

Review

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Selenium Biofortification as a Sustainable Solution to Combat Global Selenium Malnutrition

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Review

Se Biofortification as a Sustainable Solution to Combat Global Se Malnutrition

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Abstract: Selenium is an essential micronutrient that is critical for the maintenance of human health. It has a significant impact on immune function and is effective in the prevention of several metabolic-related illnesses. Furthermore, Se deficiency affects millions worldwide, particularly in regions such as China, Eastern Europe, and Africa. This review examines the current knowledge in Se biofortification, specifically focusing on the Se application to plants and soils, the mechanism of Se uptake and utilization, genetic variation in Se accumulation, and genetic modification to achieve high biofortification targets. Data from many studies show substantial increases in the Se levels in biofortified crops. For instance, foliar application of Se-enriched fertilizers increased Se concentration in wheat by 42–67 µg/kg and in corn by 19–36 µg/kg. Se biofortification in rice showed Se content variations ranging from 5 to 1370 ng/g, with a substantial increase observed from Se-rich soils. The qualitative analysis demonstrates that public health is improved when people have access to fortified cereals and pulses. There are many economic benefits that lead to a reduction in healthcare costs and increased productivity. Despite these promising outcomes, many challenges remain to overcome. Our findings suggest that future research should focus on developing uniform distribution of Se in major agricultural crops, optimizing the bioavailability of the nutrients and developing consumer acceptance. Furthermore, refining biofortification techniques to deliver Se into the edible parts, particularly to the grain in cereals, exploring the genetic basis of Se uptake in crops, and developing public health policies to support widespread adoption is essential. Se biofortification of agriculturally important crops is the main strategy to combat global Se malnutrition, which will have significant economic and health benefits. Continued multidisciplinary research and policy support are essential to realize this target ensuring global food and nutrient security in the long term.

Keywords: micronutrient deficiency; bioavailability; agriculture; cereals; food security

Introduction

Selenium is needed for all the living beings including microorganisms, plants, animals and humans (Fu et al. 2002; Novoselov et al. 2002; Lobanov et al. 2007). Micronutrient deficiency or malnutrition is severe among humans (Qaim et al. 2007). Iron, zinc, copper, calcium, magnesium, iodine, and selenium were found to be commonly insufficient in the human diet (White and Broadley 2009; Guerinot and Salt 2001; Goldhaber 2003). This is called chronic hunger (Stein 2009) or hidden hunger (FAO 2005), or micronutrient malnutrition (Yang et al. 2007). Children and breastfeeding mothers are the most affected groups to malnutrition (WHO 2002). Growing staple crops in soils with limited micronutrients (Mao et al. 2014), low income, lack of awareness of a balanced diet (Qaim et

al. 2007) and increased grain yield by decreasing nutrient density in cereals and legumes (Garvin et al. 2006, Fan et al. 2008a) are identified as the main reasons for micronutrient malnutrition. Micronutrient malnutrition is common in poor households who are satisfied with their food needs through cereals and pulses (Qaim et al. 2007) which leads to loss of immunity, mental impairments, and high mortality rates (Amarya et al. 2015).

Among micronutrients, deficiency in Fe, Zn, and Se was reported in 50% of the population (Zhao and McGrath 2009), and 260 million are iodine or Se deficient (Caballero 2002), billion are iron deficient, 2.7 billion are Zn deficient, and the majority is lacking vitamins (Haddad et al. 2004, Hotz and Brown 2004). According to Combs (2001), Se is deficient in 500–1000 million people worldwide and this equals to 15% of the world population (Thavarajah et al. 2011).

The World Health Organization has identified Se-deficient, Se-low and Se-adequate countries (Yuan et al. 2012). Mombo et al. (2016) have mapped the locations according to Se availability worldwide (Figure 1).

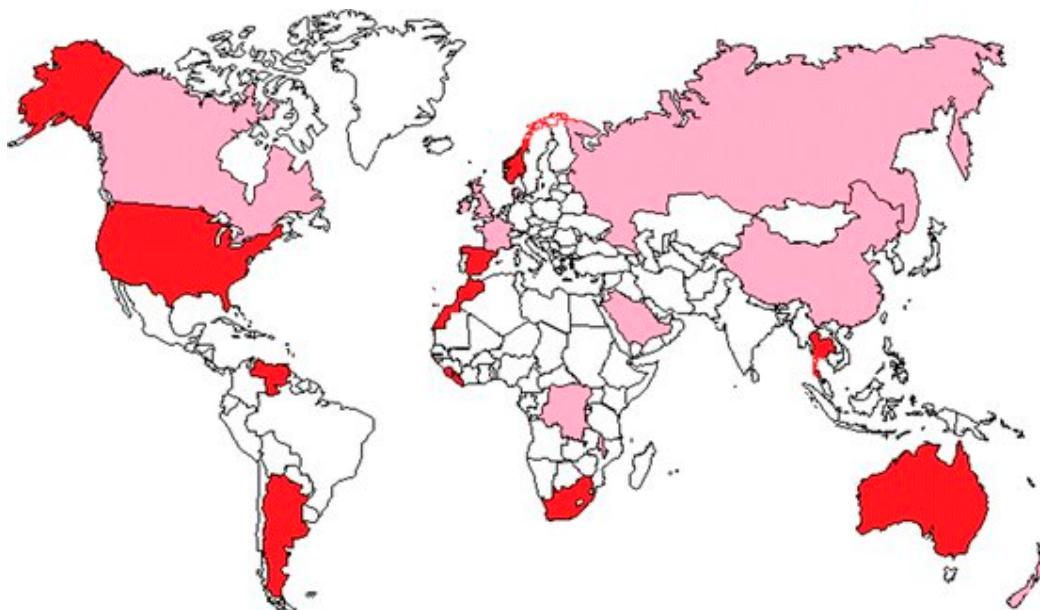


Figure 1. Soil Se levels in the world. Regions naturally rich in Selenium appear in red; pink areas correspond to regions with naturally low Se concentration and white areas correspond to regions with unknown concentration. Source: Mombo et al. (2016).

Se Dietary Intake and Health Implications

Two independent groups discovered Se in glutathione peroxidase (GPx) in 1973 (Pedrero and Madrid 2009). GPx activity is considered a feature to evaluate Se requirement in the human body (Levander et al. 1983). According to the function of GPx, the daily requirement of Se for a woman is 55 µg and for a man is 77 µg per day (Pedrero and Madrid 2009). The recommended daily intake of Se varies by region. A daily Se intake of 55 µg is recommended for Indian subtropical regions and temperate North American regions (Thavarajah 2011), and 60–75 µg for Europe, Australia, and Asia (Giray and Hincal 2004; Lyons et al. 2005a; Spallholz et al. 2004). On the other hand, more than 300 µg of Se per day is a critical level, according to findings in Europe (Thiry et al. 2012) and according to Wu et al. (2015), the recommended nutritional intake of Se is 50–200 µg/day. Hence, as a range, 55–200 µg Se per day has been recommended for humans (Rayman 2000; Thomson 2004; WHO 2009). Using the average values from two studies from China and New Zealand, Goldhaber (2003) arrived at a value of 450 µg Se per day as the Estimated Average Requirement (EAR) of Se.

The required amount of a micronutrient for a daily diet can be supplemented by adding such an amount to the food during any food processing step (Graham et al. 2007). Daily Se intake for humans

must be assessed carefully since the Se content and Se bioavailability differ with the soil in which plants were grown and the form of selenium ingested. It is not possible to recommend dietary items for Se intake because the soil in which they are cultivated determines the content of Se in the food. However, knowing the origin of, for example, wheat in the bread, the Se adequacy of the diet can be judged. For example, changes in blood Se in Hamilton, New Zealand were consistent with values calculated from variations in dietary intake of Se of wheat products from the blending of New Zealand wheat (11 ng/g Se) with imported Australian wheat (150 ng/g Se) (Watkinson, 1981). Furthermore, there was a positive correlation of selenium level in sunflower seeds with the concentration in the soil it was grown in an experiment with varying soil Se concentrations (Dhillon and Dhillon, 2009).

Se in the Human Body

Balancing Se concentration in our blood and cells has important health implications. The excess of Se can be toxic, and its deficiency can result in disease.

Se Toxicity in Humans

Integrating Se in selenocysteine (SeCys) and selenomethionine (SeMet) into the proteins (Pedrero and Madrid 2009), which alters protein structure, is the cause of Se toxicity in humans (Terry et al. 2000; Ellis and Salt 2003). Se is needed in a very small amount (Kieliszek and Błażejak 2013), and in humans, it can lead to health issues if consumed in excess. The main reason for Se toxicity is due to the narrow range of daily Se requirement (Thornton et al. 1983; Rosenfeld and Beath 2013; Yang et al., 1983). This is also called a “double-edged sword element” and an “essential toxin” (Levander and Burk, 2006). Due to its narrow requirement and intolerable toxic ranges, Se supplementation should be prescribed carefully to meet individual dietary needs. Plants cultivated in soils containing more than 3.0 mg kg⁻¹ of Se are not safe for consumption (Hawkesford and Zhao, 2007). Herbivores feeding on Se hyperaccumulator plants convert methyl-SeCys to SeCys, and SeCys integrates into proteins causing Se toxicity (Freeman et al. 2006b). The daily average Se intake of 550 µg caused selenosis symptoms in a high Se region in Hubei Province of China (Huang et al. 2013). Selenosis causes skin lesions, nerve damage, and liver enlargement (McLaughlin et al. 1999). Continuous work with some electronic industries causes acute Se intoxication (Szpunar et al. 2003). Se toxicity affects not only humans, but also fish and land animals (Yang et al. 1983; Dörr et al. 2008) and such food items are not safe for consumption.

