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## ЗМІСТ

# ЕКОЛОГІЯ, ІХТІОЛОГІЯ ТА АКВАКУЛЬТУРА

## ECOLOGY, ICHTHYOLOGY AND AQUACULTURE

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# INFLUENCE OF SELENIUM ON REDOX PROCESSES, SELENOPROTEIN METABOLISM AND ANTIOXIDANT STATUS OF AQUACULTURE FACILITIES

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*The review considers the literature data describing the mechanisms of regulation of redox processes in cells with the participation of selenium. At present, the replacement of many microelements, which have been used for a long time in inorganic forms, with organic analogs, which are much more effective and biologically available, is becoming a priority in animal feeding. The data showing the effect of inorganic and organic compounds of selenium on the synthesis of selenoproteins, the effect of selenoproteins on the optimization of redox processes, increased productivity, optimization of metabolic and immune processes in aquaculture objects. Selenoprotein W has been shown to play the role of glutathione-dependent antioxidant, which may be involved in oxyreduction processes. 25 selenoproteins have been identified in mammals, and up to 41 in teleost fishes (Teleostei). It has been established that salmon fish possess even more selenoproteins due to the doubling of the entire genome occurred during the evolution of this group. The level of glutathione peroxidase gene expression (GPx1) can be a sensitive biomarker of selenium availability and helps assess the influence of the shape and concentration of the element on its biochemical transformation and cell homeostasis. A differentiated approach to the regulation of the selenium content in the composition of fish feed is considered. It has been shown that Se in the surrounding water and in the feed itself cannot provide the required level of the element capable of maintaining stable and optimal conditions for growing aquaculture objects. It has been shown that feed additives with selenium improve growth parameters and are associated with increased synthesis of muscle selenoproteins, which provide antioxidant*

*and immune protection. The importance of the optimal expression of selenoprotein genes in the processes of the regulatory mechanism of the action of Se supplements, contributing to an increase in reproductive function and intensive growth of fish, has been established.*

***Key words:*** *redox reaction, selenium, redox interface, selenoproteomes, environmental toxicity, oxidative stress, dietary selenium, aquaculture, fish.*

***Бітюцький В.С., Цехмістренко С.І., Цехмістренко О.С., Олешко О.А., Гейко Л.М. Вплив селену на редокс-процеси, метаболізм селенопротеїдів та антиоксидантний статус об'єктів аквакультури***

*В огляді розглянуті літературні дані, що описують механізми регуляції окислювально-відновних процесів у клітинах за участю селену. Нині пріоритетним напрямом у годуванні тварин стає заміщення багатьох мікроелементів, що використовувалися в неорганічних формах, на органічні аналоги, які є значно ефективнішими та біологічно доступнішими. Наведено дані, що показують вплив неорганічних і органічних сполук селену на синтез селенопротеїнів, вплив селенопротеїнів на оптимізацію окислювально-відновних процесів, підвищення продуктивності, оптимізацію метаболічних та імунних процесів в об'єктах аквакультури.*

*Встановлено, що селенопротеїн W відіграє роль глутатіону залежного антиоксиданту, який може бути залучений до процесів оксиредукції. Ідентифіковано 25 селенопротеїнів у ссавців, у костистих риб (Teleostei) – до 41. Встановлено, що лососеві риби володіють ще більшою кількістю селенопротеїнів через подвоєння всього геному, яке відбулося під час еволюції цієї групи. Рівень експресії генів глутатіонпероксидази (GPx1) може бути чутливим біомаркером доступності селену, сприяти оцінці впливу форми та концентрації елементу на його біохімічну трансформацію та гомеостаз клітин.*

*Розглянуто диференційований підхід до нормування вмісту селену в складі кормів для риб. Показано, що Se в навколишній воді і в кормі не може забезпечити необхідний рівень елементу, він здатний підтримувати стабільні та оптимальні умови для вирощування об'єктів аквакультури. Показано, що кормові добавки з селеном покращують параметри росту, пов'язані із підвищеним синтезом м'язових селенопротеїнів, що забезпечують антиоксидантний та імунний захист. Встановлено важливість оптимальної експресії генів селенопротеїнів у процесах регуляторного механізму дії добавок Se, що сприяють збільшенню репродуктивної функції та інтенсивному росту риб.*

***Ключові слова:*** *окисно-відновна реакція, селен, окислювально-відновна поверхня, селенопротеоми, токсичність навколишнього середовища, окислювальний стрес, дієтичний селен, аквакультура, риба.*

**Formulation of the problem.** Data released by the Food and Agriculture Organization (FAO) show that global fish production peaked at 171 million tonnes in 2016, with aquaculture accounting for 47 percent of the total and 53 percent excluding non-food uses. While fishing production has remained relatively static since the late 1980s, it is in aquaculture that there has been a significant increase in the supply of fish to consumers.

