

## Effects of selenium compounds and toxicant action on oxidative biomarkers in quails

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We studied the lipid peroxidation processes, activity of antioxidant defense enzymes, energy metabolism in blood, liver, and kidney of quails under modeling of cadmium loading and correction of these processes by action of Selenium and its inorganic (sodium selenite) and organic (selenite) compounds. The feeding of the quails with the Sel-Plex preparation in the compound feed of 0.15 mg/kg of dry feed promotes the activation of anaerobic and aerobic processes in the cytoplasm and mitochondria of liver cells. Increased activity of antioxidant enzymes, in particular superoxide dismutase (SOD), catalase and glutathione peroxidase (the active center of which includes the redox-active selenocysteine residue). The use of Selenium compounds increases the total lipid content of the quail kidneys. This increases the activity of glutathione-dependent enzymes, which include Selenium that reduced the lipoperoxidation products content and restored the activity of SOD and catalase. We established that the intake of cadmium sulfate caused intensification of the processes of peroxide oxidation, which changed the activity of antioxidant enzymes of SOD and catalase in quail kidneys and livers. Under cadmium loading, the pathological effect of the toxicant was counterbalanced by the use of Selenium compounds and the general physiological state returned to the control level. This increased the antioxidant status of the quail organism and reduced the negative impact of cadmium sulfate. We proposed the green synthesis method for safe and environmental-friendly generation of the selenium nanoparticles. We proved that adding nano-selenium (Nano-Se) to the quails' feed increased the safety of livestock number and the average daily growth. We also definitely recommend using Selenium compounds for the correction of structural and metabolic poultry disorders caused by effects of heavy metals.

**Keywords:** Selenium; Cadmium; Superoxide dismutase; Glutathione peroxidase; Quails; Antioxidant system; Energy metabolism; Liver; Kidney; Blood

### Introduction

Oxidative biomarkers of stress are extremely informative in environmental toxicological studies (Ibor et al., 2019). The growth of anthropogenic activity and environmental awareness has led to a significant increase in research in this area. Antioxidant protection plays a crucial role in the body's response to pollutants. There is now a wealth of information on the antioxidant and other unique properties of Selenium. In particular, Selenium is characterized by antioxidant, anti-apoptotic, antigenotoxic (Yang et al., 2017b; Abu-El-Zahab et al., 2019), anti-inflammatory (Xu et al., 2019), antitumor (Xia et al., 2020) and immunomodulatory (Khosro et al., 2015) activities. Selenium is necessary to maintain homeostasis of the whole body. Various diseases can be triggered by Se deficiency, such as white muscle disease (Yildirim et al., 2019), cancer (Kuria et al., 2020), diabetes (Schomburg, 2019), liver necrosis (Li et al., 2020) and myocardium (Liu et al., 2020) and diseases of the immune system (Khosro et al., 2019). Selenium's involvement in the formation of certain hormones (Shokraneh et al., 2020), nucleic acid metabolism (Li et al., 2020), etc. has been established.

However, Selenium as an element is not used itself by the body. Most quantity of Selenium in the tissues of animals and birds is present in the form of selenomethionine and selenocysteine, ie the organic form of Selenium is in chemical bond with amino acids (Spallholz et al., 2019). So, Selenium is a part of various selenoproteins, selenium-containing enzymes and some other proteins, which are direct participants in vital processes in the body.

One example of selenium-containing enzymes is glutathione peroxidase (GPx), which is a component of the body's natural internal protection against oxidative stress (Brigelius-Flohé & Flohé, 2019). In particular, the thyroid gland expresses several glutathione peroxidases (GPx1, GPx3, and GPx4), which are involved in the metabolism of thyroid hormones and protect cells from the harmful effects of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and free radicals. Each glutathione peroxidase is capable of restoring potentially dangerous reactive oxygen species (eg, H<sub>2</sub>O<sub>2</sub> and lipid hydroperoxides) to harmless compounds (water and alcohol), which prevents the formation of new free radicals. The integrity of cellular and intracellular membranes is significantly dependent on glutathione peroxidase. Selenium causes the reduction of heavy metal pathogenic effects, like cadmium, on the living organisms. Whereas the cadmium accumulation in the environment is undoubtedly caused by intensive human industrial activity (Rahman & Singh, 2019), it is advisable to study the energy exchange under the action of cadmium sulfate under conditions of correction with organic Selenium compounds (Tsekhmistrenko et al., 2019; Xu et al., 2019).

Quails are an extremely interesting biological object. Low weight, high egg production (300 and more), high hatchability (85–95%), short incubation (15–18 days) and puberty period (35–45 days), resistance to various infectious and diseases, the possibility of placement in low-tiered cellular batteries make quail a versatile object for industrial and household farms. They also are used for biological, medical and veterinary research (Morris et al., 2019).

The liver is a parenchymal organ in which metabolic processes are intensively underway. The kidneys, together with the liver, are involved in the elimination and excretion of various toxicants, including Cadmium compounds. The search for factors that are capable of improving the state of energy metabolism and lipid peroxidation in poultry is relevant.

