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Some Properties of Selenium and Its Effects on Human Health

Selenyumun Bazı Özellikleri ve İnsan Sağlığı Üzerine Etkileri

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ABSTRACT

Selenium is an essential trace element that has a very important role in the homeostasis of the human body and the functioning of the immune system. It is known for its antioxidant properties and as a cofactor of many enzymes, such as glutathione peroxidase, which is an antioxidant enzyme in human metabolism. Selenium has a wide range of effects, assuring redox homeostasis, affecting hormone metabolism, especially thyroid hormones, and protecting the body against oxidative stress and inflammation. Although selenium is of vital importance for human health, deficiency and excess (toxicity) of selenium intake can cause significant health problems. Its deficiency causes cardiovascular diseases, neuromuscular diseases, cancer, infertility, diabetes, depression, and some immune diseases, while excessive selenium intake may result in the risks of liver diseases, deterioration in hematopoiesis, bone tissue deformation, some neurological disorders, and type 2 diabetes. Hence, optimum selenium consumption by taking into account factors such as age, gender, and physiological conditions of people is highly important. In this review, the importance, metabolism, daily needs, and sources of selenium were emphasized to set a source for the studies to be made on the subject.

Keywords: Human health, optimum Se intake, Selenium

ÖZ

Selenyum insan vücudunun homeostazı ve immun sistemin düzenli olarak çalışması için çok önemli role sahip olan esansiyel eser bir elementtir. İnsan metabolizmasında başta antioksidan enzimlerden olan glutatyon peroksidaz gibi pek çok enzimin kofaktörü olarak ve antioksidan özelliği ile bilinir. Selenyum, redoks homeostazı ile başta tiroid hormonları olmak üzere hormon metabolizmasını etkileyen, vücudu oksidatif strese ve inflamasyona karşı koruyan geniş bir etki alanına sahiptir. Selenyum insan sağlığı için hayati bir öneme sahip olmakla birlikte selenyum tüketiminin eksikliği ve fazlalığı (toksisite) önemli sağlık problemlerine neden olabilmektedir. Eksikliği, kardiyovasküler hastalıklar, nöromüsküler hastalıklar, kanser, infertilite, diyabet, depresyon ve bazı immun hastalıklara yol açarken, fazla selenyum alımı; karaciğer hastalıkları, hematopoezde bozulma, kemik doku deformasyonları, bazı nörolojik bozukluklar ile diyabet tip-2 riski ile sonuçlanabilmektedir. Bu nedenle insanların yaş, cinsiyet ve fizyolojik durumları gibi faktörlerin de göz önüne alınarak, optimum selenyum tüketimi büyük önem taşımaktadır. Bu derleme çalışmasında konu ile ilgili yürütülecek yeni çalışmalara kaynak oluşturmak amacıyla, selenyumun önemi, metabolizması, günlük ihtiyaç ve kaynakları tartışılmıştır.

Anahtar Kelimeler: İnsan sağlığı, optimum Se alımı, Selenyum

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Introduction

Leading a healthy life is under the influence of some factors such as heredity, environmental conditions, and nutrition. Nutrition maintains many metabolic and physiological functions of the organism in a healthy way and has a direct effect on the life span. A healthy life, growth, development, and continuity of bodily and physical functions are only possible with an adequate and balanced diet (Çelebi & Karaca, 2006, 2008). A healthy, balanced, and adequate diet can be achieved by taking adequate and appropriate proportions of protein, carbohydrates, lipids, vitamins, and minerals from the foods consumed. One of the minerals required for a healthy diet is selenium (Se), which has many critical functions in metabolism and is an essential trace mineral. This mineral is named after Selene, the ancient

Greek goddess of the moon. Selenium was discovered in 1817 by the Swedish chemist Berzelius, known as one of the founders of modern chemistry (Ilgın et al., 2010). Although the toxic effect of Se was noticed in the middle of the 19th century, its importance in nutrition as an essential element was first noticed in 1957 when it was seen that it prevented liver necrosis in rats with vitamin E deficiency (Akkuş et al., 1991; Aksoy et al., 2000).

