

Review

Ionic Selenium and Nanoselenium as Biofortifiers and Stimulators of Plant Metabolism

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Abstract: Selenium (Se) is an essential element in mammals; however, there is frequently an insufficient intake due to several factors. Different techniques have been used to deal with this problem, such as plant biofortification with Se in its ionic forms and, more recently, at the nanoscale. Additionally, despite the fact that Se is not considered an essential element in plants, it has been shown to stimulate (through still unknown mechanisms) plant metabolism, causing an increase in the synthesis of molecules with reducing power, including enzymes such as glutathione peroxidase, catalase and ascorbate peroxidase as well as non-enzymatic antioxidants such as phenolic compounds, glucosinolates, vitamins and chlorophylls. A positive correlation has also been shown with other essential elements, achieving an increase in tolerance to environmental adversities. This article describes the advances made in the field of the biofortification of horticultural crops with ionic Se and nanoselenium (nSe) from 2009 to 2019. The aspects covered include various concentrations used, the findings made regarding the impact these chemical forms have on plant metabolism, and indications of its participation in the synthesis of primary and secondary metabolites that increase stress tolerance.

Keywords: biofortification; trace element; plant nutrition; metabolism

1. Introduction

Selenium (Se) is an essential trace element in humans and other vertebrates. It fulfills various functions, especially those related to the synthesis of selenoproteins, and also includes antioxidant and anti-inflammatory properties, immune system and antiviral effects, cancer prevention, brain development and cognitive aspects [1]. The minimum daily requirement for Se in humans was established by the Recommended Daily Allowances (RDA) and the World Health Organization (WHO), and the optimal range is between 50 and 60 µg per day to reduce health risks. Currently, it is known that Se intake is less than the minimum daily requirement for most populations due to the shortage of this element in crop food sources, mainly due to the low concentration of Se in the soil. The soil Se concentration has been established as being between 0.01 and 2 mg kg⁻¹, with 0.4 mg kg⁻¹ being the global mean [2]. To deal with this problem, various Se biofortification strategies for different crops have been used, such as exogenous incorporation in ionic forms [3,4] and more recently in the form of nanoparticles [5,6], and encouraging results have been obtained to mitigate such deficiency.

During the exploration of Se biofortification, beneficial effects on plant metabolism have been found, including an increase in molecules with reducing power leading to an increase in stress tolerance [7], an increase in plant growth and fruits with greater nutraceutical value, among others [8]. The objective of this review is to analyze, compare and conclude results obtained in the last decade

(2009–2019) regarding ionic and nanoparticulated Se biofortification as well as metabolic stimulations, mainly in horticultural plants.

2. Selenium in Human Health

Selenium (Se) was discovered in 1817 by Berzelius and was considered a highly toxic and polluting element. It was not until after the 1950s that functions essential to human and animal health were attributed to Se [9], including antioxidant activity [10,11], hormonal regulation such as in the thyroid [12,13], anticancer effects [14,15], cardiovascular protection [16,17] and antiviral properties [18,19]. Nowadays, various review articles have shown and updated the latest findings on the role of Se in organic functioning [1,20–23], where such functions are carried out through the synthesis of 25 known selenoproteins derived from selenocysteine (SeCys) [24,25]. The function of most of these proteins remains unknown, but a group of these selenoproteins was shown to have oxidoreduction catalytic activity, where SeCys is located in the active site because it is more reactive than cysteine (Cys) under physiological conditions; thus, SeCys can exist as a nucleophile without electrostatic interactions and can enhance the catalytic effectiveness [26]. The enzymes related to the oxidoreduction catalytic activity include five glutathione peroxidases, which catalyze the reduction of peroxide in the presence of glutathione; three thioredoxin reductases, which reduce thioredoxin or other proteins in the presence of NADPH; three deiodinases in the thyroid, which promote the reductive de-iodization of thyroid hormones; methionine-R-sulfoxide reductase, which reduces oxidized methionine residues within proteins; selenophosphate synthase, which catalyzes the synthesis of selenophosphate and is ATP dependent. On the other hand, there is a group of selenoproteins that do not have catalytic functions, among which are K, a simple protein with a transmembrane domain; O, the largest selenoprotein; H, related to glutathione gene expression (GSH); I, a membrane protein; T, containing a predicted redox motif. The W and V proteins are related at the C-terminal, M and Sep 15 are distant homologs proteins, and the functions of the S, R and N proteins remain even more unknown [27,28].