We studied the lipid peroxidation processes, activity of antioxidant defense enzymes, energy metabolism in blood, liver and kidney of quails under modeling of cadmium loading. We also implemented the correction of these processes by inorganic (sodium selenite), organic (Selenite) and organic particles.

## Materials and Methods

The experiments were conducted in Bila Tserkva National Agrarian University vivarium and experimental industrial production (which production capacity is 1500 heads of quails). The studies were conducted on Pharaoh quail (*Coturnix japonica*) chickens of meat production. Five groups of 100 birds each were formed from the day-old birds by analogy method. All groups of poultry received standard feed. Quails of Group 2 additionally received sodium selenite ( $\text{Na}_2\text{SeO}_3$ ) for 0.15 mg/kg of feed. A Group 3 received the Sel-Plex drug in the same amount. Birds of Groups 4 and 5 received compound feed with the addition of  $\text{Na}_2\text{SeO}_3$  (Group 4), Sel-Plex (Group 5) and cadmium sulfate ( $\text{CdSO}_4$ ) at a dose of  $1/50 \text{ LD}_{50}$ .

During the first experiment we compared effects of inorganic ( $\text{Na}_2\text{SeO}_3$ ) and organic Selenium (Sel-Plex) compounds and Selenium on toxicant activity (cadmium sulfate) in the bird organisms.

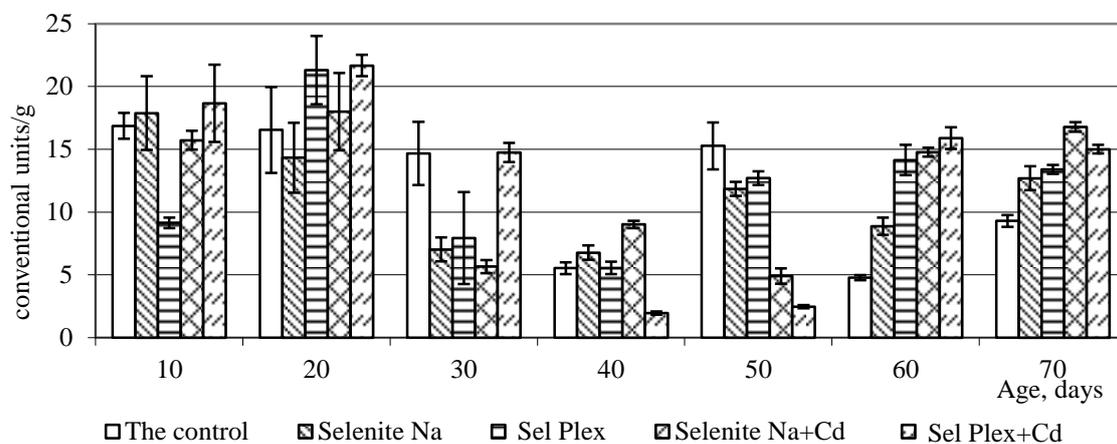
In the first experiment, the intensity of lipid peroxidation and the peculiarities of the antioxidant system were studied, as well as the energy metabolism in the blood and tissues of the liver and quail from birth to the establishment of intensive oviposition with the addition of different forms of Selenium (Sodium Selenite and Sel-Plex) into feed.

In the second experiment,  $\text{Na}_2\text{SeO}_3$  (Group 2) and Selenium nanoparticles (Group 3) obtained by the green synthesis method (Tymoshok et al., 2019) were introduced in addition to the basic diet.

Liver and kidney tissues, as well as blood serum, were used for biochemical studies. Cytoplasmic and mitochondrial fractions of liver and kidney were obtained by differential centrifugation. Sampling was performed from the first to 70th day of retention with an interval of 10 days. In the cytoplasm and mitochondria, the activity of lactate dehydrogenase (LDH), succinate dehydrogenase (SDH) and cytochrome oxidase (COX) were determined by traditional methods. The processes of lipid peroxidation were evaluated by the activity of superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase and the content of reduced glutathione, as well as total lipids, cholesterol and triacylglycerols

