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The Importance of Selenium (Se) in the Prevention and Treatment of Diseases

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Abstract

Introduction: *Numerous studies have proven the hypothesis put forward in the '70s that some human diseases are connected with selenium deficiency. Significantly lower concentration of selenium in the blood is found in patients with coronary thrombosis, diabetes, asthma, fatty liver disease and cirrhosis, malignant tumors, rheumatoid arthritis, skin conditions, neurological diseases, childhood diseases, alcoholism and nicotinism.*

Aim: *The aim of this paper is to indicate the importance of selenium (Se) in the prevention and treatment of human diseases in the light of the literature on the subject.*

Description: *Numerous studies conducted in the world concerning the role of selenium in the prevention and treatment of diseases have confirmed that selenium has the following health effects: it fights mutagenic free radicals, stimulates the immune system, increases the production of IgG and IgA antibodies, inhibits the division of cancer cells and limits their hematogenous spread due to its anticoagulant properties, and decreases the toxicity of chemotherapeutics. The recommended daily intake of selenium for adults is 50–100 μg and should not exceed 200 μg. Its maximum safe dose should not exceed 400 μg per day. In Poland, the average content of selenium in foods is too low.*

Summary: *Appropriate concentration of selenium in a human body has prophylactic and preventive effects. The results of numerous prospective studies in Poland and abroad indicate that a low intake of selenium and/or its low concentration in serum/plasma/nails are markers of high risk of developing most cancers as well as cardiovascular diseases, rheumatic diseases and psoriasis.*

Key words: *selenium (Se), prevention, disease, treatment, epidemiology.*

Introduction

Due to its essential biological functions and a thin line between the dose human organisms need to function correctly and one that is already toxic, selenium has become a research subject of great interest among toxicologists and researchers from various disciplines over recent years [1, 2, 3, 4].

Selenium, discovered in 1817 by a Swedish chemist Jöns Jacob Berzelius, was considered a toxic element for a long time. Areas of high concentration of selenium in the soil contributed to even fatal poisoning in cattle, and people suffered from hair loss, cracking nails and skin conditions. Now, several dozen of years after the Chinese publications revealed that selenium supplementation is vital in order not to develop cardiomyopathy (Kesham disease), our knowledge about this microelement is much broader [5, 6].

It was only in the middle of the 20th century that scientists presented beneficial effects of selenium in people and animals (despite the fact that the line between beneficial and toxic effects of selenium is narrow) [5].

We currently know that selenium is an essential element for life and a key component of selenoproteins, which perform diverse functions in living organisms [7, 8].

Selenium has been arousing more and more interest over recent years both as a microelement and as a natural component with a potential ability to inhibit processes of carcinogenesis [4].

The importance of this trace element needs to be emphasized in maintaining health, prolonging longevity, maintaining visual acuity or increasing potency. It is also of great significance in the prevention of cancer, cardiovascular diseases (coronary artery disease in a form of a myocardial infarction, hypertension), X-ray damage. Its beneficial therapeutic effects are noticed in the treatment of rheumatism, psoriasis, and others [9, 10].

Dietary intake of selenium is an important factor modifying the action of many drugs, including cytostatic drugs and toxic compounds.

Selenium is an essential microelement for the proper growth and development of living organisms. It acts by means of proteins, in which it is built in a form of selenocysteine. Being a component of seleloproteins, selenium occupies both enzymatic and structural roles [9].

The biological effect of this microelement is connected with defending the cell against "oxidative stress" and regulating immunological functions of a living organism, among others. Selenium deficiency causes an increase of toxic components generating active forms of oxygen in various species of animals during their oxidative metabolism. On the other hand, selenium supplementation can prevent their toxic influence [4, 5].

Selenium concentration in the group of healthy people in Poland is 73,7±15,4 ng/ml. It is far from optimal, which is 100–120 ng/ml. The average concentration of selenium in the Poles' blood serum is 70 ng/ml, and differences between regions do not exceed ±10%. The level of selenium in over 95% of Poles is lower than 105µg/l and these people are particularly recommended to supplement their diet with selenium compounds [11].

For comparison, the average concentration of selenium in the blood serum of the adult population of Eastern Germany is 81 ng/Ml. Americans have the optimal dose of Se – its average concentration in the USA is 127–178 ng/ml [11, 12].

Review methods

The article is based on Polish and English works published between 1983–2018 and selected while searching the following databases: PubMed, Web of Science, ResearchGate, Google Scholar. The keywords used were: selenium (Se), prophylactics, disease, treatment, epidemiology and their combinations. The search was carried our mainly by means of electronic databases. 34 publications were identified and those evaluated as the most adequate for the subject of this article were used.