Se Deficiency in Humans

In many regions of the world, Se consumption is lower than 40 µg per day (Combs 2001; Navarro-Alarcon and Cabrera-Vique 2008). Se has the ability to prevent heart diseases and muscle disorders (Nèvre 1996; Fernandes et al. 2014). For example, Keshan and Kashin-Beck diseases are reported in the regions with insufficient Se in the soil (Yang et al. 2007). Keshan disease is an endemic cardiomyopathy and Kashin-Beck disease reduces human working ability and well-being (Yang et al. 2007) and causes osteoarthritis (Allander 1994). In humans, having low levels of Se has been linked to a higher likelihood of contracting HIV/AIDS and other viral diseases (Gailer et al. 2000; Rayman 2000) and male infertility (Nèvre 1996; Ellis and Salt 2003). Any further reduction of Se leads to the risk of arsenic (As) toxicity in humans (Kibriya et al. 2007). Most importantly, epidemiological studies have indicated an inverse relationship between Se intake and the incidence of certain cancers in humans and tumors in mammals. Blood or plasma levels of Se are usually lower in patients with cancer than healthy humans (Whanger 2004) and inclusion of methylselenocysteine (MeSeCys) in the diet of mammals reduces the incidence of certain cancers (McKenzie et al. 2009). Various organic compounds containing Se play distinct roles within the human body involving a number of metabolic processes (Table 1).

Table 1. Se containing biological compounds and their role in the human body.

Se in biological compound	Properties	Reference
Glutathione peroxidase (GPx)	Se containing enzyme, protecting cells from oxidative damage	Parada and Aguilera 2007; Thiry et al. 2012
Thioredoxin reductases (TrxR)	Maintaining the cellular redox balance, important for various cellular processes, including DNA synthesis, repair, and cell growth.	Thiry et al. 2012; Lu and Holmgren 2014
Iodothyronine deiodinases (DIO)	Responsible for the conversion of thyroid hormones.	Lu and Holmgren 2014
Selenoprotein	Free-radical scavenging activity in the human body with cancer preventive properties	Clark et al. 1996; Rayman 2000; McKenzie et al. 2001; Abdulah et al. 2005
Methylselenol	An anticancer agent	Abdulah et al. 2005
Methylselenocysteine and selenomethionine	More anti-carcinogenic and more bioavailable compound**	Rayman 2008; Brummell et al. 2011

** Bioavailable fraction: The proportion of the available nutrient in the blood stream to ingested amount of nutrient (Parada and Aguilera 2007). *Bioactive fraction: The amount of Se that transformed into active seven metabolites are the bioactive Se (Thiry et al. 2012). Se is easily measured in biological tissues (Goldhaber 2003).

Alleviation of Se Malnutrition in Humans Through Food Intake

Se malnutrition can be addressed in five steps: finding Se-rich crop species, transformation of crop species unable to metabolize Se to enable them metabolise Se, increasing micronutrient bioavailability, raising consumer awareness of malnutrition and nutrients, and fertilizer development and application (Yang et al. 2007; Stein 2009; Brummell et al. 2011).

Food diversification is the main solution to avoid Se deficiency in poor people's diets (Meenakshi et al. 2010), while enriched supplements are administered in developed countries (Schrauzer 2001; Finley 2005). Fifty-five micrograms of daily dietary Se intake (Bendich 2001) can be supplemented in inorganic form. Inorganic sodium selenite is a commonly used form for Se supplementation that is prepared using yeast (*Saccharomyces cerevisiae*) (Hilton et al. 1982; Gatlin and Wilson 1984; Pedrero and Madrid 2009; Felton et al. 1996; Schram et al. 2008).

Se is supplied in salt in treating Kashin-Beck disease (Bawa et al. 1992). The amount of Se that is available in commercially produced Se-enriched products varies (Pedrero and Madrid 2009). The toxicity of Se has been reported due to this discrepancy (Helzlsouer et al. 1985) and the factors that interfere to reduce mineral absorption in the gut must be addressed to overcome this problem (White and Broadley 2009). Increasing pro nutrients and decreasing antinutrients such as oxalate, polyphenols or phytate are some approaches for enhancing Se absorption in the human gut (Graham 2007; Brinch-Pedersen et al. 2007; Graham et al. 2007).

Organic Se forms are more bioavailable than inorganic forms in food (Pedrero and Madrid 2009), and have a higher retention power and a lower toxicity (Brummell et al. 2011; Thiry et al. 2012). Further, the bioavailability of Se is higher in plant-based food than in meat (Combs 2001). Bioavailable Se in goat and sheep milk is greater than Se in cow milk (Shen et al. 1996). Se biofortification in crops or food fortification are reliable solutions for increasing Se availability and consumption (McKenzie et al. 2009; White and Broadley 2009). Future research need to be focused on enhancing the bioavailability of Se in both animal and plant sources. Selenoprotein production in the body can be achieved by ingestion of Se as sodium selenate, selenite, and SeCys, which is mainly

practiced for animal rearing for meat (Pedrero and Madrid 2009). The metabolic pathways of Se cycling within the human body are illustrated in Figure 2.

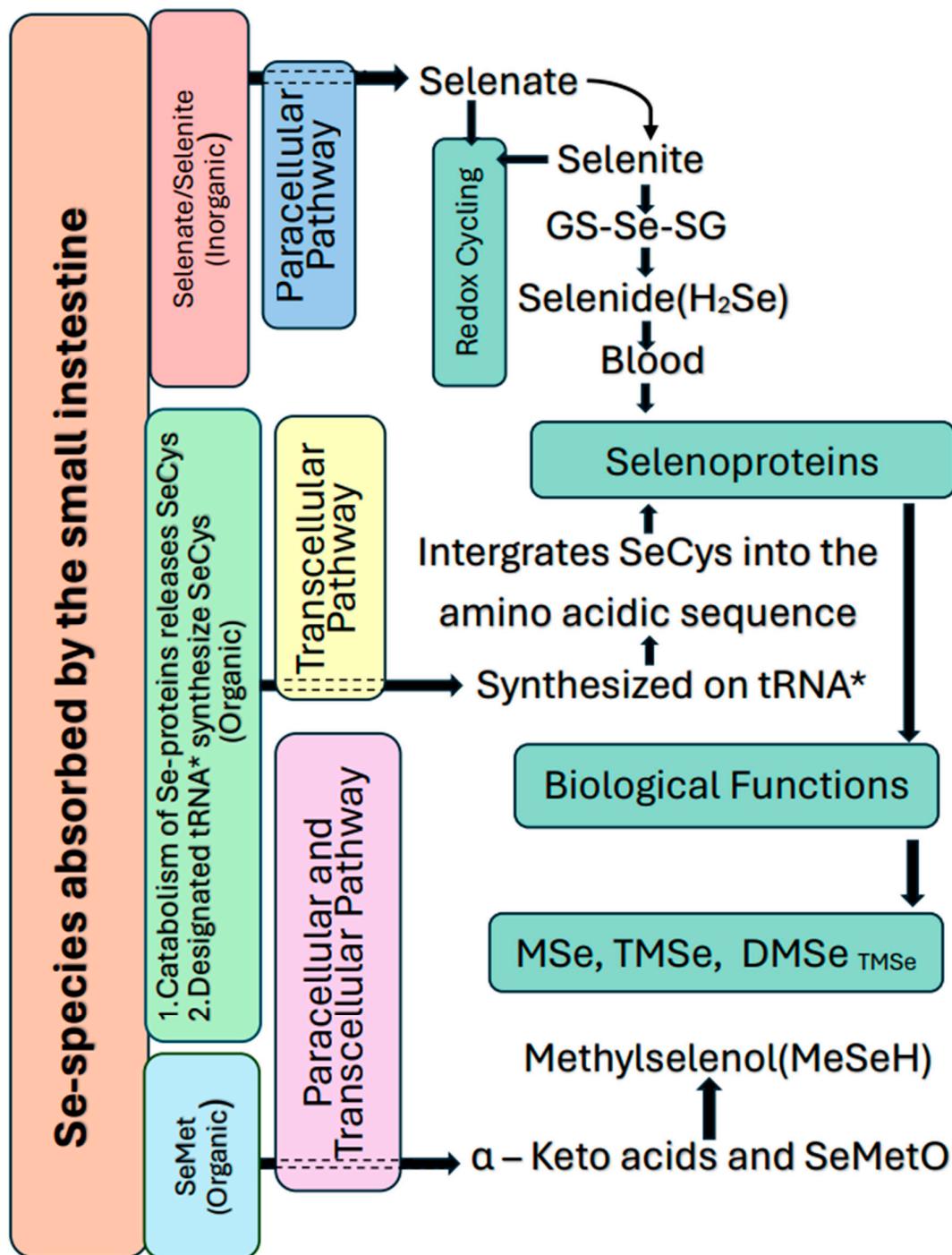


Figure 2. Cycling of selenium in the human body.

