadmium uptake by rice (Oryza sativa L.) seedlings. Environ. Sci. Pollut. Res. Int. 2017, 24, 18926–18935. [CrossRef]

196. Cui, J.; Liu, T.; Li, Y.; Li, F. Selenium reduces cadmium uptake into rice suspension cells by regulating the expression of lignin synthesis and cadmium-related genes. Sci. Total Environ. 2018, 644, 602–610. [CrossRef]

197. Gao, M.; Zhou, J.; Liu, H.; Zhang, W.; Hu, Y.; Liang, J.; Zhou, J. Foliar spraying with silicon and selenium reduces cadmium uptake and mitigates cadmium toxicity in rice. Sci. Total Environ. 2018, 631–632, 1100–1108. [CrossRef] [PubMed]

198. Tan, L.C.; Nancharaiah, Y.V.; van Hullebusch, E.D.; Lens, P.N.L. Selenium: Environmental significance, implications of interactions and future research perspectives. J. Trace Elem. Med. Biol. 2017, 40, 95–103. [CrossRef]

199. Li, Y.; Li, H.; Li, Y.-F.; Zhao, J.; Guo, J.; Wang, R.; Li, B.; Zhang, Z.; Gao, Y. Evidence for molecular antagonistic mechanism between mercury and selenium in rice (Oryza sativa L.). A combined study using 1, 2-dimensional electrophoresis and SR-XRF techniques. J. Trace Elem. Med. Biol. 2017, 50, 435–440. [CrossRef]

200. Huang, G.; Ding, C.; Guo, F.; Li, X.; Zhang, T.; Wang, X. Underlying mechanisms and effects of interaction between cadmium (Cd) and selenium (Se) on grain yield and Cd and Se accumulation in a hybrid rice (Oryza sativa L.) system. J. Agric. Food Chem. 2017, 65, 9537–9546. [CrossRef]

201. Xu, X.; Yan, M.; Liang, L.; Lu, Q.; Han, J.; Liu, L.; Feng, X.; Guo, J.; Wang, Y.; Qiu, G. Impacts of selenium supplementation on soil mercury speciation, and inorganic mercury and methylmercury uptake in rice (Oryza sativa L.). Environ. Pollut. 2019, 249, 647–654. [CrossRef] [PubMed]

202. Chapman, E.E.V.; Moore, C.; Campbell, L.M. Native plants for revegetation of mercury- and arsenic-contaminated historical mining waste—Can a low-dose selenium additive improve seedling growth and decrease contaminant bioaccumulation? Water Air Soil Pollut. 2019, 230, 225. [CrossRef]

203. Zhao, Y.; Hu, C.; Wang, X.; Qing, X.; Wang, P.; Zhang, Y.; Zhang, X.; Zhao, X. Selenium alleviated chromium stress in Chinese cabbage (Brassica campestris L. ssp. Pekinensis) by regulating root morphology and metal element uptake. Ecotoxicol. Environ. Saf. 2019, 173, 314–321. [CrossRef]

204. Cai, M.; Hu, C.; Wang, X.; Zhao, Y.; Jia, W.; Sun, X.; Elyamine, A.M.; Zhao, X. Selenium induces changes of rhizosphere bacterial characteristics and enzyme activities affecting chromium/selenium uptake by pak choi (Brassica campestris L. ssp. Chinensis Makino) in chromium contaminated soil. Environ. Pollut. 2019, 249, 716–727. [CrossRef]

205. Ulhassan, Z.; Gill, R.A.; Huang, H.; Ali, S.; Mwamba, M.; Ali, B.; Huang, Q.; Hamid, Y.; Khan, A.R.; Wang, J.; et al. Selenium mitigates the chromium toxicity in Brassica napus L. by ameliorating nutrients uptake, amino acids metabolism and antioxidant defense system. Plant Physiol. Biochem. 2019, 145, 142–152. [CrossRef]

206. Handa, N.; Kohli, S.K.; Sharma, A.; Thukral, A.K.; Bhardwaj, R.; Alyemeni, M.N.; Wijaya, L.; Ahmad, P. Selenium ameliorates chromium toxicity through modifications in pigment system, antioxidative capacity, osmotic system, and metal chelators in Brassica juncea seedlings. S. Afr. J. Bot. 2018, 119, 1–10. [CrossRef]

207. Qing, X.; Zhao, X.; Hu, C.; Wang, P.; Zhang, Y.; Zhang, X.; Wang, P.; Shi, H.; Jia, F.; Qu, C. Selenium alleviates chromium toxicity by preventing oxidative stress in cabbage (Brassica campestris L. ssp. Pekinensis) leaves. Ecotoxicol. Environ. Saf. 2015, 114, 179–189. [CrossRef]

208. Chen, Z.; Xu, J.; Xu, Y.; Wang, K.; Cao, B.; Xu, K. Alleviating effects of silicate, selenium, and microorganism fertilization on lead toxicity in ginger (Zingiber officinale Roscoe.). Plant Physiol. Biochem. 2019, 145, 153–163. [CrossRef]

209. Wu, Z.; Yin, X.; Bañuelos, G.S.; Lin, Z.Q.; Liu, Y.; Li, M.; Yuan, L. Indications of selenium protection against cadmium and lead toxicity in oilseed rape (Brassica napus L.). Front. Plant Sci. 2016, 7, 1875. [CrossRef] [PubMed]

