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REVIEW PAPERS

SELENIUM IN MEDICINE AND TREATMENT

Anna Frączek, Kazimierz Pasternak

Chair and Department of Medical Chemistry
Medical University of Lublin

Abstract

Selenium, one of non-metals, has attracted great interest among many researchers over the last years. Properties of selenium were first mentioned back in the 12th century. Selenium exists in two forms, organic and inorganic one. But whatever the form of supplementation, it is an essential micronutrient conditioning many vital functions. Large-scale research has shown that it has many important properties, including antioxidant ones, for living organisms. It is incorporated in many enzymes and proteins. Numerous studies on this element have demonstrated its beneficial effects, mainly on the cardiovascular and nervous systems. It also contributes to reduction in the incidence of many neoplastic diseases. However, despite numerous desirable effects of this element in the human body, it should be remembered that selenium is also a toxic substance with a narrow therapeutic index. Its excessive consumption contributes to the development of a condition called selenosis. The recommended dose of selenium, depending on the patient's age, ranges from 25 to 70 μg 24 h^{-1}. However, selenium in excess of 700 μg 24 h^{-1} shows strong toxicity. Therefore, adequate selenium supplementation is crucial. Nonetheless, despite numerous studies on selenium and its biological role, this trace element still raises many unresolved questions.

Key words: selenium, qualities of selenium, selenium deficiency, excess of selenium.

Anna Frączek, Chair and Department of Medical Chemistry, Medical University of Lublin, Chodźki 4a, 20-093 Lublin, Poland

Abstrakt

Selen, który zaliczany jest do grupy niemetali, na przełomie ostatnich lat stał się pierwiastkiem budzącym zainteresowanie wielu badaczy. Właściwości selenu były opisywane już w XII wieku. Selen występuje w dwóch formach, organicznej oraz nieorganicznej. Jednak bez względu na przyjmowaną formę, jest niezbędnym mikroelementem warunkującym wiele funkcji życiowych. W badaniach wykazano, iż ma on niezwykle istotne dla organizmu żywego właściwości, m.in. antyoksydacyjne. Wchodzi w skład wielu enzymów i białek. Liczne badania nad tym pierwiastkiem udowodniły jego korzystny wpływ m.in. na układ sercowo-naczyniowy i nerwowy. Przyczynia się on także do zmniejszenia występowania wielu nowotworów. Jednak pomimo wielu zalet tego pierwiastka należy pamiętać o tym, iż jest również substancją toksyczną, o wąskim indeksie terapeutycznym. Jego nadmierne spożycie przyczynia się do rozwoju choroby określanej jako selenoza. Zalecane dawki selenu, w zależności o wieku pacjenta, wahają się od 25 do 70 μg 24 h^{-1}, natomiast w dawce powyżej 700 μg 24 h^{-1} wykazuje on silne właściwości toksyczne. Dlatego niezwykle ważna jest odpowiednia suplementacja selenu, bowiem pomimo licznych badań, nadal pozostaje on nie do końca poznanym pierwiastkiem.

Słowa kluczowe: selen, właściwości selenu, niedobór selenu, nadmiar selenu.

HISTORY OF SELENIUM

Selenium was discovered in 1817 by a Swedish scientist J.J. Berzelius, who was analysing slime in a chamber that served for production of sulphuric acid. Initially, it was misidentified as well-known tellurium. However, detailed analysis showed that it was a completely different element, unknown up to that moment. Because of its frequent co-occurrence with tellurium (from the Greek name Tellus – earth), it was called selenium (from Greek Selene – moon).

But the earliest descriptions regarding proprieties of selenium and its toxicity date back to the 12th century (Reid et al. 2004).

The Venetian merchant and traveller Marco Polo, travelling along the Silk Route, reached China. There, in a mountainous area, he found a selenium-rich plant, which – when eaten by cattle – caused their hooves to drop off. In his diaries, he described different states presenting toxicity of this element such as hair loss, tooth loss or sialorrhea. However, despite the unfavourable influence of selenium on living organisms, trace amounts of selenium are essential for maintaining proper functions of the human body. In 1973, selenium was found to have antioxidant properties because of its presence in the active centre of glutathione peroxidase. This finding generated an increased interest in the role of this element in living organisms as well as in its side effects resulting from excess or deficiency of the element (Mckenzie 2000, Zagrodzki 2000a, b).