Selenium in the Environment

Se compounds in the environment are diverse (Figure 3). Se occurs both in oxidation and in organic forms in the natural environment (Qin et al. 2012). Twenty-five selenoproteins contain Se as

structural proteins and enzymes (Kryukov, Castellano et al. 2003; Lu and Holmgren 2009). Glutathione peroxidases, thioredoxin reductases and iodothyronine deiodinases are Se containing enzymes (Rayman 2012; Zhang 2009; Stein 2009). Selenoprotein production in the body can be achieved by ingestion of selenium as sodium selenate, selenite, and SeCys, which is mainly practiced for animal rearing (Pedrero and Madrid 2009). Trimethyl selenonium in the urine and dimethyl selenide (DMSe) in exhaled gases are two bodily excretions of Se (Ganther 1986; Stadtman 1991). A few Se-contained compounds in plants are SeMet, SeCys, γ -glutamyl lenomethyl selenocystine, MeSeCys, selenocystathione, selenohomocysteine and selenomethyl selenomethionine (Reeves and Baker 2000; Montes-Bayón et al. 2002). Se containing volatile gases, namely DMSe, dimethyl diselenide (DMDSe), diethylselenide (DESe) and diethyldiselenide (DEDSe) are emitted to the environment (Dauchy et al. 1994; Gómez-Ariza, et al., 1998). Microbial activities based on oxidation, reduction, methylation, and demethylation change the status of Se (Stolz et al., 2006). Some bacterial and fungal species can convert Se substrates SeO_4^{2-} , SeO_3^{2-} , Se^0 , SeS_2 , H_2SeO_3 , NaSeH into methylated products such as DMSe, DMDSe, methylselenol, dimethyl selenide sulfide (DMSeS), and DMSeDS (Eswayah et al., 2016). The predominant groups of Se-methylating organisms that can be found in soils and sediments are bacteria and fungi, while bacteria are the active Se-methylating organisms in the aquatic environments. The volatile Se compound produced by most organisms is DMSe and is non-toxic to mammals (Frankenberger and Arshad, 2001).

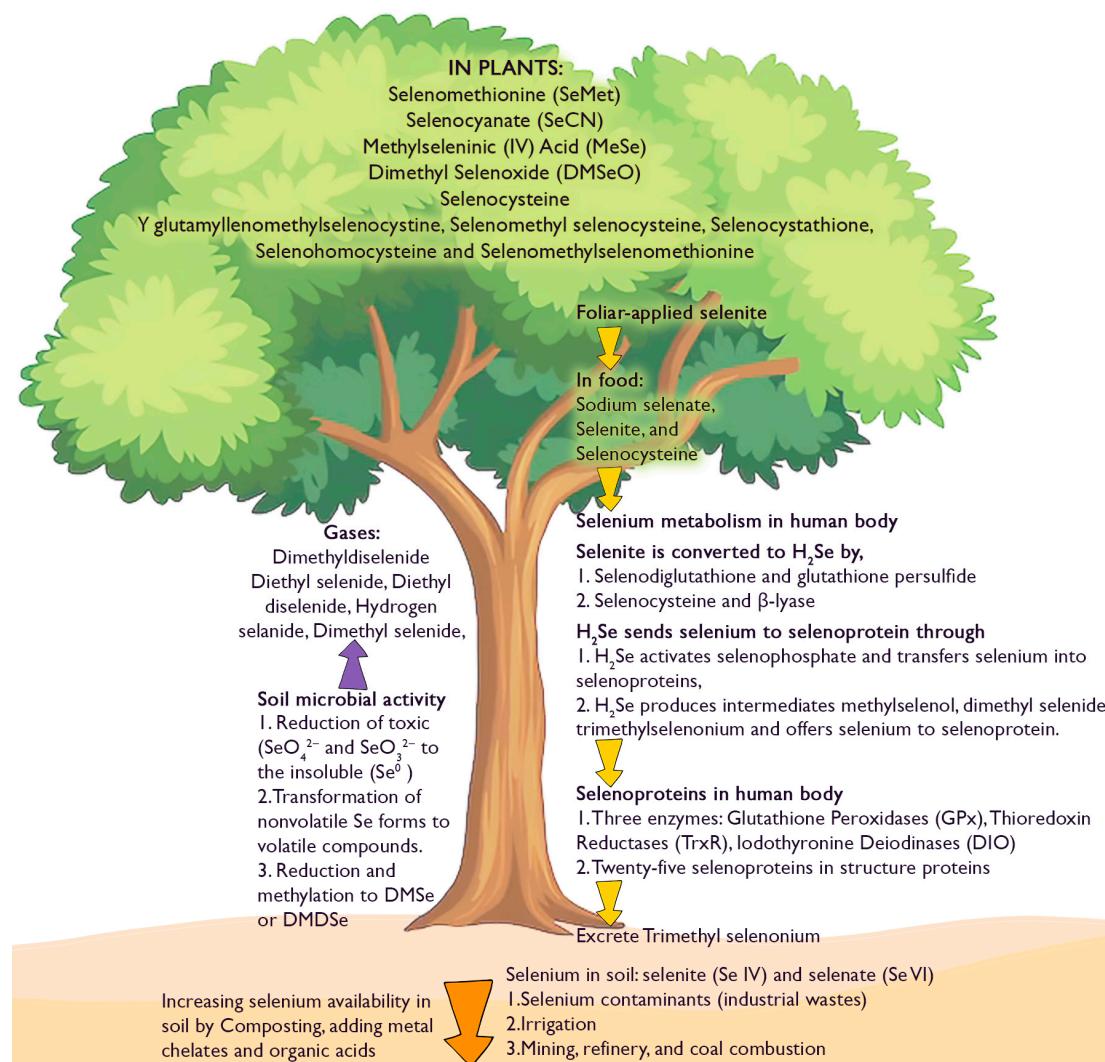


Figure 3. Diverse forms of Se in the environment.

Se in Plants

The bioconcentration factor (BCF) in the soil for Se is calculated as the proportion of Se in the plant to Se in the soil (Wang et al. 2012). BCF is reported in a range of 0.23 to 1 (Dhillon and Dhillon 2009; Sun et al. 2010; Wang, et al. 2012; Bujdoš et al. 2005). Se mainly acts as an antioxidant in plants (Xue et al. 2001; Djanaguiraman et al. 2005). Yield increment with Se application is also evident for many crops and pastures (Qaim et al. 2007) along with iron and zinc for improved plant vigour (Graham et al., 1999; Welch 2002). It has been reported that Se promotes the carbohydrate metabolism in *Solanum tuberosum* (L.) (Turakainen et al. 2004).

The most bioavailable form of Se in soils is selenate, which is taken up by plants using enzymes of the sulphur assimilation pathway since most of the transporters and enzymes involved in the uptake, translocation, and assimilation cannot discriminate between the S and the Se forms of their substrates (Sors et al. 2005; Brummel et al. 2011). Selenate is reduced to selenite and converted to SeCys (Sors et al. 2005). In Se hyperaccumulators, SeCys is methylated to MeSeCys by the action of selenocysteine methyltransferase (Neuhierl et al. 1996; Brummell et al. 2011).

Inorganic Se can be converted to the organic form of Se (e.g.; MeSeCys and glutamyl selenomethyl selenocysteine) in plants (Combs and Gray 1998; Tapiero et al., 2003; McKenzie et al. 2009; Brummell et al. 2011). The predominant compounds of Se in different crops are listed in Table 2. Various parts of plants accumulate distinct quantities of Se. For example, in corn, the order of Se accumulation changes as leaf >root>seed>stalk (Wang et al. 2012). The increasing order of Se in rice was arranged as husk>straw>bran>whole grain >polished rice (Sun et al. 2010). Typically, the seed contains a lower concentration of Se compared to other parts of cereals. This indicates that the Se deficiency in our diets is caused not by the poor intake of Se by the cereal crop, but rather in its transportation into the grain. Therefore, the mechanism responsible for loading Se into the grain endosperm is likely the factor that restricts its accumulation. Nevertheless, there is a lack of comprehensive understanding regarding these processes.

Table 2. Prominent Se compounds in different crops.

