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The role of selenium in nutrition – A review

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Abstract. The role of selenium has been changed over the last decade. The element that was previously considered to be toxic turned out to be present in the human body in amounts of 10–15 mg, and almost every cell of our body contains it. Selenium contributes to growth, supports healthy muscle activity, reproductive organs, reduces the toxicity of certain elements such as mercury, supports the immune system, and even delays the spread of certain viruses (influenza, Ebola, HIV). Selenium-deficient areas of Europe could be a risk for their populations. The recommended daily intake (RDA) of selenium is 55 µg/day, while WHO and FAO have set up the daily tolerable dose at 400 µg/day. We must count with the harmful effects of selenium overdose, but it is almost impossible to introduce this amount into our body solely with food. Our selenium sources can be refilled with food supplements or selenium-enriched functional foods. In the review article, we report about the role of selenium in the environment, selenium-enriched plants, selenium-enriched yeast, the role of selenium in animal feed and in the human body, the opportunities of selenium restoration, selenium-enriched animal products, and the selenium content of milk.

Keywords and phrases: selenium, selenium supplementations, seleno-enzymes, seleno-amino acids, selenocysteine, selenomethionine, nutrition, enriched animal products, functional foods, milk

1 Introduction

The role of selenium has been considerably appreciated thanks to recent years' research. Selenium was discovered in 1817 by *Berzelius* and *Gahn* (*Széles et al.*, 2007). In the 1930s, it was considered that selenium is a toxic heavy metal, which in higher doses leads to the destruction of the living organism (*Vernie*, 1984). In 1943, its carcinogenic effect has been described (*Nelson et al.*, 1943). Some years later, *Clayton* and *Baumann* (1949) found out that selenium supplementation decreases the number of tumorous cases. The essential role of selenium was first published in 1957, when rat experiments proved that selenium added to food prevented the necrosis of the liver (*Schwarz* & *Foltz*, 1957). From 1966, we can read about the anti-cancer effects (*Shamberger* & *Rudolph*, 1966). The activity of selenium-dependent enzyme proteins was studied in 1973 (*Turner* & *Stadtman*, 1973). Glycine reductase and glutathione peroxide is found in bacteria and mammals (*Rotruck et al.*, 1973). In 1976, the chemical characterization of the selenoprotein component of *glycine reductase* was studied, and selenocysteine as the organoselenium moiety was identified (*Cone et al.*, 1976).

Researchers have found that if so many selenium forms are known, no selenium content of the organism can be deduced from the selenium yield. According to *Thomassen* and *Nieboer* (1995), we must count with toxicity, accessibility, and the study of absorption in the organism. The oxidation state and the complex training with other substances must be investigated, and thus the distribution and volume of the selenic alterations can be determined by means of speciation analysis (*Ebdon et al.*, 2001).

2 Selenium in the environment

Selenium is rarely found in its elemental form in the environment (*Craig*, 1986). Soil, water, and all living organisms contain –2 (selenide), +4 (selenite), and +6 (selenate) oxidation status (*Gómez-Ariza et al.*, 1998), but these forms depend on the environmental effects (*Skinner*, 1999). Selenates and selenites are water-soluble, so they occur most often in these forms in water (*Gómez-Ariza et al.*, 1999).

Besides the inorganic alterations, there are so many forms of organic bindings in which selenium is present as selenide (*McSheehy et al.*, 2000; *Michalke et al.*, 2001). They are mostly seleno-amino acids or their derivatives. Foods of plant origin include selenomethionine and those of animal origin contain selenomethionine and selenocysteine. Selenomethionine is essential to humans and animals, but they can produce selenocysteine from selenomethionine in the organism (*Beilstein* & *Whanger*, 1986).

3 The role of selenium in the human body

Selenium plays a significant role in many physiological processes in a direct or indirect way. Our foods contain selenomethionine and selenite. Selenite is reacting in our organism with the thiols in the effect of glutathione, and then it forms H_2Se. Selenocysteine is formed from selenomethionine through various processes. Selenocysteine decomposes into hydrogen selenide as the result of the β-*lyase* enzyme. Approximately 90% of selenocysteine integrates into the proteins of our organism (*Mitchell et al.*, 1976). The amount of these selenoproteins decreases when the diet is incomplete. Most of them have been identified in the 20th century, such as the *iodotyrosine deiodinase*, which is responsible for the activation of thyroid hormones (*Allan et al.*, 1999), or selenoprotein P (*Ungvári*, 2015).

With the average selenium intake, the excess is excreted in the urine as a seleno-amino sugar in large quantities, it is excreted through the respiratory processes as dimethyl-selenide, while the urine may excrete trimethylselenium ions (*Suzuki* & *Ogra*, 2002; *Kobayashi et al.*, 2002; *Bendhal* & *Gammelgaard*, 2004).