The daily intake of Se is established based on the concentration of selenoprotein P (SepP) in the blood serum, since it has been shown to be the most effective marker. A study in one province of China indicated that Se deficiency induced SepP saturation by consuming 49 µg of Se per day in people weighing 58 kg [29], which corresponds to approximately 1 µg of Se per kg of body weight. Therefore, the reference values were stipulated as follows: daily intake of 70 µg of Se for men with an average weight of 70 kg, and 60 µg of Se for adult women with an average weight of 60 kg, but this could increase up to 75 µg during pregnancy. Table 1 shows the Se intake specifications according to age and condition [30]. Additionally, it has been shown that the human body can tolerate large amounts of this element; however, amounts near 400 µg of Se per day show signs of toxicity [31].

Table 1. Recommended Se dietary allowances.

Age	Se Intake (µg day ⁻¹)
Babies up to 6 months	10
Babies from 7 to 12 months	20
Children from 1 to 3 years	20
Children from 4 to 8 years	30
Children from 9 to 13 years	45
Adolescents from 14 to 18 years old	60–70
Adults 19–50 years	60–70
Pregnant women	60
Lactating women	75
Adults over 51 years old	70

It is estimated that between 500 million and 1 billion people around the world have a deficient intake of Se, mainly due to the scarcity of this element in the soil since plants are the main source of Se in the diet [32]. The world average of Se in the soil is 0.4 mg kg^{-1} ; however, the availability of this nutrient depends on the physicochemical properties of the soil, such as the redox state, pH, content of organic matter and microbiota [33,34].

To deal with this problem, one solution has been to biofortify Se in staple crops for human consumption, and evaluations have included using different Se chemical forms, concentrations, doses and application times; application directly to soil, foliar spraying, hydroponics and direct application to the seed and the nude root by imbibition. Tables 2 and 3 show some prominent results obtained in the last 10 years on the topic of biofortification with ionic Se and nanoparticle Se (nSe).

Table 2. Biofortification of staple and horticultural crops with Se ionic species.