Crop	Prominent Se compounds	Reference
Garlic, onion, and leeks,	Selenomethyl cysteine, methyl selenocysteine (MeSeCys),	Beilstein et al. 1991; Ogra et al. 2005; Avila et al. 2013
Broccoli		
Brassica and Allium	and Glu-MeSeCys	Beilstein et al. 1991; Ogra et al. 2005; Whanger 2002; Rayman 2008
Indian mustard	Selenomethionine(SeMet) SeOMet,	Grant et al. 2004
Broccoli sprout	MeSeCys and glucosinolates	Avila et al. 2013
<i>Arabidopsis thaliana</i>	Selenite	Beilstein et al. 1991; Kahakachchi et al. 2004; Pilon-Smits and Quinn 2010
Wheat, barley, and rye	SeMet	Stadlober et al. 2001, Poblaciones et al. 2014
Brazil nuts	SeMet	Vonderheide et al. 2002
Shiitake mushrooms	SeMet	Ogra et al. 2004
Rice	SeMet (Dominant), MeSeCys, SeCys	Beilstein et al. 1991; Li et al. 2010
Radish	MeSeCys and -glutamyl S MeSeCys	Combs and Gray 1998; Tapiero et al. 2003

Se in Cereals

Around 60–80% of Se requirement in the global human diet is provided by grains (Stadlober et al. 2001). Northern Indian villagers obtain ~90% of their Se requirement solely from grains (Hira et al. 2004). In contrast, cereals contribute around 18% of the total Se intake in Finland (Eurola et al., 1990). Cereals significantly convert selenate to SeMet (Stadlober et al., 2001). Oat has an increased Se content of around 72.5–203.08% by fertilizer application (McKevith, 2004). The foliar application Se effectively increased Se content in whole wheat (42–67 $\mu\text{g}/\text{kg}$) and corn (19–36 $\mu\text{g}/\text{kg}$) (Milovac et al., 1998). The Se content in wheat is mostly influenced by the geographical region (Hawkesford and Zhao 2007). In regions where the soil is rich in Se, cereals can contribute significantly to daily Se requirements.

The required amount of Se for the human diet can be achieved by foliar application of selenate, or soil application of selenite in rice (Boldrin et al. 2013). The Se content of rice varies even within the same country, and is as follows: China 2–1370 ng/g, India 5–371 ng/g, Japan 26–109 ng/g, Thailand 6–487 ng/g and USA 6–406 ng/g (Williams et al. 2009; Kelly et al. 2002). Around 75% of the rice samples do not reach the human Se requirements according to Williams et al. (2009). This content can be boosted approximately by double through improved management practices (Fang et al. 2008). The rice bran contains a Se content that is ten times more than that found in the endosperm. This suggests that there is an important barrier in the transfer of Se into the inner endosperm of the grain. Not only Se, but other micronutrients such as Fe and Zn also exhibit similar trends (Kamral et al., 2023). The primary type of Se found in rice bran is SeMet, as reported by Li et al. (2010). SeMet is mostly accumulated in rice bran when Se is added as a fertiliser (Stadlober et al. 2001). Other forms, such as SeCys and MeSeCys, are also present in rice (Li et al. 2010; Sun et al. 2010). However, MeSeCys and SeCys are present in lower concentrations (Sun et al. 2010). Though 80% of Se is SeMet (Guzmán et al. 2009), up to 50% of MeSeCys (~50%) has also been reported in rice in other studies (Williams et al. 2009).

The nutritive value of Se in the crop depends on the conversion of inorganic to organic Se (Whanger 2002; Hawkesford and Zhao 2007). Inorganic Se is easily converted into organic Se by rice (Li et al. 2010). The spatial distribution pattern of Se in rice grains has been demonstrated by applying selenite, SeMet, and MeSeCys (Carey et al., 2012). It has been demonstrated that the form of Se application decides Se localization in the rice grain: In selenite-treated grains, ovular vascular trace region accumulates Se and, in the SeMet applied rice plants Se is high in seed external layers and in the endosperm. In MeSeCys applied plants, Se was high in the aleurone layer and the embryo (Carey et al. 2012). These findings suggest that the high molecular mass of MeSeCys might impede the passage into the inner endosperm of the grain.

The rice husk inorganic Se content is ~10 times greater than the endosperm inorganic Se and outer pericarp and aleurone tissues also contain higher Se than the endosperm (Carey et al., 2012). Rice endospermic Se is mainly organic, while rice bran contains both organic and inorganic Se (Williams et al. 2009). These findings indicate that either the transfer of Se into the grain or the synthesis of organic Se in the inner endosperm is the component that limits the organic Se content in the cereal grain. Moreover, these findings also suggest that cereals, specifically grains such as wheat and rice, have a major role in fulfilling the global Se dietary needs. These needs can be partially met through agronomic fortification methods, such as applying Se fertilizers, implementing specific cultivation practices, and utilizing cultivars with increased potential to accumulate Se.

Se in Soil

The Se speciation is determined by the physical features of the soil (Frankenberger and Benson 1994) (Table 3). Se is found in soil primarily as selenide, selenite, and selenate ions, while it is typically present as selenate or selenite ions (Hopper and Parker 1999). The availability of Se species in the soil is given as selenate > SeMet > SeCys > selenite > elemental se > selenide (Kabata-Pendias, and Szteke, 2015). Selenate ions (SeO_4^{2-}) can form salts with various cations (eg; Na_2SeO_4). Selenite is a Se-containing ion with oxygen (SeO_3^{2-}), found in salts (eg; Na_2SeO_3), while selenide (Se^{2-}) is a compound

formed by the combination of Se with another element, typically a metal or non-metal, in the form of a selenide ion (eg; H_2Se , ZnSe).

Table 3. Se speciation in soil.

Valency	Remarks	Reference
Se (0)	Produced by microbial activities Produced by the physical reduction of both Se (+4) and Se (+6) becomes oxidized forms Insoluble, immobile and poorly bioavailable Very common and found everywhere at the concentration range of 0.01 to 2.0 mg kg^{-1} Elemental Se is prominent in anaerobic soils	(Chen et al. 2009; Mishra et al. 2011). Chen et al. 2009; Mishra et al. 2011 Kulp and Pratt 2004; Lenz and Lens 2009 (Fordyce 2005). Elrashidi et al. 1987
Se (+2)	Very slightly mobile in acid soils, forms stable minerals and organic compounds. The selenide minerals produced after biotic reduction, and selenide minerals are bioavailable. Major species: HSe^- , $\text{H}_2\text{Se}^\circ$ Selenide is prominent in anaerobic soils	Kulp and Pratt 2004; Lenz and Lens 2009; Kabata-Pendias, and Szteke, 2015 Elrashidi et al. 1987; Wu et al. 2015
Se (+4)	The most toxic valence state	He et al. 2010; Wu et al. 2015
Selenite (SeO_3^{2-})	oxidizes. Easily absorbed hydrous sesquioxides and organic matter Bound with oxides and oxyhydroxides of such metals is dissolved by microorganisms at later stages Major species: HSeO_4^{2-} , SeO_2^{3-} Selenite becomes predominant in acidic to neutral soils Selenite is available in acidic soils. Acid soluble fraction of Se (VI) is approximately 44%	Wang et al. 2012; Kabata-Pendias, and Szteke, 2015; Elrashidi et al. 1987 Elrashidi et al. 1987; Wang et al. 2012
	Selenite increases arsenic in rice	Hu et al. 2014
Se (+6)	The dominant species that are highly and slowly absorbed by the plants. Alkaline soils solubilize Se (+6). Highly water soluble and highly bioavailable. Not adsorbed on hydrous sesquioxides (mainly $\text{Fe}_2\text{O}_3 \cdot \text{H}_2\text{O}$)	Elrashidi et al. 1987; Séby et al., 1997; Se speciation in soils after alkaline extraction. Science of the Total Environment, 207(2-3), pp.81-90. Dhillon and Dhillon 2009 Kabata-Pendias, and Szteke, 2015

major species: SeO_4^{2-}

Selenate is the predominant in oxidized and alkaline soils

Selenate species are available in aerobic Wang et al. 2012 neutral or alkaline soils

Under submerged or waterlogged Mikkelsen et al. 1989b; Jayaweera conditions, selenate is converted to and Biggar 1996 elemental Se, selenite or selenide

Se (+6) prevents arsenic penetration into rice Hu et al. 2014 roots

Acid-soluble fraction of Se (IV) is Séby et al., 1997 approximately 15%

Se Content in Upland and Lowland Soils

The levels of oxidized Fe and Mn bound to Se are greater in upland soil compared to lowland soil (Wang et al. 2012). For example, exchangeable Se is around 1% in the upland soils (Wang et al. 2012). It has been demonstrated that adding selenate to aerobic soil is the best way to boost grain Se content in rice (Li et al. 2010). When Se is applied with the fertilizer to upland soils, the retention of Se in the seeds is higher than when added to submerged soils (Li et al. 2010). It has been proposed that under dryland conditions, microbial activity is enhanced in the presence of CaCO_3 accelerating the release of Fluvic acid-Se into inorganic and organic Se that increases Se absorption by roots (Qin et al. 2012). Alternatively, under anaerobic conditions, particularly in rice, grain nutrient dilution occurs, resulting in increased biomass and grain yield, which in turn may lead to a decrease in Se concentration in the grains. Hence, aerobic rice (upland rice) retains a higher Se content in the seeds than in submerged soils (paddy rice) (Li et al. 2010).