The most important role of selenium is its antioxidant effect. This is expressed by the interaction with various enzymes (*Awashti et al.*, 1975; *Molnár*, 2013; *Rigó*, 2002). It plays a key role in the function of the *glutathione peroxidase* enzyme, which responds to hydrogen peroxide and other harmful lipids and phospholipid hydroxides to prevent harmful free radicals, inhibit DNA damage and the development of metabolic active carcinogens (*Karag et al.*, 1998). The amount is determined by the amount of selenium and reduced glutathione in our body (*Meister* & *Anderson*, 1983). Selenium is incorporated into the enzyme as selenocysteine, where the sulphur is located. In the body's antioxidant defence system, the biochemical property provides the importance of selenium to reduce the amount of sulphur more easily (*Cser* & *Sziklai-László*, 1998).

The *iodotyrosine deiodinase* enzyme assists in the production and function of T_3 and thyroxin hormones, wherefore selenium is essential for growth and normal thyroid function (*Wilson et al.*, 1992; *Holben* & *Smith*, 1999). *Thioredoxin reductase* regulates cell growth (*Mustacich* & *Powis*, 2000), while selenoprotein N is responsible for normal muscle development (*Zhang et al.*, 2012).

The antioxidant effect of selenium can prevent the oxidation of LDL cholesterol (*Gey*, 1998), reduce inflammation, strengthen the immune system, help protect the body against oxidative stress, and thereby indirectly reduce HIV virulence (*Dworkin*, 1994; *Stone et al.*, 1997; *Weeks et al.*, 2012). Selenium reduces some toxic elements, such as mercury toxicity, via inhibiting their absorption by forming insoluble compounds (*Feroci et al.*, 2005).

In the case of people on a healthy diet, the risk of selenium deficiency is small, but in selenium-deficient areas, such as Hungary or Germany (*Gondi et al.*, 1992), there may be a health risk of persistent selenium nutrition (*Ellis* & *Salt*, 2003).

Selenium deficiency affects about half a billion people annually (*Combs*, 2001). Many diseases may develop and exacerbate, for example, depression (*Finley* & *Penland*, 1998), cardiovascular disasters, tumour disorders, thyroid dysfunction, or spread of viruses (influenza, HIV, Ebola) (*Tamás*, 2000); it weakens the viability of sperms (*Reilly*, 1998), but some studies also write about the selenium's capability of delaying ageing (*Bankhofer*, 1988).

Selenium deficiency may cause Keshan disease, which has been discovered in China – it mainly affects children and causes cardiopulmonary dysfunction, leading to myocardial infarction. The Kashin–Beck syndrome (degenerative joint disease) can also be linked to selenium deficiency (*Burke* & *Opeskin*, 2002). Recent studies have shown that inadequate selenium supply can be associated with Down's syndrome and the development of infant cretinism (*Ani et al.*, 2007, *Chanoine*, 2003).

The normal human body (60–70 kg) contains 10 to 15 mg of selenium. Almost every cell of our body contains it, but most of the selenium accumulates in the kidneys, liver, spleen, pancreas, and testes. According to Codex Alimentarius Hungaricus (*152/2009* (*XI. 12*) *FVM*), the recommended daily intake (RDA) of adults is 55 μg/day. According to the Institute of Medicine, Food and Nutrition Board (2000), the maximum limit of Se is 400 μg/day over which negative selenium effects are expected (*Arthur*, 1991). The first symptoms of selenium poisoning are metallic mouth taste, garlic smell breath, in chronic cases, hair loss, the loss of nails, skin rashes, discolouration of the teeth, and ultimately neurological disorders. Acute selenium toxicity only rarely causes death, and the lethal dose of selenium is 5–10 mg/kg (*Olson*, 1986). This quantity cannot be taken in with food (*Ungvári*, 2015).

Table 1: Comparison of Recommended Sun Intake (RDA) and Maximum Tolerable Volume (UL) by age

Age (year)	RDA (µg Se/day)	UL (µg Se/day)
1–3	20	90
4–8	30	150
9–13	40	280
14–18	55	400
19–	55	400