Selenium is an element commonly found in nature. It is obtained as an intermediate product during the purification of metal ores, especially copper. Selenium in group VI A of the periodic table shows great similarity with sulfur in the same group in terms of physical and chemical properties. It is found in nature as −2, 0, +4, and +6 valence compounds. H_2SeO_3 and H_2SeO_4, which are inorganic forms of Se; analogous to hydrogen sulfide, sulfites and sulfates however, selenoamino acids such as Se-methionine, Se-cystine, Se-cysteine and other organic Se compounds such as selenoglutathione, dimethylselenide, trimethylselenium are generally less stable and more reactive than their sulfur analogues. Selenium is found in a wide range of concentrations in various geological materials such as water, soil, and rocks, but its distribution varies widely (Hıncal & Ataçeri, 1989). Accumulation of Se above 50 ppm in plants has a toxic effect. Therefore, the consumption of these plants, which contain high levels of Se, poses a danger to living beings (Gissel-Nielsen et al., 1984). The amount of Se in plants varies greatly depending on the type of soil and plant in which they grow. Although Se is found in every region of the world, its distribution varies greatly between regions. Grassland plants contain twice as much Se as grains. Crucifers contain about two to five times as much Se as meadow plants and cereals. The pH of the soil affects its selenite fixation. Alkaline, dehydrated, and dry soils contain toxic levels of Se. Since selenate compounds are soluble in these soils, they are easily taken up by plants growing in these soils (Alloway, 1973). The regions where it is most common are the USA, Ireland, some parts of China, and Turkestan. Plants that accumulate toxic levels of Se and are able to grow on these seleniferous soils have evolved tolerance to Se. Between 20,000 and 30,000 ppm, Se can accumulate in the dry matter of these plants that are called Se hyperaccumulators.

Selenium, which has major importance for metabolism, is included in metabolism through nutrition by passing from soil to plants in the food chain. Nutritional functions of Se in humans are provided by selenoproteins containing Se in their structure (Uslu & Aktaç, 2020). Proteins containing a Se compound in their active site are defined as selenoproteins, and these proteins absolutely need a Se compound to function. It is estimated that there are around 100 selenoprotein compounds in the human body, but only 30 of them have been identified, and the biological functions of these have not been fully determined yet (Bal et al., 2015; Kangalgil & Yardımcı, 2017). Among these, glutathione peroxidase (GPx) is the selenoprotein whose physiological functions are the most well-known. Besides having antioxidant effects and taking part in plasma Se transport, these selenoproteins are also the biomarkers that best reflect the plasma Se level. Glutathione peroxidase is a powerful Se-bound antioxidant enzyme found in many tissues in mammals that protects cells from oxidative stress and contains 4 atoms of Se that best reflect the level of plasma Se (Kasnak & Palamutoğlu, 2015; Rayman, 2000; Sung, 2000). This enzyme is a component of a multi-component antioxidant defense system, such as catalase, superoxide dismutase, and vitamin E, which protects the cell tissues and therefore the organism against oxidative stress. In this system, it protects polyunsaturated fatty acids, phospholipids containing saturated fatty acids, critical proteins, and deoxyribonucleic acid in the cell against the harmful effects of free radicals formed as a result of biological oxidation in the cell. The GSH-Px reduces hydrogen peroxide (H_2O_2) to water, which is formed as a result of biological oxidation and some metabolic reactions in cells, and which combines with a free radical, superoxide anion (O^-), to form a much stronger free radical hydroxyl (OH^-). $H_2O_2 + GSH \xrightarrow{\text{GSH-Px}} GSSH + 2H_2O$ prevents the formation of the more dangerous OH^-. Likewise, GSH-Px, which provides the reduction of hydroperoxides $\left(ROOH + 2GSH \xrightarrow{\text{GSH-Px}} GSSH + ROH + H_2O\right)$, is mostly cytosolic and is also found in mitochondria (Çaylak, 2011; Çelebi et al., 2016). The GHS-Px is also the most important biomarker for determining body Se level because more than 60% of Se in plasma is in GSH-Px. Also, in addition to antioxidant enzymes such as GPx and selenoprotein P, Se also takes part in the functions of enzymes that take a role in more specialized biochemical events such as iodine deiodinase, which plays a role in the metabolism of thyroid hormones, GPx-4, which plays a role in spermatogenesis, and selenophosphate synthetase-2, which plays a role in the biosynthesis of selenoproteins (Kangalgil & Yardımcı, 2017, Xia et al., 2010). In addition, Se, with its antioxidant effect, provides cell integrity, protects endothelial cells from hydroxynitric damage, reduces the activities of many reactive oxygen species such as H_2O_2 and lipid hydroperoxide, protects immune cells and therefore the immune system from oxidative damage, reduces cytokine release, and functions in many metabolic events such as prostaglandin and leukotriene metabolism in some tissues (Hıncal & Ataçeri, 1989; Kangalgil & Yardımcı, 2017).