Fisheries have been declared an important source of food, nutrition, income and livelihoods for millions of people around the world. With a strong increase in aquaculture production, which now provides half of all fish eaten, and some improvement in the status of a number of fish stocks through improved fisheries management, fish supply has reached a new record level. In addition, fish remains one of the world's most traded food commodities, with more than half of the value of fish exports to developing countries.

The aquaculture industry is constantly transforming to cope with increasing challenges such as environmental pollution, climate change, and pathogenic infestations are increasing stressors that lead to reduced productivity. Oxidative stress is the most common form of stress associated with reduced productivity in aquaculture. Essential micronutrients play a crucial role in combating oxidative stress.

In aquaculture farming, pathogens, bacterial and viral in nature, pose a constant threat to production. The mechanism of action of many fish viruses is currently not fully understood, and research is ongoing and the search for possible solutions to enhance the natural protection of fish. Functional foods can provide an alternative to improve

the natural defenses of the fish. They are special dietary compositions containing substitutes or additives in order to improve the physical fitness and immune defense of fish. Elements such as Se, provided at optimal and above-optimal levels, but not reaching toxic levels, may represent a necessary solution to improve fish health [1].

**Analysis of recent research and publications.** In biological systems, the most common reactions are Redox Reaction (RR). The main feature of biological systems is that RR in most cases catalyzes proteins, which indicates the presence of genetic control over redox processes. Oxidoreductases, which catalyze the reactions of oxyreduction, have characteristic properties. The primary amino acid sequence of their apoenzyme determines the conformation of "pockets" specific for coenzymes. This interaction is a prerequisite for the catalytic activity of oxidoreductases. In the spatial organization of the protein, the interaction of amino acid residues (Cys, His, etc.) is of great importance, what determines the specificity and effectiveness of the intra- and intermolecular electron transfer pathways.

The balance of redox processes (redox status) determines cellular redox homeostasis, on which bioenergetic and essential cell functions, including differentiation of proliferation, proteostasis, apoptosis, and autophagy, depend to a large extent [2]. The leading role in maintaining redox homeostasis is played by the ratio of the processes of generation and catabolism of reactive oxygen species (ROS), catalyzed by enzymes and enzymatic systems. Their imbalance can lead to an increase in the level of intracellular ROS and an increase in oxidative processes, and ultimately to oxidative stress, which disrupts the harmonious cell defense system, which leads to instability of the genome and the onset of cancer [3] and other pathologies [4].

**Presentation of the main research material.** Oxidation-reduction of proteins (proteome) is considered as an important element of the organism's adaptation to the environment [5; 6]. The change in the redox status of proteins is the result of environmental factors, including an adaptive response with the participation of cell signaling systems. Thus, the unifying link between the effect of the exposure on the genome is the change in the redox state of the proteome [5]. The redox homeostasis of proteins is supported by a variety of oxidizing and reducing agents. Oxygen is the main oxidant of biomolecules in aerobic organisms. The active participation of oxygen in redox reactions is realized due to the high reactivity of active forms of oxygen, which are formed in numerous biochemical processes both spontaneously and deliberately.

Active forms of oxygen, such as superoxide anion radical ($O_2$), hydrogen peroxide ($H_2O_2$), peroxynitrite ($OONO^-$) and hydroxyl radical ($HO^{\bullet}$), are formed in biological systems and are involved in both reversible physiological signaling processes and in pathologies associated with oxidative stress [7].

Selenium (Se) is a redox metalloid involved in redox (redox) processes in the body. Due to the different oxidation states of Selenium in its compounds (-2, +2, +4 and +6), they exhibit specific biological properties, forming a complex redox system of the body's adaptive response to environmental signals (exposure), causing an adequate response, optimizing homeostasis at the level of the genome, epigenome, transcriptome, metabolome, and exposome. DNA methylation is a common epigenetic mechanism by which gene expression is regulated.