Source: Institute of Medicine, 2000

4 Opportunities of selenium restoration

The selenium content of foods is highly varied. The South American Brazilian walnut (*Bertholletia excelsa*) has the highest selenium content, more than 100 µg per piece (*Chang*, 1995). The richest selenium source among our foods is animal organs (animal meat) and seafood. Since the content of selenium in foods consumed during a daily meal is not significant, increasing the amount of food cannot increase selenium intake. Our selenium needs can be covered with dietary supplements and foods enriched with selenium. Dietary supplements can be used to satisfy our needs of nutrients and physiological substances since the 1980s. Nowadays, excellent products are available in capsules or tablets for this purpose (*Horacsek et al.*, 2006). Selenium-encapsulated food supplements have already been produced at the University of Debrecen (*Eszenyi et al.*, 2011). These products mainly contain selenium, selenate, selenomethionine, or selenium-enriched yeast. Selenium occurs naturally or in near natural form in selenium-enriched functional foods (*Csapó et al.*, 2016). When preparing foods with this technology, the plant or animal is supplied with selenium as a nutritional supplement that undergoes several transformations and reaches its natural form. During the transformations, the oxidation state of the selenium may change, and so it is important to track what form the plant or animal product contains. The cancer-preventing effect of selenium-enriched garlic has been reported (*Clement* & *Lisk*, 1995), but selenium-enriched bread, pastry, eggs, and margarine had already been on the market by then in Hungary.

5 Selenium-enriched plants

Plants can transform selenite into organic selenium form by fertilization or spraying. It is safe for animals and humans because the chances of overdose with selenium consumed with plant foods are low (*Terry et al.*, 2000). Even in selenium-rich soils, the selenium content of plants does not reach 10 mg/kg in dry matter. Most plants contain only 1–2 mg/kg of Se, but there are some that can accumulate a larger amount. Plants belonging to the family of *Brassicaceae* and *Fabaceae* can produce up to several thousand milligrams of selenium in a kilogram of dry matter (*Ellis* & *Salt*, 2003). This can be explained by the fact that the plants mainly synthesize methylselenocysteine, which is stored for a long time (*Brown* & *Arthur*, 2001), but it is not incorporated into plant tissues; they can also be used for the purification of toxic soils (*Bañuelos et al.*, 2011). In the case of normal Se content, the element is incorporated into the plant proteins as selenocysteine and selenomethionine. Selenium-enriched garlic and green onion, chive and broccoli contain selenium in the form of methylselenocysteines. Wheat, maize, rice, and soybean selenium forms (*Beilstein et al.*, 1991; *Tamás* & *Csapó*, 2015) were investigated, and it was found that selenium is mostly present as selenomethionine in these plants.

In the case of plants, fertilizers or foliar fertilizers with different selenium contents may be used to increase the selenium content. In the case of animals, inorganic selenium formulations can be used to increase the selenium content of animal tissues, but this is better if the feed contains organically bound selenium such as selenium-enriched fodder (*Hidiroglou* & *Jenkins*, 1975).

6 The role of selenium in animal feed

How selenium deficiency does affect the function of animal organisms? *Florian* and his colleagues (2010) found that lesion of the colon has occurred in mice raised with selenium-poor feed. In the case of animals, selenium shortage can lead to muscular dystrophy anaemia, growth disorders, infertility, heart diseases, and increasing taint of diseases (*Dredge*, 2005). As for cattle, the shortage of selenium negatively influences the production of milk, the risk of udder inflammation increases, and fertility decreases.

The supplement of the minerals can be done by salt lick in addition to forage. Before the appearance of salt lick, grinded salt was given to the animals. Since 1920, there are salt licks that are manufactured especially for animals. The researchers noticed that animals' needs of minerals are more efficiently satisfied by blocks rather than grinded salt added to their forage (*Sampson*, 1923). Moreover, the NaCl makes animals drink more water, which promotes the milk production and the health of the livestock. On the market, many salt licks of different ingredients are available. In the USA, the colours of the salt licks indicate the different types in the following way:

- The white only contains NaCl.
- The yellow contains Sulphur.
- The red has iron and iodine added to it.
- The blue contains cobalt and iodine.
- The brown contains cobalt, iodine, copper, molybdenum, magnesium, and potassium.
- The black one contains the ingredients of the brown and selenium (*Keyes*, 2012).

It is customary in Hungary that cattle farms and bull nurseries have 60 mg/kg of selenium-containing salt blocks for animals. By adding a small amount of selenium (and partially vitamin E), lambs can be protected from white muscular disease (WMD) and pigs can be treated with vitamin E deficiency (VESD syndrome). Its effect is similar to the human mechanism through selenium-containing enzymes. In the case of selenium deficiency, the absence of thyroid hormones T3 and T4 in animals may also occur, which may also affect the animal weight benefits as well.

7 Selenium-enriched animal products

By feeding with selenium feed additives, we could produce selenium-enriched meat, eggs, or cow's milk (*Csapó & Albert*, 2018). As most of our foods contain little selenium, it would be necessary to develop functional products in order to increase the Hungarian population's selenium intake. The production of foods with an increased selenium level is relatively complicated. One of the forms of selenium is added to animal feed, whereafter it undergoes transformation in the body until it finally reaches a natural form. Since the oxidation state of selenium changes during the transformation, it is necessary to monitor what form of selenium is present in animal products.

