EJONS
Uluslararası Matematik, Mühendislik ve Doğa Bilimleri Dergisi
International Journal on Mathematic, Engineering and Natural Sciences

Review Article | e-ISSN: 2602 - 4136 | https://doi.org/10.5281/zenodo.15761884

Human Health and Selenium

Ibrahim AKTAS *[1], Sedat BILGIÇ [2]

[1] Adıyaman University, Vocational School of Health Services, Adıyaman, Türkiye
[2] Adıyaman University, Vocational School of Health Services, Adıyaman, Turkiye
Sorumlu Yazar Email: iaktas@adiyaman.edu.tr

Article Info

Received: 30.04.2025
Accepted: 12.06.2025

Keywords
Selenium,
Oxidative Stress,
Human,
Disease

Abstract: Selenium (Se) is a trace element essential for human reproductive and growth functions. The term " Se" originates from the Greek word selene, meaning "moon." Se is represented by the chemical symbol Se, has an atomic number of 34, and an atomic mass of 78.96. It is located in period 4 and group 6A of the periodic table. In nature, Se exists in various oxidation states, including -2, +2, +4, and +6. The -2 oxidation state is typically found in selenides, the +4 state in selenites, and the +6 state in selenates. Additionally, a +1 state can be observed in some sel Se enium compounds, such as s Se elenium chlorides. Plant-based foods contain Se primarily in its organic form, selenomethionine (SeMet), which has a bioavailability of approximately 90%. Inorganic forms such as selenate and selenite also exist in foods and are known for their high bioavailability. The antioxidant properties of selenoproteins play a crucial role in preventing cellular damage caused by free radicals. It is estimated that there are approximately 30–50 selenoproteins in the human body. Of these, about 12 are believed to be involved in processes related to viral infections, cancer, and immune function. The primary Se -containing protein in tissues is glutathione peroxidase (Gpx), which serves as a key biomarker for determining Se status at the cellular level. Furthermore, Gpx plays a vital role in protecting cells from oxidative stress-induced damage.

1. Introduction

Selenium (Se) is an essential trace element involved in the regulation of reproductive and growth functions in living organisms (Küçük, 2014; Zachara, 2018; Berzelius, 2020). In plant-based foods, selen Se is predominantly present in its organic form, selenomethionine (SeMet), which demonstrates approximately 90% bioavailability. Additionally, Se supplements often utilize inorganic forms such as selenate and selenite, which also exhibit high bioavailability.

Se exerts its biological effects in tissues primarily through selenoproteins. These are Se -containing enzymes and proteins that play critical roles in various physiological processes. In animals, Se acts as a constituent of these selenoproteins, contributing to DNA synthesis, reproductive and thyroid function, and overall metabolic regulation. Moreover, Se has a protective role against oxidative cellular damage and infections, underscoring its significance in immune defense and antioxidant systems (Shreenath et al., 2023).

Se deficiency in plants is closely linked to the Se content of the soil in which they grow. Research has shown that children from families residing in areas with Se -deficient soils tend to exhibit slower growth rates compared to those living in Se -rich regions. Furthermore, certain types of cancer have been reported to occur more frequently in populations living in Se -poor regions compared to those in Se -abundant areas.

In addition to its role in plant and human development, Se deficiency has been associated with significant physiological consequences. It can lead to severe muscle weakness and decreased elasticity of the heart and blood vessels. Notably, Se deficiency has been confirmed as a causative factor in the development of fetal cardiomyopathy in children (Minich, 2022).

1.1. Selenocysteine

In the scientific literature, selenocysteine (Se-Cys) is commonly abbreviated as Se-Cys. It is structurally analogous to the amino acid cysteine, in which a Se atom replaces the sulfur atom. Se-Cys is primarily derived from animal sources and serves as an essential component of various selenoproteins.

Se-Cys is present as a residue within many enzymes, including Se-Cys -containing Gpx, tetraiodothyronine 5'-deiodinases, and thioredoxin reductases. These enzymes play crucial roles in redox regulation, thyroid hormone metabolism, and cellular antioxidant defense mechanisms. Selenoproteins typically contain a single Se-Cys residue, which is integral to their catalytic activity.

Containing Se-Cys residues are predominantly classified as selenoproteins, and those involved in enzymatic reactions are referred to as selenoenzymes. Importantly, the redox potential of Se-Cys is lower than that of cysteine, enhancing its reactivity and making it particularly suitable for incorporation into antioxidant enzymes. This unique chemical property renders Se-Cys especially valuable in biochemical systems that require efficient redox regulation (Hariharan and Dharmaraj, 2020).

1.2. Selenomethionine

Selenomethionine (SeMet) is a naturally occurring Se -containing amino acid. The biologically active L-enantiomer, L-SeMet, is considered the principal dietary form of Se. This form is commonly found in cereal grains, Brazil nuts, pasture legumes, and soybeans. Another significant Se compound, Se-methyl Se-Cys (along with its γ-glutamyl derivative), constitutes the main Se source in plant species belonging to the genera *Brassica*, *Allium*, and *Astragalus*.

In biological systems, SeMet can be nonspecifically incorporated into proteins in place of methionine during protein synthesis. This substitution occurs due to the chemical similarity between Se and sulfur. However, SeMet is also highly susceptible to oxidation, a characteristic that influences its stability and metabolic processing in vivo (Hadrup and Ravn-Haren, 2020).

Additionally, Se can be considered as an element that is stored in the form of selenomethionine (SeMet). When Se absorption in the body is impaired due to any physiological or pathological condition, SeMet serves as a Se reservoir, supplying Se to the organism as needed. SeMet is primarily obtained from plant-based sources (Hadrup and Ravn-Haren, 2020; Çakına, 2022).

The scientific literature identifies approximately 30 to 50 selenoproteins, with at least 12 of them known to play critical roles in viral pathogenesis, carcinogenesis, and immune system regulation. Among these, Gpx is recognized as the major selenoprotein present in a wide range of tissues. Gpx incorporates Se into its structure and is frequently used as a biomarker for evaluating Se status at the cellular level.

Gpx plays a pivotal role in protecting cells from oxidative stress by neutralizing reactive oxygen species (ROS). Its activity is particularly important in maintaining the function of muscle tissues, male reproductive biology, and the central nervous, endocrine, immune, and cardiovascular systems. The antioxidant capacity of SeMet is attributed to its ability to scavenge ROS. Moreover, both Se and methionine contribute to the synthesis and recycling of glutathione, a key endogenous antioxidant in the body (Küçük, 2014; Uslu and Aktac, 2020).

