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Biological role of selenium in the organism of animals and humans

O. Sobolev*[1], B. Gutyj[2], R. Petryshak[2], J. Pivtorak[2], Y. Kovalskyi[2], A. Naumyuk[2], O. Petryshak[2], I. Semchuk[2], V. Mateusz[2], A. Shcherbatyy[2], B. Semeniv[2]

[1]*Bila Tserkva National Agricultural University, Soborna sq., 8/1, Bila Tserkva, 09100, Ukraine*
[2]*Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies*
*Pekarska Str., 50, Lviv, 79010, Ukraine, *e-mail: sobolev_a_i@ukr.net*
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Scientific studies of foreign and domestic scientists convincingly proved, that selenium is a vitally necessary microelement with a wide spectrum of biological action. Despite the small concentrations in the body, selenium has unique multi-functional functions - catalytic, structural, regulatory, - in the process of which he activates the action of many enzymes, vitamins, hormones and thus ensure the normal functioning of various biological systems, the implementation of numerous physiological and biochemical reactions in the living organism. The biochemical functions of selenium are not determined by the trace element itself, but by selenium proteins that contain the selenocysteine residue as an integral part of their active center. For today more than thirty such specific selenoproteins have been identified and identified in their pure form, the main of which are glutathione peroxidase, thioredoxine reductase, 5-iodothyronine deiodinase, selenoprotein P, and others. Glutathione peroxidases are the main antioxidant enzymes involved in peroxide oxidation of lipids in biological membranes, catalyze the reduction of hydrogen peroxide and almost all organic hydroperoxides, thus protecting the body's cells from reactive oxygen species. Thioredoxin reductase restores the SH-group in a specific thioredoxin protein, which is responsible for maintaining the oxidative-reduction potential in the cell, affects the products of eicosanoids, modulates the processes of inflammation and chemotaxis. Dayon dentiases of the I-III type are responsible for the exchange of thyroid hormones, are involved in the transformation of the "prohormone" of thyroxine into a more active form of influence - triiodothyronine, regulate and maintain a constant concentration of other thyroid hormones. Selenoprotein P is involved in the transport of selenium to various tissues, acts as an agent that helps neutralize toxic effects and remove heavy metals (Pt, Hg), protecting Leydig cells from active forms of oxygen, indirectly affects the synthesis of testosterone and the processes of spermatogenesis. Selenium plays an important role in the functioning of a nonspecific and specific immune system, prevents mutation of viruses and the emergence of new high-pathogenic strains. Selenium inhibits the formation of hyperplastic and enzyme-altered cells caused by aflatoxin B1 or T-2 toxin, capable of destroying molds producing aflatoxins. Selenium is involved in the formation of mechanisms that determine the reproductive function, in particular, stimulates the hormonal function of the fetoplacental complex towards increasing the synthesis of estrogens, activates childbirth and postnatal involutional processes in the organs of the reproductive system, maintains the active function and structural integrity of the sperm, and thereby ensures their high mobility, preservation, and active penetration into the egg cell. The discovery of the biological properties of selenium has become the basis for its use initially in the prophylaxis and treatment of many illnesses and pain symptoms associated with the deficiency of this trace element, and subsequently - in order to increase the productivity of farm animals and poultry, improve the quality of their products and produce dietary food products of a functional purpose, with bio-correcting effect. Despite the considerable amount of conducted research, mechanisms of action of selenium on some metabolic processes in the body are still not fully clarified.
Key words: selenium; properties; mechanism; action; organism

Introduction

Scientific researches of domestic and foreign scientists in the field of physiology, biochemistry, medicine and veterinary sciences have convincingly proved, that selenium is a trace element with a wide spectrum of biological action, which includes physiological regulation of the enzymatic chain of antioxidant defense, signal transduction, transcription, cell growth and processes of apoptosis, hormonepoesis, spermatogenesis, immunogenesis, etc. According to the modern classification of trace elements, the basis of which is their biological significance for the organism and the impact on the immune system, selenium is classified as vital, or essential elements. It answers all the criteria for the biogenicity of chemical elements (Kudrin et al., 2000).

Selenium, which is contained in the body in small quantities, performs unique multi-functional functions - catalytic, structural, regulatory, - in the process of which it activates the action of many enzymes, vitamins and hormones, and thus ensure the normal functioning of different biological systems, the implementation of numerous physiological and biochemical reactions in a living organism (Reilly, 2013; Gutij, 2013).