## Results and Discussion

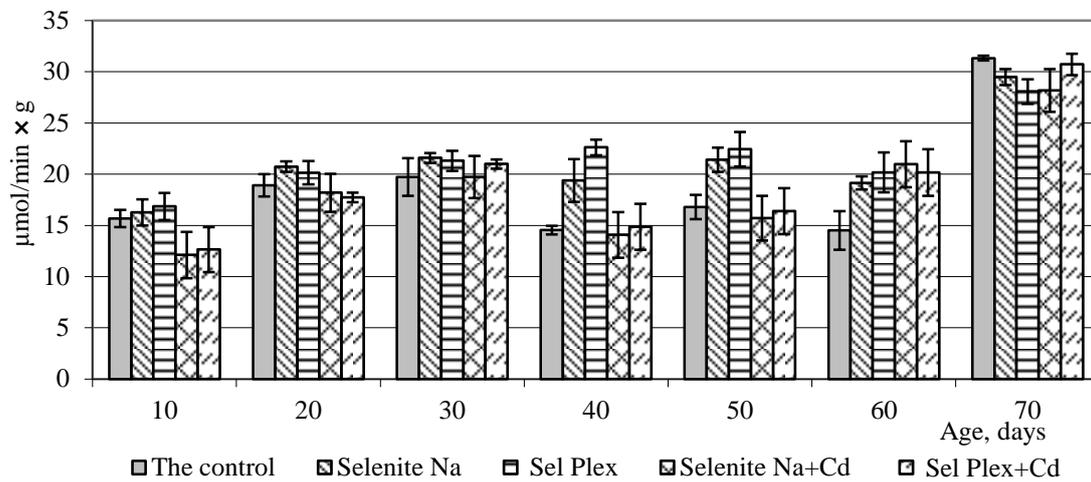
When selenium compounds were added to the quail diet, SOD activity in the kidney tissues varied slightly within the intact bird index, increasing significantly in the quails of the 2nd and 3rd experimental groups at the end of the experiment ( $p < 0.001$ ) (Figure 1). The cadmium load contributes to a significant decrease in SOD activity, which necessitates the effective protection against reactive Oxygen forms formed during the process of superoxide dismutation by catalase and glutathione peroxidase (GPx).



**Figure 1.** Superoxide dismutase activity in quail kidneys (here and then the values are  $M \pm m$ ;  $n = 5$ ).

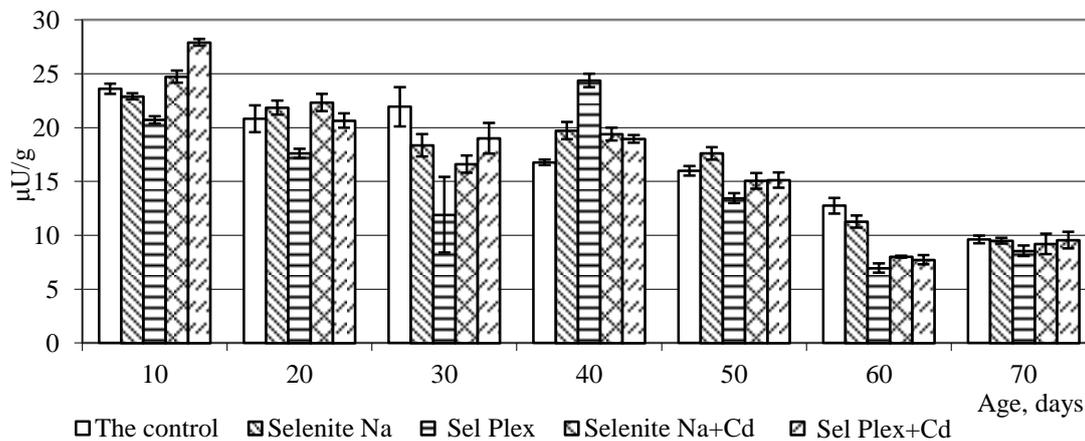
The kidneys are an effective link to the complex mechanisms of regulation of water-salt and acid-base balance (Lew & Radhakrishnan, 2020). In addition to maintaining the persistence of the ionic composition of the aquatic environment of the body, the kidneys directly regulate the homeostasis of proteins, carbohydrates and lipids (ibaeribaşı et al., 2020). These features determine the feasibility of studying the activity of the kidneys and their biochemical composition in the event of adverse effects on the organism, or heavy metals. Selenium is a known antioxidant that causes a reduction in the content of free radicals and, as a result, products of lipoperoxidation, which helps to restore the activity of enzymes of the antioxidant protection system, in particular catalase and SOD.

The activity of the glutathione-dependent link of AOS also indicates a negative effect of the chronic action of cadmium sulfate (Figure 2). During the experiment, the activity of the GPx in groups 4 and 5 was reduced compared to the intact bird. Significant growth of it over the 6th decade with dominance over control may be a compensatory reaction to changes in SOD and catalase activity.



**Figure 2.** Glutathione peroxidase activity in quail kidneys.

Toxic kidney damages are accompanied by significant inhibition of catalase activity at all stages of the study (Figure 3). One of the reasons for the decrease in catalase activity due to the action of the toxicant may be the degradation of ribosomes responsible for enzyme synthesis (Zhu et al., 2019). The addition of Selenium compounds eliminated the inhibitory effect of cadmium sulfate on catalase activity during critical periods of development, whereas without cadmium loading, there was a constant decrease in its activity (group 3), compared with intact birds. The low activity of catalase is offset by an increase in the activity of GPx.