Bioavailability of selenium depends on many factors, but mainly on its form, which conditions its assimilation. It may occur in an inorganic form as selenites (Me_2SeO_3) or selenates (Me_2SeO_4) and in an organic form as selenomethionine (SeMet) and selenocysteine (SeCys). It is the best absorbed in the organic form as well as in the presence of vitamin A, D and E (Haratake 2007, Holben, Smith 1999, Kabata-Pendias, Pendias 1999, Zaporowska 2002).

The recommended dose of selenium (RDA – Recommended Dietary Allowances) is 25 µg/p.d. for children, 50 µg/p.d. for women and 70 µg/p.d. for men (Boyle, Holben 2004, *Panel on Dietary*…1996, 2000, Scholl, Reilly 2000, Zaporowska 1997).

The threshold between the due and a toxic dose is small. Daily consumption of selenium below 0.1 mg kg^{-1} b.w. may induce symptoms of its deficiency, whereas quantities above 1.0 mg kg^{-1} b.w. may have toxic effects on the human organism.

An essential and safe dose of selenium in the human organism is from 55 to 200 µg 24 h^{-1}, depending on the place of residence. Many authors underline that consumption of selenium in the above doses has a preventive effect in the course of different neoplastic diseases (Drake 2006). Doses of selenium above 700 µg 24 h^{-1} are defined as toxic for the human organism (Seńczuk 1994, Więckowski 1995).

Recommended daily consumption of selenium is different depending on the geographical region. The recommended dose of selenium in Great Britain is 75 µg a day for men and 60 µg a day for women. In the United States, the supply of selenium slightly exceeds due doses and is 90 µg a day, although in Finland the intake of selenium is even higher: 125 µg a day (Bergqvist et al. 2003, Mckenzie et al. 1998).

Therefore, adequate Se supplementation is very important. Protein products like milk, meat, fish, sea food and also cereal products or nuts are the main dietary sources of selenium (B'Hymer, Caruso 2006, Cabrera et al. 1996, Haratake et al. 2007, Pappa et al. 2006, Rayman 2000, Ventura et al. 2007).

Supply of this element can occur indirectly, owing to soil fertilization with selenium or animal fodder enrichment. Other forms of Se supplementation are direct ones, that is together with vitamins and other microelements. Some researchers suggest superiority of the organic form of selenium over the inorganic one (Leeson et al. 2008, Rezanka, Sigler 2008, Slavik et al. 2008, Taylor et al. 2009).

However, irrespective of the form, selenium is an indispensable microelement, needed to maintain normal life functions.

PROPERTIES OF SELENIUM

Selenium belongs to non-metals. It is similar to sulphur in its proprieties. It occurs in three allotropic forms as silver-grey fragile metal, red amorphous body and glassy grey and pink solid body. In nature, it exists in two forms: organic and inorganic. The organic form is more easily accessible to the human body than the inorganic one.

Dihydrogen selenide, selenium dioxide, selenous acid (IV), selenic acid (VI), sodium selenite (IV), sodium selenate (VI) are the most common inorganic forms, although for living organisms the most important organic selenium compounds are selenocysteine, methylselenocysteine, selenomethionine, methylselenomethionine, selenocystyne, selenourea, selenoniocholine, selenobetaine (Pyrzyńska 1996, Wesołowski, Ulewicz 2000).

Selenium is widespread in nature. Penetrating from the atmosphere to oceans, seas and lakes, it is absorbed by plants and then, through the food chain, it reaches animals and humans. Plants can store Se in amino acids (Masłowska et al. 1998, Wachowicz 1993, Wesołowski, Ulewicz 2000).

Selenium supplied with food or through the respiratory system is attached to erythrocytes and plasma proteins: albumins and globulins, and then it is distributed to tissues. It is mainly eliminated with urine and some amounts are also removed from the body with sweat and exhaled air (Wesołowski, Ulewicz 2000).