As part of biocatalysts, he participates in tissue and molecular levels in oxidative-reduction processes, respiration, hematopoiesis, metabolism of nutrients and biologically active substances, protective reactions of the organism, plays a role in the transmission of photo signals of the retinal eye (converts world energy into electric), is a cancersostatic agent. The ability of selenium to reduce the toxicity of heavy metals has been confirmed (Murah et al., 2002; Baraboj, 2004; Kuz'menok, 2008; Gutyj et al., 2016).

Antioxidant properties of selenium

The biological effect of selenium and its effects on various functions of the body largely depend on the relationship of this micronutrient with sulfur - a constant component of the tissues. Chemically, selenium is close to sulfur - their atoms have a close configuration of the outer electron shells, almost identical sizes, ionization potentials, and electron closeness. In the body selenium compounds are usually restored, and sulfur - to oxidation. Selenovuden is a stronger (active) compound than hydrogen sulfide. Selenium has the ability to replace (under certain conditions) sulfur in amino acids - cystine and methionine. As a result, the sulfur-containing amino acids acquire activity that is inherent in their pure form (Johansson et al., 2012).

The biochemical functions of selenium are determined not by the micronutrient itself, but by selenium proteins that contain the selenocysteine residue as an integral part of their active center (Hatfield et al., 2002). Today, more than 30 specific selenoproteins have been isolated and identified, but only 15 of them are known (Rocha et al., 2017).

Their general feature is, firstly, strictly stoichiometric covalent inclusion of selenium in certain places in the polypeptide chain, and secondly, a special form of expression under the action of selenium contained in the diet. Synthesis of selenium-specific proteins in the body is regulated by a genetically unique mechanism involving cis-factors (UGA codon, mRNA) and transiting elements (monoselenophosphate synthetase, tRNA, selenocysteine sintezase) (Burk, 2002).

The first open selenium-specific protein was glutathione peroxidase (GSH-Px). There are four main types of glutathione peroxidase: classical cytosolic (GSH-Px1), gastrointestinal (GSH-Px2), plasma (GSH-Px3) and phospholipid hydroperoxide (GSH-Px4) (Brigelius-Flohe, 1999; Lavryshyn et al., 2016).

Searches of homogeneous preparation have shown that GSH-Px is a homotheartramine selenenzyme with a molecular mass of 74-105 kD, formed by four subunits (molecular mass of the subunit of 21-25 kD). Each subunit consists of 178-201 amino acid residues. Selenium is a part of GSH-Px in the form of selenocysteine - 4 atoms of the trace element per molecule of the enzyme. Chromatographically, it was found that about 70% of the introduced selenium was bound to the enzyme (Men'shikova et al., 2006).There are two hypotheses regarding the inclusion of selenium in glutathione peroxidase - translational and posttranslational. According to the first, the synthesis of selenocysteine occurs by transferring selenium hydride to an appropriate acceptor, for example, on O-acetyl-serine. Then selenocysteine, formed by means of transport RNA, is included in the polypeptide chain.

Posttranslational hypothesis supposes the inclusion of selenium in the polypeptide chain in the process of posttranslational modification. Glutathione peroxidase (GSH-Px1-4) is a major antioxidant enzyme (Suira et al., 2008).

It has been established that GSH-Px1 is involved in the peroxidation of lipids in biological membranes, catalyzes the reduction of hydrogen peroxide (H_2O_2) and almost all organic hydroperoxides (ROOH), which protects the body's cells from reactive oxygen species and thus provides a pronounced carcinogenic effect. In addition, its role in prostaglandin metabolism in platelets has been proven (Lubos et al., 2008).

The activity of GSH-Px1, in comparison to other glutathione system enzymes, is more dependent on selenium content in the diet. Therefore, determination of its activity in erythrocytes is considered as a sensitive marker for assessing the selenium status of the animal and poultry organism (Pilarczyk et al., 2012; Suchý et al., 2014).

However, some scientists assert that this classic test can no longer be considered sufficiently correct and call for more reliable criteria for assessing the availability of animals and poultry with selenium. They explain this because GSH-Px1 activity does not change proportionally to the amount of selenium absorbed by the body. It comes out on the plateau after reaching a certain concentration of selenium in the blood and no longer increases with an increase in the level of the trace element in the diet. In addition, it has been found that prolonged feeding of animals and poultry with rations of low selenium content does not lead to a rapid decrease in the activity of this enzyme (Holovska et al., 2003).