Organic matter-bound Se is higher than Fe and Mn-bound Se in lowland soils (Wang et al. 2012). Releasing Se from organic matter is faster than releasing it from Fe or Mn oxide-bound Se (Munier-Lamy et al. 2007). Elemental Se and selenide are more stable in lowland soils in their less accessible forms (Elrashidi et al. 1987). For example, when lowland soil is supplied with selenite, the observed Se types were selenite, SeMet, and Se oxide (Li et al. 2010), suggesting that two species are the immediate transformed products in an organic background. Soil adsorption of Se is prominent in lowland soils since the clay fraction is comprised of Fe and Al oxides (Mouta et al. 2008). However, adding selenate or selenite to lowland soil is not effective (Li et al. 2010) since selenite (SeO_3^{2-}) is thermodynamically stable (Kirk 2004). Exchangeable Se is around 16.1% in lowland soils (Wang et al. 2012). Waterlogged and submerged soil conditions with high selenium (Se) levels are more effective in mitigating excessive selenium entry of Se into plants (Williams et al. 2009). Under anaerobic conditions, soil pH decreases (Li et al., 2010), soil redox potential decreases subsequently (Mikkelsen et al., 1989b) and oxide and hydroxide forms of iron are released into the soil solutions, and Se is adsorbed to oxides and hydroxides (Grybos et al., 2007; Fendorf et al., 2008; Grybos, et al., 2007). Se is more available in sandy soils than in sandy clay soils (Fernandes et al. 2014) high in cretaceous shale (Ohlendorf et al. 1986) and in volcanic tuff and in the black carbonaceous soils (Kunli et al. 2004). Therefore, it is essential to take into account the chemical and physical features of the soil while formulating strategies for Se agronomic fortification.

Approaches to Manipulation of Se in Plants for Better Human Health, Crop Yield and Soil Remediation

As Se can be deficient in diets or excessive, manipulating its content in plants is important for better health outcomes for humans.

Improving Bioavailability of Se in Soil

The bioavailability of Se in soil was reported as 1.1–3.4% in UK soil samples by Stroud et al. (2010). The bioavailable forms of Se are less than the total Se contents in the soil and this is the case for any soil type (Zhang and Moore 1996). In general, the availability of Se for plants is primarily determined by the redox potential and pH of the soil, soil parent material, soil type, and climatic conditions, as well as Se speciation (Mikkelsen et al. 1989b; Tan et al. 1994; Terry et al. 2000; Wang and Gao 2001). Continuous irrigation also increases Se availability in the soil (Ohlendorf et al. 1986). For example, the soils of the Hubei province, Ziyang and Daba regions of South Qinling in China (Kunli et al. 2004), and Punjab region in India (Sharma et al. 2010) and South Dakota in USA (Gerla, et al. 2011) are all rich in Se. Further, the type of fertilizer and fertilizer application time also determines the Se availability in the soil (Wang et al. 1996; Kahakachchi et al. 2004; Kápolna and Fodor 2006). The bioavailability of Se can be improved through the implementation of crop management practices. The retention of Se in grain is more effective when Se is applied closer to the heading stage than when it is applied during soil preparation. Drainage during the maturity period allows increased Se accumulation in rice grains. SeO_4^{2-} -enriched N-fertilizers improve Se uptake; this is particularly prominent at the heading stage (Premarathna et al. 2012). The rhizosphere is the narrow region of soil that surrounds and influenced by the plant roots. Selenobacteria in this zone can be used to enhance the bioavailability of Se in soil (Acuña et al. 2013). It has been established that Fulvic acid- Humic acid-, and organic matter-bound Se is the available Se sink in the soil (Qin et al. 2012). Consequently, the addition of chelating chemicals to soil has the potential to enhance the bioavailability of Se.

Se Uptake by Plants

Plants absorb Se from the soil and distribute it to other parts through xylem and phloem. Selenate and selenite are the two main forms for the absorption of Se by plants (Ellis and Salt, 2003). Selenite is the main form of Se found in anaerobic soils, and selenate is more common in aerobic soils (Avila et al. 2013). The most abundant form of Se for plants is selenate, as selenite tends to bond with oxides or hydroxides of iron or manganese (Barrow and Whelan 1989). The availability of Iron oxyhydroxide Se is also greater in soils (Rayman 2008). BCF is higher in selenate-treated soils than in selenite-treated soils (Munier-Lamy et al. 2007), suggesting that Se is actively, not passively, transported in the plant. Se is a sulfur analogue and selenate (SeO_4^{2-}) is a sulfate (SO_4^{2-}) analogue and Se transportation and accumulation follow sulfur metabolic pathway in the plant cell (Sors et al. 2005). The similarity in structure and charge between selenate and sulphate leads to competition for uptake and assimilation in plants (Ellis and Salt 2003; Hoewyk et al., 2007; White et al. 2007; Tamaoki et al., 2008; White and Broadley 2009; Eiche et al., 2015). The preference of sulphate transporters for selenate and sulphate may vary among plant species and under varying nutritional conditions (Zhu et al., 2009). The absence of sulfate transporters prevents selenate from being absorbed into the cell. (Shibagaki et al. 2002; Yoshimoto et al. 2002; Bell et al. 1992). High sulfur doses reduce the Se contents in plants when Se is applied as selenate (Avila et al. 2013). However, some plants have Se-specific transporters (Feist and Parker 2001; Schiavon et al. 2015; Pilon-Smits and Quinn 2010). *SULTR1* is the dominant selenate transporter in *Arabidopsis thaliana* (Barberon et al. 2008).

An antagonist uptake pattern of selenate and selenite in plants has been reported (Zayed and Terry 1992). Selenate is transported to shoot, and selenite has an affinity to accumulate in the roots (Li, et al. 2008). Further, selenate is better than selenite in the accumulation process (Zhu et al. 2009). Selenite uses both passive diffusion (Sors et al. 2005; Li et al. 2010) and phosphate transporters (Li et al. 2010) to enter the plant. The adsorption affinity of selenite with the soil particles is greater than selenate (Kamei-Ishikawa et al. 2007). Further, compared to selenate, rhizosphere microbes volatilize selenite significantly (Azaizeh et al., 2003). Se translocation to shoot is limited once applied as selenite (Arvy 1993; de Souza et al. 1998; Hopper and Parker 1999). Glutathione is important to convert selenite to selenate (Ellis and Salt 2003; Whanger 2004; White et al. 2007).

The organic forms of Se are deposited in roots when selenite is applied (Zayed et al. 1998). The mobility of organic Se (SeMet or MeSeCys) is greater in the plants than inorganic Se. Organic Se species are transported exclusively through phloem whereas inorganic form of Se is transported through both phloem and xylem (Carey et al. 2012). Se enters grain through both the xylem and phloem sap (Krishnan and Dayanandan 2003). SeMet and MeSeCys are dispersed throughout the external grain layers and in the endosperm and MeSeCys also gets deposited in the embryo (Carey et al. 2012).

Se Toxicity in Plants

Substitution of cysteine (Cys) and methionine (Met) by SeCys and SeMet, respectively, results in Se toxicity (selenosis) in plants (Brown and Shrift 1981). According to Guptha and Guptha (2017) Se toxicity manifests due to either malformed selenoproteins or oxidative stress. Many studies indicate that Se toxicity is a cause of oxidative stress (Chen et al., 2008; Schiaven et al., 2012; Gupta and Gupta 2017). Se is volatilized in plants after converting SeMet to DMSe, and several other forms (Ellis and Salt 2003; Zhu et al. 2009; Rayman et al. 2008; Terry et al. 2009). Most of the metabolic activities associated with Se processing within the plant cell take place inside the chloroplast (Leustek et al. 2000) (Figure 4).