Selenium in the form of SeMet increases liver DNA methylation, increasing the S-adenosylmethionine / S-adenosylhomocysteine ratio, increasing the serine hydroxymethyltransferase mRNA level [8] and maintaining genome stability. The complexity of metabolic reactions involving various forms of selenium interferes with an accurate understanding of the mechanism of the processes; therefore, the use of integrated approaches involving proteomics and metabolomics can improve this understanding.

Se promotes genome regulation by activating and repressing transcription factors that control gene expression. Se at optimal concentrations blocks the activation of the transcription factor NF-κB, which regulates the expression of inflammatory genes. Quantitatively, the most important link between proteome and animal metabolome occurs through two key Se-containing amino acids, selenocysteine (SeCys, Sec) and selenomethionine (SeMet) [9].

Selenium (Se) is found in proteins in two forms: as the amino acids selenocysteine SeCys) and selenomethionine (SeMet). The term selenoprotein is used only for proteins containing selenocysteine residues, as this is the main biologically active form of selenium in proteins. SeCys is encoded by a triplet codon (UGA), which is usually a translational stop codon.

As 21 amino acids, selenocysteine is incorporated into the polypeptide chain of proteins using a special molecular insertion mechanism. The SeCys insertion sequence occurs with the participation of SeCys-recognition proteins as specific elongation factors and binding to the transport RNA. SeCys is present as a stem loop in the 3 untranslated region or UTR of the selenoprotein mRNA. The amount of selenoproteins (selenoproteomes) differs in different species of living organisms [10]. It has been established that aquatic organisms usually have larger selenoproteomes than terrestrial ones; moreover, in mammalian selenoproteomes, a tendency towards a reduction in the use of selenoproteins is noted.

Among the selenoproteins, glutathione peroxidase (GPx) and thioredoxin reductase (TrxR) are the most studied [11], being an irreplaceable component of the cellular glutathione and thioredoxin systems. They perform important regulatory functions in the intracellular redox environment [12; 13], affect the balance of the endocrine system, determine the degree of insulin resistance [14]. Selenoprotein P (SelP) is the main protein in the body responsible for Se homeostasis and its transport in the body [15]. Selenoprotein P is found in two different isoforms in fish, SelPa and SelPb; which have differences in structure and presumably play different roles in Se homeostasis in fish [16].

In mammals, 25 selenoproteins have been identified, in teleost fishes (Teleostei) – up to 41. Some salmonids have even more selenoproteins, which is the result of the doubling of the entire genome that occurred during the evolution of this group [11, 17].

The genes that encode selenoproteins are involved in various metabolic processes such as redox-dependent signaling. Selenium-containing glutathione peroxidases, from the family of multiple isozymes, are encoded by several genes (GPx1a, GPx1b, GPx4a, and GPx4b) in teleost fish [18], TRXRD1, TRXRD2 [19], whose expression products are involved in protein folding and degradation, metabolism, which, in turn, alter the regulation and expression of genes [6, 20].

The chemical form of the delivered Se can greatly affect its bioavailability and therefore, the entire body. The main form of Se in the most common feed ingredients is SeMet, which makes up more than 50% of the total amount of Se in corn, soy, wheat, barley etc. [21]. It was established that inorganic forms of Se are less bioavailable than organic selenium compounds and this means that they can be more easily excreted from the body. In addition, inorganic selenium compounds exhibit toxicity at lower concentrations compared to organic forms [1].

The priority in feeding farm animals is the replacement of many trace elements which have been used for a long time in inorganic forms with organic analogues that are much more effective and biologically available and nanoforms of elements synthesized by green chemistry methods [22]. Numerous scientific and industrial trials have shown that selenomethionine (an organic form of selenium) is an effective source of selenium to improve the health and productivity of animals and birds [23; 24].

To date, discussions are underway on rationing selenium in compound feeds for fish. Many fundamental principles have been proposed for linking selenium concentrations in the whole fish organism or in the diet with adverse effects on fish. Different points of view of researchers form a differential approach to rationing the content of this element in the diet. Separate studies were examined and the basic principles for selenium concentrations in the whole body of the fish and in the diet, which were higher than those proposed by other researchers (≈4 μg/g in the whole body and 3-4 μg/g in the diet), were recommended. This article also recommends sharing the basic principles for cold-water fish (6 μg/g for the whole body and 11 μg/g in the diet) and heat-loving (9 μg/g for the whole body and 10 μg/g in the diet). Most selenium literature maintains a full-body threshold of 4 μg/g in fish and 3 μg/g in the diet [25].

