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SIGNIFICANCE OF SELENIUM IN DISEASE PREVENTION IN BREEDING ANIMALS AND HUMANS

Bożena Muszyńska[1], Dorota Bederska-Łojewska[2], Piotr Zięba[3]

[1]Jagiellonian University Medical College, Faculty of Pharmacy, Chair and Department of Pharmaceutical Botany, ul. Medyczna 9, 30-688 Kraków
[2]National Research Institute of Animal Production, Department of Nutrition Physiology, 32-083 Balice near Kraków
[3]University of Agriculture, Faculty of Biotechnology and Horticulture, Department of Vegetable and Medicinal Plants, al. 29 Listopada 54, 31-425 Kraków

Selenium is one of the essential trace elements that play an important role in maintaining proper functions in the mammalian organism. It should be supplied to the human body with food of plant and animal origin. It is a component of many enzymes with antioxidant activity, such as: glutathione peroxidase, selenoprotein P, thioredoxin reductase and phospholipid hydroperoxide glutathione peroxidase. In its free form, it does not show its biological activity. The problem of Poland and the neighbouring countries lies in relatively low selenium content in the soil. In addition, due to the lack of selenium (IV) in the soil and its bioavailability for plants, their species and varieties, plant feeds are not a good source of this element. Due to low selenium content in plants and also in feeds intended for farm animals, plant and meat products may be deficient in this element in the aspect of proper human nutrition. Chemical abilities of various forms of selenium compounds to adequately meet the dietary requirements of pregnant cattle and their offspring are evaluated using indicators such as selenium supply, and the efficiency and effectiveness of selenium crossing through the placenta. The results of studies with participation of sheep and goats showed that the values of these indicators are modulated by the type of administered organic/inorganic selenium compound. The development of an effective animal feed additive supplementing this element, taking into account its narrow therapeutic range and bioavailability, is becoming a challenge for scientists dealing with this subject.

Key words: immunostimulatory effect, ruminants, selenium, breeding animals

Biological importance of selenium (IV)

Selenium is an element belonging to the sixteenth group of the periodic table. In the environment it occurs in three allotropic variations which do not show biological activity. In 1960s selenium together with other elements, among others, magnesium or iodine, was named “the element of life”, because it has been proved that it is essential for maintenance of proper functions of mammalian organism, including the appropriate growth and development. It was considered as the indispensable trace element which plays the main role as the component of 30 selenoproteins which have antioxidant, anti-inflammatory and chemoprotective properties (Czauderna et al., 2017; Reeves and Hoffmann, 2009; Kumar et al., 2009).

This element is a component of amino acids that are important for the proper functioning of organisms, such as selenocysteine and selenomethionine, which in turn are a structural element of several dozen proteins that play both structural and enzymatic role. Selenium is also the ingredient of many antioxidant enzymes: glutathione peroxidase, selenoprotein P, thioredoxin reductase and phospholipid hydroperoxide glutathione peroxidase. Being a part of glutathione peroxidase, it plays an important role as the antioxidant and participates in free radical scavenging. Its action consists in the inhibition of harmful processes of peroxidation of lipids, nucleic acids (DNA, RNA), and therefore it protects the cells against deformation and genetic damage (Hatfield et al., 2016).