1.3. Pharmacokinetics

Following oral administration, Se is absorbed primarily in the small intestine and subsequently transported to the liver, where it is metabolized and incorporated into selenoproteins. From the liver, Se is distributed to peripheral tissues via the bloodstream. This transport is facilitated through binding to specific plasma proteins, including serum albumin, selenoprotein P (SEPP1), and glutathione peroxidase-3 (Gpx-3).

The bioavailability of Se from dietary sources is estimated to be approximately 14% of the ingested amount, with adult daily Se intake typically ranging between 2 to 20 mg. Se levels in the body can also be monitored through biological samples such as urine, nails, and hair.

Studies indicate that measurable increases in enzyme activity related to Se intake, such as Gpx activity, become apparent only after 4–6 weeks. Se also plays a crucial role in the activity of deiodinase enzymes, which are responsible for the activation of thyroid hormones. Notably, over 80% of the thyroid hormone thyroxine (T4) is converted into its active form, triiodothyronine (T3), in a Se -dependent process. In states of Se deficiency, an elevation in T4 levels accompanied by a reduction in T3 concentrations has been observed, indicating impaired hormone activation.

Finally, Se is primarily excreted from the body via the urinary system, which plays a key role in maintaining Se homeostasis (Kaya et al., 2013; Uslu and Aktac, 2020).

1.4. Selenium deficiency

Se deficiency has been associated with various impairments in the human immune system (Avery and Hoffmann, 2018). During pregnancy, insufficient Se levels and reduced antioxidant enzyme activity may lead to increased oxidative stress in maternal tissues, contributing to adverse outcomes such as miscarriage, premature birth, preeclampsia, and intrauterine growth restriction (Zachara, 2018).

Studies have shown that children residing in regions with Se -deficient soils exhibit slower physical development compared to those from Se-rich areas. These children often present with significant muscle weakness and reduced elasticity of cardiac and vascular tissues, increasing their risk of developing fetal cardiomyopathy.

Furthermore, Se deficiency has been linked to a higher prevalence of psychological disorders in humans. It is also associated with increased mortality rates among individuals suffering from chronic hepatitis and acquired immunodeficiency syndrome (HIV). Research indicates that Se deficiency contributes to a higher incidence of microbial infections and elevates the risk of various cancers, including those of the colon, lymphatic system, lungs, breasts, skin, prostate, liver, and stomach (Aktaş and Yahyazadeh, 2022).

In addition to these effects, Se deficiency has been associated with an increased incidence of common infections such as influenza and the common cold, as well as a heightened risk of contracting viral agents such as the human papillomavirus and herpes simplex virus. It is also linked to increased sensitivity to environmental chemicals and a greater predisposition to autoimmune diseases.

The thyroid gland plays a key role in regulating essential physiological functions, including body temperature, appetite, weight, sleep, and energy levels. Se contributes significantly to thyroid health by protecting the membrane regions of thyroid cells where autoantibodies tend to bind and initiate immune-mediated damage. Therefore, Se is essential for the regulation of thyroid hormone synthesis and concentration.

Although iodine is the primary element responsible for the prevention of thyroid gland enlargement, Se deficiency—particularly in individuals with adequate iodine intake—can lead to the development of thyroid gland hypertrophy and goitrous nodules.

Se deficiency is also associated with certain endemic diseases. Keshan disease (KD), a type of cardiomyopathy, and Kashin-Beck disease, a condition affecting joint and bone health, are both strongly linked to insufficient Se intake. Moreover, Se is vital for muscle function, and its deficiency may result in muscle weakness and myopathy.

Finally, Se plays a role in reproductive health, and its deficiency has been reported to contribute to infertility in both men and women (Kieliszek, 2021).

1.5. Side effects and toxicity

Chronic excessive intake of Se can result in elevated blood Se levels exceeding 100 µg/dL. Oral doses linked to lethal toxicity range between 1–100 mg Se per kilogram of body weight. Fatal outcomes have been associated with blood Se concentrations above 300 µg/L (normal range: ~100 µg/L) and urinary Se levels exceeding 170 µg/L (normal: 20–90 µg/L) (Hadrup and Ravn-Haren, 2020).

The primary mechanism underlying Se toxicity involves structural alterations in proteins due to the substitution of sulfur with Se in sulfur-containing amino acids, thereby disrupting normal protein function (Minich, 2022). This biochemical interference can contribute to the onset of chronic diseases, including diabetes.

Caution is advised when administering Se to individuals with chronic health conditions such as skin cancer, hypothyroidism, or chronic kidney disease, as dose adjustments may be necessary. Se supplementation should be discontinued approximately two weeks prior to surgical procedures. Additionally, concurrent use of Se and vitamin E is not recommended in individuals with allergy sensitivities due to potential adverse reactions.

Clinical manifestations of Se toxicity (selenosis) may include gastrointestinal disturbances (abdominal pain, nausea, vomiting), dental anomalies, a characteristic garlic-like odor on the breath, alopecia (hair loss), brittle nails, splenomegaly (enlarged spleen), hepatotoxicity (liver deformation), fatigue, irritability, and mild neurological symptoms. More severe signs include dizziness, muscle pain, tremors, flushing of the face, a burning sensation, paresthesia (numbness and tingling), altered reflexes, and partial paralysis (Spiller and Pfiefer, 2007; Uslu and Aktac, 2020).

1.6. Daily selenium requirement

Se intake requirements vary by age, sex, and physiological condition. The recommended dietary allowances are as follows:

- Children aged 1–3 years: 20 µg/day
- Children aged 4–8 years: 30 µg/day
- Children aged 9–13 years: 40 µg/day
- Individuals aged 14 and above: 55 µg/day
- Women: 60 µg/day
- Men: 75 µg/day
- Lactating women: 70 µg/day

Although the optimal serum Se concentration is approximately 85 µg/dL, intakes exceeding 400 µg/day may pose toxicological risks. Moreover, studies have indicated that when serum Se levels exceed 137 µg/dL, the risk of developing type 2 diabetes may increase.