In Europe, the use of feed additives is regulated by European feed legislation. The maximum limit of total Se in animal feed, including fish feed, was set at 0.5 mg/kg (Council Directive 70/524/EC and amendments). The European Food Safety Authority (EFSA) had published several scientific findings on the use of organic selenium yeast forms as feed additives. Based on the obvious higher bioavailability of organic Se compared to inorganic forms, it was found that the level of additives should be limited to a maximum of 0.2 mg/kg feed to ensure consumer safety. Subsequently, the European Union regulated the use of several Se feed additives, mainly selenized yeast, with an additive level of not more than 0.2 mg/kg feed [26].

A study on rainbow trout (*Oncorhynchus mykiss*) studied the uptake of the organic form of selenium as part of Sel-Plex and its effect on the expression of fish selenoproteomes [1]. Rainbow trout was fed a control diet containing Se at 0.9 mg/kg of feed, or the same diet enriched with three different Sel-Plex concentrations: 0.5 mg/kg, 4 and 8 mg/kg, which corresponds to the concentration of Se 1.4 mg/kg (low-Se diet), 4.8 (middle-class diet) and 8.9 mg/kg (high-Se) diet), respectively.

The added additives of organic selenium (Sel-Plex) did not affect the survival and growth of fish. The distribution of selenium in organs is as follows: liver, kidney, muscle, and blood cells. With a high level of Se in the diet (4.8 and 8.9 g/kg) and a longer exposure time, the liver is not able to regulate the content of selenium, and the concentration of the element in the tissues increases. In order to investigate the body's biological response to Sel-Plex supplementation, the authors studied the effect of Sel-Plex supplementation on mRNA expression of selected trout selenoproteins.

The liver was the most sensitive tissue at the transcriptome level, followed by kidneys, blood cells, and muscles. This directly reflects the accumulation of Se in these tissues described previously, and additionally confirms the importance, especially of the liver and kidneys, in the exchange of Se in fish. The study was carried out in order to clarify the dosage of selenium, based on the assumption that fish, in particular salmon, may require higher Se levels than mammals and more than the dosage allowed by current legislation (0.5 mg/kg dry feed weight) [27].

A study by Mechlaoui et al. [28] was aimed at determining the effect of dietary inclusion of selenium (Se) in the form of inorganic Se (sodium selenite, $Na_2SeO_3$) and organic Se (hydroxyselenomethionine, HO-SeMet) on sea bream (gilthead seabream) (Sparus aurata). The control diet for fish (without Se supplementation) contained 0.8 mg selenium/kg feed and was used as a basal diet. Up to 2 groups of experimental feeds introduced selenium in the form of $Na_2SeO_3$ in an amount of 0.2 mg Se/kg and 0.5 mg Se/kg. Two more feed groups contained a similar amount of selenium in the form of OH-SeMet.

The highest growth rate was observed in fish fed OH-SeMet at a level of 0.2 mg/kg, but without significant differences with fish which were given a control diet without

adding Se. The smallest growth was observed in fish treated with sodium selenite, up to 0.5 mg/kg. An increase in Se in the diet, especially in the form of OH-SeMet, led to an increase in Se in the liver and muscles. The inclusion of OH-SeMet in the diet led to a significant ($p<0.05$) decrease in the content of malondialdehyde (MDA) in the liver and muscles.

The inclusion of Se in the form of selenite at a dose of 0.2 mg/kg is not as effective as the organic supplement Se to improve the oxidative status of muscles. The dietary inclusion of Se at a dose of 0.2 mg/kg significantly reduced plasma cortisol levels after 2 hours of acute stress, regardless of what form of Se was given. Serum lysozyme activity decreased with an increase in the amount of added Se additives in the diet. Thus, the addition of Se to 0.2 mg/kg (1-1.1 mg/kg of the analyzed dietary Se), especially in the form of OH-SeMet, had a beneficial effect on growth, maintaining liver morphology and improving fry protection (of juvenile) dorado from acute or chronic stress. In addition, it was found that OH-SeMet is more effective than $Na_2SeO_3$ in protecting against oxidative stress in fish muscles [28].