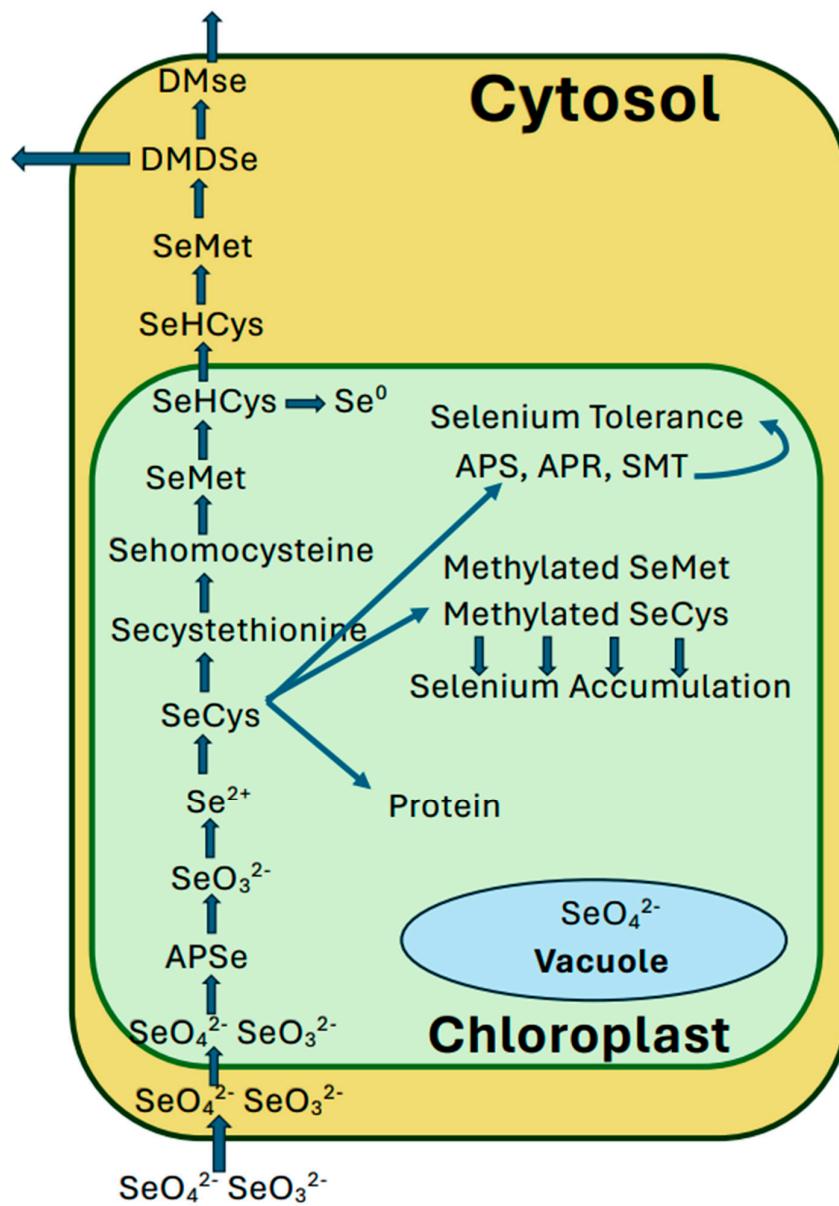


Figure 4. Se metabolism in plant cell. DMSe: Dimethylselenide, DMDSe: Dimethyldiselenide, SeMet: Selenomethionine, SeHCys: Selenohomocysteine, SeCys: Selenocysteine, APSe: Adenosine phosphoselenate, APR: Adenosine phosphosulfate reductase, SMT: Selenomethyltransferase.

The Ability of Different Plants to Metabolize and Accumulate Se

Depending on their ability to absorb and metabolise Se, plants are divided into three groups (Terry et al. 2000; Ellis and Salt 2003). The majority of plants are 'non-accumulators' of Se. They can only accumulate low levels of Se from the soil; less than $100 \text{ mg Se kg}^{-1} \text{ DW}$, and usually much less (McKenzie et al. 2009). These plants take up Se non-specifically via the sulphur (S) assimilation pathway (White et al. 2007), ultimately forming SeCys and SeMet, which are mis-incorporated into proteins resulting in Se toxicity symptoms such as stunting, necrotic lesions on the leaves and reduced root growth (McKenzie et al. 2009). In contrast, Se hyperaccumulators, such as *Astragalus bisulcatus* and *Stanleya pinnata*, when grown in Se-rich soils can take up and accumulate large quantities of Se (up to several $\text{g Se kg}^{-1} \text{ DW}$) without apparent symptoms of toxicity (Pickering et al. 2003; Freeman et al. 2006b). A plant having non protein MeSeCys amino acid can tolerate Se (Montes-Bayón, LeDuc et al. 2002, Pedrero and Madrid 2009) and are Se hyperaccumulators (Terry et al. 2000;

White et al. 2004). The third group, which is intermediate are called secondary Se accumulators. They can grow on soils with moderate Se levels and accumulate moderate quantities of Se (up to 1 g Se kg⁻¹ DW) without showing signs of toxicity. Certain Alliaceae (e.g. garlic - *Allium sativum*) and Brassicaceae such as. Indian mustard (*Brassica juncea*), broccoli (*B. oleracea* var. *italica*) and canola (*B. napus*) are in this group (McKenzie et al. 2009).

Three parameters are used to identify Se-hyperaccumulators: plant Se:S ratio, shoot Se concentration compared to that in roots, and leaf Se content (Galeas et al. 2007; White et al. 2007). It has not been documented as Se hyperaccumulation being essential for the plant (Brown and Shrift 1981; Anderson 1993). However, hyperaccumulation is considered as beneficial for antioxidant properties, developing antiherbivore for arthropods and antipathogenic for fungi (Hanson et al. 2003; Hanson et al. 2004; Hartikainen 2005; Freeman et al. 2006a; Quinn et al. 2007; Quinn et al. 2008). They have the advantage of surviving in high Se soils. It is worthwhile understanding the fundamental mechanism of how plants accumulate such large amounts of Se; the process will be immensely helpful in developing Se-rich cereals and pulses as well as phytoremediation of high Se-contaminated soils (Trippe & Pilon-Smits, 2021). Se hyperaccumulating plants in the families of Asteraceae, Brassicaceae and Leguminosae (Reeves and Baker 2000) are important research materials for in-depth analysis of Se hyperaccumulation, Se fortification, and Se phytoremediation.

Prevention of Se Pollution

Se pollution is one of the growing concerns across the globe, particularly in mining and agriculture areas (Lemly, 2004). Improved water management practices, such as reducing excessive irrigation or applying Se-free water have reduced Se leaching from the soil (Dhillon and Dhillon, 2001). The application of organic amendments to Se-contaminated soil mitigates the adverse impacts of Se (Sharma et al., 2011). The incorporation of crop residue or animal manure into selenated soils leads to a significant reduction in Se accumulation by plants (Ajwa et al., 1998). Bioreactors can be developed to harness microbial activities as a biological method to remove excess Se (Staicu et al., 2017; Nkansah-Boadu et al., 2019). Selenate, a highly soluble and bioavailable form of Se, can be reduced to selenite and further to less toxic elemental Se using chemical or biological methods (Hageman et al., 2013; Zhang et al., 2020). Hence, it is essential to maintain a proper equilibrium between selenite and Se in order to prevent Se toxicity in plants.

Se Phytoremediation by Se Hyperaccumulators and Se tolerance

In phytoremediation, plant extraction (phytoextraction), filtration (hemofiltration or rhizofiltration) or volatilization (phytovolatilization) mechanisms are utilized (Dhillon and Bañuelos 2017; LeDuc and Terry 2005). For example, Indian mustard (*Brassica juncea* Czern L.) can be used for Se-contaminated soil phytoremediation. Subsequently, harvested mustard can be used as animal feed (Banuelos 2006; Banuelos and Lin 2009), biofuels (Searchinger et al. 2008), or bioavailable Se source (Bañuelos et al. 2015). Other plants that can be grown to reduce Se content substantially are giant reed (*Arundo donax*), creeping saltbush (*Atriplex semibaccata* R. Br. L.), old man saltbush (*Atriplex nummularia* Lindl. L.), tall fescue (*Festuca arundinacea* Schreb. L.), canola (*Brassica napus* L.), birdsfoot trefoil (*Lotus corniculatus* L.), and kenaf (*Hibiscus cannabinus* L.) (El-Ramady et al., 2015; Banuelos, 1996). Also, plants of the *Astragalus* genus and *Neptunia amplexicaulis* (Domin.) of the family Fabaceae, which hyperaccumulate Se as MeSeCys are efficient plants for phytoremediation of Se (Peterson and Butler 1967; Neuhierl and Böck 1996). Further investigating the genetic variability in the accumulation of Se among a wider range of plant species will open up further opportunities to remediate Se contamination through phytoremediation.

Se hyperaccumulation or Se tolerance in *Astragalus bisulcatus* is due to the selenocysteine methyltransferase gene expression (Ellis et al. 2004; McKenzie et al. 2009). Se uptake, hyper accumulation and emission collectively maintain Se tolerance in such plants (Pilon-Smits and LeDuc 2009).

Se Reduction by Microbes

Microbial Se transfer mechanism plays an important role in Se reduction in the environment (Huang et al., 2012; Etteieb et al., 2021; Li et al., 2022). Rhizospheric microbes accelerate Se uptake and volatilization (Pilon-Smits, 2005). Se hyperaccumulator plants colonize with a diverse community of endophytic bacteria that promote plant growth (Sura-de Jong et al., 2015; Li et al., 2022). Specific strains of soil bacteria have the ability to transform soluble forms of Se into insoluble, less toxic forms, reducing the bioavailability of Se. These microorganisms decrease the amount of Se contamination in the surface environment by converting it into a volatile form through methylation (Bañuelos et al. 2007). In general, bacteria play a more prominent role than fungi in Se volatilization, and aerobic conditions accelerate bacteria-mediated Se volatilization. For example, experiments using the antibiotic ampicillin in Indian mustard showed that bacteria facilitated 35% of plant Se volatilization and 70% of plant tissue accumulation of Se (de Souza et al. 1999). Bioaugmentation of such bacteria is important for lowering Se bioavailability in soils. These findings suggest that the Se transformation process and its rate determine Se bioavailability. Se volatilization changes from $\text{SeMet} > \text{selenite} > \text{selenate}$ in soil (Azaizeh et al., 1997). However, there is very limited understanding of this process in different agricultural systems.

Utilizing Se Detoxification in Plants for Phytoremediation

Once Se is released from SeCys and SeMet, toxic conditions arise in plants (Brown and Shrift 1981; White et al., 2004). For their survival, plants have developed Se detoxification mechanisms. One of the main Se detoxification mechanisms is volatilization as gases. Dimethyl diselenide, diethyl selenide and dimethyl selenide are emitted by such plants (Dauchy et al. 1994). It has been suggested that plants with these traits can be utilized for Se phytoremediation and Se fortified foods (Pilon-Smits and LeDuc 2009). The enzyme cystathione gamma synthase (cgs) that converts SeCys to SeMet in the volatilization pathway prevents Se toxicity by decreasing Se accumulation by 40% (Pilon-Smits and LeDuc 2009).