**Figure 3.** Catalase activity in quail kidneys.

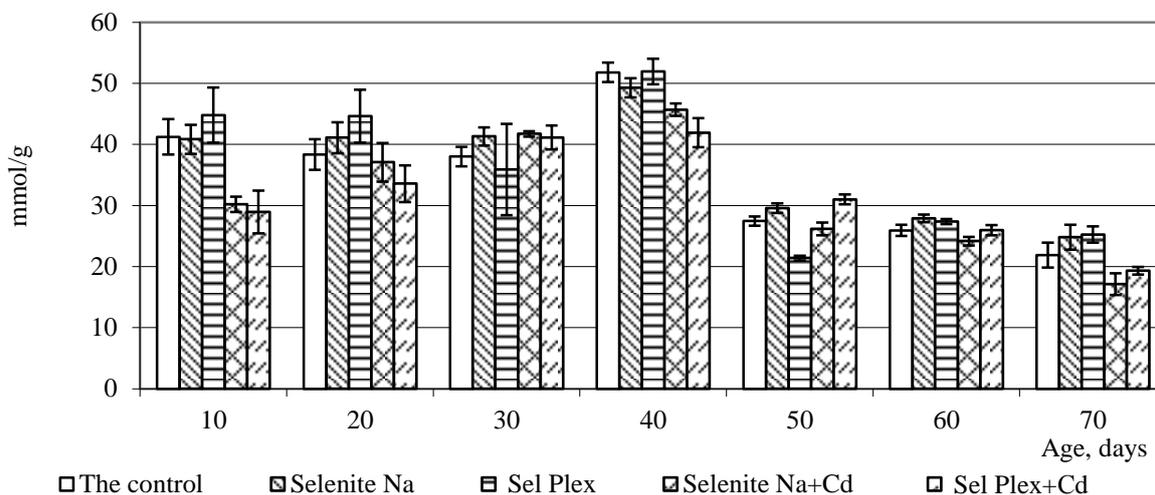
Ceruloplasmin (CP) is one of the markers of exposure to Selenium (Hackler et al., 2020). Changes in the content of ceruloplasmin were noted after selenium compounds were administered. In the cadmium load simulation, the CP content decreased at 30 days of age and likely at 50 days ( $p < 0.01$ , Group 4). At other stages of the experiment, sodium selenite and Sel-Plex contributed to the increase in the concentration of ceruloplasmin, including critical periods of quail development such as 10 days ( $p < 0.001$ ), 40 days - oviposition ( $p < 0.001$ ) and 50 days ( $p < 0.01$ ). When added to the diet of Selenium compounds, there is a likely increase in the content of CP in the quails of the Group 3, including during the critical periods of development, and a tendency to decrease its content in the quails of Group 2 relatively with intact birds. Increasing the content of ceruloplasmin in the kidneys may indicate its compensatory effect against the background of the decrease in the activity of other antioxidant enzymes, including SOD and catalase (Fotakis & Timbrell 2006).

The prolonged addition of Selenium compounds caused a change in the activity of the enzymes of the antioxidant defense system, both individually and cadmium loading. The gradual decrease in SOD and catalase activity is offset by an increase in the activity of glutathione-dependent enzymes.

Significant concentrations of hydrogen peroxide and organic hydroperoxides which are neutralized by GPx, as well as inhibition of glutathione reductase activity led to a decrease in the content of reduced glutathione (Figure 4). A significant decrease in the content of this tripeptide and the activity of its associated enzymes provides cadmium neutralization in the kidneys, preventing their cytotoxic effects on cells.

The toxic effects of  $\text{CdSO}_4$  as well as other heavy metals occur due to the oxidation of heme Ferum, caused by chemical hypoxia, and may also be related to the processes of damage to membranes and subcellular structures due to lipoperoxidation (Tsekhmistrenko et al., 2018a; Zhang et al., 2018a; 2019; Zhang et al., 2018a;). Toxic concentrations of Cadmium induce astrocytic apoptosis by depleting intracellular glutathione levels, increasing intracellular calcium levels, altering mitochondria of membrane potentials, and activating JNK and PI3K/Akt signaling pathways. Cadmium inhibits cell proliferation in kidney epithelial cells, lung fibroblasts, and primary myelocytes. Toxic concentrations of cadmium induce astrocytic apoptosis by depleting intracellular glutathione levels, elevating intracellular calcium levels, altering mitochondria membrane potentials, and activating JNK and PI3K/Akt signaling pathways. Cadmium suppresses cell proliferation in kidney epithelial cells, lung fibroblasts, and primary myelocytes (Ospondpant et al., 2019) The data obtained may indicate the crucial role of the relevant glutathione-dependent

enzymes in the body's overall antioxidant potential. These results are consistent with the statement about the protective role of glutathione redox cycle enzymes against enhanced free radical formation and reactive oxygen species (Shekhar et al., 2019).



**Figure 4.** The content of reduced glutathione in quail kidneys.

The effect of Selenium compounds on the activity of individual oxidoreductases has been identified (Wang et al., 2019). The results of studies on the dynamics of indicators of the state of the energy system in the subcellular structures of quails' liver indicate that the activity of cytoplasmic lactate dehydrogenase (LDH) exceeds the activity of the mitochondrial form of this enzyme (Table 1).