The best-known metabolic pathway of selenium compounds delivered with food is reduction of selenites (IV) to hydrogen selenide H_2Se and then its methylation. In a non-enzymatic route: selenite (IV) reacts with glutathione (GSH) and is transformed into selenodiglutathione (GS - Se - SG), which in the presence of glutathione reductase undergoes transformation to selenoglutathione (GS - SeH). Hydrogen selenide, an indirect metabolite of the reaction, is then ethylated and eliminated with urine. It can also be used for synthesis of selenoproteins (Daraga, Szymańska 2003).

The main function of selenium is its inclusion in numerous proteins and enzymes. Selenium-dependent enzymes are glutathione peroxidase, selenoproteine P, selenoproteins as well as tetraiodothyronine 5'-deiodinase (Bruk, Hill 1994). It has been discovered that over half of selenium in the blood serum occurs as selenoprotein P. Selenoprotein P is the protein transporting and storing selenium; it has the ability to bind to special biological receptors and it shows antiradical activity (Bruk, Hill 1994, Taylor 1995, Van Cauwenbergh et al. 2004).

Selenoproteins W occur mainly in muscles and in the spleen**,** heart and brain (Vandeland et al. 1993).

Selenium influences activities of selenium-dependent proteins, which are indispensable to the proper functioning of immunological system, mainly lymphocytes T (Mckenzie et al. 1998)

DEFICIENCY AND EXCESS OF SELENIUM

Medical literature contains much information on the role of selenium in the human organism. The physiological role of selenium in a human body, demand for this element, its influence on the development of various diseases and pathological conditions have been studied.

It has been shown that development of tumours, fully manifested AIDS symptoms in patients with the HIV virus or pathologies of the cardiovascular system are more common in patients with low values of selenium (Allovena et al. 1995, Combs et al. 1997, Combs, Gray 1998, Combs 2005, Reilly 1998, Taylor 1995, Zimmerman 2007).

Numerous studies confirm that after absorption in the alimentary tract selenium is distributed with red blood cells and its highest concentration occurs in the thyroid. It is the main component of thyronine 5'–deiodinase, an enzyme catalyzing conversion of thyroxine T4 into its active form of 3,3',5-triiodothyronine (T3). Thus, selenium deficiency causes decrease in triiodothyronine in the blood and symptoms of hypothyreosis, which manifests itself through dry skin, hypersensitivity to cold, wrong heart functioning and disturbed fat metabolism (obesity) (Behne, Kyriakopulos 2001, Berry et al. 1991, Floriańczyk 1996, Hordyjewska, Pasternak 2004, Seńczuk 1994).

Therefore, production of triiodothyronine, an active thyroid hormone, in the presence of the enzyme deiodinase, of which selenocysteine is the main component, depends on the proper level of selenium in the human organism (Duntas 2006).

Duntas et al. (2003) tried to resolve the problem whether the selenium concentration in blood can affect autoimmune thyroiditis. Patients with autoimmune thyroiditis were divided into two groups. For 6 months, one group was given selenometionine in the dose of 200 mg as well as L-thyroxine and the other group received placebo. In the first group, a decrease in the count of antibodies against thyroidal peroxidase was observed: by about 46% after 3 months and about 55.5% after 6 months. It the second group, the analogous decrease was 21% after 3 months and 27% after 6 months. Combination of selenomethionine with L-thyroxine was proven to produce beneficial effects in treatment of the autoimmune thyroid disease.

A low level of thyroid hormones unfavourably influences the functioning of nervous tissue, decreases intellectual efficiency and causes emotional disorders such as depression. A low level of selenium has also been implied in Alzheimer's disease. It is mainly connected with the harmful influence of free radicals on mitochondria (Rayman 2000).

Selenium plays an unusual role in the proper functioning of the cardiovascular system. It is connected mainly with its antioxidant function. The protective role of this element against prooxidants results from its presence in the active centre of antioxidant enzymes like glutathione peroxidase (GSH-

-Px) (Hartikainen 2005, Mckenzie et al. 2002, Navarro-Alarcon et al. 2000, Van Cauwenbergh et al. 2004).