The importance of introducing selenium supplements based on a plant ingredient for parent forms of rainbow trout had been demonstrated, which not only affected the reproductive functions of producers, but also ensured parental transmission of Se to offspring for the possibility of antioxidant metabolism from the very beginning of feeding [29]. Three groups of rainbow trout received a diet with or without selenium supplements (control, basal level of Se – 0.3 mg/kg of feed), a group with the addition of Se in the form of sodium selenite ($Na_2SeO_3$) in the amount of 0.3 mg/kg of feed, as well as a third the group received food, in which selenium was additionally added in the form of OH-SeMet in an amount of 0.7 mg/kg of food.

Trout was fed with this food for 6 months before spawning. In Se supplemented groups, the total number of spawning females was significantly higher compared to the negative control group, and females treated with OH-SeMet started spawning earlier than females treated with $Na_2SeO_3$ or control diet. Concentrations of total Se were significantly higher in the muscles of females from the group to which additional OH-SeMet was added. Higher concentrations of Se in oocytes of both groups with the addition of Se confirmed maternal transfer of Se, while the total concentration of Se in samples of seminal fluid did not differ significantly between the groups of fish.

The Se supplement enhances the expression of the hepatic SelPa gene of the uterine population of males and females along with the genes of such important selenoproteins as cytosolic and mitochondrial methionine sulfoxide reductase (MsrB1 and MsrB2), which play a critical role in protein redox regulation; glutathione peroxidase isoform genes (GPx1a, GPx4a2), catalase antioxidant enzyme, Glutamate-cysteine ligase catalytic subunit (Gclc), glutamate-cysteine ligase, also known as gamma-glutamylcysteine synthetase K1, which is the first ECH associated protein an element of the Keap1-Nrf2 signaling pathway, which is the main regulator of cytoprotective reactions to oxidative and electrophilic stress triggered by protein genes (MsrB1, GPx1a, GPx4a2, CAT, Gclc, Keap1) expressed in the liver of males.

In fry, which switched to active swimming, the addition of organic Se led to higher gene expression for SelPa, GPX1a, GPX1b2, CAT, and MsrB2. Organic supplementation of Se led to a significant increase in the level of α-tocopherol and vitamin C in the offspring. These results show that the addition of selenium to broodstock feeds affects the stimulation and course of spawning, and the transfer of selenium from parents to offspring affects some features of the new generation [29].

The study of D. Pacitti et al. [17] determined the expression of the constitutive mRNA of glutathione peroxidase (GPx) genes in different trout tissues and their reactions. Glutathione peroxidases are the largest and most studied family of selenoproteins. Cytosolic glutathione peroxidase (cGPx, GPx1) and phospholipid hydroperoxide glutathione peroxidase (PHGPx, GPx4) are widely distributed throughout the tissues and play a key role in regulating the oxidative status in the cell. The authors cloned the GPx1 and GPx4 genes in rainbow trout (Oncorhynchus mykiss). Accessibility to Se was analyzed using rainbow trout liver cell line (RTL).

The non-organic form of selenium (sodium selenite $Na_2SeO_3$) and the organic form (selenocysteine, Cys-Se-Se-Cys) were used as Se sources. Activity was studied to test the effect of transcript changes on the enzymatic function of these molecules. To understand whether the results obtained from the analysis of transcript expression were due to the bioavailability of Se or the formation of reactive oxygen species (ROS), the cytotoxicity of the two selenium compounds was tested by measuring the effect of Se on the integrity of cell membranes.

In addition, the bioavailability of Se was quantified by mass spectrometry to determine the amount of Se in cell culture media, and the contribution of the two selenium compounds used in the treatment. Three gene isoforms were identified for GPx1 (GPx1a, 1b1 and 1b2) and GPx4 (GPx4a1, a2 and b). The discovery of a third gene encoding GPx1 and GPx4 indicates that salmonids may have the largest selenoproteome among all vertebrates. The results of these studies indicate that the expression level of transcripts of trout GPx1 may be a sensitive biomarker for selenium consumption, helping to assess whether selenium concentration and chemical speciation affect cell homeostasis.