Se Biofortification

Elevating Se biofortification in crops can be achieved through a variety of effective strategies. These include soil or foliar application of Se, crop management practices, as well as advancements in plant breeding and genetic transformation and editing techniques.

Genetic Biofortification or Breeding for Biofortification

Genetic biofortification of Se implies the selection and use of genotypes that have an ability to accumulate higher Se contents. It purely depends on available genetic resources for breeding purposes (White and Broadley 2009). Varying Se content in the different genotypes is advantageous for genetic biofortification (Eurola et al. 1991; Lyons et al. 2005b). As an example, wild relatives of wheat such as *Aegilops tauschii* have higher Se contents than durum and bread wheat (Graham et al. 1999; Lyons et al. 2003; White & Broadley, 2005a; White et al. 2007). Hence, interbreeding elite crop cultivars with Se-rich wild-relatives or landraces is one of the strategies to produce Se-enriched staple crops. Selection of genotypes that can produce MeSeCys using inorganic Se is the basis for biofortification (Roberge et al. 2003; Ramos et al. 2011). However, Se must be available in the soil for screening the grains (or other edible parts) for Se in breeding programs (Cakmak 2008). So, Se variation across diverse environmental conditions is a barrier to breeding for biofortification (Lyons et al. 2005a).

Gene Transformation for Se Biofortification

Development of food crops intended to increase dietary Se intake is Se biofortification. This can be achieved through traditional breeding but more efficiently using gene transformation technologies. Considering its anticancer properties, it would be much more beneficial if a proportion

of this supplementary Se were present as MeSeCys (Bhattacharya, 2011; Poluboyarinov et al., 2020) or other organic forms (Poluboyarinov et al., 2020). Therefore, most of the plant transformation work in this area has been directed at increasing the organic Se levels. Sulfur and Se metabolism related genes were overexpressed in *Brassica juncea*, resulting in increased Se accumulation and Se tolerance (Lyons, et al. 2005a; Banuelos and Meek 1990). *Adenosine triphosphate sulfurylase (APS)*, *SeCys methyltransferase (SMT)*, and *cystathionine gamma synthase (CgS)* genes are used for gene transformation for Se biofortification (Neuhierl and Böck 1996; Van Huysen et al. 2003; Banuelos et al. 2005). APS is an enzyme that catalyzes sulfate and selenate (Pilon-Smits et al. 1999) for Se assimilation (Banuelos et al. 2005). Overexpressing APS in Indian mustard has been successful for Se biofortification (Pilon-Smits, et al. 1999). *SMT* gene from the Se hyperaccumulator plant, *Astragalus bisulcatus*, has often been used for inducing Se tolerance (Ellis et al. 2004; LeDuc et al. 2004; McKenzie et al. 2009). Cystathionine gamma-synthase (CgS) converts SeCys to SeMet, and Se volatilization is increased by 2 to 3 folds in transgenic *A. thaliana* by overexpressing CgS (Van Huysen et al. 2003). Gene pyramiding of *APS* and *SMT* accelerates selenate accumulation (LeDuc et al. 2006). When a cDNA encoding the *SMT* from Se hyperaccumulator *A. bisulcatus* was overexpressed in tomato (*Solanum lycopersicum*), transgenic plants' accumulation from soil-supplied selenate was found to increase the assimilation of Se into leaves and fruit. Relative to wild-type, Se accumulation from soil-supplied selenate was increased by ~1.53-fold in both leaves and fruit but MeSeCys accumulated in the fruit but not in the leaves. Depending on the transgenic line and Se treatment, up to 16% of the total Se in the fruit was present as MeSeCys. MeSeCys was produced more effectively from selenite on a percentage conversion basis, but greater accumulation of MeSeCys could be achieved from selenate due to its better translocation from the roots (Brummell et al. 2011). Quantitative Trait Loci for Se tolerance have been identified (Agalou et al. 2005; Zhang et al. 2006) for potential dissecting of major genes. However, strict regulations for genetically modified crops and intellectual property rights problems are a hindrance to their commercialization (Cohen and Paarlberg 2002; Potrykus 2009; Stein 2009).

Agronomic Se Biofortification

Agronomic Se biofortification is adding Se to the soil through the application of Se-enriched fertilizers or soil amendments to increase Se in the edible parts of food crops. Micronutrient-enriched fertilizer application is an initial step for micronutrient fortification (Lyons et al. 2005a; Hawkesford and Zhao, 2007; White and Broadley 2009, Mao et al. 2014). Application of inorganic fertilizers in Se poor soils enhances Se absorption more than 100 times for many crops (Liu et al. 2010). Developing crop varieties that are more efficient at absorbing and accumulating Se from the soil is a long-term strategy. Se can be added to current fertilizer recommendations as an additional ingredient (Cakmak 2008; 2009). Finland achieved enough Se in food for its population after introducing such fertilization programmes since the mid-1980s, the first country to do so (Zhao and McGrath 2009, Alftan et al., 2015). New Zealand also achieved Se-enriched crops through Se-enriched inorganic fertilizers (Hartikainen 2005; Premarathna et al. 2012). Adding Se with Zn and/or I gave a similar effect as added Se alone (Mao et al. 2014). Most of the time soils that contain Se as selenite exhibit less bioavailability than the presence of Se as selenate (Li, et al. 2008; Mao et al. 2014). Se is applied at the rate of 10 to 20 g Se ha⁻¹ as selenate, but for receiving the same Se increment in grains, selenite should be applied at over 100 g Se ha⁻¹ (Yläränta 1985). A 35.9% increment of grain Se in barley by applying selenate was reported in comparison to selenite application (Chen et al. 2002). However, the same effect of grain Se accumulation was reported in soil-applied selenate and foliar-applied selenite in many crops (Mao et al. 2014). The conversion ratio of Se to MeSeCys in broccoli is greater when applied as selenite compared to selenate (Avila 2013), but it was controversial in the case of rice. The difference would be anaerobic soil condition in rice (Li et al. 2010). Adding Se into the soil is more efficient in Se increment in grains than using it as a foliar application, and selenate increases grain Se while selenite increases root Se in rice (Boldrin et al. 2013).

Plants of the family Brassicaceae have the capacity to produce S-rich glucosinolates known to have significant human health benefits. Selenate application to three Brassicaceae crops; broccoli (*Brassica oleracea* L. var. *italica*), cauliflower (*Brassica oleracea* L. var. *botrytis*) and forage rape (*Brassica napus*) and analysing glucosinolates produced in four tissues demonstrated that the distribution of Se-containing glucosinolates is different among the three crops, and broccoli florets and forage rape roots accumulated more of these (McKenzie et al. 2015). Understanding these differences in Se accumulation is important in agronomic biofortification programmes using different crops. Increasing bioavailability of the element at the rhizosphere also facilitates greater uptake of Se (Meenakshi, 2010). Adding metal chelates increases Se availability (Zhao and McGrath, 2009). Composting and adding organic materials to the soil improve the bioavailability of Se in the soil, making it more accessible to crops (Wang et al. 2018). Organic acids act as chelates to increase Se uptake efficiency in fertilizers (Morgan et al. 2005, Lynch, 2007) and organic acids improve root volume (Kirkby and Johnston 2008). Using Se-enriched water sources can also contribute to increased Se uptake by crops (Zhou et al. 2018). Further, rotating Se-accumulating crops with other crops in the same field can help maintain soil Se levels and reduce the risk of soil depletion (Bañuelos and Dhillon 2011).

Factors Affecting Biofortification

Biofortification has been recognized as a promising approach for improving the nutritional quality of edible crop species (Yang et al. 2007). Several factors can significantly impact the success of biofortification initiatives. Among them the choice of crops is very important as many crop species do not have the same ability to effectively accumulate and enhance the specific nutrients in the edible organs (White and Broadley 2005). In addressing Se deficiency, lentils have been identified as a potential candidate for Sri Lanka (Thavarajah, et al., 2011).

The most important factor is the nutrient availability in the soil, which determines the crop's ability to take up those nutrients. Further the soil composition and the soil pH and nutrient interactions can also influence the success of biofortification targets (White and Broadley, 2005). Environmental factors like climate, temperature, and precipitation can influence nutrient uptake and crop growth. Different geographic regions may require specific biofortification strategies tailored to their environmental conditions as well as cultivated crops. Furthermore, the acceptance and willingness of people to consume nutrient rich food is crucial for the success of biofortification effort (Meenakshi et al. 2010). Special precautions are also needed in biofortification programmes. For example, micronutrients can be contaminated with heavy metals, which could pose a major challenge for biofortification. This is mainly due to some of the transporters common to other nutrients' uptake could easily facilitate heavy metal uptake. Thus, biofortification with Se could also facilitate the increase of heavy metals in food, such as cadmium (Zhao and McGrath, 2009). Se can be found excessively in polluted soils and phytoremediation and biofortification cannot be expected simultaneously (Vamerali et al. 2014). Because plants cannot be grown in Se remediated substrates though such substrates are rich with Se and other heavy metals and micronutrients. Heavy metals use the same transporters of Se (Zhao and McGrath, 2009). Further, though the seeds are fortified with Se, Se concentration is higher in the husk and aleurone layer of seed and most of the time aleurone layer is discarded during processing. Milling and processing must be minimized for higher retention of Se in the diet (White and Broadley 2009; Qaim et al. 2007).