Atherosclerotic changes as a side effect of the vascular endothelium dysfunction are the background of all cardiovascular disorders. High concentration of LDL fraction, excessive activity of shear stress, arterial hypertension, diabetes, hyperhomocysteinemia, anoxaemia, free radicals and also mechanical damage have adverse effects on the endothelium (Naruszewicz, Zapolska-Downar 2006).

More intensive oxidation processes as well as elevated generation of free radicals induced by enzymes such as NADPH oxidase, xanthine oxidase, cyclooxygenase as well as nitrogen oxide synthase in sites affected by arteriosclerosis intensify the destructive changes in the endothelium (Skoczynska 2006).

Positive effects of selenium use were noticed by Huang et al. (2002) while analysing the relation of Se supplementation with changes in blood vessels. Examinations were conducted on Wistar rats with selenium deficiency. They were fed with selenium for 13 weeks. A significantly lower blood selenium concentration, decrease in glutathione peroxidase activity as well as decrease in the HDL and plasma prostacyclins concentrations were stated in the group of selenium-deficient rats in comparison with the control. However, such parameters as the level of lipid peroxides, cholesterol LDL fraction, total cholesterol as well as the thromboxane concentration significantly increased. The lumen of the aorta in selenium-deficient rats was observed with scanning electron microscopy and numerous damages to the endothelium cells were found. They were swollen, contained a vacuole in the cytoplasm and demonstrated lack of integrity in the most severely damaged places. Selenium and selenoproteins were reported to play an extremely important role in the cytoprotective activity against the unfavourable influence of cholesterol on endothelium cells. This is highly important because maintenance of the proper structure of vessels is absolutely necessary for preventing atherosclerotic changes (Huang et al. 2002).

According to other researchers, the unfavourable influence of cholesterol on the endothelium of vessels remains an important clinical problem. Selenium and selenoproteins are hoped to be factors preventing arteriosclerosis development (Wu, Huang 2006).

The human organism possesses many mechanisms controlling free radical formation. Glutathione peroxidase (the GSH - the Px) is an important element of the defence system (Kohrle et al. 2000).

Peroxidase occurs in 4 isoforms. The first form is classic peroxidase (GPx), which is found in the cytosol and participates in reactions of hydrogen peroxide and organic hydroxides reduction. However, it cannot reduce lipid hydroxides. The second form is glutathione peroxidase (PH - GPx), which occurs in the cytosol, too, and is partly attached to the cellular membranes.

It can reduce phospholipid hydroxides. The third isoform is glutathione peroxidase (GPx), also called extracellular peroxidase, located in the plasma. It catalyzes reactions of lipid hydroxides and hydrogen peroxide reduction. The fourth isoform of peroxidase, most recently discovered, is gastric peroxidase (GI - GPx) (JAESCHKE et al. 2002, SAITO et al. 1999).

Glutathione peroxidase is a tetrameric protein of the molecular mass of 84 kDa. Each of the four subunits contains selenocysteine in its catalytic centre. The highest activity of peroxidase was found in the liver, blood and lungs, and the lowest appeared in the brain and eye lenses. Glutathione peroxidase is part of an enzymatic system connected with glutathione (COHEN 1993, FLOHE 1988).

Glutathione peroxidase (GSH - Px) is an antioxidant enzyme, which in the presence of reduced glutathion (GSH) catalyzes reduction of hydrogen peroxide (H_2O_2) to water or organic peroxides (ROOH) to appropriate alcohols (ROH), thus participating in the antioxidant defence of the cardiovascular system.

Glutathione peroxidase breaks the route of phospholipase A2, preventing the liberation of phospholipids of arachidic acid, which in the presence of cyclooxygenase and lipooxygenase could be metabolized to prostaglandins. Thus, the production of inflammatory process mediators, which affect adversely the cardiovascular system, is limited.