The physiological function of GSH-Px2, which is localized mainly in the intestinal mucosa, liver and heart, is to neutralize lipid hydroperoxides that are adsorbed from the feed and partly formed in the intestine itself. It regulates the production of arachidonic acid and reduces inflammatory processes in the body (Voloshin et al., 2008).

The functions of plasma glutathione peroxidase (GSH-Px3) have not yet been fully understood, suggesting that it metabolizes hydroperoxides, for example, hydroperoxides of phosphatidylcholines (Krynkov et al., 2003).

GSH-Px4 is an enzyme that has a broad substrate specificity. It restores oxidative fatty acid residues directly from the structure of membranes and lipoproteins - hydroperoxides of esterified fatty acids and cholesterol, as well as tamin hydroperoxide (Lushchak, 2012; Papazjan et al., 2009). The highest activity of GSH-Px4 was recorded in the testicles (Nayernia et al., 2004). Two types of GSH-Px4: mitochondrial and non-mitochondrial have been differentiated in recent years (Imai et al., 2003). The mitochondrial GSH-Px4 plays an important role as an anti-apoptotic enzyme. Not mitochondrial GSH-Px4 is linked to a nuclear membrane and regulates the production of leukotrienes. In addition, it has been established that GSH-Px4, which is contained in the testicles, has a dual function depending on the stage of spermatogenesis: as an oxidant enzyme in spermatoses and as a proteinaceous sperm (Ufer et al., 2003; Ufer et al., 2011).

Relatively recently (in 1996), selenium-dependent thioredoxin reductase (TrxR) has been isolated and has different isoforms: cytoplasmic and two mitochondrial ones, which has different isoforms: cytoplasmic and two mitochondrial. All three isoforms have the same domain structure and are characterized by the presence of selenocysteine in the C-terminal active center, which explains the unique properties of this enzyme (Gromova, 2007). The main biological function of TrxR is the catalysis of the oxidation / reduction of SH-groups in a specific thioredoxin protein, which is responsible for maintaining the oxidation-reduction potential in the cell. TrxR is found to be the key enzyme for selenium metabolism. It affects the products of eicosanoids, modulates the processes of inflammation and chemotaxis (Nalvarte et al., 2015), restores various low molecular weight compounds (antibacterial polypeptides, cystine, aloxane, vitamin K), regulates antioxidant functions of vitamins C and E (Kalinina et al., The ability to inhibit DNA- and RNA-nucleotidyltransferases, which results in the leveling of the amplification of the tumor genome, probably determines the participation of this enzyme in the mechanism of antitumor activity (Kudrin et al., 2000).

An important selenogenzime is 5-iodothyronine deiodinase (ID), which is responsible for the exchange of thyroid hormones. There are three types of deiodinase, I, II and III, whose synthesis is regulated by different genes (Germain et al., 2009; Larsen et al., 2013).

Type I dyeodinase is localized in the liver, central nervous system, kidneys and thyroid gland. It is the main regulator of the transformation of the "prohormone" of thyroxine (T4) into a more active form of exposure - triiodothyronine (T3) (Maia et al., 2011).

Type II diiodinase predominates in the central nervous system, the pituitary and adipose tissue. It catalyzes the formation and maintains a constant concentration of intracellular T3 required for the functioning of the nervous and endocrine systems (Larsen, 2009).

Daydinase of type III is detected in the placenta, glial cells of the nervous system, and skin. It is considered, that this enzyme inactivates triiodothyronine and reduces the activity of other thyroid hormones, and thereby regulates their concentration throughout the gestation period (Huang et al., 2008).

Deiodinase I-III, whose activity is determined by the content of selenium in organs and tissues, by transforming thyroxin into triiodothyronine, indirectly affects energy, carbohydrate, lipid and protein metabolism, as well as on a number of physiological functions that are regulated by hormones of the thyroid gland (Kravciv et al., 2008). The role of selenium in the functioning of tissue deiodinase suggests a close relationship between the exchange of this trace element with iodine exchange (Pashkovs'ka, 2015; Hatfield et al., 2016).