The current review discusses the biological functions, metabolism, needs, and health benefits of Se, and diseases resulting from the deficiency and toxicity of this trace mineral, along with its distribution in different regions of the world. This study is a significant source for the studies to be carried out on the effects of Se on health.

Selenium Metabolism

Selenium is a trace element that is taken by diet. Since biological systems are not able to fully distinguish selenites and sulfides, there is competition between the absorptions of Se and S. Selenium absorption is quite high as it occurs via active transport similar to selenomethionine analogues (Stadtman, 1980). The protein content of the diet with vitamins A, E, and C increases the absorption of Se (Robinson & Thomson, 1983). Likewise, it has been reported that organic forms of Se such as selenomethionine, methylselenocysteine, and γ-glutamyl methyl selenocysteine obtained through natural sources have higher bioavailability than inorganic forms such as sodium selenite (Davis et al., 2017). Pérez-Corona et al. (2011) reported that the absorption of Se in organic form from the intestines is 85%–95%, while Se in inorganic form is only 10%. Selenium absorbed from the intestines is transported to the liver, where Se is metabolized and selenoproteins are synthesized by binding to erythrocytes, glutathione, globulin, and albumin in the plasma (Fairweather-Tait et al., 2011) and from there through the blood to organs and tissues such as the pancreas, kidneys, testicles, and thyroid glands (Combs et al., 2011). However, in order for Se to bind to plasma proteins, it must initially be uptaken by erythrocytes and metabolized by reduced glutathione to be reduced to H_2Se. Following reduction, free Se binds to plasma proteins and is transported to the liver. The liver has a central role in the metabolism of Se. Selenium is used for the synthesis of selenocysteine, an amino acid found in the active sites of selenoenzymes (Seale et al., 2018). Selenoprotein-P comprises approximately 60% of Se in plasma and acts as the main carrier protein (Ilgın et al., 2010). An adult human body contains about 2–20 mg of Se. The selenium level of the human body is estimated by measuring the Se levels of tissues such as urine, hair, and nails. Under physiological uptake conditions, the homeostasis of Se in the body is regulated through urine. Due to its high solubility, 20%–50% of the Se excreted in the urine is in the form of $(CH_3)_3$ Se+. But, $(CH_2)_3$ Se, which has volatile properties, is excreted through the lungs. However, the excretion of Se in this way is important in case of high Se uptake (Hıncal & Ataçeri, 1989).

The main source of Se is dietary nutrients, and in some regions and countries, drinking water also contains small amounts of Se. For example, 3.5 µg/L Se is reported in drinking water in the USA. There is insignificant level of Se in the air in terms of nutrition (Roman et al., 2014). Selenium is found in two organic forms: selenocysteine in foods of animal origin and selenomethionine in foods of plant origin. It is estimated that approximately 50% of Se in the diet is selenomethionine (Kangalgil & Yardımcı, 2017). The amount of Se contained in plants varies greatly according to the condition of the soil they grow and the type of plant. For example, meadow plants contain two times more Se than cereals, while citrus fruits contain four to five times more Se than meadow plants and cereals (Gissel-Nielsen et al., 1984). The inorganic sources of Se in diet are substances in the form of salts such as sodium selenite and sodium selenate. These inorganic compounds are generally used to increase the Se content of foods. However, their absorption is lower than the Se in organic form (Cardoso et al., 2016). Table 1 shows the Se contents of some animal and plant foods.