Crop, Vegetable	Chemical Specie and Dose	Application Form	Highlighted Findings	Reference
Lettuce	Na ₂ SeO ₃ 0.86 mg L ⁻¹ and Na ₂ SeO ₄ 3.7 mg L ⁻¹	Nutrient solution	The two forms of Se increased the biomass production, ascorbate peroxidase (APX) and glutathione peroxidase (GPX) activities, and reduced the lipoperoxidation. Na ₂ SeO ₄ was more efficient than Na ₂ SeO ₃ to accumulate 15 and 2.5 mg Se per kg (DW), respectively.	[35]
Lettuce	Na ₂ SeO ₄ 0.5 mg L ⁻¹	Nutrient solution	Accumulation of 0.53 mg Se per kg (DW), increase in biomass production, reduction in ethylene concentration.	[36]
Lettuce	Na ₂ SeO ₃ 0.7 mg L ⁻¹ and Na ₂ SeO ₄ 1.5 mg L ⁻¹	Nutrient solution	The two forms of Se increased the SOD and catalase (CAT) activities. The aerial part biomass increased 3.5% with Na ₂ SeO ₃ and 5.6% with Na ₂ SeO ₄ .	[37]
Lettuce	SeO ₂ 5 mg L ⁻¹ + quitosán	Nutrient solution	Accumulation of 24 mg Se per kg in leaves (DW).	[38]
Tomato	Na ₂ SeO ₃ 10 and 20 mg L ⁻¹	Foliar, every 20 days	Increase by 3.48 times the Se accumulation in the fruit (DW), and greater total antioxidant capacity.	[39]
Tomato, cucumber and lettuce	Na ₂ SeO ₄ 10 to 20 mg kg ⁻¹	Applied directly to peat	Accumulation in edible parts were 29.3–48.0 µg kg ⁻¹ for cucumber, 22.7–53.4 µg kg ⁻¹ for lettuce leaves and 15.2–19.9 µg kg ⁻¹ . Higher shelf life in lettuce and increased content of vitamin A in tomato	[40]
Tomato	Na ₂ SeO ₄ 1 mg L ⁻¹	Hydroponics	Delay in the onset of fruit ripening, lower content of β-carotene. Se accumulation of 58 µg/100 g fresh fruit	[41]
Tomato	Na ₂ SeO ₄ 1 mg L ⁻¹	Foliar	Increased enzymatic and non-enzymatic antioxidants. Control of gray mold rot	[42]
Tomato	Na ₂ SeO ₄ 1 mg L ⁻¹	Foliar	Delayed fruit ripening due to reduced ethylene production and respiration rate	[43]
Tomato	Na ₂ SeO ₄ 1 and 1.5 L ⁻¹	Hydroponics	Delayed postharvest ripening due to physiological process such as respiration, ethylene synthesis. Reduced weight loss post harvest	[44]
Tomato	Na ₂ SeO ₄ 0.9, 1.8, 4.7, 9.4 and 18.8 mg L ⁻¹	Hydroponics	Increased synthesis of phenolic compounds in leaves. Reduction in Mo, Fe, Mn, Cu in roots	[45]
	Na ₂ SeO ₄ 2 y 20 mg per plant	Foliar	The biofortification of tomato fruit (19 and 256 mg kg ⁻¹ , respectively) increased flavonoids.	

Table 2. Cont.

Crop, Vegetable	Chemical Specie and Dose	Application Form	Highlighted Findings	Reference
Tomato	Na ₂ SeO ₃ 2 and 5 mg L ⁻¹	Nutrient solution	Increase in plant growth and enzyme antioxidant activity, and average accumulation of 35.8 µg Se per g of fruit (DW).	[46]
Transgenic tomato and wild tomato	Na ₂ SeO ₄ 940 mg L ⁻¹	To soil, from the fruit filling twice a week for 10 weeks	The Se concentration increased from 0.7 to 137 mg per kg of fruit (DW) in transgenic tomato and from 0.3 to 60 mg per kg of fruit (DW) in wild tomato. The transgenic tomato was more efficient than the wild tomato to the overexpression of methyl-selenocysteine transferase (Me-Sec) with 10.9% and 1.5%, respectively.	[47]
Seeds and seedlings of melon, lettuce and tomato	Na ₂ SeO ₃ 0.1 and 1 mg L ⁻¹ , 2 mg L ⁻¹ , and 5 mg L ⁻¹	Seed imbibition, nutrient solution and foliar, respectively	Positive effect on the antioxidant status and vitamin C concentration in the seedlings.	[48]
Strawberry	Na ₂ SeO ₄ 1.9 and 19 mg L ⁻¹	Nutrient solution	Excessive accumulation of Se in fruits (46 µg per g DW) with 1.9 mg L ⁻¹ , and adequate accumulation (60 µg per 150 g FW) with 19 mg L ⁻¹ . The lower dose increased the biomass and nutraceutical quality, while the higher concentration did not modify the ionomics or growth, and increased the growth regulators, amino acids (phe and arg) alkaloids and isoflavones.	[49]
Strawberry	Na ₂ SeO ₃ 2 mg L ⁻¹	Nutrient solution	Accumulation of 31.2 mg Se per kg in fruits (DW) and increase in antioxidant potential.	[50]
Peas	Na ₂ SeO ₃ 10 g ha ⁻¹ and Na ₂ SeO ₄ 10 g ha ⁻¹	Foliar at the beginning of flowering on sunny days	Na ₂ SeO ₄ was more efficient than Na ₂ SeO ₃ to accumulate 148 and 19 µg Se per kg of pea (DW) for each g of Se applied, respectively.	[51]
Brassica sprouts	Na ₂ SeO ₄ 8.54 mg L ⁻¹	Germination of seeds in soaked paper and 1 mL every 24 h	Increased the accumulation of organic Se: selenocysteine and reduction in glucosinolates.	[52]
Carrot and Broccoli	Powdered of <i>Stanleya pinnata</i> 25–200 g (equivalent to 700 mg per plant)	Soil	Increase in accumulation from 0.5 to 3.5 mg Se per kg in broccoli (DW) and from 0.3 to 22.3 mg Se per kg in carrot (DW). There was no effect on growth.	[53]
Carrot	Na ₂ SeO ₄ 1 mg L ⁻¹	Foliar	Increased yield, reducing root ripening and increased titrable acidity.	[54]