Assessment of Biofortification

Assessing biofortification is a comprehensive process that requires interdisciplinary collaboration. Local agricultural and health authorities, as well as international organizations like the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) should play important roles in guiding and monitoring biofortification programs to prevent both deficiency and excess Se intake (WHO, 2006).

Usually, enhancement of crop yield quality doesn't ensure an economic gain in agriculture (Unnevehr, 1986). Quality improvements of field crops are rare, and one example is golden rice production for Vitamin A enrichment in rice (Dawe et al. 2002). DALYS methodology has explicated the economic benefit of golden rice (Zimmermann and Qaim 2004) and found that people were still below the micronutrient threshold after introduction of Golden rice (Fiedler et al. 2000). Success of biofortification programmes is assessed using following steps: Assess biofortified crop nutrient content and ensure their productivity and marketability, evaluate nutrient concentrations in plant tissues, test nutrient retention during food processing, study consumer acceptance, and measure nutritional impact. It is also important to monitor health outcomes, environmental effects, economic feasibility, market demand, and programme progress. Strategies have to be adapted as needed, regulatory compliance, and long-term sustainability have to be ensured. Engaging communities and collaboration among stakeholders for shared knowledge and best practices are an integral part of biofortification programmes.

When there is no consumer acceptance of biofortified food, micronutrients are neglected in the diet (Qaim et al. 2007). Most of the crop improvement programmes targeted at increasing yield have resulted in the decrease of the concentration of micronutrients in the grain. Sometimes inhibitory effects of soil reduce the Se intake of the plant. For example, slight doses of sulfur increase Se uptake and extra doses of sulfur inhibit Se uptake (Lyi et al. 2005). This happens when selenate is applied (Avila et al. 2013). SeO and SO_4^{2-} analogues also reduce Se accumulation in plants (Pilon-Smits and Quinn, 2010). Biofortification is not important for farmers unless crops have farmer-preferred agronomic characteristics, including high yield (Stein 2009). Widespread acceptance for Se biofortification must be earned harder (Nestel et al. 2006; Qaim and Stein 2009; Qaim et al. 2007) and community approaches must be carried out for such an effort (Stein 2009).

Economic Benefits of Se Biofortification

The economic benefits of Se biofortification have been supported by several studies around the world. Horton and Ross (2003) demonstrated that poor health in the developing world associated with micronutrient deficiency has a major impact on the economies of countries. It has been demonstrated that there is a strong relationship between dietary energy used in the population and national economic growth (Wang and Taniguchi 2003). For instance, around 30% of British per capita increment was gained due to the overall nutrition assurance of the nation (Fogel 2004). According to Horton and Ross (2003), a 4% loss of gross domestic production in 10 developing countries is due to national nutrition problems. Globally, one billion people are suffering from micronutrient malnutrition (Williams et al. 2009). In Sri Lanka, it has been documented that 24-40% of the female population in the tested regions with reported goitre is Se deficient (Fordyce et al. 2000). Se deficiencies play a role in goitre pathogenesis (Fordyce et al. 2000). Se insufficiency levels ranging from 5% to 50% have been documented in various districts across Sri Lanka (Diyabalanage et al., 2020). Nutrient insufficiency has a direct impact on the economy by increasing healthcare costs and reducing workforce productivity, as it leads to a higher prevalence of chronic illnesses. Additionally, it can strain social safety nets and public resources, diverting funds away from other critical economic development initiatives. Hence, the economic benefits of Se fortification are evident in terms of improved health outcomes, reduced healthcare costs, increased productivity, and efficient allocation of public resources. However, the specific economic impact of Se fortification may vary based on the context and the population characteristics, emphasizing the need for further research and development.

Knowledge Gap

While Se biofortification holds significant promise as a solution to combat global Se malnutrition, there are several areas within this field that require further research and investigation to refine and optimize strategies. Understanding the factors that affect the bioavailability of Se in fortified crops is important. Research should focus on improving the efficiency of Se absorption and

incorporation into edible plant parts. This also involves investigating the interaction between soil, plant, and human physiology to maximize the health benefits of Se fortification. Further, research should explore the most effective forms and sources of Se for fortification. Different forms of Se, such as selenate and selenite, have varying bioavailability. Additionally, alternative Se sources, like organic Se compounds, should be investigated to determine their suitability for fortification.

Different crops accumulate Se in different forms and quantities in different tissues. Identifying and breeding crop varieties that efficiently absorb Se from the soil and accumulate in edible parts is essential. Another important aspect needs attention is developing and promoting improved Se accumulating crop varieties that can thrive in different geographic regions, considering local soil and climate conditions. Developing and optimizing agronomic practices for such varieties (varietal agronomy) is also important for Se biofortification. This includes determining the appropriate timing and method of Se application, as well as studying the effects of other soil amendments, such as pH adjustments and organic matter content on Se uptake by plants.

The threshold levels for Se requirement and toxicity are very narrow. Research should provide guidelines for safe and effective Se fortification levels in staple crops. Over-fortification can lead to Se toxicity, which can have adverse health effects. It is important to establish the maximum allowable Se levels to prevent unintended health risks. Se is not a well-known element in human health. Hence, investigating consumer attitudes and acceptance of Se-fortified crops is important. Research should address concerns related to biofortified products among different cultural and demographic groups not to waste investments on Se biofortification efforts. Se has not been added to any food item so far. Long-term epidemiological studies are necessary to assess the health outcomes over extended periods including the side-effects of Se in populations that consume Se fortified crops regularly. These studies should explore non-communicable diseases over extended periods since the side-effect of Se over consumption is unknown. The socioeconomic impact of Se fortification needs to be studied to ensure that it does not inadvertently lead to social inequities or disrupt traditional farming practices. Intellectual property rights and equitable access to fortified crops should also be examined and documented in advance. The region-specific fortification strategies must be formulated to utilize them for diverse soil Se contents, soil conditions, crops and environments. Se can be toxic to some plants and aquatic life, so research should evaluate the ecological consequences of increased Se in agricultural runoff and its potential effects on ecosystems. Hence, developing regulatory frameworks for Se fortification is another essential socio-economic aspect. By addressing these research areas, scientists and policymakers can better tailor Se fortification strategies to diverse geographic regions and populations, ensuring the safe and effective delivery of this essential micronutrient to those who need it most.

Conclusions

Se is a trace element that is essential for human health, yet it often goes unnoticed in discussions about nutrition and global health. It plays an essential role in various physiological processes in the human body. Se is an essential component of selenoproteins, which act as antioxidants and have been linked to various health benefits. Inadequate Se intake in the diet (less than 15–30 µg/day) can lead to weakened immune system and is considered as an etiological factor in some cardiovascular, cancer, neurodegenerative and osteoarticular diseases in humans. In severe cases, Se deficiency can result in a condition known as Keshan disease, which affects the heart and can be fatal.

The prevalence of Se deficiency is not limited to one region or population; it is a global concern. Many areas of the world, including parts of China, Eastern Europe, UK, Canada, New Zealand, Russian Federation and parts of Africa, are known to have Se-deficient soils. As a result, crops grown in these regions are often low in Se, and the deficiency is subsequently passed on to the people who depend on these crops as their primary source of sustenance.

One of the most promising and sustainable solutions to combat global Se malnutrition is Se fortification of staple crops, particularly rice. Rice is a staple food for more than half of the world's population and fortifying it with Se has the potential to reach large populations, making it a practical

and effective strategy. Se biofortification, the process of enhancing the Se content of crops through agronomic practices, has been successful in increasing Se levels in rice and other staple foods.

Comprehensive Se fortification strategies involve not only increasing Se content in crops but also ensuring that the bioavailability of Se is optimized. It's not just about adding Se to the soil but also understanding how plants absorb and incorporate it into their edible parts. This approach requires a combination of soil management techniques, plant breeding, and crop selection to achieve the desired Se levels. For instance, selecting rice varieties that efficiently accumulate Se from the soil and those that can partition more Se into endosperm can make significant improvement in diets. The potential impact of Se fortification in rice crops on public health is substantial. By increasing the Se content of a widely consumed staple food, we can address the issue of Se deficiency at its source. This has several significant benefits. Se fortification can lead to improved overall health and reduced risk of diseases associated with Se deficiency. Enhanced immune function, better cardiovascular health, and reduced risk of cancer are some of the potential benefits. Fortifying rice and other staple crops is a cost-effective and sustainable approach to combat Se deficiency. It leverages existing agricultural systems and distribution channels, making it accessible to a large portion of the population. By increasing the nutritional content of staple crops, Se fortification contributes to food security, ensuring that communities have access to a more nutritious and balanced diet. As public health improves, healthcare costs associated with Se deficiency-related diseases can decrease. This can alleviate the burden on healthcare systems and improve the overall well-being of communities. Further, healthier individuals are more productive and have better educational outcomes. 15-30 $\mu\text{g}/\text{day}$ Thus, Se fortification can contribute to economic growth by creating a healthier and more capable workforce. Hence, Se fortification, particularly in rice crops, is a sustainable solution to combat global Se malnutrition.

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