210. He, Y.; Xiang, Y.; Zhou, Y.; Yang, Y.; Zhang, J.; Huang, H.; Shang, C.; Luo, L.; Gao, J.; Tang, L. Selenium contamination, consequences and remediation techniques in water and soils: A review. Environ Res. 2018, 164, 288–301. [CrossRef]

211. Tan, L.C.; Nancharraiah, Y.V.; van Hullebusch, E.D.; Lens, P.N.L. Selenium: Environmental significance, pollution, and biological treatment technologies. Biotechnol. Adv. 2016, 34, 886–907. [CrossRef] [PubMed]
212. Henry, B.L.; Wesner, J.S.; Kerby, J.L. Cross-ecosystem effects of agricultural tile drainage, surface runoff, and selenium in the Prairie Pothole Region. *Soil Syst.* 2020, 4, 57. [CrossRef]

213. Etteieb, S.; Magdouli, S.; Zolfaghari, M.; Brar, S.K. Monitoring and analysis of selenium as an emerging contaminant in mining industry: A critical review. *Sci. Total Environ.* 2020, 698, 134339. [CrossRef]

214. Sharma, V.K.; Sohn, M.; McDonald, T.J. Remediation of selenium in water: A review. In *Advances in Water Purification Techniques, Meeting the Needs of Developed and Developing Countries*; Ahuja, S., Ed.; Elsevier Inc.: Amsterdam, The Netherlands, 2019; pp. 203–218. [CrossRef]

215. Malhotra, M.; Pal, M.; Pal, P. A response surface optimized nanofiltration-based system for efficient removal of selenium from drinking water. *J. Water Process Eng.* 2020, 33, 101007. [CrossRef]

216. Paul, T.; Saha, N.C. Environmental arsenic and selenium contamination and approaches towards its bioremediation through the exploration of microbial adaptations: A review. *Pedosphere* 2019, 29, 554–568. [CrossRef]

217. Solovyev, N.; Prakash, N.T.; Bhatia, P.; Prakash, R.; Drobyshev, E.; Michalke, B. Selenium-rich mushrooms cultivation on a wheat straw substrate from seleniferous area in Punjab, India. *J. Trace Elem. Med. Biol.* 2018, 50, 362–366. [CrossRef]

218. Chawla, R.; Filippini, T.; Loomba, R.; Cilloni, S.; Dhillon, K.S.; Vinceti, M. Exposure to a high selenium environment in Punjab, India: Biomarkers and health conditions. *Sci. Total Environ.* 2020, 719, 134541. [CrossRef] [PubMed]

219. Loomba, R.; Filippini, T.; Chawla, R.; Chaudhary, R.; Cilloni, S.; Datt, C.; Singh, S.; Dhillon, K.S.; Vinceti, M. Exposure to a high selenium environment in Punjab, India: Effects on blood chemistry. *Sci. Total Environ.* 2019, 716, 135347. [CrossRef] [PubMed]

220. Yasin, M.; El Mehdawi, A.F.; Jahn, C.E.; Anwar, A.; Turner, M.F.S.; Faisal, M.; Pilon-Smits, E.A.H. Seleniferous soils as a source for production of selenium-enriched foods and potential of bacteria to enhance plant selenium uptake. *Plant Soil* 2015, 386, 385–394. [CrossRef]

221. Statwick, J.; Sher, A.A. Selenium in soils of western Colorado. *J. Arid Environ.* 2017, 137, 1–6. [CrossRef]

222. Chang, C.; Yin, R.; Wang, X.; Shao, S.; Chen, C.; Zhang, H. Selenium translocation in the soil-rice system in the Enshi seleniferous area, Central China. *Sci. Total Environ.* 2019, 669, 83–90. [CrossRef]

223. Chang, C.; Yin, R.; Zhang, H.; Yao, L. Bioaccumulation and health risk assessment of heavy metals in the soil-rice system in a typical seleniferous area, central China. *Environ. Toxicol. Chem.* 2019, 38, 1577–1584. [CrossRef]

224. Dhillon, K.S.; Dhillon, S.K.; Singh, B. Genesis of seleniferous soils and associated animal and human health problems. *Adv. Agron.* 2019, 154, 1–80. [CrossRef]

225. Wang, X.; Wang, S.; Pan, X.; Gadd, G.M. Heteroaggregation of soil particulate organic matter and biogenic selenium nanoparticles for remediation of elemental mercury contamination. *Chemosphere* 2019, 221, 486–492. [CrossRef]

226. Wang, X.; Pan, X.; Gadd, G.M. Immobilization of elemental mercury by biogenic Se nanoparticles in soils of varying salinity. *Sci. Total Environ.* 2019, 668, 303–309. [CrossRef]

227. Wang, X.; Pan, X.; Gadd, G.M. Soil dissolved organic matter affects mercury immobilization by biogenic selenium nanoparticles. *Sci. Total Environ.* 2019, 658, 8–15. [CrossRef]

228. Wang, X.; Liu, B.; Pan, X.; Gadd, G.M. Transport and retention of biogenic selenium nanoparticles in biofilm-coated quartz sand porous media and consequence for elemental mercury immobilization. *Sci. Total Environ.* 2019, 692, 1116–1124. [CrossRef] [PubMed]