Table 1.
Selenium Contents of Some Animal and Plant Foods (µg/100 g) (TÜRKOMP, 2021)

Food	Se Content (µg)	Food	Se Content (µg)
Edible offal (calf's kidney)	155.3	Ostrich meat (leg)	21.7
Lentil (green/dry)	102.0	Cheese (goat)	21.0
Mussel (black)	48.9	Needlefish	20.8
Sardine (canned)	47.5	Sesame	19.8
Anchovy (canned)	46.6	Cowpea (dry)	19.0
Tuna (canned)	43.9	Linseed (dry)	18.8
Sesame seed (dry)	40.8	Pea nut (dry)	17.0
Lentil (red/dry)	40.4	Rabbit meat (unhidebound)	16.6
Acorn	39.2	Mushroom (cultivated)	15.0
Turbot	37.8	Chub	14.9
Goat meat (Fore shank)	35.6	Pea (dry)	11.8
Red mullet fish	33.3	Oat (White)	9.4
Saurel	31.2	Parsley (dry)	7.8
Chickpea (dry)	31.1	Barley (six-row)	6.6
LouferAQ:	28.8	Table salt (iodized)	6.1
Egg (Ostrich)	28.6	Tomatoes (dry)	5.6
Quail meat (unhidebound)	27.6	Pea (canned)	4.5
Shrimp	26.9	Vetch (dry)	4.5
Egg (hen)	26.9	Rye	3.8
Anchovy	26.4	Corn (flint, dry)	3.8
Haddock	23.4	Walnut (kernel, dry)	3.1
Broiler meat (wing)	22.8	Milk (cow)	2.5

Selenium Needs

Selenium is one of the essential elements that have a very important role in the homeostasis of the human body and the regular functioning of the immune system. However, scientific studies have shown that taking this element more or less than needed causes important health problems (Holben & Smith, 1999). Selenium deficiency causes a decrease in the activity of GPx which is an antioxidant enzyme activated by this element, and this situation results in an increase in the amount of H_2O_2, which is a free radical. As a result, it causes inflammation and could result in the initiation of many health problems such as diabetes, depression, and cardiovascular diseases. On the other hand, excessive intake of this element causes many other health problems such as hair loss, nail loss, bone deformation, diarrhea, nausea, fatigue, irritability, anemia, and reproductive disorders (Sur et al., 2020). Considering such disorders, it is of great importance to determine the Se need carefully.

Selenium needs of people vary according to age, gender, physiological condition, and nutritional habits. For example, a breastfeeding woman has a higher Se requirement than a woman of the same age. The World Health Organization recommends that a daily intake of 400–700 µg of Se will cause toxic effects, and the amount of Se that an adult should consume must not exceed 70 µg/day (Kieliszek & Błażejak, 2013). Recommended daily intakes of Se according to age, gender, and physiological status are presented in Table 2.

Table 2.
Daily Selenium Requirement (µg/Day) by Age, Gender, and Physiological Status (TÜBER, 2015)

Age	Gender	Requirement (µg/Day)
1–3	Female	15
	Male	15
4–6	Female	20
	Male	20
7–10	Female	35
	Male	35
11–13	Female	55
	Male	55
14–15	Female	55
	Male	70
15–70	Female	70
	Male	70
>70	Female	70
	Male	70
Pregnant	Female	70
Lactating mother	Female	85

Deficiency and Toxicity of Selenium

Although Se is an essential element for human metabolism, excess or deficiency of Se intake can cause significant health problems. In order to lead a healthy life, avoid these health problems, and slow down the aging process, daily Se intake should be at a sufficient level. As with many other nutrients, the need for Se varies depending on factors such as age, gender, and physiological condition. Therefore, the fine line between deficiency and toxic concentration of dietary Se amount should be considered (Vinceti et al., 2017). Results of studies on the subject indicate that the minimum amount of Se required for the absence of symptoms related to Se deficiency in humans is 10 µg/day, and the maximum tolerable amount is 400 µg/day (Mueller et al., 2009). Rocourt and Cheng (2013) reported that normal plasma Se level should be around 125 ng/mL on average, if it falls below 100 ng/mL, Se deficiency and if it exceeds 125 ng/mL, selenosis (toxicity) occurs.