There are organic forms of selenium in food, such as selenomethionine (Se-Met) and selenocysteine (Se-Cys) (bioavailability: 85-95%) and inorganic selenites or selenates (bioavailability: 40-60%). Selenomethionine and selenocysteine are building blocks of several dozen structural and enzymatic proteins. Selenomethionine, selenocysteine, selenites and selenates are transformed to hydrogen selenides that are a direct selenium donor during selenoprotein synthesis (Lu and Holmgren, 2009). Methyl selenium derivatives as products of metabolism are removed from the organism with urine or exhaled with air. Bioavailability of this element is varied and depends on the form of occurrence and composition of food, water and soil content as well as human nutritional status. Conditions predisposing to chronic selenium deficiency include: chronic malnutrition, parenteral nutrition, impaired nutrient absorption in the intestines (Crohn's disease, resection of the small intestine), conditions associated with liver cirrhosis, neoplasms, inflammatory bowel diseases, chronic renal insufficiency, neoplastic metastases. Selenium deficiency may lead to depression, myopathy, muscular dystrophy and calcification, it favours myocardial contraction disorders, vascular degeneration, the occurrence of Keshan disease, impotence and overall decrease in vitality. This element participates in metabolism of thyroid hormones as a catalyst in the synthesis of their active forms (Bianco et al., 2002). It stimulates the immune system showing the anti-inflammatory and antiviral properties (for example, it inhibits the progression of HIV infection restricting the development of AIDS disease). Selenium is also necessary for the proper growth of neurons and plays an important role in the transmission of nerve impulses in the central nervous system. Moreover, it participates in elimination of free radicals and heavy metals, such as arsenic, cadmium, silver and mercury (Opoka et al., 2015; Molenda and Muszyńska, 2017; Muszyńska, 2012).

Therefore, selenium is a trace element that should be provided to human organism together with food of plant and animal origin. However, the main problem in the therapeutic application of this element is its narrow therapeutic range. Its concentration in human blood should amount to between 80 μg/L and

120 μg/L. Any abnormalities are associated with an increased risk of the occurrence or progression of serious diseases (Opoka et al., 2015; Muszyńska, 2012).

Anticancer activity of selenium (IV) is also worth noting. A growing number of cases of neoplastic diseases and the incomplete effectiveness of classical methods of treatment (chemotherapy and radiotherapy) induce the scientists to search for the new effective therapeutic and preventive methods, including these based on a properly balanced diet. It has been demonstrated that in Japan, where the average selenium consumption amounts to approximately 500 μg per day, cancer incidence rate is 5-fold less compared to the other countries where people take half of the above-mentioned dose together with food. Selenium doses over 800 μg/day cause intoxications. In the late 1960s it was observed that this element plays a significant role in prevention of the processes of neoplastic proliferation and growth. Selenium inhibits the process of proliferation of neoplastic cells through the effect on the expression of *p53* – the tumour suppressor gene and *Bcl-2* – the apoptosis suppressor gene. Regardless the cell type, selenium stops cell division at the G1 checkpoint phase of cell cycle, inhibiting the expression of genes for numerous proteins (including cyclins). However, it increases the expression of genes for P19 protein, P21 protein, superoxide dismutase, glutathione-S transferase, inhibits the synthesis of osteopontin – the protein that is significant in metastasis formation (Opoka et al., 2015). Already in 1949 it was proved that selenium may prevent liver tumour formation in rodents – Dr. Klaus Schwartz observed that liver necrosis in rats might be prevented with the use of an extract containing this element (McDowell, 2017). Dr. Jon Martin from the Colorado State University discovered that the animals in which neoplastic diseases had been evoked for scientific purposes and then were administered with appropriate selenium doses, started to produce 20-30 times more immune bodies than mice from the other control group (Martin, 2015). Selenium (IV) is also a factor preventing the processes of proliferation and growth of neoplastic cells. Its preventive action towards colorectal cancer, lung cancer, laryngeal cancer, prostate cancer, gastric cancer and oesophageal cancer was proved (Flis-Borsuk et al., 2016). Manufacturers of selenated dietary supplements obtained the approval from the Food and Drug Administration Agency in the USA to report health indications that "selenium supplementation may reduce the risk of certain types of cancer". Daily selenium consumption for adults recommended by this Agency amounts to 55 μg. What is more, when dosed properly, selenium prevents the development of atherosclerosis, diminishes the risk of myocardial infarction and brain stroke (Abrams et al., 1992). Selenium deficiency in serum (regardless the genotype) is associated with high risk of neoplastic diseases – lung cancer, laryngeal cancer, colorectal cancer, gastric cancer, pancreatic cancer and ovarian cancer. In turn, excess selenium causes such symptoms as gastrointestinal ailments, nervous system disturbances, skin problems, brittle nails, hair loss and fatigue. Its high concentration increases the risk of, among others, the development of breast or prostate cancer (Knekt et al., 1998).

