Research Article

Dependence of Antioxidant and Biochemical Status on Selenium Content in the Blood of Animals

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Abstract | Inadequate nutrition of the body with selenium can adversely affect the oxidant-antioxidant status of the animal since this microelement belongs to the most important antioxidant defense enzyme glutathione peroxidase. This article examines the intensity of lipid peroxidation processes and the functioning of the antioxidant defense system in pregnant and calved cows in the area with selenium favorable agrobiocenoses (Voronezh region, Russian Federation) and selenium-deficient biogeochemical province (Kirov region, Russian Federation). The LPO-AOS parameters were evaluated in 89 Black-Motley cows at the age, corresponding to 2 to 3 lactations, with mean or great live market quality and a weight of 500 to 650 kg. The content of microelements, malonic dialdehyde, enzymatic and non-enzymatic components of the antioxidant defense system in the blood was investigated. Biochemical analysis of the blood was also performed to estimate the functional state of the cow's organism. In animals from the selenium-deficient region, the microelement content did not exceed 44.2–81.9% of the level in animals from the satisfactory region throughout all studied groups. Besides, an increased accumulation of lipid peroxidation products was observed. In particular, malonic dialdehyde increased by 17.9–96.6%. Also, the malfunction of the glutathione system was noted, manifested in the reduced activity of glutathione peroxidase and glutathione reductase. The consumption of Vitamin E as a non-enzymatic element within the antioxidant defense system increased significantly by up to 2.27 times. Study results of the blood biochemical composition show that selenium deficiency may facilitate the development of pathologies in the liver and excretory system . Therefore, food additives as an additional source of micronutrients may be recommended to maintain the antioxidant defense system capability in animals with low selenium levels in agrobiocenoses.

Keywords | Antioxidant protection, Biochemical composition, Cows, Pathology, Peroxidation, Selenium

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INTRODUCTION

Micronutrients play a significant role in living systems since co-enzymes involved in various metabolic processes have antioxidant and immunoprotective effects. Selenium is considered one of the essential micronutrients with many biophysical, metabolic, and energy functions. The body-nutrient need is associated with the content of unsaturated fatty acids, tocopherols, and such micronutrients as sulfur and arsenic in the diet, which can adversely affect the availability of selenium for the body. The available data on selenium levels in cattle allow stating its significant variability and dependence on some factors, including age, physiological condition, geochemical characteristics, the shared influence of other chemical elements (Jovanović and Ermakov, 2020; Petzer and Ferreira, 2019; Sadvokasova et al., 2014). It should be noted that under conditions of increased stress of physiological and metabolic processes in the cow's body, the need for selenium can rise dramatically.

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A satisfactory level of selenium in cattle has been shown to have a positive impact on reproductive qualities. Notably, it decreases the number of infertility days in cows and the incidence rate of reproductive diseases (Ventsova and Safonov, 2021). Besides, selenium reduces the frequency of mutations, has anticarcinogenic, radiation-protective, and antitoxic effects . The synthesis and activity of selenium-containing proteins and enzymes are best achieved with selenium intake close to the lower limit of optimum intake. For beef cattle, the selenium content in fodder is 100 mg/kg dry matter, for dairy cattle 300 mg/kg dry matter (Suttle, 2010). The use of selenium additives enhances the nutritional value and quality indicators of milk. In particular, the selenium content increases in milk, making it possible to produce dairy products enriched with selenium. The use of micronutrient compounds in the diet increases selenium content in milk and dairy products from 29.7% to 38.2%. The consumption of these products may prevent cardiovascular disease, osteoarthropathy, and decreased immune protection in humans (Azorín et al., 2020; Benstoem et al., 2015). Injections of medications or food additives with inorganic and organic selenium contribute to reduced accumulation of lipid peroxidation (LPO) products as diene conjugates and malonic dialdehyde (MDA). To date, the antioxidant properties of selenium have been confirmed in numerous studies (Kireev et al., 2016; Safonov, 2018; Sevostyanova et al., 2020).