Primary dietary sources of Se include cereal grains, meat, and seafood. Specifically:

- Beef and lamb: 20–35 µg Se/100 g
- Chicken: 10–24 µg Se/100 g
- Dairy products: ~3.7 µg Se/100 mL
- Bovine kidney: up to 155.3 µg Se/100 g
- Freshwater fish: >12 µg Se/100 g
- Canned tuna: >70 µg Se/100 g

Gpx, which accounts for over 60% of total Se content in serum and plasma, is considered the most reliable biomarker for assessing Se status in humans (Uslu and Aktaç, 2020).

Se intake and serum levels vary considerably among different countries and regions, influenced by dietary habits and soil Se content. For instance, Se supplementation programs have been implemented in Se -deficient regions such as the Keshan area in China and certain parts of Central Asia and Europe, including Finland. These interventions have led to significant improvements in public health by preventing Se -related disorders. In countries like China, soil heterogeneity results in regional variations in both dietary Se intake and serum Se concentrations (Minich, 2022).

Table 1. Selenium use and blood levels in different regions of the world

Country	**Daily intake (µg)**	**Blood/serum (µg/liter)**
Russia	15-130	67-106
Germany	38-47	89-98
USA	60-160	100-350
China*	2-6990	5-7800
Japan	27-89	80-155
Canada	113-220	143
Tibet	5-15	5-47
Finland until 1984	40	69
Finland after 1984	80	109

1.7. Alternative medicine

In contemporary complementary and alternative medicine practices, Se is utilized for its potential therapeutic effects in various conditions. One of its primary uses is in the management of hypercholesterolemia (high cholesterol levels), where Se's antioxidant properties may contribute to cardiovascular health.

Another common application is in the treatment of Hashimoto's thyroiditis (HD), an autoimmune disorder affecting the thyroid gland. Se supplementation in patients with Hashimoto's disease has been shown to reduce thyroid peroxidase antibody (TPOAb) levels, which may alleviate the progression of the disease. Furthermore, Se is used to assist in the regulation and reduction of elevated thyroid hormone levels, particularly in cases of subclinical hyperthyroidism or autoimmune-related thyroid dysfunction.

These alternative uses underscore Se's emerging role in integrative medicine, especially for patients seeking complementary approaches to chronic endocrine and metabolic disorders.

1.8. Storage

The total Se content in the human body is estimated to range between 13 and 30 milligrams. A significant portion of this Se —approximately 28% to 46%—is stored in skeletal muscle tissue, highlighting the importance of muscle as a primary Se reservoir.

Plasma Se concentrations of 8 µg/dL or higher are considered sufficient to support optimal protein synthesis, particularly the synthesis of selenoproteins, which are critical for various physiological functions, including antioxidant defense and thyroid hormone metabolism.

1.9. Vitamin E

Vitamin E is a potent antioxidant that serves as the first line of defense against the peroxidation of membrane phospholipids. A critical contributor to this protective mechanism is Se, specifically through its role as an integral component of the Gpx enzyme. Within the Gpx molecule, the Se ion maintains enzymatic activity, thereby assisting in neutralizing lipid hydroperoxides and indirectly reducing the antioxidant burden on vitamin E.

Furthermore, Se plays a supportive role in the exocrine function of the pancreas, which is essential for proper digestion and nutrient absorption (Aktaş et al., 2020). Se enhances the absorption and metabolism of dietary fats and vitamin E, while also promoting the retention of vitamin E within plasma lipoproteins.

By exerting its antioxidant function, particularly in sulfur-containing amino acids such as cysteine, Se helps reduce the overall demand for vitamin E in maintaining cellular redox balance (Akici et al., 2012).

1.10. Biochemical effects of selenium

1.10.1. Antioxidant

Oxidative stress refers to the destruction of normal cells caused by the excessive production of ROS in damaged cells (Aktaş and Sevimli, 2020). This condition arises when reactive species such as hydroxyl radicals, metal-oxygen complexes, superoxide anions, and hydrogen peroxide interact with metal ions, resulting in cellular damage (Aktaş and Bayram, 2020). Cells in human tissues possess complex detoxification systems that neutralize these reactive intermediates and prevent oxidative injury (Aktaş and Gür, 2021). Among these systems, Se plays a crucial role due to its incorporation into key antioxidant enzymes. Organic Se forms, such as Se -enriched yeast, have been shown to offer superior protection against oxidative damage compared to inorganic forms like sodium selenite (Gür and Bilgiç, 2022). Moreover, organic Se has been demonstrated to be less toxic while retaining effective antioxidant capacity (Hosnedlová et al., 2017; Çakına, 2022).

Several Se -dependent enzymes—such as thioredoxin reductase, Gpx, and iodothyronine deiodinase—function as intracellular antioxidants, playing a pivotal role in mitigating oxidative damage. Consequently, Se supplementation is considered to enhance the endogenous antioxidant defense mechanisms of the body (Wang et al., 2017).

1.11. Selenium and its relationship with diseases

1.11.1. Immunity

Elevated Se concentrations have been observed in immune-related organs such as the lymph nodes, spleen, and liver during disease states. Supplementation with Se, in conjunction with standard therapeutic approaches, has been shown to enhance immune responses and improve clinical outcomes. In Se -deficient individuals, the progression and severity of viral infections, including influenza, tend to worsen.

Se has been reported to reduce the risk of hepatocellular carcinoma induced by hepatitis B and C viruses. Regular dietary intake of Se -rich foods is therefore essential for sustaining a robust and responsive immune system.

Moreover, Se exhibits a protective role against DNA damage and mutagenesis by interacting with other antioxidants such as vitamin E. It is actively involved in modulating inflammatory responses and mitigating oxidative stress. The enzyme Gpx, a Se -dependent protein, protects lipid-containing organelles and cell membranes by neutralizing peroxidative damage through its redox functions.

Together with vitamin E, Se contributes to maintaining cellular integrity by strengthening cell membranes and neutralizing hydrogen peroxide via redox reactions involving glutathione. This mechanism also contributes to decelerating the aging process at the cellular level. In conditions of Se deficiency, the toxicity of redox by-products increases, resulting in significant oxidative damage to cell membranes.

Furthermore, Se is critical for individuals living with HIV, as it facilitates the differentiation of CD4+ T lymphocytes into T-helper 1 cells. This transformation plays a role in reducing the incidence of opportunistic mycobacterial co-infections. Se also enhances the cytotoxic activity of natural killer cells, T lymphocytes, and macrophages.

In addition to its immunomodulatory properties, Se has been found to reduce the toxicity of various harmful substances, including heavy metals (lead, cadmium, arsenic, mercury) and environmental toxins such as paraquat herbicides (Shreenathet al., 2023).