**Table 1.** Lactate dehydrogenase activity in subcellular structures of quail liver under effect of Sel-Plex and Sel-Plex with Cadmium.

Age, days	Lactate dehydrogenase, $\mu\text{U/g}$					
	control		Sel-Plex		Sel-Plex + Cd	
	cytoplasm	mitochondria	cytoplasm	mitochondria	cytoplasm	mitochondria
10	$0.94 \pm 0.02$	$0.13 \pm 0.01$	$0.84 \pm 0.03^*$	$0.14 \pm 0.01$	$0.79 \pm 0.03^*$	$0.29 \pm 0.02^{*\wedge}$
20	$1.85 \pm 0.14$	$0.25 \pm 0.02$	$1.75 \pm 0.11$	$0.33 \pm 0.03^*$	$1.93 \pm 0.06$	$0.37 \pm 0.03^*$
30	$2.10 \pm 0.03$	$0.95 \pm 0.09$	$2.06 \pm 0.06$	$0.87 \pm 0.04$	$1.99 \pm 0.07$	$0.82 \pm 0.06$
40	$1.89 \pm 0.03$	$0.56 \pm 0.03$	$1.85 \pm 0.02$	$0.45 \pm 0.04$	$2.03 \pm 0.05$	$0.42 \pm 0.06$
50	$2.24 \pm 0.06$	$0.26 \pm 0.02$	$2.29 \pm 0.05^*$	$0.33 \pm 0.02$	$2.17 \pm 0.03^\wedge$	$0.14 \pm 0.01^{*\wedge}$
60	$1.64 \pm 0.09$	$0.30 \pm 0.03$	$2.98 \pm 0.05^*$	$0.71 \pm 0.04^*$	$1.24 \pm 0.16^\wedge$	$0.61 \pm 0.03^*$
70	$2.38 \pm 0.21$	$0.20 \pm 0.02$	$2.74 \pm 0.26$	$0.53 \pm 0.04^*$	$1.95 \pm 0.13^\wedge$	$0.16 \pm 0.01^\wedge$

\* Difference is significant against control at  $p < 0.05$ ;  $\wedge$  the difference is significant relative to the experimental group at  $p < 0.05$ .

We registered a 10.6% decrease in LDH activity ( $p < 0.05$ ) in the cytoplasm of quail liver cells treated with the Sel-Plex compound feed on 10th day. Such a decrease in activity may be due to the slowing down of glycolytic breakdown of glucose and the activation of aerobic processes in the cell under the action of Selenium (del Puerto et al., 2016). Significant increase in enzyme activity in the Sel-Plex group was observed from the 50th to the 60th day of the bird's life. In suspensions of mitochondria of hepatocytes of the quails of this group, an increase of LDH activity by 32% compared to the control ( $p < 0.05$ ) was detected. The probable increase in activity of this enzyme compared to the control was observed in the 60th and 70th day of life by 2.4 and 2.6 times, respectively. It should be noted that the ratio of cytoplasmic LDH to mitochondrial in the 30-day age group in the 2nd group was 2.4, and at the 50-day age - 6.9. In the control of the same age, this ratio was 2.2 and 8.6, respectively. In the cytoplasmic fraction of quail liver, which together with the drug Sel-Plex received cadmium sulfate for the 10th day of life, there was a 16% decrease in LDH activity ( $p < 0.01$ ). However, from the 50th to the 70th day a significant decrease in the activity of this enzyme was found compared to the group receiving Selenium. The lack of difference between the control group explains the correcting effect of Sel-Plex on energy metabolism in cells under the condition of chronic loading of Cadmium salts. In the mitochondria of liver cells of the quails of the same group on the 10th and 20th days of life, there was a probable increase in LDH activity compared to the control. This is due to the fact that Selenium, despite Cadmium's ability to block the flow of oxygen to cells, improves the redox processes in the cells. In the third decade, there was a markedly probable fluctuation in LDH activity. On 60th day, the level of this enzyme increased compared to control 2-fold ( $p < 0.001$ ). The ratio of cytoplasmic and mitochondrial LDH activity was highest at 50 days of age (15.5) versus 8.6 in controls. This indicates a high activity of this enzyme in the cytoplasm of cells when blocking the cadmium salts with glycolytic glucose cleavage. From the 50s to the 70s, there was a marked fluctuation in LDH activity in both study groups. At 70 days of age, the activity of cytoplasmic LDH exceeded on average 9.7 times the activity of the mitochondrial form of the enzyme. This indicates that in the cytosol of quails' liver cells, the conversion of pyruvate to lactate with LDH is much more intense. The activity of GPx in the cytoplasm of Sel-Plex quails' hepatocytes increased by 66% ( $p < 0.001$ ) at the age of 20 days. At the beginning of the oviposition, there was a marked decrease in its level and by the 50th day it was 3 times smaller than in the control. At the end of the study period, the activity of GPx in the cytoplasm of Sel-Plex quails' liver cells increased by 46.2% ( $p < 0.001$ ) relative to control. In the mitochondria of the liver there was a significant increase in the activity of GPx: in the 40-day period - by 29.3% ( $p < 0.001$ ), on the 70th day - by 52.4% ( $p < 0.001$ ) according to the control. Characteristic is that in the mitochondria of hepatocytes of the quail group, which were fed by selenium organic compounds, the activity of GPx reached its highest level on the 40th day

(the beginning of oviposition), and in the cytoplasm it was the lowest during the whole experimental period. This means that mitochondria under the influence of Sel-Plex take on the function of antioxidant protection because they have a higher content of GPx.