Natural selenium sources

Organic selenium complexes and amino acids containing selenium are considered as the most bioavailable sources of this element.

Both plant and animal raw materials are sources of selenium. The content of this element in food is very variable and depends on, among others, the type of soil (pH, oxidation-reduction potential, content of organic substances, clay elements, etc.), climatic conditions, as well as species and variety diversity of plants intended for cultivation, animal husbandry conditions and technological processes to which the food is subjected. The best sources of selenium include animal protein: kidneys, liver, cheese, eggs and also fish, seafood as well as plant protein that is present in cereal products. The sources of selenium for human body are also nuts (Brazilian nuts, hazelnuts, cashews), lentils, sesame seeds, wheat germ, wheat bran, corn grains, barley, soy, tomatoes, red grapes, egg yolks (containing also vitamin E), sea salt and stone salt, whole grains and wholemeal bread, sea and ocean products, celery, onion, garlic (Fairweather-Tait et al., 2011).

Selenium content determined in Polish drinking milk was very low and insufficient, ranging from 4.67 to 16.60 μg/L, with the mean concentration amounting to 9.01 μg/L. Such low selenium level in milk, resulting from its low content in feed rations for cows, may have an effect on the increase in disease incidence in consumers. According to the authors, lack of selenium addition to feed may also decrease milk yield of cows (Brzóska et al., 2018).

Under the appropriate conditions, fungi, including yeast, are able to store large amounts of trace elements, such as selenium, and incorporate them to organic compounds. It was observed that if selenium salt dissolved in water is added to culture medium, yeasts are able to accumulate a considerable amount of this element. If culture medium is supplemented with 30 μg/mL of sodium – selenite added during the logarithmic growth phase – it leads to the accumulation of selenium at the amount of 1200-1400 μg/g of dried baker's yeast *(Saccharomyces cerevisiae)* measured by ICP-AES method (Suhajda et al., 2000).

Recently, there has been a growing interest in the introduction of edible mushrooms as feed additives (Bederska-Łojewska et al., 2017). Studies concerning approximately 200 species from 21 families of edible mushrooms have demonstrated that selenium is always present in their sporocarps. Selenium content in Boletaceae family, e.g. in *Boletus edulis* - penny bun – amounts to 20 μg/g d.m., in wild growing common mushrooms 5 μg/g, and in the other species it amounts to not less than 1 μg/g d.m. To compare, food of plant origin contains from 0.02 to 0.12 μg/g d.m. of selenium; for example, selenium content in vegetables ranges from 0.01 to 0.09 μg/g d.m., whereas fruit almost do not contain this element at all. Higher selenium content was determined only in sea fish and seafood (from 0.56 to 2.00 μg/g d.m.) (Muszyńska, 2012).

Selenium and ruminant diet

Feeds of plant origin play an essential role in cattle nutrition, however, the amount of selenium supplied in feed from plants grown in Central Europe is insufficient. In Poland and neighbouring countries, this element is lacking in the soil. Additionally, due to the lack of selenium in the soil, plants and fodder obtained from them are not a good source of selenium and intensify the problem of its deficiency. For this reason, there is not enough selenium in the organisms of herbivorous animals – such as farm animals, and its lack in the meat of these animals causes selenium deficiency in the human body as well Muszyńska and Molenda, 2017).

The first country where selenium was widely applied was New Zealand (1967). In the same year, Finnish veterinarians used selenium for the treatment of muscular diseases in farm animals and in 1969 selenium was approved as an additive to animal feeds (Koller and Exon, 1986).