Table 2. Cont.

Crop, Vegetable	Chemical Specie and Dose	Application Form	Highlighted Findings	Reference
Radish	Na ₂ SeO ₄ 5 mg per plant	Foliar, an application when the radish was red	Accumulation of 1200 mg Se per kg of leaves (DW) and 120 mg Se per kg of root (DW). Increased the Cys and GSH activities by 2 and 3 times, respectively. Increased 35% the glucosinolates and Me-SeCys.	[55]
Basil	Na ₂ SeO ₄ 4, 8 and 12 mg L ⁻¹	Nutrient solution	The Se accumulation values in the leaves were 2.8, 7.9 and 16.9 µg per g (DW) in the 4, 8 and 12 mg L ⁻¹ treatments, respectively. All Se treatments did not affect the growth.	[56]
Sweet basil	Na ₂ SeO ₄ 4 mg L ⁻¹	Nutrient solution	Se application increased antioxidants, reduced ethylene synthesis and increased leaf Se in the first cut.	[57]
Nopal	Se 0.8 mg L ⁻¹	To the soil contaminated with Se and salts	Accumulation of 3.9 mg Se per kg of fruit (DW) and cladode 15.9 between 16% and 24% in the form of Me-Sec. There was no effect on antioxidant potential or vitamin C concentration.	[58]
Rice	Na ₂ SeO ₃ 30 g ha ⁻¹ and Na ₂ SeO ₄ 30 g ha ⁻¹	Soil, foliar spray, with granulated urea and nutrient solution in the soil	Accumulation of 0.4 to 0.6 mg Se per kg of grain (DW) when applied as Na ₂ SeO ₄ with granulated urea, the predominant specie was selenomethionine.	[59]
Rice	Na ₂ SeO ₃ and Na ₂ SeO ₄ 120–300 g ha ⁻¹	Foliar	Increased Se in grains, total lipids mostly oleic, linoleic and palmitic acid, and sugars.	[60]
Barley	Na ₂ SeO ₃ 40 g ha ⁻¹ and Na ₂ SeO ₄ 40 g ha ⁻¹	Soil in tillering	Accumulation of 0.069 mg to 0.52 and 2.3 g per kg of grain (DW) with Na ₂ SeO ₃ and Na ₂ SeO ₄ , respectively.	[61]
Winter wheat	Na ₂ SeO ₄ 100 g ha ⁻¹	Drench route during early stem extension	Accumulation of 1.6 to 2.6 µg Se per g of grain (DW). Biomass and yield were not affected.	[62]
Wheat	Na ₂ SeO ₄ 40 g ha ⁻¹	Foliar, an application at the end of the tillering state	Increased the accumulation of Se by 90% in the form of SeMet from 0.089 to 5.5 mg per kg of grain (DW).	[63]
Wheat	Na ₂ SeO ₄ 10 g ha ⁻¹	Soil	Accumulation of Se in grains close to 50% of Se applied with 10 g ha ⁻¹ , and between 46% and 61% of Se.	[64]
Wheat	Na ₂ SeO ₄ + surfactante 21 and 120 g ha ⁻¹	Foliar, two applications at 36 and 41 days after sowing (DAS)	The lower dose increased the production by 48% and biomass by 30%, while the higher dose increased the accumulation from 0.08 to 2.86 mg Se per kg of grain (DW) and the biomass by 31%.	[65]

Table 3. Biofortification of staple and horticultural crops with nSe.