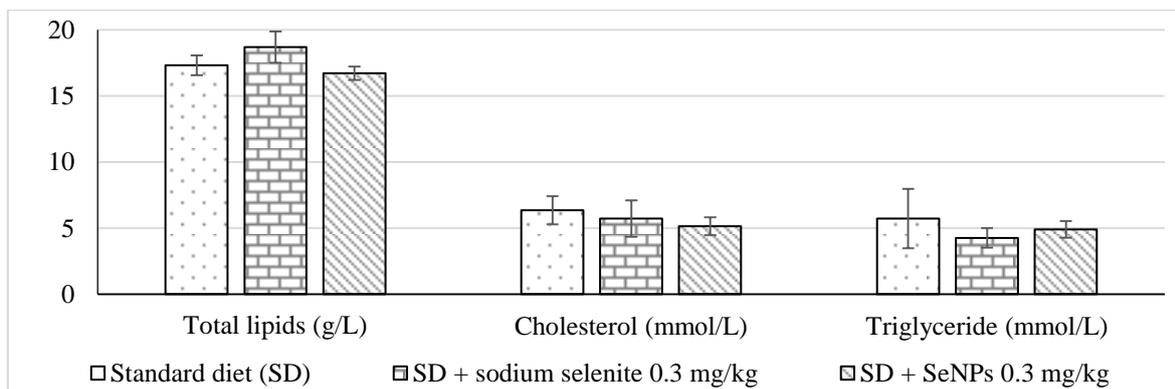
The group that received cadmium sulfate together with Sel-Plex demonstrated significant increase in cytoplasmic GPx activity by 30-40 days relative to the control and Sel-Plex group. On the 50th day the activity of this enzyme in the cytoplasm decreased by 3.4 times ( $p < 0.001$ ), and on the 60th - it increased significantly compared with the control and Group 3. By the 70th day of the experiment, the level of mitochondrial GPx had decreased, but was 49% ( $p < 0.01$ ) higher relative to control. In the mitochondria of the quails liver of the Group 5 at 10 days of age, an increase in the activity of GPx by 53% ( $p < 0.001$ ) relative to the control and 7.2% ( $p < 0.01$ ) relative to the Group 3 was detected. At day 20, enzyme activity decreased but was probably higher than control. At the beginning of oviposition (40 days), activity of mitochondrial GPx growth in the Group 5 was found to be 11.4% ( $p < 0.01$ ) relative to the control, and its activity was significantly lower compared to the Group 3. When the bird reached puberty (70 days), the activity of mitochondrial GPx in Group 5 was significantly higher compared to control group. This indicates that under the action of salts of heavy metals, the drug Sel-Plex is able to activate antioxidant protection in birds' bodies. In the study of the reduced glutathione content in the cytoplasm of quails' liver treated with Sel-Plex, on the 10th day it was found a decrease of its content by 32.1% ( $p < 0.05$ ) compared with the control (Table 2). At the age of 40 days, the content of reduced glutathione in the cytoplasm of this experimental group increased significantly, and at the end of the experiment it was 2.2 times higher than in the cytoplasm of the liver of the control group ( $p < 0.001$ ). In the liver mitochondria of birds from Group 3 (40 days) an increase in glutathione recovered by 37.6% ( $p < 0.05$ ) was also observed relative to controls. In contrast to the cytoplasm, in the liver mitochondria the level of this indicator decreased by 33.8% ( $p < 0.001$ ) in 70-day quails compared to the control. In group, treated with Sel-Plex and cadmium, cytoplasmic glutathione content decreased significantly in the first decade of the birds' life and increased 6-fold ( $p < 0.001$ ) during puberty and intensive reproduction. In the mitochondria of hepatocytes of the birds from Group 5 there was an increase in the content of reduced glutathione by 35.1% ( $p < 0.05$ ) compared with the control on the 40th day of the experiment. Unlike the cytoplasm in the mitochondria of hepatocytes of the quails of Group 5 this indicator decreased by 25.9% ( $p < 0.01$ ) relative to the control on the 70th day. The glutathione content was higher in the mitochondria than in the cytoplasm. The period of reaching the maturity of puberty was characterized by an increase in the content of reduced glutathione in the cytoplasm, which indicates the regular dynamics of the activity of the antioxidant defense system.