1.11.2. Selenium-cancer relationship

Scientific literature has identified Se -containing compounds found in garlic, particularly γ-glutamyl-Se-methyl Se-Cys and Se-methyl Se-Cys, as having notable anticancer properties (Taban et al., 2013). These compounds have demonstrated potential in inhibiting carcinogenesis through various mechanisms, including antioxidant activity and modulation of cellular redox balance.

Se plays a significant role in the prevention of several cancer types—most notably breast, liver, lung, colon, and prostate cancers—due to its ability to neutralize free radicals and protect cellular DNA from oxidative damage. Clinical studies have confirmed that a daily Se intake of approximately 200 µg (not mg) can reduce the risk of cancer development associated with genetic mutations and oxidative stress.

Furthermore, epidemiological data indicate that cancer incidence is higher in populations living in regions with low soil and dietary Se levels. Adequate antioxidant intake through diet has been shown to protect healthy cells from transformation into malignant forms.

Garlic, in particular, is a rich source of Se, as well as vitamins E and C—both of which possess strong antioxidant capabilities. These nutrients collectively contribute to cellular defense mechanisms against oxidative stress and DNA damage, reinforcing the importance of a Se -rich diet in cancer prevention strategies (Vinceti et al., 2018).

1.11.3. Selenium and alzheimer’s disease

Alzheimer’s disease (AD) is a progressive neurodegenerative disorder primarily associated with the accumulation of amyloid-β plaques, which contribute to neurotoxicity. A key mechanism underlying this neurotoxicity is oxidative stress, often accompanied by neuroinflammation. In addition, AD has been linked to disruptions in the intestinal microbiota, suggesting a potential gut-brain axis involvement in disease progression (Ferrari, 2020).

Aging is accompanied by a physiological decline in Se levels in the human body. This reduction in Se compromises the antioxidant defense system, contributing to structural and functional impairments in brain tissues. As Se is preferentially utilized by the brain in deficiency states, insufficient levels can lead to decreased turnover of neurotransmitters, adversely affecting cognitive processes.

Se intake has been shown to alleviate lipid peroxidation-related damage at neuronal synapses and to enhance neurotransmitter transport. These effects collectively support improved central nervous system (CNS) function. Dietary sources rich in Se —such as Brazil nuts and seafood—have demonstrated potential benefits in improving cognitive performance in individuals with mild cognitive impairment.

Gpx, a Se -dependent antioxidant enzyme, plays a critical role in protecting neural tissues by catalyzing the reduction of hydrogen peroxide and limiting lipid peroxidation. Other selenoproteins, including thioredoxin reductase and various GPx isoforms, contribute to cellular defense mechanisms by mitigating oxidative stress and preserving neuronal integrity.

Thus, Se supplementation and adequate dietary intake may offer neuroprotective benefits and contribute to the maintenance of cognitive function, particularly in the aging population (Uslu and Aktac, 2020; Shreenath et al., 2023).

1.11.4. Selenium and thyroid function

Among all tissues in the human body, the thyroid gland contains the highest concentration of Se per gram of tissue, primarily due to its abundance of selenoproteins. The thyroid gland plays a crucial role in regulating fundamental physiological functions, including body temperature, metabolism, appetite, weight, energy levels, and sleep cycles.

Se is essential for the synthesis and regulation of thyroid hormones. A deficiency in Se can disrupt thyroid function and lead to clinical conditions such as hypothyroidism, hyperthyroidism, and thyroiditis (inflammation of the thyroid gland) (Wang et al., 2023).

Of the 35 known human selenoproteins, three are iodothyronine deiodinases that are directly involved in thyroid hormone metabolism. These enzymes catalyze the activation and inactivation of thyroid hormones:

1. **Type I Deiodinase (D1):** Converts the inactive form of the hormone, T4, into its active form, T3, facilitating hormonal balance.
2. **Type II Deiodinase (D2):** Highly expressed in the CNS, skeletal muscle, and brown adipose tissue, D2 plays a major role in intracellular T3 production and local thyroid hormone activation.
3. **Type III Deiodinase (D3):** Inactivates excess thyroid hormone by converting T4 and T3 into their inactive metabolites, thus maintaining thyroid hormone homeostasis.

These Se -dependent enzymes are critical in maintaining a balanced thyroid hormone environment and ensuring proper endocrine function. Therefore, adequate Se intake is essential for optimal thyroid health and overall metabolic stability (Bilgic et al. 2024; Shreenath et al. 2023).

1.11.5. Hashimoto's thyroiditis

HT, also known as autoimmune thyroiditis, is a chronic inflammatory condition of the thyroid gland characterized by immune-mediated destruction of thyroid tissue. The disease is primarily marked by the presence of autoantibodies, particularly anti-thyroid peroxidase antibodies (TPOAb) and anti-thyroglobulin antibodies (TgAb). Among individuals diagnosed with HT, approximately 90% exhibit elevated levels of TPOAb in circulation. Although TgAb may also be present, it is generally considered less sensitive and less specific than TPOAb for diagnostic purposes.

As inflammation progresses, thyroid follicles are gradually destroyed and replaced by infiltrating lymphocytes, leading to impaired hormone production and often resulting in hypothyroidism.

Se, particularly in the form of SeMet, has been investigated for its potential therapeutic role in patients with HT. Studies suggest that Se supplementation may help reduce TPOAb titers and modulate the autoimmune response. Such supplementation is especially recommended for individuals with adequate iodine intake but who are Se -deficient, as Se supports thyroid hormone metabolism and enhances antioxidant defenses within thyroid tissue (Yang, 2009; Bilgiç and Aktaş, 2022).

1.11.6. Heart

Se plays a vital role in cardiovascular health, primarily due to its potent antioxidant properties that reduce oxidative stress—a key contributor to endothelial dysfunction and atherosclerosis. By enhancing antioxidant enzyme activity, Se helps protect myocardial tissue and vascular structures from oxidative damage (Aktaş et al., 2024).

Se also supports cardiovascular function by promoting healthy blood flow and inhibiting platelet aggregation, thereby reducing the risk of thrombosis and related cardiovascular complications.

Se deficiency has been consistently linked to an increased incidence of cardiovascular diseases. One well-documented example is KD, an endemic cardiomyopathy first identified in Se -deficient regions of China. This condition is characterized by myocardial necrosis, heart enlargement, and, in severe cases, sudden cardiac death, particularly among children and women of reproductive age (Bilgic et al., 2021).