Selenoprotein P (SelP) is the main selenium-specific protein in the blood. This is the only protein, containing more than one selenium atom (with high content of the trace element can contain up to 10-11 atoms). It acts as an antioxidant factor and selenium depot in the extracellular space (Gogoleva et al., 2009; Hill et al., 2012), participates
the transport of selenium to various tissues, mainly to the brain (Renko et al., 2008). This protein acts as an agent that helps neutralize the toxic action of heavy metals (Pt, Hg) (Mostert, 2000; Burk et al., 2009).

Protecting Leydig cells from active oxygen compounds, SelP indirectly affects the synthesis of testosterone and the processes of spermatogenesis (Nishimura et al., 2001). It has been found in vascular endothelial cells, where it is involved in regulation of intracellular signal transduction and protection of cells from peroxynitrile (Baraboj et al., 2004).

Another important protein that contains selenocysteine in its structure is selenoprotein W (SelW). It is present in many tissues, but predominates in the muscles, brain and heart (Lu et al., 2009). It is assumed that this protein, like selenoprotein P, functions as an antioxidant, but not in the bloodstream, but on the tissue level. It is established, that SelW is involved in the growth and differentiation of muscle tissue, protects myoblasts from oxidative stress (Chung et al., 2009). It has proven to be an important buffer against the poisoning methyl mercury in the brain (Kim et al., 2005).

One more Selenoprotein - Methionine-Sulphoxide Reductase B (MSRB) was discovered in 2003. It performs a unique function - the restoration of oxidized residues of methionine to the active state, thereby protecting proteins from oxidation (Suraj et al., 2007; Medvid et al., 2017).

Over the past ten years, a number of selenocysteine-containing proteins (SelH, SelI, SelK, SelM, SelN, SelO, SelR, SelS, SelT, SelV, SelU, SelX, Sel15) have been identified, the functions of which are either unknown or not disclosed to the end (Kuczynska et al., 2007).

Selenium can perform many functions of alpha-tocopherol (vitamin E). Interaction between selenium and vitamin E occurs indirectly due to the activity of classical glutathione peroxidase, phospholipid hydroperoxide-glutathione peroxidase, thioredoxine reductase and selenomethionine (Papazjan et al., 2009).

It is established, that the antioxidant effect of selenium and vitamin E is synergistic, but not identical. While vitamin E carries its protective effect only on the cellular membrane of polyunsaturated fatty acids, selenium produces a protective effect both on their membrane and on the cytoplasm. Modern data suggests that vitamin E breaks free radical chain by neutralizing superoxide radicals at the time of their formation, thus preventing the subsequent process of lipid peroxidation, whereas selenium catalyzes the cleavage of already formed hydroperoxides and hydrogen peroxide. Selenium contributes the antioxidant activity of vitamin E and reduces its cost to the protective function (Hutyi and Hufrii, 2005; Gunchak et al., 2007; Sokyrko, 2009; Huberuk et al., 2017; Khariv and Hutyi, 2017).

In many processes, occurring in an organism of farm animals and poultry, selenium and vitamin E usually work together within the limits of one enzymatic system of oxidation - α-ketoglutaric acid. They increase the overall activity of the oxidase system of α-ketoglutaric acid, activate decarboxylation of the pyruvate by catalytic oxidation of lipoic acid and thiogroups of dehydrogenase (Baynes et al., 2014; Hariv et al., 2016; Martyshuk et al., 2016; Nazaruk et. al., 2016).

However, there are a number of cases where the presence of selenium is mandatory. In particular, in stress conditions, when oxidation of proteins occurs, selenium can not be replaced by vitamin E, since the latter is localized exclusively in the lipid portion of the protein. In addition, with selenium deficiency, even high doses of vitamin E can not replace it, since it is an integral part of antioxidant enzymes (Cheng et al., 1999; Nazaruk et al., 2012; Nazaruk et al. 2015; Guberuk et al. 2015; Shcherbatyy et al., 2017).

Today, for a more efficient use of nutrients from fodder, improving the immune system and increasing the resistance of farm animals and poultry to various diseases, a number of scientists recommend using selenium supplements in conjunction with vitamin E (Tufarelli et al., 2011; Urso, 2015; Gutyj et al., 2017).

Anti-carcinogenic and radioprotective properties of selenium

The scientific literature widely discusses the anti-carcinogenic effect of selenium, which manifests itself only in a certain physiological range of dosing. The anti-carcinogenic effects of selenium are due to many mechanisms (Micke et al., 2009; Ognerubova et al., 2009). One of the mechanisms is based on increased accumulation of selenium in tumor cells and direct toxic effects on them. Moreover, the destructive effects of this trace element are not only proliferating but also interphase tumor cells (Wallenberg et al., 2014).