Epidemiology and requirement for selenium. Pathophysiologic importance of selenium compounds

As it was mentioned in the introduction, selenium was discovered in 1817 by a Swedish chemist Jöns Jacob Berzelius and named after the Greek goddess of the moon. However, it was only in the last 30 years that it became irrefutable that selenium is of fundamental importance for the proper development and functioning of living organisms, and that its deficiency adversely influences the spread of diseases, particularly cancers. Selenium is considered to be the least known trace element in the human body. In excess, it is a dangerous toxic microelement. In the late 1950s, beneficial properties of Se received substantial attention and Se was recognized as a trace element of key importance for human health. Noteworthy, routine checks hardly ever detect selenium deficiency [5, 6].

Selenium needs to be supplied with food. However, selenium levels in foods depend on its content in the soil, among others. There are regions with high soil concentrations of selenium (e.g. the USA, Canada, Eastern Ukraine, some regions in China), but there are also selenium deficient ones (e.g. Finland, Sweden) [13]. Poland belongs to the second group and the Pomerania region has particularly selenium-deficient soils. Low selenium level in soil means that Poles have its low concentration in their bodies. Selenium deficient areas are common worldwide, particularly some regions in South America, New Zealand, and Scandinavia. The average soil concentration of selenium ranges from 0.2 to 0.6 ppm. Increased concentration of selenium is observed in the soil rich in iron and organic substances, and in alkaline soil. In potable and ground water in Poland, the concentration of selenium is 0.05 μg/l on average, which is not much compared to other countries. The largest amount of selenium enters the atmosphere due to its oxidation from the surface of the sea [14, 15, 16].

Physiological role of selenium in plants has not been strictly defined yet. Selenium can replace sulfur in some metabolic processes, taking its position in amino acids. The reason why the existence of selenium in plants arouses significant interest is that it occupies an important role in the human and animal nutrition. It is assumed that, most commonly, the concentration of selenium in plants reflects its level in soils. Lower plants (e.g. funguses) tend to accumulate selenium. Wheat seeds exhibit a moderate amount of selenium. A relatively large amount of Se is found in tea leaves. The analysis of the average content of selenium in particular groups of foods leads to a conclusion that the highest levels of selenium are found in fruit and vegetables, then in leaves, flowers and finally plant roots. Herbs and flowers are also a rich source of selenium. The lowest amount of selenium is found in roots. The highest amount of Se in Polish vegetables is found in pea and bean seeds [11, 17].

Residents of selenium deficient regions are diagnosed with cardiomyopathy and immune system deficiencies. Moreover, Se deficiency causes liver necrosis, increases the risk of cardiovascular diseases and cancers, and affects the activity of thyroid [17].

In the United States, the daily recommended allowance for selenium is 70 μg for men, and 55 for non-pregnant women. The situation is similar in Poland. Pregnant women are recommended to increase its daily dose by 10 μg. In infants, the demand for selenium is not strictly defined and ranges from 4 to 35 μg per day. Up until now, there are no strict data concerning recommended daily amounts of selenium intake with foods, but most scientific publications assume that the doses recommended by Food and Nutrition Board of the National Research Council developed in 1980 are safe and appropriate for people. They range from 50 to 200 μg per day (Table 1) [16].

Table 1. Safe and appropriate amounts of selenium intake in diet, broken down by age [16]

Period of development	Age (years)	Recommended daily intake (μg)
Infants	0.0–0.5 0.5–1.0	10–40 20–60
Children	1–3 4–6 7–11	20–80 30–120 50–200
Adults	-	50–200

Factors influencing an increased demand for Se include: gestation, age, vitamin E deficiency, and oxidative stress caused by UVB radiation [12].

Selenium is a particularly important element of pregnant women's diet due to the fact that the demand for this microelement increases significantly during gestation and confinement [12, 18].

It has been already mentioned that the distribution of selenium is uneven on the globe, which is reflected in the content of selenium in foods. People living in some regions (e.g. Scandinavia, New Zealand, China) have a low supply of selenium, about 30 μg per day, whereas others (e.g. in Venezuela, North America) live in seleniferous areas with its high supply (over 150 μg per day). Therefore, it is not surprising that the majority of scientific studies into the role of selenium in the incidence of diseases has been carried out in countries with a relatively low supply of selenium, particularly in Scandinavia. Noteworthy, a standard supply of selenium in the UK ranges from 50 to 70 μg per day. Selenium supply in some regions depends not only on its content in the soil, but also on the dietary habits of the population – the Japanese selenium-rich diet is based on consuming large amounts of deep-sea fish from the Pacific Ocean which are a rich source of selenium [13, 19, 20].