Therefore, adequate Se intake is considered essential for maintaining cardiovascular health and preventing Se -deficiency–related heart disorders (Bomer et al., 2020; Gür et al., 2022).

1.11.7. Keshan disease

KD is a form of congestive cardiomyopathy predominantly observed in Se -deficient regions. It is clinically characterized by symptoms such as cardiac enlargement, heart failure, arrhythmias, electrocardiographic abnormalities, and in severe cases, cardiogenic shock. In addition to its cardiac manifestations, KD may also result in musculoskeletal complications, including deformities in cartilage, bones, and joints, often leading to restricted mobility due to joint enlargement. Intermittent myalgia is also reported as a common symptom.

The disease primarily affects children and women of reproductive age and is associated with a high morbidity rate, estimated at approximately 50%, along with significant mortality.

Research suggests that environmental and viral cofactors—such as exposure to toxic chemicals and infection with the Coxsackie virus—may exacerbate the severity and progression of KD. Importantly, public health interventions using Se -enriched salt have demonstrated a significant reduction in the incidence of KD, particularly in endemic regions (Wang et al., 2023).

These findings underscore the essential role of Se in cardiovascular and musculoskeletal health, and highlight its importance in preventing endemic deficiencies that can lead to severe clinical outcomes (Bilgic et al., 2023).

1.11.8. Fertility

Se is a crucial micronutrient in male and female reproductive health. It plays a fundamental role in testosterone biosynthesis and contributes to the formation, maturation, and motility of spermatozoa. Testicular tissue contains relatively high concentrations of Se, which is vital for maintaining sperm integrity and functionality, primarily through its involvement in antioxidant defense mechanisms that protect sperm cells from oxidative damage.

In males, Se deficiency has been linked to reduced sperm count, impaired sperm motility, and infertility. Similarly, in females, insufficient Se levels are associated with an increased risk of miscarriage, impaired follicular development, and reduced embryo viability.

Interestingly, both deficient and excessive Se levels can negatively affect reproductive outcomes. Elevated Se concentrations may lead to toxicity and hormonal imbalance, while deficiency compromises sperm quality and female reproductive success. Therefore, maintaining an optimal Se status is essential for fertility in both sexes (Gür et al., 2022; Shreenath et al., 2023).

1.12. Rich foods containing selenium

Se is an essential trace element found naturally in a variety of foods. The Se content of these foods can vary depending on factors such as soil Se concentration, geographic origin, and food processing methods. According to the literature, the following foods are recognized as rich sources of Se:

- Eggs
- Liver (particularly from beef and poultry)
- Walnuts
- Organ meats (offal)
- Dairy products
- Whole wheat flour and whole grain breads
- Fresh vegetables and fruits
- Red meats (beef, lamb)
- Sunflower seeds
- Mushrooms
- Poultry (especially chicken breast and turkey)
- Seafood, including rockfish, tuna, herring, and salmon
- Brazil nuts (noted as the richest natural source of Se)
- Onions and garlic

These foods, when included in a balanced diet, contribute significantly to meeting daily Se requirements and supporting antioxidant, thyroid, immune, and reproductive health (Berzelius, 2020).

Table 2. Se concentrations in foods

Sources	***Se density (mg/kg)***	***Types of Se***
Brazil nuts	*0.03–515*	*SeMet*
Bread	0.01–30	SeMet/selenate
Cereals	0.02–35	SeMet/selenate
Rice	0.05–0.08	SeMet
Onions	0.02–0.05	SeMet/Sec
Garlic	0.05–1.0	SeMet/Sec
Broccoli	0.5–1.0	SeMet/selenate
Potatoes	0.12	SeMet
Lentils	0.24–0.36	SeMet/selenate
Meat and meat products		
Beef	0.42–0.142	SeMet
Chicken	0.081–0.142	SeMet/Sec
Fish	0.1–5.0	SeMet/selenite/selenate
Eggs	3–25	SeMet/Sec
Lamb	0.033–0.260	SeMet
Milk and dairy products	0.01–0.03	Sec/selenite
Yeast	0.6–15	SeMet

.

1.12.1. Brazil nuts

Brazil nuts (*Bertholletia excelsa*) are widely recognized as the most Se -rich food source known in human nutrition. It is recommended to consume 1–4 Brazil nuts per day, as this amount is generally sufficient to meet or exceed the recommended daily Se intake.

Beyond their exceptional Se content, Brazil nuts are nutritionally dense and contain:

- Fat (60–70%)
- Protein (~17%)
- Dietary fiber
- Minerals: magnesium, zinc, phosphorus, iron, calcium, copper, potassium
- Vitamins: niacin, thiamine, vitamin B6, and various forms of tocopherol (vitamin E)

Brazil nuts also contain phenolic compounds and flavonoids in both free and bound forms, contributing to their strong antioxidant capacity. Additionally, they are rich in phytosterols such as squalene and tocopherol, which are known to support cardiovascular and metabolic health.

Due to their antiproliferative and antioxidant properties, Brazil nuts may reduce the risk of chronic diseases such as cancer and atherosclerosis, supporting their inclusion in preventive nutrition strategies (Yang, 2009; Ferrari, 2020).

1.12.2. Fortified foods

Fortified foods are an important dietary strategy for addressing micronutrient deficiencies, including Se. Various cereal products—such as whole wheat breads, breakfast cereals, and pasta—are commonly enriched with Se and other essential minerals to improve their nutritional value.

Grains naturally contain Se in variable amounts depending on the Se content of the soil in which they are cultivated. However, in many countries with low soil Se levels, Se fortification of grain-based products has become a standard public health practice. These fortified products serve as an effective Se supplement, particularly for populations at risk of deficiency (Azirak et al., 2019).

Therefore, regular consumption of Se-enriched grains can contribute significantly to maintaining adequate Se status and supporting overall health (Tanbek et al., 2017).

1.12.3. Garlic

Garlic (*Allium sativum L.*) is widely utilized both as a culinary ingredient and in traditional medicine due to its numerous health-promoting properties. One of the primary bioactive compounds in raw garlic is allicin, which is responsible for its characteristic pungent taste and odor. Allicin is formed enzymatically when garlic is crushed or chopped, and it contributes to garlic's well-documented antimicrobial and antioxidant effects.

Garlic is also a natural source of Se, which acts synergistically with its sulfur-containing compounds to enhance its antioxidant capacity. These compounds play a role in neutralizing free radicals, reducing oxidative stress, and modulating inflammatory responses.