Selenium inhibits the activation of oncogenes and malignant cell transformation, protects DNA and other cellular components from damage by active radicals of oxygen, reduces the frequency of chromosomal aberrations in leukocytes, as well as the frequency of breaking of DNA strands (Bespalov, 2008; Schlicht et al., 2004). It has been suggested that high levels of selenium in the poultry diet can stimulate the repair of a carcinogen-damaged DNA (Shackih et al., 2007). It is investigated, that selenium-containing enzymes are involved in the clearance of carcinogens, control of cellular respiration, inhibit the formation of carcinogenic nitroso compounds, stimulate immune responses and induce apoptosis of tumor cells (Philchenkov et al., 2007).

Finally, inhibition of selenium carcinogenesis is associated with inhibition of the activity of micro-organism enzymes that carry out metabolic activation of pro-carcinogens (Baraboj et al., 2004).

In addition to the anti-carcinogenic effect of selenium, its radioprotective properties were detected in areas of high radioactive contamination and in the treatment of tumors by isotopes (Vanhanen et al., 2003; Graupner et al., 2016). It has been found that selenium compounds reduce DNA damage in blood lymphocytes (Rostami et al., 2016).

The results of animal studies indicate that organic compounds of selenium have a higher radioprotective activity than inorganic compounds. The time required to achieve the maximum radioactive activity for various selenium compounds depends on the degree of oxidation in the compound. The optimal term for prophylactic administration of drugs with a degree of oxidation Se + 4 is 24 hours, and Se + 2 - 1 hour. The mechanism of anti-radiation action of selenium-containing compounds may be related to the effect on hemopoiesis and antioxidant properties of selenium (Drachjov et al., 2013).

It has also been experimentally proved that additional administration of selenium into the diet of irradiated animals increases the duration of their life (Brown et al., 2010).

Immunostimulants and antiviral properties of selenium

Selenium plays an important role in the functioning of a nonspecific and specific immune system. The stimulating effect of selenium on non-specific cellular immunity consists in increasing phagocytic and bactericidal activity of micro- and macrophages, lysozyme activity of natural "killers," neutrophil migration, and their production of superoxide ion radicals. In addition, it stimulates the lymphocytic system, bringing it to a higher level of activity (Kovalenko et al., 2008; Surai et al., 2008; Khariv et al., 2016; Khariv et al., 2017).

The increase in the number of T- and B-lymphocytes under the influence of selenium indicates its positive effect on the cellular and humoral chains of specific immunity (Bobade et al., 2009). According to scientists, Selenium supports cellular immunity through three mechanisms: regulating T-cell expression and providing transport for their enhanced response; prevention of oxidative stress-induced damage to immune cells; a change in platelet aggregation and a decrease in the rate of thromboxane-leukotriene formation (Ferencik et al., 2003; Huang et al., 2012).

The activation of selenium by the humoral chain of immunity is associated with enhanced immunosuppression of immunoglobulins and, consequently, an increase in their concentration in serum, especially the classes IgA, IgG, IgM (Khan et al., 2007; Sobolev et al., 2017).

Selenium supplements help increase the number of helpers (CD4) and reduce the number of suppressors (CD8), which results in normalization of the immunoregulation (the immunoreactive index increases - Th / Tc) (Gill et al., 2008).

Under the action of selenium, activation of synthetic processes and proliferative response of cells and immunobiological reactivity in response to the action of a typical antigen occurs (Shackih et al., 2008).

The positive effect of selenium feeding in the composition of feedstuffs on the development of lymphoid organs of the poultry - thymus and fabric bag is determined, which is to increase their mass and size (Ahtjamov et al., 2006). The development of primary organs of immunity and their morpho-functional status are the main factors that determine the immunological reactivity of the organism. In addition, its stimulating effect on the activity of the cellular and tissue structures of these immunocompetent organs, which are experienced in the poultry in the age-old involution, was revealed (Drozdova et al., 2009).

The resistance of the poultry organism to viral infections depends on the level of selenium in the diet. In particular, it affects the genetic sequence of pathogens (blocking transcription of the virus), which allows maintaining high immunocompetence and prevents mutation of viruses and the emergence of new high-pathogenic strains (Fisinin et al., 2007).