Activation of inflammatory potential within a cell can be also modified by products of lipid peroxidation. They modify the physical proprieties of cellular membranes by enhancing their permeability to hydrogen ions. The multiradical process of lipid oxidation is partly dependent on excessive generation of reactive forms of oxygen. Lipid peroxidation can be initiated by hydroxyl, alloxil, alkyl radicals, ozone, nitrogen oxide and dioxide, sulphur dioxide or hypochlorite. Glutathione peroxidase acts protectively on the endothelium of vessels by reducing the peroxynitrite anion (BARTOSZ 2003, SHEVCHUK et al. 2002, SKOCZYNSKA 2006).

Beneficial influence of glutathione peroxidase was also noted in relation to cholesterol hydroxides or its esters or oxysterols. Oxysterols show apoptotic activity on cells of vessels in smooth muscles. Studies conducted on rats state that oxysterol-induced apoptosis is inhibited by increased activity of selenium-dependent enzymes (TANG et al. 2005).

Therefore, maintenance of a proper level of selenium in blood serum is essential for the correct functioning of the antioxidant enzyme glutathione peroxidase.

Numerous studies concerning evaluation of selenium influence on the occurrence of cardiovascular system pathology were conducted. TANGUY et al. (2004) in experiments conducted on Wistar rats examined whether selenium consumption influences the degree of necrosis of the heart muscle caused by transient ischaemia. Animals were divided into two groups. For 10 weeks,

one group received a high dose of selenium (1.5 mg Se kg^{-1}) and the other group – a low selenium dose (0.05 mg Se kg^{-1}). The rats' coronary arteries were ligated for 30 minutes in order to cause ischaemia. The conclusions of the experiment were as follows: infarct size in the group of animals receiving the higher selenium dose was about 25% smaller in comparison with the group receiving the lower selenium supplementation, and the ratio of reduced glutathione to its oxidised form was more beneficial in the first group.

Selenium attracts attention of researchers all around the world. A German research team has tried to estimate the influence of the blood serum selenium concentration in patients with stable angina pectoris or severe coronary syndrome on distant prognosis. Six-year-long observations of a group of 1,700 persons enabled the researchers to conclude that the blood serum selenium level in patients who died because of cardiovascular disorders was low. Therefore, a low level of selenium was stated to correlate with cardiovascular future (LUBOS et al. 2010).

The influence of selenium supplementation on glutathione peroxidase and thioredoxin reductase was analyzed in an experiment carried out on Wistar rats. Male rats were fed a diet including 0, 50, 240 and 1000 mg of sodium selenate kg^{-1} b.w. Then, a 22.5-minute heart muscle ischaemia incident followed by 45 minute-long reperfusion were induced. The examinations resulted in the following conclusions: the heart muscle of animals with selenium deficiency was more vulnerable to damage in comparison with the control group. However, supplementation with higher selenium doses caused intensification of the activity of glutathione peroxidase and thioredoxin reductase as well as acceleration of repair processes in the ischaemic heart muscle. Decrease in the enzymatic activity was closely correlated with impairment of repair functions in the heart after ischaemia and reperfusion (VENARDOS et al. 2004).

Disturbed balance between production and removal of reactive oxygen forms leads to development of oxidative stress, which plays an essential role in pathogenesis of numerous illnesses. Its intensification is noted in myocardial infarction or ischaemia after reperfusion. Glutathione peroxidase participates in reduction of the unfavourable influence of stress on cardiomyocytes. Venardos et al. examined influence of selenium supplementation on mRNA expressions of glutathione peroxidase and thioredoxin reductase in the rat ischaemic myocardium. In the experiment, rats were fed with various doses of selenium for 5 weeks. Then, RNA was extracted by the PCR quantitative method. Selenium rich diet was found to contribute to increase in activities of the examined enzymes of the antioxidant system in comparison with the control group, which did not receive selenium supplementation. Therefore, selenium improves the tolerance to ischaemia after reperfusion by modulating mRNA expression of thioredoxin and peroxidase (VENARDOS et al. 2005).

The relationship between selenium deficiency and the range of ischaemic heart disease has been studied in rat models.

Arterial hypertension, stable coronary disease, myocardial infarction or arteriosclerosis are still a serious health problem. They affect more and more young persons, limiting their professional activity. Therefore, it seems to be essential to perform studies to explain causes of these states.