Residents of selenium deficient regions should eat a diet rich in: various types of cabbage, broccoli, onion, garlic, wholegrain cereals, wheat sprout, offal (liver), and sea fish [19, 20].

It is justified to generalize that the recommended daily intake of selenium in adults is 50–100 μg and should not exceed 200 μg. Its maximum daily dose should not exceed 400 μg. It is commonly believed that the average content of selenium in foods in Poland is too low. Table 2 presents Se concentration in the blood serum in adult inhabitants of Poland, according to various authors [7, 11, 21, 22, 23].

Table 2. Concentration of selenium in the blood serum of healthy adults in Poland

Region of Poland	Selenium concentration in the blood serum (ng/mL)	Authors
Pomerania	73.7±15.4	Łabędzka 1991
Pomerania	52.0	Zachara et al. 1983
Lodzkie Region	50.0–55.0	Wojtczak 2003
Upper Silesia	63.5±18.1	Kłapcińska et al. 2005
Lubelskie Region	51±8.26	Kapka et al. 2007
West Pomerania	70.0	Gertig et al. 2006

Source: Authors' original work according to various authors.

Table 3 and 4 present the recommended daily allowance for selenium in Poland by gender and age. As puberty progresses, it increases among both males and females. The demand for selenium is high during gestation, particularly during confinement among breastfeeding mothers [24, 25].

Table 3. Current updated *Recommended dietary allowance* (RDA) for selenium according to the data provided by the National Institute of Food and Nutrition (Instytut Żywności i Żywienia) in Warsaw for the Polish population [24]

Age / gender	Daily recommended allowance for selenium Se (μg)
Infants 0–0,5	15
Infants 0.5–1	20
Children 1–3	20
Children 4–9	30
Boys and girls 10–12	40
Boys and girls 13–18	55
Adults (women and men)	55
Pregnant women	60
Lactating women	70

Table 4. Daily recommended allowance for selenium in Poland [25]

Gender and age	Daily demand for selenium (μg)
Infants	10–15
Children	20–30
Girls aged 10–12	45
Girls over 12	60
Pregnant women	65
Lactating women	75
Boys aged 10–12	45
Boyes aged 13–15	60
Boys over 15 and men	70

Table 5 presents a daily supply of selenium in some European countries (according to various authors). Compared to other European countries, the Polish population has approximately the lowest daily supply of selenium in diet, which is only 11–24 μg [4].

Table 6 presents the content of Se in selected foods. The highest amount of Se is found in salmon, chicken eggs and buckwheat [19].

Table 5. Daily supply of selenium in some European countries [4]

Country	Supply (μg per day)
Great Britain	29–39
Belgium	28–61
France	29–43
Germany (Bavaria)	35
Denmark	38–47
Sweden	38
Switzerland	70
Poland	**11–24 (approximately)**
Slovakia	38

Table 6. Selenium content in 100 g of selected food products [19]

Food product	Selenium µg
Fresh salmon	32.2
Smoked salmon	26
Chicken egg	23.3
Buckwheat	20
Cocoa, powder	14.3
Smoked ham	12.1
Cheese, emmenthal (full-cream)	9.5
Rice (white)	6.0
Cheese, brie (full-cream)	5.8
Plain chocolate	4.5
Milk chocolate	4.5
Milk 1.5% fat	1.54
Yoghurt with fruit	1.3

Selenium and carcinogenesis processes

It is assumed that 35% of all cancers are connected with the diet. The anti-cancer potential of nutrients seems to be relatively high owing to the fact that their consumption in adequate and large amounts may decrease the incidence of certain types of cancers. Selenium and vitamins A, C and E belong to the nutrients which have anti-cancer properties and therefore change the incidence, diversity and progression of the disease. Antioxidants may also turn out to be beneficial in the course of treatment or cancer prevention [15, 16, 26]

The importance of selenium in the functioning of a human body is revealed only when abnormalities in its absorption, transport and excretion are detected [27, 28].

Over recent years, selenium has gained recognition as an effective tool in the fight against cancers. Numerous studies suggest that selenium can influence the risk of developing the disease owing to the fact that, being an antioxidant, it protects the human body against the adverse effect of free radicals. Moreover, it boosts the activity of immune system cells and slows down the development of blood vessels in tumours. The protective role of this element against pro-oxidants results, among others, from the fact that selenium is present in the active site of antioxidant enzymes, e.g. in glutathione peroxidase, GPX, which is one of the best known enzymes and whose function is to protect cell components (DNA, lipids) against the damaging activity of H2O2 and various organic peroxides produced during metabolic processes within living organisms [29, 30].