Crop, Vegetable	nSe Dose	Application Form	Highlighted Findings	Reference
Peanuts	nSe 40 mg L ⁻¹	Foliar at 45 and 60 DAS.	Increase in the plant growth, unsaturated fatty acids and antioxidant potential. No toxicity was evidenced.	[66]
Tomato	nSe 10 mg L ⁻¹	To the substrate every 15 days	Increased the tolerance to salinity stress, better in growth, enzymatic antioxidants (APX and SOD) and non-enzymatic (flavonoids) and fruit quality.	[67]
Lubia	nSe 1.18 mg L ⁻¹	Imbibition of seeds for 2 h	Increased the length of the seedlings as well as the activity of the enzymes α , β amylase and protease, total sugars and total proteins.	[8]
Wheat	nSe chemically and biologically synthesized 5 μ M	Imbibition of seedling bare root	Aquaporins are involved in nSe absorption, and Se chemical species such as SeMet and Se IV were accumulated.	[68]
Peppermint	2 and 20 mg L ⁻¹	Foliar 8-leaf seedlings, 15 times every 2 days	Increase in the size of the plant, increase in enzymatic activity of peroxidases and proline at an application concentration of 2 mg L ⁻¹ . Adverse effects on growth and chlorophylls at 20 mg L ⁻¹ were obtained.	[69]
Pepper	20 mg L ⁻¹	Foliar. Plants were sprayed four times at 10 d intervals	Increased chlorophyll, activated phenylpropanoid and capsaicinoid pathways, enhanced photosynthesis.	[70]
Radish, arugula, eggplant, cucumber, tomato and chili pepper	0.001, 0.005, 0.01 and 0.025 mg kg ⁻¹	Directly to soil	0.01 mg kg ⁻¹ increased tolerance to high temperature and increased leaf plate surface.	[71]
Coriander	nSe 25 and 50 mg L ⁻¹	Foliar + surfactant tween80 0.005%, twice every 15 days	The growth of plants subjected to salinity stress was not improved, but the yield, AsA content and electrolyte loss were improved.	[72]
Peanuts	nSe 20 and 40 mg L ⁻¹	Foliar at 30 DAS	Different varieties were tested, the growth was improved, increases in chlorophylls, carotenoids and total sugars, as well as in enzymatic antioxidants.	[6]

Table 3. Cont.

Crop, Vegetable	nSe Dose	Application Form	Highlighted Findings	Reference
Pomegranate	nSe 1 and 2 μM	Foliar one week prior to flowering, in two consecutive years.	The application of 2 μM increased the number and quality of fruits, leaf area, total sugars, phenolic compounds, antioxidants and anthocyanins.	[73]
Broad beans	nSe 10 and 20 mg L^{-1}	Imbibition of seeds	The cytotoxicity and mutagenicity of seedlings intoxicated with the herbicide atrazine were reduced.	[74]
Lime	nSe 50 mg L^{-1}	Imbibition of seeds	The impact of gamma radiation was reduced, and the germination, damping off, percent of albino plants and growth were improved.	[75]
Sorghum	nSe 10 mg L^{-1}	Foliar 10 days before appearance of the pinnacle	nSe reduced the stress due to high temperatures, increased the SOD, CAT, POX and GPX activities, the unsaturated phospholipids and the pollen germination, and decreased the oxidants.	[76]
Watercress	nSe 10, 50 and 100 mg L^{-1}	Spraying seeds twice a day for 8 days	Growth was not affected, phenolic compounds increased at 50 mg L^{-1} and antioxidant capacity at 10 and 100 mg L^{-1} .	[77]

3. Results and Discussion

3.1. Biofortification with Ionic Se and nSe in Crops

3.1.1. Ionic Selenium

Se biofortification in crops for human consumption has yielded encouraging results, including from the nutraceutical perspective to the increase in metabolites that enhance tolerance to adverse factors. Interesting results have been found with foliar application to crops, such as cereals, where both Na_2SeO_3 and Na_2SeO_4 work in a range between 30 and 300 g ha⁻¹. In this range, it is possible to find an increase in the accumulation of Se in grains and stimulation of metabolism. On the other hand, to obtain the same result in vegetables, it is necessary to apply the aforementioned chemical species between 1 and 20 mg L⁻¹ once or twice per cycle.