According to the scientific literature, regular consumption of Se-rich garlic may provide protective effects against several types of cancer, including:

- Brain tumors
- Skin cancer
- Esophageal cancer
- Colorectal cancer
- Prostate cancer
- Gastric (stomach) cancer
- Thyroid cancer

These protective effects are attributed to garlic's ability to modulate carcinogen metabolism, promote DNA repair, and support the immune system, in addition to its Se content (Akan, 2014; Tanbek et al., 2017).

2. Discussion

Scientific research has consistently demonstrated that Se is an essential trace element required for the proper regulation of reproductive and growth functions in living organisms. Beyond these fundamental roles, Se is also recognized for its pleiotropic effects, notably its anti-inflammatory and antioxidant properties (Mikulska et al., 2022).

Despite these known benefits, neither the American nor European Thyroid or Endocrinology Societies currently recommend Se supplementation for the treatment of HT (Iraz et al., 2015; Filipowicz et al., 2021). However, individual clinical trials have reported promising outcomes. For instance, a study administering 100 µg of Se daily for six months to 29 women with newly diagnosed, untreated HT demonstrated a significant reduction in TPOAb levels. This suggests that Se may play a protective role in delaying or preventing the progression to hypothyroidism in such patients (Van Zuuren et al., 2014; Kryczyk-Kozioł et al., 2021). Nevertheless, further large-scale, randomized controlled trials are required to confirm the clinical efficacy of Se supplementation in HT management.

In relation to KD —a cardiomyopathy endemic in Se -deficient regions—multiple studies have demonstrated that Se supplementation significantly reduces disease incidence (Zhou et al., 2018). In a notable clinical trial conducted in China, the administration of sodium selenite to

KD patients resulted in an increase in Gpx activity and marked clinical improvement, further supporting Se's therapeutic potential in Se -deficiency-related conditions.

These findings collectively emphasize the crucial role of Se in human health. However, they also highlight the need for context-specific guidelines and further scientific evidence, particularly for its therapeutic use in autoimmune and cardiovascular diseases (Chen, 2012).

In general, Se supplementation is considered an immunostimulatory agent, enhancing immune system functions (Huang et al., 2012). Research indicates that the prevalence of autoimmune thyroiditis, including HT, is higher in regions with low Se levels, suggesting a possible correlation between Se deficiency and the development of autoimmune disorders (Wichman et al., 2016).

Moreover, Se has been shown to modulate inflammatory pathways, particularly those associated with inflammation-related carcinogenesis. It appears to influence the molecular mechanisms underlying chronic inflammation, thereby reducing the progression of inflammation-driven cancers (Gao et al., 2016).

Epidemiological and clinical studies further suggest that individuals with higher Se intake and tissue Se levels are at lower risk for developing various cancers. Additionally, Se has been shown to exert antiproliferative effects by inhibiting the growth of cancer cells through mechanisms that include induction of apoptosis, suppression of angiogenesis, and modulation of cellular redox status.

These findings underscore Se's potential role as a preventive and therapeutic agent in immune regulation and cancer biology, while also highlighting the need for controlled clinical trials to validate its efficacy in diverse populations (Vinceti, 2018; Li et al., 2021; Yuan et al., 2022).

Se is a critical micronutrient for brain function, yet its effects are dose-dependent and may be neurotoxic at excessive levels. Although the brain contains only approximately 2.3% of the total Se found in the human body, this small amount is vital for maintaining neuronal integrity and function.

Se deprivation can lead to irreversible damage to neuronal tissue, particularly due to increased susceptibility to oxidative stress. This mechanism is of particular concern in the pathogenesis of neurodegenerative diseases such as AD. Oxidative stress is a well-established contributor to neuronal degeneration in AD and similar conditions.

Selenoproteins, which act as endogenous antioxidants, may help prevent or slow the progression of AD by neutralizing ROS and protecting neurons from oxidative damage. However, while Se supplementation may offer neuroprotective benefits, it must be approached with caution.

Excessive Se intake has been associated with adverse neurological effects, including neurotoxicity, as well as a heightened risk of developing type II diabetes and amyotrophic lateral sclerosis. These findings emphasize the importance of maintaining optimal Se levels, as both deficiency and excess can negatively impact neurological and systemic health (Solovyev et al., 2018).

There is a positive correlation between sperm count and Se concentration in seminal fluid. Studies have shown that sperm count reaches its optimal level when seminal Se concentration is within the range of 50 to 69 μg. Deviations from this range—whether lower or higher—have been associated with reduced sperm motility, which consequently increases the risk of asthenospermia, a condition characterized by impaired sperm movement (Hansen and Deguchi, 1996).

Women, Se deficiency has also been linked to adverse pregnancy outcomes. These include an increased risk of low birth weight, spontaneous abortion, and developmental damage to the fetal nervous and immune systems. Furthermore, Se deficiency during pregnancy may contribute to various maternal health risks and complications, such as gestational hypertension, preeclampsia, and preterm birth.

These findings highlight the critical importance of maintaining adequate Se levels in both men and women to support fertility, healthy pregnancy, and fetal development (Lima et al., 2022; Bilgic et al., 2022).

3. Conclusion

Adequate daily intake of Se is essential for maintaining overall health, preventing various diseases, and potentially slowing the aging process. The biological effects of Se are primarily mediated by selenoproteins that contain the amino acid Se-Cys. Dietary Se intake is influenced by both the amount of food consumed and the Se content of those foods, which can vary depending on geographic and environmental factors.

Se plays a vital role in several key physiological systems, including immune function, antioxidant defense, and thyroid hormone metabolism. According to the Turkish Nutrition Guide, the recommended daily Se intake for both adult women and men is 70 µg.

In recent years, research on Se has expanded significantly. The identification and characterization of numerous new selenoproteins—ranging from plants to humans—have enhanced our understanding of Se's roles in biological systems. These discoveries have underscored the multifaceted importance of Se in health and disease.

Se compounds have shown promising potential in the diagnosis and treatment of cancer, and are expected to play a critical role in cancer prevention and therapy in the near future. Moreover, the development of new Se -based pharmaceuticals may provide effective treatment options for various Se -related deficiencies and diseases.

In conclusion, ensuring optimal Se intake through balanced nutrition and, when necessary, supplementation can contribute significantly to public health and medical advancements.