Smoking cigarettes is undoubtedly one of the risk factors of ischaemic heart disease development. The relationship between low blood selenium concentration and the risk of infarct was estimated by researchers from New Zealand. Examinations were carried out in reference to tobacco smoking as a risk factor of heart diseases. And the conclusion of the study was that a decrease in the blood selenium level with simultaneous smoking is a risk factor of ischaemic heart disease (Beaglehole et al. 2001).

However, not all investigations confirm a strong relationship between blood selenium concentration and a risk of myocardial infarction occurrence.

Another health problem implicated as resulting from a low blood serum selenium level is Keshan and Kashin-Back diseases, which cause changes in the osteoarticular system leading to cartilage degeneration within upper and lower limbs (Li et al. 1985, Nelson et al. 1996, Xu et al. 1991, Zhai et al. 1990).

Keshan disease is defined as a childhood cardiomyopathy. First, the symptoms of the disease were observed in Keshan, a province in China, where the selenium concentration in local soils was extremely low. The disease afflicts children and women at child-bearing age. It attacks the heart muscle, leading to an increase in the heart size and occurrence of numerous necrotic focuses. Against the background of these changes, the development of congestive heart failure occurs (Xia 1994, Zaporowska 2002).

Low selenium levels contribute to the development of another disease, Friedreich disease (FRDA), i.e. hereditary ataxia. Foyer found many histological similarities between Friedrich disease and Keshan disease (Fryer 2002).

The crucial role in the pathogenesis of ataxia is attributed to the mitochondrion. As a result of mutations in the first intron of FXN gene, encoding a mitochondrial protein called frataxin, an excessive number of repetition of three nucleotides GAA occurs. Consequently, the absence of frataxin causes iron accumulation in mitochondria and thereby more intensive oxidative stress (Cooper, Schapira 2003, Lodi et al. 2006).

Thus, disturbances in the functioning of the mitochondrial respiratory chain, oxidative damage and accumulation of iron play an important role in the pathogenesis of ataxia (Cooper, Schapira 2007). Friedrich ataxia, a degenerative disease, apart from producing a devastating effect on the nervous system, affects the heart (González-Cabo et al. 1997).

Another important issue is the role of selenium in preventing neoplasic diseases. Selenium as an antioxidant, reduces lipids and limits DNA and RNA peroxidation processes, thus having a protective effect against genetic damage. Being a component of numerous redox enzymes, cytochrome b and c, selenium is involved in metabolic processes at the cellular level. All types of macromolecular damage resulting from oxidative stress contribute to cancer development. The protective effect of selenium is not only limited to the action of the antioxidant enzyme glutathione peroxidase. Other selenoproteins, such as selenomethionine or selenocysteine, have protective properties. Selenium has beneficial influence on health during many stages of carcinogenesis, both at both initiation and during tumour growth, by blocking the synthesis of DNA in cancer cells (Bartosz 2003, El-Bayoumy 1994, Masłowska et al. 1998). Selenomethionine and selenocysteine are components available in many foodstuffs such as cereals, broccoli and garlic.

While analysing the causal relationship between selenium and cancer, Whanger noted significant relationships. The level of blood plasma selenium in patients with malignant cancer is significantly lower than in the healthy control group. However, inconsistent results were provided by tests determining the selenium level in nails and its relationship with the incidence of cancer (Whanger 2004).

Consuming selenium-rich foods significantly reduces the risk of cancer. Beneficial effects of a diet rich in broccoli and therefore in selenium have been reported. This was confirmed by an experiment in which rats with a chemically induced colon cancer were fed with selenium-rich diet. A 50% decrease in incidence of irregular crypts compared with the control group was stated. Consumption of selenium-enriched plant food also reduced the incidence of breast cancer (Finley 2003, Finley et al. 2005).

Reactive oxygen species, which contribute to the development of oxidative stress, can be generated as a result of external factors (UV light, ionising radiation, etc.) as well as internal ones (defensive reactions of the immune system). Their increased concentration in an organism activates a series of reactions leading to pathological changes in the structure of DNA and mutations. Thus, it seems very important to know all the available forms of defence and reduce the incidence of cancer.