It has been found that the application of Se in the form of sodium selenite (Na_2SeO_3) between 0.86 and 5 mg L⁻¹, as well as sodium selenate (Na_2SeO_4) in a range of 0.5 to 18 mg L⁻¹, in hydroponic cultures increases the accumulation of this element and the antioxidants in the edible parts of species such as lettuce (*Lactuca sativa*), tomato (*Solanum lycopersicon* L.), strawberry (*Fragaria x ananassa*) and basil (*Ocimum basilicum*).

Similar encouraging results were shown, regarding accumulation and stimulation linked to metabolism, for Se application directly to the soil with both sodium selenite (Na_2SeO_3) or sodium selenate in cereals from 10 to 100 g ha⁻¹ and vegetables in the range of 20 to 940 mg L⁻¹.

The 24 h seed imbibition technique using Na_2SeO_4 at concentrations ranging from 0.1 to 8.54 mg L⁻¹ has been found to be both easy to perform and convenient due to its accumulation and stimulation of the metabolism.

3.1.2. Selenium Nanoparticles (nSe)

Recently, nanotechnology has revolutionized a wide range of areas such as pharmaceuticals, energy, communications engineering, medicine, the environment, chemical industry and plant nutrition, among others, due to the low area/surface ratio, states of aggregation and stability of nanoparticles. The synthesis and use of nSe as a nutrient and biofortifier has proven to be an interesting strategy because, additionally, it has been found to possess greater chemical stability, biocompatibility, rapid absorption and less toxicity compared to the ionic forms of this element [78,79]. As can be seen in Table 3, foliar applications range from 10 to 50 mg L⁻¹ in species such as coriander (*Coriandrum sativum*), pomegranate (*Punica granatum*), peanut (*Arachis hypogaea*) and wheat (*Triticum aestivum*).

Different studies have been carried out by imbibing seeds or bare roots at nSe concentrations ranging from 1.18 to 50 mg L⁻¹; results have shown no changes in growth, but increases in Se in the edible parts and antioxidant content. In addition, various works have been carried out where nanoparticles are applied directly to the substrate in ranges as wide as 10 to 100 ppm between horticultural species.

Information regarding nSe application in biofortification and improvement in plant metabolism (e.g., the appropriate concentrations in hydroponic or soil cultures) is still lacking.

In the same way, the mechanism by which these nanoparticles are absorbed is still not fully elucidated. One of the widely accepted options is that absorption happens both intra- and extracellularly through the tissues, until reaching the xylem; the way in which nanoparticles pass through the casparian strip is not yet clear, but it could be through the meristematic zone. The cell wall acts as a physical barrier; however, it contains pores with diameters between 5 and 20 nm, and nanoparticles smaller than this will enter freely [80]. It is also possible that nanoparticles greater than 20 nm enlarge the pores, inducing the formation of cavities to enter via endocytosis or even through transmembrane proteins or ionic channels [81].

As described above, to date, encouraging results have been obtained in the field of biofortification with ionic selenium in horticultural species widely consumed by humans, such as lettuce and tomato,

as well as in the stimulation of redox metabolism, which leads to an increase in tolerance to adverse factors. However, a promising alternative is the use of selenium nanoparticles, where a reduction in application complexity may be achieved, and this leads to important results in the potentiation of antioxidant metabolism, the promotion of agronomic sustainability and a reduction in waste. Therefore, more research should be carried out on the plant cell level as well as interactions within the entire trophic chain and environment [82].