Modern science considers free-radical oxidation (FRO) a process that arose during the evolutionary adaptation of living systems to oxygen respiration. The active forms of oxygen appear during its progressive reduction. Later, they come into reaction with the polyunsaturated fatty acids and phospholipids of the biological membrane bilayers, changing their permeability and disturbing the normal functioning of the cells. That results in the formation of peroxide radicals the primary, secondary, and ultimate LPO products. The enzymatic and non-enzymatic components of the antioxidant defense system (AOS) (Karpenko et al., 2008; Kireev et al., 2016; Martinovich and Cherenkevich, 2008) prevent damage to cell structures and maintain low levels of LPO.

Selenium is critical for antioxidant enzyme production and its physiological role in free radical metabolism. A major indicator of selenium availability in the body is the activity of glutathione peroxidase (GPx). This enzyme contains selenium in the active center and participates in reducing hydroperoxides of polyunsaturated fatty acids and the interruption of the LPO chain (Golova et al., 2010; Sevostyanova et al., 2020). It is known that the intensity of the LPO process increases in the organism of down-calving cows. In this case, selenium plays a stabilizing role in FRO, maintaining the balance of production and active forms of oxygen by replenishing the enzyme bond of AOS. Besides glutathione peroxidase, selenium is present in some antioxidant-reductase enzymes and neutrophilic peroxidase. Therefore, selenium deficiency affects the ability of blood and dairy neutrophils to withstand pathogenic bacteria (Petzer and Ferreira, 2019; Postrash et al., 2008).

Antioxidant vitamins also play an essential protective role within the AOS. Among other antioxidant properties, ascorbic acid as a non-enzymatic element within AOS is known for its ability to restore the oxidized form of α-tocopherol or vitamin E (Khurtsilava et al., 2012). Vitamin E has the greatest biological activity among all the non-enzymatic components. It acts as a singlet oxygen form quencher, an anion-radical acceptor, and intercepts free radicals by reacting with them at the chain-breaking stage. Vitamin A and carotenoids also have an antioxidant effect. Feeding additional sources of vitamin A contributes to the reduction of lipid hydroperoxides, active products of thiobarbituric acid, and the growth of superoxide dismutase and glutathione peroxidase activity (Anurieva et al., 2019; Bolieva et al., 2008; Smolyaninov, 2015).

Low levels of vitamin A and selenium in the blood of cows are associated with an increased probability of stillborn calves. Selenium is closely linked to thyroid hormonal homeostasis. In hypothyroidism, there are cases of sudden fetal death without apparent causes. Such cases of prenatal death may be related to degenerative processes in the myocardium, including necrosis (Uematsu et al., 2016).

The data collected showed that low selenium provision in agrobiocenoses of biogeochemical provinces becomes the most significant cause of deficiency of this most crucial biogenic element in human and animal organisms. Lack of selenium in cattle negatively affects the economic efficiency of productive cattle breeding through decreased reproduction rates and the number of young animals, increased morbidity, reduced milk productivity, and qualitative characteristics of milk (Ermakov and Jovanović, 2010; Petzer and Ferreira, 2019; Plemyashov et al., 2019; Safonov, 2018; Safonov et al., 2018). All of these factors explain the importance of in-depth research on micronutrients for the scientific community. Thus, several studies have been conducted confirming an increase in milk productivity from 7.3% to 7.9% (Aleksandrova and Sotnikov, 2014) and higher milk quality characteristics when adjusting cow selenium status (Serdyukova, 2013). The present study continues the topic development on the influence of selenium availability in animals on the balance of lipid peroxidation, antioxidant defense system, and homeostasis.

This work aimed to examine the intensity of LPO, the enzyme and non-enzyme links of AOS, and the blood biochemical composition of dairy cows during pregnancy and postpartum in areas where the selenium content in agrobiocenoses is different. As GPx production and activity are highly dependent on the level of this microelement, its deficiency is expected to have a negative effect on AOS capacity.

Sampling

For comparative analysis of selenium content in the blood and its influence on LPO-AOS indices, dairy cows from 2 farms in the Voronezh (regional agrobiocenoses with sufficient selenium content) and Kirov regions (biogeochemical province, deficient in selenium content) of the Russian Federation were selected for the study . According to the literature, soil monitoring in the Kirov area has shown an extremely low supply of raw selenium forms, with the content ranging from 28 to 51 µg/kg (Aristarkhov et al., 2018).