**Table 2.** The content of reduced glutathione in subcellular structures of quail liver under Sel-Plex and Sel-Plex with cadmium added to the diet.

Age, days	Reduced glutathione, nmol/g					
	Control		Sel-Plex		Sel-Plex + Cd	
	cytoplasm	mitochondria	cytoplasm	mitochondria	cytoplasm	mitochondria
10	0.84 ± 0.07**	2.31 ± 0.22	0.57 ± 0.08 <sup>^</sup>	1.90 ± 0.14	0.60 ± 0.04 <sup>^</sup>	1.72 ± 0.14
20	0.54 ± 0.05	2.64 ± 0.24	0.74 ± 0.07	2.56 ± 0.26	0.41 ± 0.03 <sup>^#</sup>	2.05 ± 0.26
30	0.59 ± 0.06	2.16 ± 0.10	0.64 ± 0.08	2.42 ± 0.20	0.38 ± 0.04 <sup>^#</sup>	0.29 ± 0.01
40	0.49 ± 0.04	2.31 ± 0.16	0.68 ± 0.05 <sup>^</sup>	3.18 ± 0.45 <sup>^</sup>	0.55 ± 0.03 <sup>#</sup>	0.32 ± 0.03 <sup>#</sup>
50	1.15 ± 0.08***	3.37 ± 0.33*	1.03 ± 0.08	3.48 ± 0.19	1.07 ± 0.10	0.50 ± 0.03 <sup>#</sup>
60	1.23 ± 0.10	3.70 ± 0.31	0.73 ± 0.05 <sup>^</sup>	3.77 ± 0.31	1.44 ± 0.06 <sup>#</sup>	0.89 ± 0.06
70	0.33 ± 0.02***	3.66 ± 0.15	0.71 ± 0.04 <sup>^</sup>	2.42 ± 0.16 <sup>^</sup>	1.99 ± 0.09 <sup>^#</sup>	2.71 ± 0.23 <sup>^</sup>

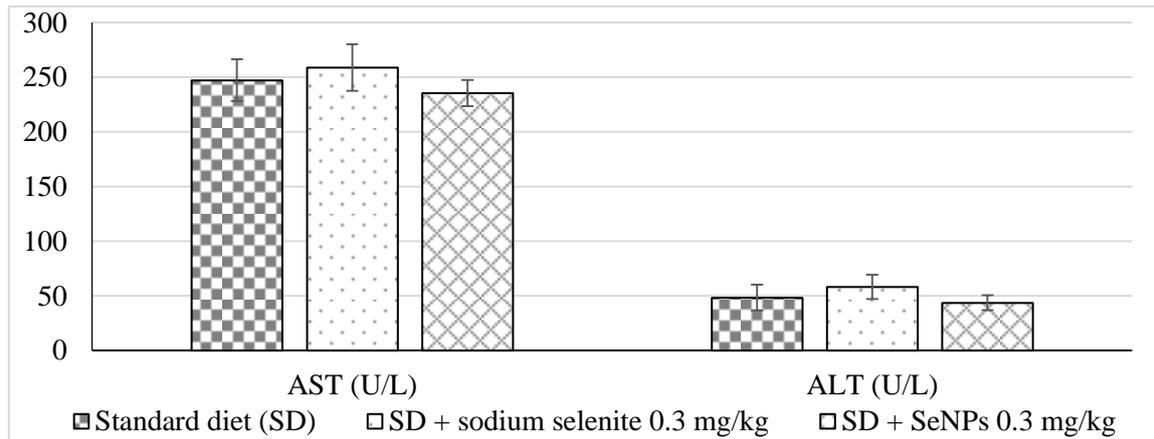
<sup>^</sup> Difference is significant with respect to control at  $p < 0.05$ ; <sup>^^</sup>  $p < 0.01$ ; <sup>^^^</sup>  $p < 0.001$ ; \* difference is significant with respect to previous age; # difference is significant with respect to study group.

In subsequent studies, the effect of Selenium nanoparticles on the quail organism was studied. The advantage of nano-selenium (Nano-Se) is the possibility of its use in the zero state of oxidation ( $Se^0$ ), which causes low toxicity and high bioavailability compared to other oxidation states ( $Se^{+4}$ ,  $Se^{+6}$ ) (Wang et al., 2007; Torres et al., 2012; Hosnedlova et al., 2018). However, it is proved that at this stage, it is unstable and easily transformed into an inactive form, although its stabilization can be achieved by encapsulation into the corresponding shells (Zhai et al., 2017). The biological properties of Selenium nanoparticles (SeNPs) depend on their size: smaller particles have high activity (Torres et al., 2012). The smaller size of SeNPs increases the ability to capture free radicals with greater antioxidant effect (Tsekhmistrenko et al., 2020). We observed the the tendency to decrease of the triacylglycerols and cholesterol content in experimental groups of birds during the analysis of the lipid spectrum of quails blood (Figure 5). While the triacylglycerols and cholesterol are indispensable components of cell membranes, the fats have an energy function and cholesterol serves as a starting material for the biosynthesis of steroid hormones (cortisol, progesterone, and estosterone), vitamin D, and bile acids. Thus, the introduction of avian nanoparticles of Selenium into the birds' diet did not affect the permeability of cell membranes.