Se anti-cancer (antiproliferative) properties are widely recognized and used for therapeutic purposes. Low Se level is observed in numerous diseases. However, it is often difficult to prove whether the deficit is of primary or secondary nature. Generally, it is known that it is caused by abnormalities in absorption, nutritional mistakes, excess use, or pathological states with a strictly defined role of selenium [31, 32].

Numerous studies demonstrate the following health effects of selenium:

1. fights mutagenic free radicals. Cell damage caused by active forms of oxygen can lead to carcinogenic transformations of the cells;
2. stimulates the immune system increasing the production of IgG and IgA antibodies;
3. slows down the division of cancer cells;
4. shows anticoagulant properties and decreases the hematogenous spread of cancer cells;
5. decreases the toxicity of chemotherapeutics [32].

Antioxidants, supplied to living organisms with food, enhance the synthesis of prostacyclins by means of preventing the influence of lipid hydroperoxides on inhibiting the activity of prostacyclins. Clinical research indicates that supplementation with antioxidants enhances the production of prostacyclins. In the light of evidences that the aggregation of platelets supports the implementation of hematogenous metastasis, additional use of antioxidants should also slow down the spread of cancer. The aforementioned activity is additionally enhanced by the immunostimulating influence of these nutrients. Because of their anti-cancer, immunostimulating and antimetastatic properties, antioxidants slow down the development of cancer at all stages. Moreover, deficiency of selenium inhibits the release of prostacyclins and enhances the production of PAF (*Platelet Activating Factor*) by endothelium cells of platelets [32, 33, 34].

Conclusions

The hypotheses put forward in the 1970s have been confirmed – some diseases in human being are related to the deficiency of selenium. It has been demonstrated that selenium concentration in the blood is much lower in patients with: coronary thrombosis, diabetes, asthma, fatty liver disease and cirrhosis, malignant tumours, rheumatoid arthritis, skin conditions, neurological diseases, childhood diseases, alcoholism and nicotinism [15, 16, 28].

Selenium protects against detrimental effects of ultraviolet radiation and its fundamental role in the metabolism of thyroid hormones needs to be particularly emphasised [16].

Studies conducted on rat aortas indicated a high production of lipid hydroperoxides in atherosclerotic platelets, whereas the production of PGI_2 (prostaglandin I_2) in the diseased tissues was significantly lower than in the healthy ones. It was demonstrated that even a slight increase in the concentration of lipid hydroperoxides could influence the biochemical path of arachidonic acid and support an increased production of TXA_2 (Tromboxane A_2). Selenium supplementation led to an increase in the synthesis of PGI_2 [1, 20].

Preventive and therapeutic effects of selenium is also shown in the treatment of coronary thrombosis. The use of coenzyme Q_{10} and selenium for one year improves long term prognosis after a myocardial infraction. Clinical research leads to a conclusion that treatment with the use of antioxidants (selenium, vitamin E, coenzyme Q_{10}) improves the prognosis in a significant way and decreases mortality after the myocardial infraction Therefore, it should become a permanent component of the complex clinical treatment. It needs to be emphasized that the aforementioned procedure is recommended in all forms of coronary thrombosis [20].

Results of numerous studies conducted over recent years show that the role of selenium in medicine and recommendations concerning its supplementation in the aforementioned diseases ought to be reassessed [16, 28].

A review of publications on the subject indicates that the majority of authors show a beneficial effect of selenium as a therapeutic agent in the treatment of numerous diseases [14, 15, 16, 25, 27].

While analysing the aforementioned relations, a range of other factors should be taken into account, which include:

1. selenium concentration in a given patient, compared to the whole population,
2. the kind as well as optimal and adequate amount of other nutrients, particularly vitamins A and E;
3. influence of environmental factors;
4. virulence and the course of a disease;
5. influence of the intake of other medicines;
6. proper control of therapeutic trials with selenium [7].

It needs to be emphasized that selenium is of fundamental importance in chemoprevention. Chemoprevention means reducing the risk of cancers by means of chemical compounds provided in a form of supplements, food additives, or medicines (e.g. tamoxifen decreases the incidence of breast cancer in the higher-risk group). A properly balanced diet and supplementation can decrease the so-called "penetration" – i.e. the possibility of developing cancers in people with higher risk of the disease [4, 19].

Abbreviations:

Se – selenium
GPX – glutathione peroxidase
H2O2 – hydrogen peroxide
DNA – deoxyribonucleic acid
PAF – Platelet Activating Factor
PGI_2 – Prostaglandyny I2

TXA_2 – Tromboksan A2
Ig G – Immunoglobulines G
Ig A – Immunoglobulines A

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