Anti-toxic properties of selenium

In the literature there is evidence that organic and inorganic forms of selenium are now considered to be the most promising drugs for reducing the depressive effects on the body of animals and poultry of mycotoxins. Selenium may inhibit the formation of hyperplastic and enzyme-altered cells caused by aflatoxin B1 or T-2 toxin. In addition, it is capable of destroying molds that produce aflatoxins (Chena et al., 2014; Kovaljov et al., 2006).

The therapeutic effect of selenium compounds is due to its ability as a cofactor to be part of enzymes that are directly involved in stabilizing the physicochemical structure of plasma membranes of cells and subcellular organelles, as well as enhancing regenerative synthetic processes in them (Guljushin et al., 2009; Hariv and Gutyj, 2016).
It is assumed, that selenium activates the system of glutathione, indirectly performs the function of "absorber" of superoxide radicals and thus protects cell membranes from toxin-induced damage (Uysal et al., 2005).
The enrichment of the selenium diet in doses 2-3 times higher than the physiological need inhibits the process of oxidation of lipids induced by mycotoxins (Weber et al., 2006) and reduces their toxic effect on albumin and lipid metabolism in the liver (Faixova et al. ., 2007). It has been experimentally proved that the action of selenium reduces the duration of decomposition and detoxification of mycotoxins in the body (Mubarak et al., 2009).
The antioxidant properties of selenium also appear in relation to environmental contaminants of natural and anthropogenic origin, in particular heavy metals such as mercury, cadmium, bismuth, argentum, arsen and plum (Suira et al., 2007; Gutyj, 2013; Gutyj, 2016; Gutyj et al., 2016).A number of scientists, investigating the antidote effect of selenium, concluded that, when interacting with heavy metal salts, it easily formed biologically inactive (low-toxic) selenides, which accumulate in the form of insoluble compounds and rapidly excreted from the body (as a result of their exclusion from biochemical processes) (Bochkarjova a et al., 2009; Bjorklund, 2015).It has been established that in the presence of selenium, the binding of cadmium and plumbum in the organism of animals and poultry increases with metallothioneins (rich in cysteine, low molecular weight proteins with pleiotropic functions), in which they do not exhibit toxic effects. It is also believed that the detoxification effect of selenium may be related to the ability of this trace element to recover disulfide bonds in proteins in the SH group, which then "capture" heavy metals (Bochkarjova et al., 2004; Galachiev et al., 2005; Vasyl'ceva et al., 2008). In addition, selenium, as an antioxidant, slows down the process of lipid peroxidation caused by heavy metals (Perepelkina ai et al., 2010).
So, selenium drugs reduce digestion, neutralize and enhance the removal of heavy metals from the body. At the same time, scientists have researched that the use of drugs, which contain only selenium, is more effective than combined medications, such as selenium complex with vitamins E and A (Sobolev et al., 2004).
There are reports in the scientific literature, that the inclusion of mineral selenium in the composition of fodder for broiler chickens not only reduces the concentration of plumbum and cadmium in their muscle tissue, respectively, but also improves the quality of the meat and its preservation (Bokova et al., 2004; Suchý et al., 2014).

Selenium and osteogenesis

There are direct clinical evidence of the effect of selenium on osteogenesis through increased proliferation and activation of osteoblasts - germ cell of bone tissue (Zeng et al., 2013).
In experiments with labeled selenium (75Se), conducted on a cell culture of osteoblasts of animal and human fetus, it has been found that these cells contain at least nine selenium-containing proteins with a molecular weight of 14, 18, 21, 24, 54, 56, 70 and 80 kD, among which there are cGSH-Px, pGSH-Px, TrxR, SelP. Some of them are involved in the regulation of transcription, peroxide and antioxidant defense, carry the transport role in transferring selenium from biological fluids to mineralized tissues, affect on the activity of osteocalcin (marker of bone exchange) and γ-carboxylase (Liu et al., 2012; Petrovich et al., 2004).
Selenium is an indispensable cofactor of sulfotransferase, which carries the transfer of sulfur residues to the molecule of glycosaminglycans, indicating its involvement in the metabolism of cartilage tissue and its components (Ivchenko et al., 2008).
Due to the lack of selenium in the diet of animals and poultry there is a violation of metabolic processes in bone tissue, a delay in growth, a decrease in calcium in the blood, hypercalciuria is indicated, indicating the association of selenium with absorption and excretion of calcium by the kidneys (Moreno-Reyes et al., 2001).