The important role of selenium in increasing immunity in fish growth has been demonstrated. A growth study was conducted to determine the need for selenium in feed for black sea bream fish (*Acanthopagrus schlegelii*) in juvenile age [30, 31]. The basal diet was supplemented with Se polysaccharide at levels of 0.34 mg/kg; 0.52; 0.68; 0.91; 1.08 and 3.06 mg/kg. Concentrations of Se≤0.91 mg/kg of feed significantly influenced the increase in weight gain in fish, while higher levels of selenium incorporation showed a decrease in growth trends. The activity of superoxide dismutase, glutathione peroxidase, catalase, and glutathione reductase in serum and liver increased significantly and leveled out in fish fed ≥1.08 mg Se/kg ration, while the content of malondialdehyde in the liver and serum decreased significantly with increasing Se levels. The content of Se in the liver and muscles increased linearly with increasing levels of Se in the diet. Based on the results, it can be concluded that the need for Se diet for juvenile black sea bream is 0.86 mg/kg per weight gain [30].

Studies by Lee et al. [32] postulated the importance of the addition of trace elements, selenium (Se) to fish feed, because Se from the surrounding water and the feed itself cannot provide the optimal level required for cultivated aquatic species. The experiment showed that juvenile Nile tilapia has special requirements for the presence of Se in the body, which cannot be provided with normal food or water from the environment. The inclusion of dietary Se at optimal concentrations is a prerequisite for effective growth, saturation of tissues and ensuring normal enzyme in Nile tilapia. The addition of Se to fish feed in excess of the required level can have toxic effects on freshwater aquaculture organisms.

Researchers Wang et al. [31] proposed an experimental test of the hypothesis about the possibility of other selenoproteins, in addition to deiodinase, also participate in the regulation of fish growth. In this study, rainbow trout (*Oncorhynchus mykiss*)

was fed with graduated Se levels (2, 4, or 6 mg/kg, from selenium yeast, Se-yeast) for 10 weeks. At the end of the feeding test, fish growth and the expression of 28 selenoprotein genes in tissues were evaluated.

The results showed that dietary Se-yeast significantly increased fish growth ($P<0.05$). Correlation analysis showed that the growth of rainbow trout significantly and positively correlated with only 4 genes of selenoprotein in the liver, but with all 11 differentially expressed genes of selenoprotein in muscles ($p<0.05$) does not cause oxidative stress in fish tissues. In addition, Se dietary supplements elicited an overall upregulation of selenoprotein gene expression in the liver (10 genes) or muscle (11 genes) ($p<0.05$) and it showed the strongest correlation with mRNA levels of the W-like selenoprotein gene in muscle ($P<0.05$). Selenoprotein W plays the role of glutathione (GSH) – dependent antioxidant, which may be involved in the redox process.

These results indicate that nutritional supplements with Se yeast are useful for the growth of rainbow trout, and improved growth rates are closely related to the expression of muscle genes of selenoprotein, in particular, the selenoprotein W-like gene. This study reveals the importance of muscle gene expression of selenoproteins and offers a new concept for the regulatory mechanism of Se diet for fish growth [31]. The effect of bioaccumulation of selenium on tilapia of Mozambique was studied. Se induces an oxidative stress effect such as (of lipid peroxidation (LPO) and protein carbonyl (PCO) lipid peroxidation (LPO) and oxide modification of proteins and (PCO) in fish gills and liver exposed to Se. Se exposure increases the activity of SOD, GPx, GST, metallothionein, GSH and inhibits CAT activity [33].

When organic selenium is introduced into the diet of barramundi (juvenile barramundi (*Lates calcarifer*), their weight, growth rate (final weight, specific growth rate and weight gain), as well as protein digestibility coefficient increase, the activity of glutathione peroxidase, creatinine kinase [34].

**Conclusions and suggestions**. Thus, a literature review shows that Se and its various forms interact with the functional genome through a complex structure of the metabolic network response with the participation of selenoproteins [35]. The research results demonstrate that the inclusion of Se in compound feed for fish at optimal concentrations is a prerequisite for ensuring effective growth, saturation of tissues and optimization of the activity of selenoproteins, contributing to an increase in the reproductive function of broodstock, ensuring the possibility of effective functioning of the antioxidant and immune system of juvenile fish from the very beginning of feeding.

It is assumed that adequate analysis and management of data on controlled exposure to Se will help developing a strategy for its effective use in fish feeding, calculating possible risks from exposure to excessive doses of Se and in a broader sense, serving as a working paradigm for experimental research and practical use in aquaculture.

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