The LPO-AOS parameters were evaluated in 89 Black-Motley cows at the age, corresponding to 2 to 3 lactations, with mean or great live market quality and a weight of 500 to 650 kg. Pregnant cows under study were at different stages of fetal formation: an initial period of fetogenesis at two months of pregnancy, the period of fetoplacental complex formation at five months, and the maturation period of important organs and fetal systems, as well as its enhanced growth at 8.5 months. In the postpartum period, the animals were selected for the experiment based on their clinical condition and the presence or absence of postpartum pathology. Major biochemical parameters of blood have also been studied in cows. All animals were fed following zootechnical standards for dry and dairy cows. Cattle rations were based on forage used locally in each region: meadow hay, barley straw, corn silage, peas, barley, wheat, sunflower cake, molasses, and sodium salt in plenty. In both farms, all animals were kept using the same tethering system during the housing period.

Research methods

The clinical condition of the animals was assessed using traditional methods. Purulent catarrhal endometritis was diagnosed when the body temperature and pulse increased. In addition, the mucous tissue of the internal genitals became peculiar, the color of the bursa changed, and there was a mixture of pus and a serene smell. Reproductive status was evaluated through external examination and transrectal palpation. Blood for laboratory testing was collected from the jugular vein in the morning following the aseptic and antiseptic measurements. For assessing the LPO-AOS capacity, the selenium level was estimated by spectrofluorimetric method, and that of malonic dialdehyde through the reaction with thiobarbituric acid. The activity of superoxide dismutase (Sirota, 1999) glutathione peroxidase and glutathione reductase was asseses accoding to (Kruglikova et al., 2012) that of catalase as per Korolyuk et al. (1995). Concentration of vitamin A was estimated by spectrophotometric method, that of vitamin E by method based on formation of quinones during oxidation of tocopherol molecules by iron chloride, and vitamin C using titration with 2.6-dichlorophenolindophenol). The main indices of biochemical blood composition were observed on a Hitachi-902 biochemical analyzer to assess metabolic activity.

The animal handling was carried out under the principles of human treatment laid down in the EC Directive (86/609/EEC) and the Helsinki Declaration.

Mathematical methods recognized in biological and medical research were applied to process and interpret the collected indicators using Statistica 6.0 and Microsoft Excel analytical software. The significance of the differences was determined by the Student t-criterion using a matched comparison method.

RESULTS AND DISCUSSION

According to the literature, soil monitoring in the Kirov area has shown an extremely low supply of raw selenium forms, with the content ranging from 28 to 51 µg/kg (Aristarkhov et al., 2018). Table 1 shows the blood analysis results for cows at different gestational periods and recently calved cows. The presence or absence of uterine inflammatory processes in the uterus was also taken into account.

Table 1: Selenium content in the blood of cows at various reproductive stages under different selenium supply conditions, µg%.

Reproductive stages	Voronezh region (Se-favourable)	Kirov region (Se-defficient)
Pregnancy term		
2 months	16.0±0.87	10.0±2.44
5 months	17.2±1.16	7.6±0.82
8.5 months	14.4±0.79	7.7±1.14
Postpartum period		
Normal condition	16.0±0.73	13.1±1.08
Pathology	14.3±0.42	9.4±1.13

It was established that the content of selenium in the blood of cows in the 2nd month of pregnancy was 62.5% ($P<0.05$) in the deficient region, in the 5th month 44.2% ($P<0.001$), in the 8.5th month 53.5% ($P<0.001$) compared to similar figures in the selenium-favorable region. In the postnatal period with its ordinary course, the selenium level in cows of the deficient area was 81.9%. In the case of inflammatory processes in the uterus (endometritis), 65.7% compared to similar indicators in animals from the favorable region. Also, cows' lowest amount of selenium was observed during

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an intensive formation of the fetal complex and in the final pregnancy stage. In cows with postpartum pathology, the content of the microelement was reduced. Purulent-catarrhal endometritis occurred when the selenium level lowered by 10.6% (P<0.05) in animals from the favorable region and by 28.2% (P<0.05) in those from the deficient region (in comparison with healthy animals from these regions).