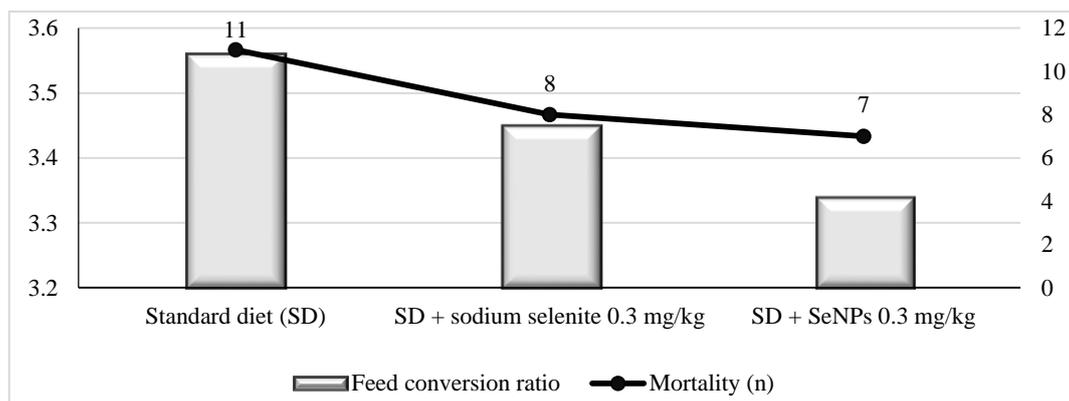
**Figure 5.** Indicators of lipid metabolism of 35-day-old quails.

A number of enzymes performs the regulation of metabolic processes in birds. The condition of the liver, kidneys, pancreas, skeletal muscle and myocardium can be assessed by studying transaminases. The results of the studies show that the activity of AST and ALT does not undergo significant changes due to the introduction of quails of various forms of Selenium into the organism. This indicates that there is no negative impact (Figure 6).



**Figure 6.** Blood transaminases activity of 35-day-old quails.

When growing quails' meat, the main indicator of poultry productivity is live weight. Feeding of compound feed with the content of nano-selenium has been found to provide the highest growth rates (Mohapatra et al., 2014). Thus, at 35 days of age, the quails of this group by live weight probably ( $P < 0.001$ ) exceeded the indicator of the first group by 7.5% and by 4.2% the indicator of the 2nd group. They were also characterized by the highest increase in live weight and feed consumption per head, as well as lower bird consumption (Figure 7).



**Figure 7.** Feed conversion ratio and mortality of supplemented with different Se.

Thus, a living organism is capable of adapting to the action of toxicants or pharmacological compounds that are manifested by adaptation, addiction, or tolerance (Van de Water et al., 2006). The decrease in the "response" of the birds' organism to heavy metal compounds upon long-term admission should receive a broader explanation, from an addictive standpoint. Addiction has been observed with low intensity toxic substances for a long time (Fotakis & Timbrell 2006), which was the case in our studies. This condition is due to the mobilization of protective and adaptive mechanisms and the activation of reparative processes under stress of various origins (Polishchuk et al., 2020). The manifestation of addiction with the participation of the antioxidant system depends on the relationship between the intensity of these processes (Tsekhmistrenko et al., 2018b).

The toxic effect of cadmium sulfate on its chronic receipt is likely to be associated with the formation of a large amount of ROSs, which initiate processes of radical damage to cellular structures. The reaction to the action of Cadmium ions is the activation of the body's protective and compensatory forces, which is explained by a decrease in the activity of antioxidant defense enzymes and a decrease in the content of reduced glutathione.

## Conclusion

We observed high activity of enzymes of energy metabolism, in particular COX, SDH and LDH when quenched with selenium compounds in the cytoplasmic and mitochondrial fractions of the liver. We suggested that the Sel-Plex has a pronounced effect on the energy metabolism of the poultry, resulting in improved meat and egg productivity. We also proved corrected effect of the organic form of Selenium on the energy metabolism under chronic loading of Cadmium.

We also found that if selenium supplements were included in the quail diet alone and under cadmium load adjustments, the birds had a greater body weight gain and increased livestock population. More pronounced changes were observed in poultry with added Sel-Plex and nano-selenium. Sel-Plex and nano-selenium use in the quail diets increased birds' antioxidant status and improved the absorption of nutrients. We also detected the nano-selenium has a more pronounced effect than sodium selenite.

Nevertheless, the mechanisms of assimilation and metabolism of Selenium compounds need further investigation; further research is also needed to determine the mechanisms of transformation of inorganic and nanoforms into selenoprotein and to check the biosafety of selenium nanoforms as feed additives in poultry.

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