3.2. Stimulation of Plant Metabolism

It has been shown that the application of selenium in plants, via foliar, hydroponic cultures, directly to the soil or by imbibition, stimulates plant metabolism, resulting in improved growth, improved synthesis of molecules involved in defense [83] and an increase in stress tolerance [84]. However, the exact mechanics under which these processes occur are unclear. The main pathway of selenium's impact will be pointed out below, when it is applied in ionic form and in nanoparticles.

3.2.1. Ionic Selenium

Several research works have been carried out to demonstrate the effect of selenium on plant metabolism, more specifically the impact on phytochemicals, and the results have been quite varied. In a relatively constant way, it has been established that low concentrations of Se can act as an antioxidant and high concentrations as a pro-oxidant [85]. However, establishing the values of "high" or "low" concentrations is difficult. According to what is shown in Table 2, each form of application tolerates different selenium concentration ranges, taking into account the following pattern: imbibition > hydroponics > foliar > soil.

The application of Se and its impact on antioxidant metabolism in plants have been linked to both primary and secondary metabolites.

Primary Metabolites

Regarding primary metabolites, there is an increase in the activity of glutathione peroxidase (GPX), an enzyme that involves selenic acid (PSeOH) in its catalytic cycle. This reacts with glutathione, a tripeptide that functions as a coenzyme in this reaction and contains a sulfhydryl functional group (-SH), to form a selenyl-sulfide adduct. At this point, a second GSH molecule intervenes, and here selenol (PSeH) is formed in the active site where peroxide reduction takes place [86]. In addition, it has been reported that the application of selenium promotes an increase in the activity of enzymes with an antioxidant capacity, such as ascorbate peroxidase, catalase, superoxide dismutase, dehydroascorbate reductase, glutathione reductase and monodehydroascorbate reductase [87].

Although not as thoroughly studied, it has also been related to the increase in other non-catalytic antioxidant proteins, such as thioredoxin (TrxR) and P protein, the latter containing more than 10 Se atoms [88].

In a study carried out in rapeseed (*Brassica napus*), important effects on primary metabolism were elucidated, including a higher concentration of glucose, coupled with higher ATP production; increased superoxide dismutase activity in the mitochondria and potentiation in the pentose pathway phosphate, which supplies a large number of non-enzymatic antioxidants; as well as a reduction in the tricarboxylic acid (TCA) cycle [89].

An increase has also been found in the synthesis of sulfur amino acids (Cys and Met) and selenoamino acids such as SeCys and Semet, which are incorporated into proteins. However, there is also evidence of other non-protein amino acids being synthesized, such as γ -glutamyl methyl seleniocysteine (γ -gluMetSeCys), methyl-SeCys and methyl-Semet, mainly in hyperaccumulator families of S, such as *Brassica* and *Allium*. In addition, these metabolites have shown powerful anticancer activities [47,52]. Within this same group of plants, volatile species such as dimethyl-diselenide (DMDS) are produced, which partly controls selenium accumulation. In non-accumulating plant species (those

that accumulate < 100 mg Se per kg DW), the methylated species of selenium, dimethyl selenide (DMSe), is synthesized [90].

It is known that the presence of Se promotes increases of sulfur transporters sultr 1 and 2 as well as ATP sulfurylase at the transcriptomic level, which leads to greater absorption of sulfur and, therefore, the synthesis of both primary and secondary metabolites that contain these elements [91]. However, it is important to highlight the balance between Se and S concentrations. It has been found that high Se and low S concentrations promote competition, avoiding adequate absorption of sulfur and, in this case, a reduction in the synthesis of the mentioned metabolites [92].

In a study carried out in rice (*Oryza sativum*), a three-fold increase in fatty acids (oleic, linoleic and linolenic) was found after the application of selenite and selenite; however, the metabolic pathway that was affected is not clear [60].