Numerous reports on the effects of antioxidants on the development of cancer can be found in the literature.

The Nutritional Prevention of Cancer Trial group tried to determine whether selenium supplementation affects the incidence of prostate cancer. Cases of men whose initial plasma selenium concentration was low and the PSA ratio (prostate specific antigen) lower or equal to 4 ng/mL were analysed in details. The conclusion of that study was that selenium supplementation has a beneficial effect on decreasing the incidence of prostate cancer in the examined group (Duffield-Lillico et al. 2003).

Similar conclusions were drawn by researchers from Canada. They determined the impact of mineral supplementation including selenium and antioxidant vitamins on the incidence of prostate cancer in SU.VI.MAX study. Men were divided into two groups, with normal and elevated PSA. In the group of men with normal baseline PSA receiving selenium-enriched diet, statistically significant reduction in the incidence of prostate cancer was found. However, in men with elevated PSA no such relationship was verified. Moreover, they were observed to present an increased incidence of cancer. Thus, the earlier hypothesis that consumption of antioxidant vitamins and minerals, including selenium, reduced the risk of prostate cancer has been confirmed (Mayer et al. 2005).

The study conducted in Holland on 59 thousand men born between 1955 and 1969 evaluated the level of selenium in segments of nails. After 6 years of observations, it was found out that a higher selenium intake may reduce the risk of prostate cancer (Van Den Brandt et al. 2003).

However, not all studies verify the correlation between selenium intake and incidence of prostate cancer. Peters et al., when examining a group of about 35 thousand men, tried to find out if there was a relationship between selenium and vitamin E intake and reduced incidence of prostate cancer. They found out that vitamin E and selenium supplementation is not related to the risk of cancer (Peters et al. 2008).

Neoplastic prostatic hyperplasia is a serious clinical problem. But begin prostate hyperplasia, which is characterized by the following symptoms: hiperuresia, nocturia, inability to stop micturition, dysuria, etc, is another serious and common disorder. Therefore, it seems worth investigating the problem whether selenium supplementation may have beneficial effects on the human health in the case of lower urinary tract pathology. Rohrmann et al. (2004) determined the protective effect of selenium in begin prostatic hyperplasia. The study covered a group of 2,497 aged over 60, who demonstrated symptoms of begin prostatic hypertrophy. Before the test, concentrations of vitamins A, C and E, carotenoids and selenium had been determined. The control group were men without dysuric symptoms. The results demonstrated that the concentration of selenium was much lower in the group with the lower urinary tract pathology than in the control group. In contrast, men with a higher selenium concentration showed the symptoms of dysuria significantly less often. Thus, selenium was claimed to exert protective effects on prostate cancer as well as beneficial effects on benign prostatic hyperplasia patients (Rohrmann et al. 2004).

Clinical problems discussed above are more common in men over the age of 50. But in the group below 50 years of age, infertility is frequently a clinical problem. Many external factors, environmental or nutritional ones, lead to a reduction in the number of sperm cells in semen. Selenium supplementation was found to have positive influence on sperm motility and consequently on sexual functions. Research conducted by Ammar-L Keskes

on a group of 54 infertile men was designed to determine the effect of selenium and vitamin E supplementation on the improvement of sperm parameters. Vitamin E in a dose of 400 mg and selenium in a dose of 200 μg were given to 28 men for 3 months. The marker of lipid peroxidation, i.e. concentration of malondialdehyde (MDA), was determined in the study. Selenium and vitamin E supplementation caused a significant decrease in the MDA level and thus improved sperm motility. The authors emphasize the protective effect of selenium on semen quality, indicating a high potential of this element use in infertility treatment (KESKES-AMMAR et al. 2003).

Similar conclusions were reached by Safarinejad MR et al. while examining 468 men with infertility, who were given 200 μg of selenium and 600 mg of N-acetylcysteine for 26 weeks. Supplementation with selenium and N-acetylcysteine positively correlated with improvement of sperm quality (SAFARINEJAD, SAFARINEJAD 2009).