Declaration of Author Contributions

All authors declare that they have contributed equally to this manuscript, have reviewed the final version, and have approved it for publication.

Declaration of Conflicts of Interest

The authors declare that there is no conflict of interest regarding this study.

References

Akan, S., 2014. Siyah sarımsak. *Gıda*, 39(6): 363-370.

Akici, A., Akova, M., Duman, D.K., Erdemli, İ., Babaoğlu, M.Ö., Birincioğlu, M., 2012. E vitamini. In O. Kayaalp (Ed.), Akılcı Tedavi Yönünden Tıbbi Farmakoloji. (13th ed., p. 1365). Pelikan Yayınevi, Ankara, Turkey.

Aktaş, I., Bayram, D., 2020. Investigation of the effects of silymarin on valproic acid-induced kidney damage in rats. *Harran Üniversitesi Veteriner Fakültesi Dergisi,* 9(1): 42-8.

Aktas, I., Gur, F.M., 2021. The effects of thymoquinone and β-aminoisobutyric acid on brain tissue of streptozotocin-induced diabetic rats. *International Journal of Veterinary and Animal Research*, 4: 1-6.

Aktaş, I., Gur, F.M., Özgöçmen, M., 2020. Silymarin ameliorates valproic acid-induced pancreas injury by decreasing oxidative stress. *International Journal of Veterinary and Animal Research*, 3(2): 34-8.

Aktaş, I., Sevimli, M., 2020. Protective effects of silymarin on brain injury in rats. *Van Veterinary Journal*, 31(2): 87-92.

Aktaş, I., Yahyazadeh, A., 2022. Protective potential of misoprostol against kidney alteration via alleviating oxidative stress in rat following exposure to paclitaxel. *Tissue and Cell*, 79: 101966.

Aktaş, I., Gür, F.M., Bilgiç, S., 2024. Protective effect of misoprostol against paclitaxel-induced cardiac damage in rats. *Prostaglandins and Other Lipid Mediators*, 171: 106813.

Avery, J., Hoffmann, P., 2018. Se, selenoproteins, and immunity. *Nutrients*, 10(9): 1203.

Azirak, S., Bilgic, S., Tastemir Korkmaz, D., Guvenc, A.N., Kocaman, N., Ozer, M.K., 2019. The protective effect of resveratrol against risperidone-induced liver damage through an action on FAS gene expression. *General Physiology and Biophysics*, 38(3): 215-225.

Berzelius, J.J., 2020. Lettre de M. Berzelius à M. Berthollet sur deux métaux nouveaux (Letter from Mr. Berzelius to Mr. Berthollet on two new metals). *Annales de Chimie et de Physique*, 2(7): 199–206.

Bilgiç, S., Aktaş, İ., 2022. Investigation of protective effects of misoprostol against paclitaxel-induced ovarian damage in rats. *Annals of Medical Research*, 29(3): 233-239.

Bilgiç, S., Özgöçmen, M., Ozer, M.K., 2023. Thymoquinone ameliorates amikacin induced oxidative damage in rat brain tissue. *Biotechnic and Histochemistry*, 98(1): 38-45.

Bilgic, S., Tastemir Korkmaz, D., Azirak, S., Nilay Guvenc, A., Kocaman, N., Kaya Ozer, M., 2021. Olanzapine-induced renal damages and metabolic side effects: the protective effects of thymoquinone. *Annals of Medical Research*, 25(1): 0070-0075.

Bilgic, S., Aktaş, I., Yahyazadeh, A., 2024. Protection of lutein against the neurotoxicity of cisplatin in the rat brain. *Tissu and Cell*, 91: 102609.

Bilgiç, S., Gür, F.M., Aktaş, I., 2022. Biochemical and histopathological investigation of the protective effect of lutein in rat kidney exposed to cisplatin. *Medical Records-International Medical Journal*, 4(3): 433-438.

Bomer, N., Grote Beverborg, N., Hoes, M.F., Streng, K.W., Vermeer, M., Dokter, M.M., IJmker, J., Anker, S.D., Cleland, J.G.F., Hillege, H.L., Lang, C.C., Ng, L.L., Samani, N.J., Tromp, J., van Veldhuisen, D.J., Touw, D.J., Voors, A.A., van der Meer, P., 2020. Selenium and outcome in heart failure. *European Journal of Heart Failure*, 22(8): 1415-1423.

Chen, J., 2012. An original discovery: selenium deficiency and Keshan disease (an endemic heart disease). *Asia Pacific Journal of Clinical Nutrition: APJCN*, 21(3): 320-6.

Çakına, S., 2022. The relationship between oxidative stress and selenium. *Environmental Toxicology and Ecology*, 2(1): 22-29.

Ferrari, C.K.B., 2020. Anti-atherosclerotic and cardiovascular protective benefits of Brazilian nuts. Front Biosci (Schol Ed), 1(12), 38–56.

Filipowicz, D., Majewska, K., Kalantarova, A., Szczepanek-Parulska, E., Ruchała, M., 2021. The rationale for selenium supplementation in patients with autoimmune thyroiditis, according to the current state of knowledge. *Endokrynologia Polska*, 72: 153–62.

Gao, X., Zhang, Z., Li, Y., Shen, P., Hu, X., Cao, Y., Zhang, N., 2016. Selenium deficiency facilitates inflammation following s. aureus infection by regulating tlr2-related pathways in the mouse mammary gland. *Biological Trace Element Research*, 172: 449–57.

Gür, F.M., Aktaş, İ, Bilgiç, S., Pekince, M., 2022. Misoprostol alleviates paclitaxel-induced liver damage through its antioxidant and anti-apoptotic effects. *Molecular and Cellular Toxicology*, 18: 393-400.

Gür, F.M., Bilgiç, S., 2022. A synthetic prostaglandin E1 analogue, misoprostol, ameliorates paclitaxel-induced oxidative damage in rat brain. *Prostaglandins and Other Lipid Mediators*, 162: 106663.

Hadrup, N., Ravn-Haren, G., 2020. Acute human toxicity and mortality after selenium ingestion: A review. *Journal of Trace Elements in Medicine and Biology*, 58: 126435.

Hansen, J.C., Deguchi, Y., 1996. Selenium and fertility in animals and man a review. *Acta Veterinaria Scandinavica*, 37(1): 19-30.

Hariharan, S., Dharmaraj, S., 2020. Selenium and selenoproteins: it's role in regulation of inflammation. *Inflammopharmacology*, 28(3): 667-695.