Secondary Metabolites

After the application of ionic species of selenium, both positive and negative effects have been reported on the concentration of secondary sulfur metabolites such as glutathione and glucosinolates. For the first, examples of increased concentrations were evidenced in radish (*Raphanus sativum* L.) [55] and plum trees (*Prunus domestica*) [93]. On the other hand, the reduction in GSH found in strawberry plants was associated with an increase in the concentration of its oxidized form: glutathione disulfide (GSSH) [94].

Various S hyperaccumulating plants, such as broccoli (*Brassica oleracea*), show increased synthesis of glucosinolates with exogenous application of Se, which participate in defense against herbivores and are synthesized mainly from methionine and phenylalanine [95].

There is a close relationship between the metabolism of sulfur and nitrogen; the proportion of these in most plant species is preserved between 1:45 and 1:30, respectively. About 80% of S and N assimilation is directed to the production of protein amino acids. After modifications in the absorption of S due to the aforementioned effect on transporters with the application of Se [96], the content of metabolites dependent on these elements, such as glucosinolates, is also affected.

It has also been found that selenium modifies the phenylpropanoid pathway, increasing the enzymatic activity of phenylalanine ammonium lyase (PAL), which is why several investigations have found a positive correlation with phenolic compounds, which act as non-enzymatic antioxidants [49]. Similarly, an increase in the synthesis of ascorbic acid has been found, which functions as a direct scavenger of reactive oxygen species and a cofactor of enzymes with antioxidant activity, such as APX [97].

In summary, selenium stimulates metabolism in two ways: (1) via antioxidants, where it participates in the catalytic cycle of enzymes such as APX, and (2) via pro-oxidants, where selenite and selenate probably mimic moderate oxidative stress and the detection of synthesized reactive species will trigger signaling to achieve the formation of all antioxidant machinery [98].

3.2.2. Selenium Nanoparticles (nSe)

Unlike readily available research on Se applications in its ionic form, research on its nanoparticulate (nSe) form is much more recent and scarcer. Although results have been favorable, even more than that observed in the ionic form, there is still a long way to go. It is generally known that nSe have a strong impact on antioxidant metabolism, which is why they have probably been successfully tested in various species to cope with different types of stress. Examples of this are reported in sorghum (*Sorghum bicolor*) subjected to high temperatures [65]; strawberry, tomato, coriander, basil and barley (*Hordeum vulgare*) under stress by salinity [57,62,76–78]; increase in tolerance to stress caused by pathogens such as *Alternaria solani* [79], *Meloidogyne incognita* [80] and *Botrytis cinerea* [99]. The reason why Se can trigger these beneficial effects could be related to a change in the redox status of the cell, causing a greater stimulation in the synthesis of non-enzymatic antioxidants such as lycopene and carotenoids. It could also be related to an increase in the activity of the main enzymes involved in the antioxidant

pathway such as glutathione peroxidase, where selenium acts as a cofactor, and it is possible to obtain ionic selenium from nanoparticles [66]. A reduction in the loss of photosynthetic pigments such as chlorophyll a and b has also been noted during adverse conditions, which leads to an improvement in the photosynthetic rate, maintenance of homeostasis and improvement in growth [62]. This can be explained, at least partially, by nSe being stored in the thylakoid membranes, providing them with stability. A reduction in lipoperoxidation has also been proposed as protecting and stabilizing some enzymes that catalyze the synthesis of these photosynthetic pigments [6].

4. Conclusions

This review addressed the doses and forms of application of selenium ionic (Na_2SeO_3 and Na_2SeO_4) and nanoparticulate in the main crops, for biofortification purposes as well as the implications in the synthesis of molecules with reducing power that entails an increase in nutraceutical quality and stress tolerance.

5. Outlook

When the available information regarding ionic Se and nanoselenium (nSe) applications in different crops is analyzed in parallel, it can be seen that there is a need to address the missing information in order to more precisely understand the absorption, assimilation and metabolism of both selenium forms.

It is necessary to test the Se nanoparticle application more extensively, especially in crops widely consumed by humans, such as vegetables. The recommended form of application based on a cost–benefit analysis is the foliar route at concentrations less than 10 mg L^{-1} and monitoring the genomic and metabolomic behaviors around this process.

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