Thus, selenium supplementation may be a significant factor in improving sperm condition and decreasing infertility among men.

By analogy to prostate cancer in men, breast cancer is an extremely serious and dangerous disease in women. It is the most frequently occurring cancer among women. Genetic predisposition as well as hormonal and environmental factors underlie tumour development. Many carcinogens have direct impact on the tumour transformation, which is then modulated by hormones. Due to a high incidence of breast cancer, particularly among women over 50 years of age, it becomes essential to search for any factors which could prevent the disease. Japanese researchers assessed the impact of eating selenium-enriched vegetables and tried to determine the role of selenium in chemoprevention of cancer. Japanese radishes grown on a medium enriched in selenium were given to rats with artificially induced breast cancer (by administration of 10 mg or 14 mg DMBA 7,12-dimethylbenz (α) anthracene). The experiment showed that the incidence of breast cancer was statistically significantly lower in the group eating the selenium-enriched diet than in the control group. They suggest that consumption of selenium-enriched products can be an effective diet component in the prevention of breast cancer (YAMANOSHITA et al. 2007).

Selenium is hoped to be a dietary component that can prevent development of tumours. Many studies have shown positive correlations between selenium-enriched diet and reduction in the frequency of tumour occurrence. However, not all examinations have yielded consistent results.

Influence of selenium supplementation on the prevention of basocellular cancer of skin was studied by a team of scientists from New York. About 1,300 persons from the eastern part of the United States participated in randomized examination. They were given selenium in the dose of 200 μg a day. The results showed that selenium supplementation was ineffective in prevention of basocellular cancer. Moreover, it was demonstrated to increase the risk of planoepithelial cancer (DUFFIELD-LILLICO et al. 2003).

Beneficial effects of selenium supplementation can result from its detoxification role. It reduces toxicity of xenobiotics and heavy metals by affecting their metabolism in a living organism. Glutathion and co-operating enzymes e.g. glutathione peroxidase, in which selenocysteine is the catalytic centre, play an unusually important role in cells (ŁUKASIEWICZ-HUSSIAN 2003).

Selenium beneficially influences the metabolism of cadmium, reducing its immunotoxicity (BOSCOLO et al. 2004). It also reduces the toxicity of mercury in the human organism by forming quite stable chemical bonds with this heavy metal (BUKOWSKA 2003).

The protective influence of selenium against ionization and UV radiation in alleviation of the side-effects of chemotherapy and nitrosoamine poisonings has also been reported (MCKANZIE 2000, MICKE et al. 2004). Research also shows that selenium is an unusually important vestigial element in many cases of diseases.

However, it should be remembered that it is also a toxic substance of a narrow therapeutic index. First records about the toxic influence of selenium can be found in the diaries of Marco Polo written in the 12th century. Numerous investigations have shown that excessive consumption of selenium has unfavourable influence on the human organism, causing selenosis. Selenium toxicity symptoms, as J.K. MacFarquhar et al. stated, are diarrhoea (78%), fatigue (75%), hair loss (72%), pain of joints (70%), change of colour of nails and their fragility (61%) as well as nausea (58%) (MACFARQUHAR et al. 2010, ZAWIERTA et al. 1997). Full-blown selenosis is most common in Venezuela, Colombia, United States and in China (LEE et al. 1996, ZIMMERLI et al. 1997).

The mechanism of the toxic activity of selenium is connected with the competent cooperation of the element with sulphur, causing disorder of its metabolism. In the synthesis of mercapto acids selenium from selenite (IV) can displace sulphur and enter into reactions with thiol groups. Large quantities of selenium disturb the metabolism of methionine, catalyze oxidation of hydrosulphurs and cause inhibition in protein synthesis (THOMSON 2004, VILLA et al. 1999). The excess of selenium interferes with processes of catecholamine amine alkylation and stimulates the synthesis of toxic alkyloselenic compounds (MASŁOWSKA, JANIAK 1991).

Despite numerous intensive investigations on selenium, in many aspects the element remains unknown. Many metabolic routes as well as a range of its action within cells await examination. Therefore, elucidation of the selenium physiology and pathology is a challenge for many researchers.

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