As for pigs, feed supplementation uses organic and inorganic selenium-containing substances to increase the amount of Se in meat. In piglets and sows, the selenium content of the offal and the muscles increases with the addition of an appropriate quantity and quality of selenium (*Surai*, 2006). In laying hens, they act in the same way so as to increase the selenium content of the egg, whereas in cattle this is a common method of selenium-enriching meat and milk.

Selenium supplementation increases the activity of selenium-containing enzymes such as *glutathione peroxidase*. Selenomethionine is incorporated into the body's protein, thereby providing the body's selenium supply.

Despite the decrease in milk consumption, it is also a main source of selenium, and so it is advisable to increase its selenium content. Knowing the selenium concentration, the health status of the stock and the udder is measurable. The addition of selenium to the feed of dairy cows allows the production of selenium-enriched milk.

8 Selenium-enriched yeast

The most commonly marketed selenium source is selenium yeast (*Schrauzer*, 2000). Selenium-enriched yeast is produced by fermenting *Saccharomyces cerevisiae* in high sodium selenite, sodium selenate, and selenomethionine medium. Yeast cells are destroyed by heat treatment, then spray dried, and finally checked for the organic and inorganic selenium content of the product. Selenomethionine can integrate into the body proteins and serve as a selenium source (*Thomson*, 2004 a,b). The total selenium content can be up to 3,000 mg/kg, which is found as selenomethionine in yeast proteins (*Polatajko et al.*, 2004), while selenocysteine is only present in small amounts (*Kotrebai et al.*, 2000). The inorganic selenium content of selenium yeast is also useful in the formation of proteins but does not become a selenium reserve (*Varo et al.*, 1988). In some European countries, selenized yeast has already been authorized as a feed additive to produce functional food. The absorption of selenium is influenced using yeast strain, the technology of production, and the selenium form (*Fox et al.*, 2005). They also found that selenium-enriched yeast is more efficiently incorporated into the body than the inorganic form, and so it is available for a longer period.

In 1993, a research group studied the use of selenium yeast and selenomethionine in breast-feeding and non-breast-feeding mothers. It was found that the levels of selenium in blood increased because of treatments. Each of the groups receiving selenomethionine increased the blood plasma selenium level; however, this was only observed in non-lactating mothers consuming selenized yeast. The amount of selenium in the milk of selenium-treated mothers increased (*Mcguire et al.*, 1993).

From the above examples, you can see that the addition of selenium yeast activates the selenium enzymes in the body and selenomethionine builds on the protein of the body to provide continuous selenium replacement, and it is slowly excreted. The absorption of selenized yeast is slower than that of selenomethionine because the former has to be dissected before the valuable substances can be released. Slower absorption is also caused by the presence of inorganic salts in addition to organic selenium formulations.

9 Milk as selenium source

In Hungary, according to the latest figures of the Central Statistical Office, milk consumption per capita was 161.0 litres in 2015. This shows a decreasing tendency compared to previous years; nevertheless, milk is a selenium source for humans as part of our basic diet. The average selenium content of milk is 25 μg/l – milk and dairy products amount to 6–10% of the daily selenium intake (*Csapó* & *Csapóné*, 2002). Selenium supplementation in cattle feed provides an opportunity to increase the Se content of milk. Se supplementation can be accomplished by feeding with selenium-enriched plants or inorganic sodium selenite or by addition of organic selenomethionine, selenocysteine, or selenium-enriched yeast. However, when selecting the additive, it is important not to ignore that selenium in the rumen of ruminant animals may be reduced to insoluble selenide or elemental selenium. Hydrogen selenide is released as rumen and intestinal gases, and the elemental selenium leaves the faeces. It is practical to favour the organic form because its absorption is more satisfying than that of inorganic form (*Bokori et al.*, 2003). Several scientists carried out experiments to measure the change of milk selenium level in selenium supplementation. *Surai* (2006) published that organic and inorganic selenium treatments increase plasma selenium level.

In 2010, Australian researchers investigated the elimination of selenium in cattle. They found that 66% of selenium intake left the body with urine, faeces, and gases, 17% of which were excreted in the milk, and 17% were incorporated into animal tissues (*Walker et al.*, 2010). An Italian research team published their results in 2010 and 2011, in which the effects of sodium selenite and selenized yeast were investigated on selenium status and milk selenium content. The incorporation of SeCys and SeMet, or selenium yeast, is more effective than inorganic forms and reduces heat stress in dairy cattle (*Calamari et al.*, 2010, 2011).

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