Selenium deficiency is frequently seen in countries where soils are poor in Se, such as Siberia and some parts of China (Mistry et al., 2013). Its deficiency can cause functional and structural disorders in many organs and systems. Diseases frequently seen as a result of Se deficiency are diarrhea, cardiovascular diseases, arrhythmia, stroke, sudden infant death, male infertility, gastrointestinal and prostate cancers, neuropathy, aging, diabetes, thyroid hormone diseases, autoimmune diseases, depression, neurodegenerative diseases, and inflammation (Hendricks et al., 2013; Kangalgil & Yardımcı, 2017; Mistry et al., 2012; Rayman, 2000; Roman et al., 2014; Ruseva et al., 2013). On the other hand, cardiomyopathy (Keshan disease) and endemic osteoarthropathy (Kashin–Beck disease) are also common disorders seen in Se deficiency (Chen, 2012).

Keshan disease is congestive cardiomyopathy in women of reproductive age and children over the age of 10 (Chen, 2012). It was determined that the Se levels in the hair, nails, and blood of the people with Keshan disease were lower than the control groups and the Gpx activities were also reduced. Kashin–Beck disease is characterized by shortening of the fingers and toes and rheumatoid arthritis-like changes. Due to oxidative stress, joint lesions can lead to cartilage necrosis and bone deformations in the future. This disease is more common in 13-year-old age groups than in other age groups (Akkuş et al., 1991; Navarro-Alarcon & Cabrera-Vique, 2008). It is reported that a minimum of 30 mg of Se should be consumed daily for the prevention of Keshan and Kashin–Beck diseases (Simmer et al., 1990). As with Se deficiency, the geographic region is also important in the high intake of this mineral. In countries and regions such as India where the soil contains a high amount of Se, high levels of Se uptake and a blood Se concentration of more than 100 mg/dL cause toxicity (Selenosis) (Uslu & Aktaç, 2020). High levels of Se in the blood show pro-oxidant properties and cause DNA damage by inducing free radical production. In addition, high levels of Se replace the sulfates in the thiol (SH) groups found in proteins that repair DNA, causing them to become inactive. Likewise, when Se is taken at high levels, it replaces the sulfides in the structure of sulfoproteins and can also lead to the inhibition of respiratory enzymes such as NADH dehydrogenase, succinate dehydrogenase, and cytochrome oxidase, which are especially involved in oxidative phosphorylation (Sur et al., 2020).

Selenium toxicity can occur acutely or chronically. Symptoms such as gastrointestinal pain, muscle aches, fatigue, weakness, nausea, vomiting, and diarrhea seen in acute selenosis can be seen together with serious toxic effects such as neurological dysfunctions (Fordyce, 2013; Navarro-Alarcon & Cabrera-Vique, 2008; Sur et al., 2020). In chronic excess Se exposure, many symptoms such as liver damage, deterioration in hematopoiesis, hair loss, infertility, nail breakage, skin redness, garlic-like bad breath, bone deformations, tooth decay, and neurological disorders are observed (Davis et al., 2017; Duntas & Benvenga; 2015; Li et al., 2012; Nazemi et al., 2012; Spiller & Pfiefer, 2007). In addition, Drutel et al. (2013) reported that high levels of Se intake, even for therapeutic purposes, have a significant toxic effect on the endocrine system and increase the risk of type 2 diabetes.

Conclusion and Recommendations

Selenium plays a role in the metabolism of thyroid hormones and the endocrine system, which have an important role in brain development, continuity of brain functions, and the regulation of the body's metabolic rate. In addition, it is one of the basic components of many main metabolic pathways such as the antioxidant defense system and the immune system, the reproductive system, the musculoskeletal system, and the continuity of liver and kidney functions. It is only possible for the aforementioned mechanisms to fulfill their functions by taking sufficient daily Se. Sources of Se in diet are selenoproteins containing selenocysteine and selenomethionine.

Attention should be paid to the amount of foods consumed and the Se content of these foods in the daily intake of Se because it is very important to consume a sufficient amount of Se daily in order to fulfill its functions. According to the Turkish dietary guidelines, a daily average of food containing an average of 70 µg Se is recommended for adult women and men. In addition, in the treatment of diseases related to Se deficiencies, the type, amount, and duration of treatment should be well-adjusted. Otherwise, in long-term overconsumption, the blood Se level may increase in excessive amounts and cause serious toxic effects.

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