Table 2 presents the values of key indicators characterizing the condition of the LPO-AOS system in pregnant animals. The calf-bearing period in cows from the Voronezh region is accompanied by increased intensity of LPO processes, which is evident from the increase in MDA concentration in the blood of animals with the increase in gestational age. Thus, the MDA level increased by 17.9% at five months of pregnancy and 36.6% at 8.5 months (P<0.001). These changes occur due to hormonal reorganization and increased intensity of metabolic processes. The activity of enzyme components in the antioxidant defense system maintaining basic acid homeostasis of the body intensified as well. For instance, the level of glutathione peroxidase increased statistically significantly by 35.4% at 8.5 months of pregnancy, that of glutathione reductase (GR) by 31.9%, superoxide dismutase (SOD) by 28.3%, and catalase by 10.9%. Higher activity of the glutathione system coincides with a drop of selenium content in the blood (Table 1), which may be due to the consumption of microelements to synthesize selenium-containing enzymes.

Table 2: LPO-AOS indices for pregnant cows under different selenium supply conditions.

Indicator	Pregnancy term		
	2 months	5 months	8.5 months
MDA, μM/l	1.34±0.09	1.58±0.08	1.83±0.05
	2.62±0.12	1.90±0.11	2.55±0.26
GPx, mM G-SH/ l×min	11.7±0.75	10.3±0.30	15.8±0.93
	8.2±0.82	10.0±0.45	11.1±0.52
GR, μM G-SS-G/ L×min	273.0±8.51	267.0±15.22	360.0±8.44
	143.0±6.51	144.6±4.40	144.0±6.81
SOD, units/mg Hb	0.92±0.04	0.81±0.04	1.18±0.05
	0.92±0.06	0.86±0.06	1.06±0.05
Catalase, mM H_2O_2/L× min	34.9±1.16	36.0±0.96	38.7±0.74
	33.2±1.68	32.4±1.04	37.0±1.01

Note: Hereinafter, the upper values are the values of cows from the agrobiocenoses of the selenium-favorable region, and the lower values are the values of cows from the agrobiocenoses of the selenium-deficient region; *MDA: malonyldialdehyde; GPx: glutathione peroxidase; GR: Glutathione peroxidase; SOD: superoxide dismutase.

Compared to animals in the Voronezh region, cows in the Kirov region exhibited more intense lipid peroxidation processes. At two months of pregnancy with selenium deficiency, the MDA concentration in the blood was 95.5% higher (P<0.001); at five months 20.2% higher (P<0.05), and at 8.5 months 39% higher (P<0.05) compared to animals with sufficient selenium supply. The lowest activity of the glutathione system was observed in down-calving cows: GPx was 42.3% lower (P<0.01), GR – 2.5 times lower (P<0.001), and the enzyme activity of SOD and catalase did not differ significantly.

The effect of selenium on the antioxidant protection of cows was also observed in the analysis of non-enzymatic AOS binding components (Table 3). One of the most critical indices is vitamin E as a selenium synergist, which helps optimize its uptake in the body. Cows displayed a reduction of blood selenium levels throughout the whole pregnancy period. Namely, there was a 34.7% decrease in the level of selenium (P<0.001) by the 2nd month of pregnancy, followed by a 16.2% decrease (P <0.001) at 5 months and a 38.2% drop (P <0.001) at 8.5 months. The content of vitamin A (52.5–38.5% vs. 27.0–18.5% in the group of cows from the favorable region) and carotin (44.4–50.41% vs. 19.0–5.2%) decreased more intensively with increasing pregnancy period.

Table 3: Levels of non-enzymatic AOS elements in the blood of cows at different reproductive cycle stages under different selenium supply conditions.