Selenium and reproductive function

The results of experimental studies and the publication of scientists from different countries of the world suggest that selenium is involved in the formation of mechanisms that determine the reproductive function of animals and poultry (Rassolov et al., 2009; Suchý et al., 2014). In female animals, selenium preparations, introduced into the diet, initiate oogenesis, activate the functional activity of the morphological structures of the ovaries, stimulate the generative function of the ovarian glands, secretory activity of the epitheliocytes of oviducts, the glands of the horns and the body of the uterus, promote the synthesis of DNA and RNA, increase the functional potential of cells (Ivanova, 2005).
The experiments conducted in vito showed that selenium, regulating the activity of selenium-containing enzymes, affects the regulation of the ovary by the folliculostimulating hormone. It has been found that selenium compounds stimulate proliferation of granular ovarian follicle cells, and also increase the effect of gonadotrophin on estradiol secretion (Basini et al., 2000).
We can assume, that the basis of the normalizing action of selenium drugs on the reproductive functions of animals lies in their ability to influence the intensity of metabolic processes in the body, as well as the ability to stimulate the hormonal function of the fetoplacental complex towards increasing the synthesis of estrogens, to intensify the reproductive activity and postnatal involutional processes in the organs of the reproductive system (Lysenko et al., 2006).
In males and poultry, the inadequate level of selenium in the diet disturbs the synthesis of steroid hormones, reduces sexual activity, and impairs the quality of sperm (El-Sharawy et al., 2017; Petrosjan, 2006). For a deeper understanding of the role of selenium in spermiogenesis, it is necessary to mention that it is an integral part of selenoproteins, which, being localized in the testicles, sperm and semen fluid, not only provide their antioxidant protection, but also play a structural role (Kaur et al., 2004).
Three types of antioxidant protection are responsible for maintaining the active function of the sperm. The first line - glutathione peroxidase together with superoxide dismutase and catalase prevents the appearance of free radicals; the second one - glutathione peroxidase, together with natural antioxidants (vitamin E, glutathione, etc.) contained in the sperm, limit the formation of free radicals and their distribution; the third is based on enzymatic systems that are responsible for removing damaged cell molecules (Papazjan et al., 2007).

The lack of selenium or its excess leads to morphological changes in spermatypes, in particular, the increase in the number of defective and immature sperm (Zhou et al., 2017). Selenoprotein - phospholipid hydroperoxide glutathione peroxidase (PH-GSH-Px) has been identified in the cervical sperm, which has a direct relation to the structural integrity of the sperm and thus provides them with high mobility, preservation, active penetration into the egg cell and fertilizing ability (Tramer et al., 2002).
Another selenium-dependent enzyme found in the genital organs of males, thioredoxine reductase, restores active sites of other enzymes damaged by free radicals (Das, 2004).
Practically, The introduction of the optimal amount of selenium in the composition of fodder for the parent poultry herd allows to increase the volume of ejaculate in males, the activity, concentration and resistance of sperm, and, consequently, the fertilization of eggs and the removal of young animals (Nazyrova et al., 2010).

Signs of giposelenosis

Selenium, both independently and in combination with other biologically active substances (vitamins, minerals), is effectively used in the prophylaxis and treatment of many diseases of selenium deficiency in farm animals and poultry (Klicenko et al., 2009). Selenium deficiency disorders are widespread and cause significant economic losses to livestock and poultry (McMullin, 2004).
These diseases include: exudative diathesis, muscular dystrophy, periosis, encephalomalacia, anemia, pancreatic fibrosis, muscular stomach and heart microangiopathy, fatty degeneration, liver dystrophy, slow development of immunocompetent organs (factory bags, thymus), testicular degeneration. They are characterized by a violation of the permeability of capillary and cellular membranes, manifested in edema, necrosis, massive hemorrhages, and degenerative changes in the functional structure of cells of internal organs and tissues. The deficiency of selenium is also accompanied by loss of appetite, decreased digestibility and absorption of nutrients in the gastrointestinal tract, increments in live weight of young animals, productivity and quality of sperm in adult livestock, the incubation qualities of eggs, as well as an increase in embryonic mortality and death of animals and poultry. In severe cases, paralysis is developing (Antipov et al., 2005; Lyons et al., 2007).
The introduction of selenium in food fodder completely prevents the emergence of symptoms of its deficiency. At the same time, selenium supplements contribute to the prevention of gastrointestinal diseases associated with an increase in the number of E. coli and Staphylococcus aureus in the digestive tract (Steinbrenner et al., 2015).