Selenium deficiency was diagnosed in 50% of the examined cattle from 54% of farms in the Czech Republic, including dairy cows and calves (Pavlata et al., 2002; Pavlata et al., 2005). In the 1960s, white muscle disease was diagnosed for the first time in young ruminants and it was caused by severe selenium deficiency (Muth and Muth, 1963).

Results of the following studies on animals demonstrated that selenium supplementation in cows with deficiency of this element had a positive effect on their fertility, immune function as well as development and strengthening of the immune system (Mehdi i Dufrasne, 2016). Selenium deficiency is particularly dangerous for mothers in late pregnancy, as selenium transfer to foetus occurs even in mothers who have already had selenium deficiency (Enjalbert et al., 1999; Hefnawy et al., 2014). Appropriate selenium supply in cows in late pregnancy and in newborn calves may be obtained through diet supplementation (Bayril et al., 2015).

Selenium supplements for ruminants are classified as inorganic salts (such as sodium selenate and sodium selenite) and organic compounds (such as selenomethionine and selenocysteine) that occur in selenium-enriched yeast (selenium-yeast). Recommended selenium amount in feed rations for sheep ranges from 0.1 to 0.2 mg/kg DM (Moniello et al., 2005), whereas for cattle it is 0.3 mg/kg DM (Nutrient Requirements of Dairy Cattle, 2001). Studies by Marounek et al. (2006) revealed that selenium supplementation does not statistically increase selenium level in muscles, liver or kidneys and amounts to: 0.35 vs 0.69; 1.57 vs 1.87; 2.51 vs 2.65 mg/kg, for control group and group administered with selenium, respectively.

The ability of various chemical forms of selenium compounds to adequately meet the mineral requirements of pregnant cattle and their offspring are evaluated using indicators such as, primarily, the efficiency and effectiveness of selenium transfer through the placenta (Stewart et al., 2014).

Selenium in cattle rumen is metabolised by microorganisms that may integrate it with their own proteins, and more accurately with the amino acids, or reduce selenium compounds to the non-assimilable elemental selenium which is excreted with stool (Galbraith et al., 2016). In the abdominal cavity, non-organic selenium is captured by bacteria more slowly than organic selenium sources (Panev et al., 2013).

An improvement of selenium absorption from the inorganic salts was observed in cattle which received salt granules covered with the protective coatings that were partially stable in rumen and decreased salt solubility in rumen, but effectively released selenium in the following segments of the gastrointestinal tract (Włodarczyk and Birkle, 2010).

In turn, Konecny et al. (2015) noted that the administration of organic selenium compounds increased the amount of this element in lamb blood, which had a positive effect on the postnatal dynamics of thyroid hormones within 30 days after birth.

Results of studies in sheep and goats revealed that values of these indicators are modulated by the type of chemical forms of selenium compounds, i.e. organic/inorganic bonds. The experiments showed that selenium from the organic bonds is better assimilable (Stewart et al., 2014).

Therefore, the development of an effective animal feed additive supplementing this element, taking into account its narrow therapeutic range and bioavailability, is becoming a challenge for scientists dealing with this subject.

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BOŻENA MUSZYŃSKA, DOROTA BEDERSKA-ŁOJEWSKA, PIOTR ZIĘBA

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SUMMARY

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The problem of Poland and neighboring countries lies in the lack of this element in the soil, and therefore in herbivorous farm animals, and since it is not in the meat of these animals, there are significant shortages in the human body. In addition, due to the lack of selenium(IV) in the soil, fruits and vegetables and the products obtained from them are not a good source of selenium and intensify the problem of deficiency of this element in Europeans.

The ability of various chemical and physical forms of Se compounds to adequately meet the mineral requirements of pregnant cattle and their offspring are evaluated using indicators such as selenium supply, and the efficiency and effectiveness of selenium crossing through the placenta. The results of studies with sheep and goats showed that the values of these indicators are modulated by the type of administered organic/inorganic selenium compound.

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