Hosnedlova, B., Kepinska, M., Skalickova, S., Fernandez, C., Ruttkay-Nedecky, B., Malevu, T.D., Sochor J., Baron, M., Melcova, M., Zidkova, J., Kızek, R., 2017. Summary of new findings on the biological effects of selenium in selected animal species—a critical review. *International Journal of Molecular Sciences*, 18(10): 2209.

Huang, Z., Rose, A.H., Hoffmann, P.R., 2012. The role of selenium in inflammation and immunity: From molecular mechanisms to therapeutic opportunities. Antioxid. *Redox Signal*, 16: 705–43.

Iraz, M., Bilgiç, S., Şamdancı, E., Özerol, E., Tanbek, K., Iraz, M., 2015. Preventive and early therapeutic effects of ß-Glucan on the bleomycin-induced lung fibrosis in rats. *European Review for Medical and Pharmacological Sciences*, 19: 1505-16.

Kaya, S., Pirinçci, İ., Ünsal, A., Traş, B., Bilgili, A., Akar, F., 2021. Vitaminler. In S. Kaya (Ed.), Veteriner Farmakoloji. (5th ed.). Medisan Yayınevi, Ankara.

Kieliszek, M. 2021. Selenium. *Advances in Food and Nutrition Research*, 96: 417-429.

Kryczyk-Kozioł, J., Zagrodzki, P., Prochownik, E., Błażewska-Gruszczyk, A., Słowiaczek, M., Sun, Q., Schomburg, L., Ochab, E., Bartyzel, M., 2021. Positive effects of selenium supplementation in women with newly diagnosed Hashimoto's thyroiditis in an area with low selenium status. *International Journal of Clinical Practice*, 75: e14484.

Küçük, O., 2014. Selenyum ve ruminantlarda kullanımı. *Erciyes Üniversitesi Veteriner Fakültesi Dergisi*, 11(1): 55–61.

Li, C., Wang, N., Zheng, G., 2021. Oral administration of resveratrol-selenium-peptide nanocomposites alleviates Alzheimer's disease-like pathogenesis by inhibiting Aβ aggregation and regulating gut microbiota. *ACS Applied Materials & Interfaces*, (39): 46406-20.

Lima, L.G., Santos, A.A.M.D., Gueiber, T.D., Gomes, R.Z., Martins, C.M., Chaikoski, A.C. (2022). Relation between selenium and female fertility: A systematic review. *Revista Brasileira de Ginecologia e Obstetrícia*, 44(7): 701-9.

Mikulska, A.A., Karaźniewicz-Łada, M., Filipowicz, D., Ruchała, M., Główka, F.K., 2022. Metabolic characteristics of Hashimoto's thyroiditis patients and the role of microelements and diet in the disease management-an overview. *International Journal of Molecular Sciences*, 23(12): 6580.

Minich, W.B., 2022. Selenium metabolism and biosynthesis of selenoproteins in the human body. *Biochemistry (Mosc)*, 87(1): 168-102.

Shreenath, A.P., Hashmi, M.F., Dooley, J., 2023. Selenium Deficiency. StatPearls. Neveda, USA.

Spiller, H.A., Pfiefer, E., 2007. Two fatal cases of selenium toxicity. *Forensic Science International*, 171(1): 67-72.

Solovyev, N., Drobyshev, E., Bjørklund, G., Dubrovskii, Y., Lysiuk, R., Rayman, M.P., 2018. Selenium, selenoprotein P, and Alzheimer's disease: is there a link? *Free Radical Biology and Medicine*, 127: 124-33.

Uslu, B., Aktac, S., 2020. Selenyum ve selenyumun depresyon üzerine etkileri. *European Journal of Science and Technology*, 20: 147–51.

Taban, S., Turan, M.A., Sezer, S.M., Türkmen, N., 2013. Kastamonu Taşköprü yöresinde yetiştirilen sarımsak bitkisinin selenyum içerikleri ve bazı toprak özellikleri arasındaki ilişkiler. *Journal of Agricultural Faculty of Uludag University*, 27(1): 39-47.

Tanbek, K., Ozerol, E., Bilgic, S., Iraz, M., Sahin, N., Colak, C., 2017. Protective effect of Nigella sativa oil against thioacetamide-induced liver injury in rats. *Medicine Science International Medical Journal*, 6(1): 96-103.

Van Zuuren, E.J., Albusta, A.Y., Fedorowicz, Z., Carter, B., Pijl, H., 2014. Selenium supplementation for Hashimoto's Thyroiditis: Summary of a cochrane systematic review. *European Thyroid Journal*, 3: 25–31.

Vinceti, M., Filippini, T., Del Giovane, C., Dennert, G. Zwahlen, M., Brinkman, M., Zeegers, M.P., Horneber, M., D'Amico, R., Crespi, C.M., 2018. Selenium for preventing cancer. *Cochrane Library: Cochrane Reviews*., 1(1): CD005195.

Wang, F., Li, C., Li, S., Cui, L., Zhao, J., Liao, L., 2023. Selenium and thyroid diseases. *Front Endocrinol (Lausanne)*, 14: 1133000.

Wang, N., Tan, H.Y., Li, S., Xu, Y., Guo, W., Feng, Y., 2017. Supplementation of micronutrient selenium in metabolic diseases: ıts role as an antioxidant. *Oxidative Medicine and Cellular Longevity*, 1–13.

Wichman, J., Winther, K.H., Bonnema, S.J., Hegedus, L., 2016. Selenium supplementation significantly reduces thyroid autoantibody levels in patients with chronic autoimmune thyroiditis: a systematic review and meta-analysis. *Thyroid*, 26: 1681–92.

Yang, J., 2009. Brazil nuts and associated health benefits: A review. *LWT - Food Science and Technology*, 42(10): 1573–1580.

Yuan, S., Mason, A.M., Carter, P., Vithayathil, M., Kar, S., Burgess, S., Larsson, S.C., 2018. Selenium and cancer risk: Wide-angled Mendelian randomization analysis. *International Journal of Cancer*, 150(7): 1134-40.

Zachara, B.A., 2018. Selenium in complicated pregnancy. A Review. *Advances in Clinical Chemistry*, 86: 157–178.

Zhou, H., Wang, T., Li, Q., Li, D., 2018. Prevention of Keshan disease by selenium supplementation: a systematic review and meta-analysis. *Biological Trace Element Research*, 186: 98–105.