Toxicity to selenium

Farm animals and poultry are very sensitive to both deficiency and excess selenium in the diet. Selenium is highly toxic. The lower threshold of its content in the diet, when the selenose is detected in animals and poultry, is 5 mg per 1 kg feed (Malinin et al., 2002).
The minimum lethal dose of selenium for animals in the form of sodium selenite ranges from 1.5 to 8.0 mg/kg body weight, regardless of whether this compound was administered orally, subcutaneously, intraperitoneally or intravenously (Saha et al., 2016).
Today, the estimated minimum toxic dose of sodium selenite, which is capable of causing changes in the clinical status of poultry, mg/kg body weight: indices – 0.9; broiler chickens – 1.7; ducklings – 9.4; laying hens – 33.4. In addition, the oral LD50 selenium for chickens is 9.7 mg/kg live weight (in other experiments - 24.6 mg/kg), for young turkeys and ducks - 13.5 and 64.0 mg/kg, respectively (Surai, 2002).
Characteristic symptoms of chronic and acute selenium poisoning in cattle and sheep are the garlic smell when exhaled, vomiting, significant salivation, loss of appetite, difficulty in breathing (shortness of breath), the animal can not swallow, seizures, unnatural movements, hoof deformation, lameness, diarrhea, hair loss, bloating, loss of vision, exhaustion, paralysis and death, often from respiratory failure . Pathological changes in selenium poisoning include anemia, cirrhosis of the liver, kidney inflammation, edema and hemorrhage of the heart, ovarian cystitis, erosion of joints and bones (Fordyce, 2013).
Intoxication of the body of a poultry occurs mainly for injections or when feeding it with fodder with high content of selenium. Signs of poisoning of poultry with selenium are anemia of the skin and mucous membranes followed by their cyanoticity, leakage of mucus from the beak. In the sick poultry and the one that has suffered from poisoning, the pain of joints, lameness persists for a long time; in some cases, thickening of the joints has been detected. There are disturbances of the central nervous system, muscle twitching, convulsions, accelerating the frequency of respiration and heart rate, and the lack of response to external stimuli. The poultry refuses to feed, it experiences fever loss, blindness, coma and comings and dies. At a pathologically anatomical section in broiler chickens, hyperemia of the glandular mucous membrane, enteritis with the presence of small-point hemorrhages is observed. The liver and kidneys are enlarged, on the cut - full-blooded. In chickens, turkeys and ducklings in the oral cavity and esophagus there is a thick, foamy liquid with a straw yellowish tinge. Under the epicardium and the endocardium is hemorrhage. In turkey, an enlargement of the gall bladder is observed. At the slaughter of poultry in the stage of poisoning with selenium, it is evident that carcasses of bad fatness, watery muscle, cyanotic (Tishkov et al., 1989).
The molecular mechanism of the toxic effect of selenium has not been fully studied, although it has been found that its compounds irreversibly block the sulfhydryl groups of tissue proteins enzymes (substituting SH for SeH), reduce the activity of deiodinase and induce the formation of superoxide radicals in reaction with glutathione, which results in suppressed processes of cellular respiration and oxidative phosphorylation in the body.
Another hypothesis of selenium toxicosis is based on the formation of methyl selenide, which also leads to the formation of free oxygen radicals, such as superoxide anion, which induces oxidative stress. In addition, the formation of selenium trisulfide complexes (selenium + cysteine + coenzyme A) leads to a change in the tertiary structure of enzymes and thus disrupts their function (Mézes et al., 2009; Sobolev et al., 2016).

Conclusions

The biological role of selenium and its importance for the organism of animals and poultry is much wider than described above. It probably is involved in many processes have not studied that occur in the body.
The discovery of biological properties of selenium has become the basis for its use initially in the prevention and treatment of many diseases and pain symptoms, related to the deficiency of this trace element, and later - in order to increase the productivity of farm animals and poultry, improvement of the quality of their products and production of dietary food products of functional purpose, with bio-corrective action.

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