Reproductive period	Vitamin E, mg%	Vitamin A, μg%	Carotin, mg%
Pregnancy term			
2 months	1.44±0.07	53.6±5.44	0.58±0.035
	0.94±0.12	78.7±5.59	1.33±0.101
5 months	1.05±0.12	37.1±2.96	0.47±0.067
	0.88±0.06	37.4±6.82	0.74±0.049
8.5 months	1.02±0.05	43.7±2.96	0.55±0.028
	0.63±0.05	48.4±6.03	0.66±0.039
Postpartum period			
Normal condition	1.02±0.15	50.2±5.21	0.48±0.037
	0.45±0.07	43.3±2.95	0.36±0.079
Pathology	0.66±0.04	37.1±3.61	0.30±0.038
	0.47±0.04	30.8±4.31	0.27±0.075

In the postnatal period, the level of vitamin E continued to decrease. In the absence of pathologies in animals with selenium deficiency, its content was 2.27 times lower, that of vitamin A 13.7% lower, and for carotin 25.0% lower than at a sufficient level of microelement.

During the postpartum period, the inflammatory process in the uterus and 11.9 – 39.4% lower selenium content in the blood of sick cows led to a 28.8% reduction of vitamin E content in cows from the selenium-deficient region. The level of vitamin A dropped by 17.0%, and that of carotin by 10.0% compared to cows from a favorable region.

Thus, with selenium deficiency and reduced activity of the glutathione AOS elements, substances included in the non-enzymatic link, mainly the synergistic vitamin E, are more actively involved.

Based on biochemical blood analysis of animals from different regions (Table 4), selenium deficiency was established to cause an increase of urea content by 25.9–83.4% in the blood of animals at different stages of the reproductive cycle. It was most markedly manifested during pregnancy (P<0.01-0.001). Probably, such animals have a higher renal glomerular filtration rate. Thus, compared to animals from the favorable region, the urea/creatinine ratio was twice as higher at the beginning of pregnancy, increasing to 64.5% at the end and eventually increasing by 20–76.7% after calving.

Table 4: Biochemical blood parameters of cows at different stages of the reproductive cycle under different selenium supply conditions.

Indicator	Pregnancy		Postpartum period	
	2 months	8.5 months	Normal	Pathology
*ALAT, U/L	21.8±2.74	22.7±1.74	26.6±2.28	15.5±1.51
	28.0±2.85	26.0±2.24	27.6±3.21	27.2±2.96
AsAT, U/L	68.4±2.91	61.4±3.62	71.4±2.40	82.4±4.31
	83.2±5.11	61.4±2.85	77.7±6.36	109.9±5.87
GGT, U/L	19.6±1.15	20.2±1.28	19.6±1.15	18.4±0.81
	24.0±2.36	17.5±0.61	29.2±3.98	22.9±3.22
Urea, mmol/l	4.52±0.39	3.25±0.22	3.07±0.27	3.94±0.31
	7.79±0.28	5.96±0.22	4.07±0.44	4.96±0.55
Urea/ creatinine	48.7	29.6	36	42.7
	101.5	48.7	63.6	50.8
Calcium, mM/l	2.65±0.04	2.63±0.04	2.61±0.05	2.54±0.02
	2.27±0.07	2.42±0.09	2.22±0.05	2.08±0.14
Phosphorus, M/L	2.16±0.11	2.05±0.09	2.19±0.06	2.17±0.09
	1.95±0.15	2.04±0.10	1.92±0.19	1.88±0.20

Note: *ALAT: alanine aminotransferase; AsAT: aspartate aminotransferase; GGT: gamma-glutamyltransferase.

In cows from the selenium-deficient region, a tendency of increased transaminase and gamma-glutamyltransferase (GGT) activity was observed. The ALAT activity (alanine aminotransferase) was 28.4% higher at two months of pregnancy and 14.5% higher at eight months; also, it was 75.5% higher in cows with postpartum endometritis. No significant differences per region were observed during the ordinary course of the postpartum period. AsAT activity (aspartate aminotransferase) was 21.6% higher at two months of pregnancy with established selenium deficiency and 33.4% higher in cows with postpartum endometritis. The GGT activity was 22.4% higher at two months of pregnancy and 49.0% higher after calving in the physiological course of the postpartum period or 22.4% higher in case of any pathology.

From the above, it can be concluded that selenium deficiency in cows can deteriorate the functional activity of the liver and renal perfusion. Also, some changes in mineral metabolism were observed, namely, a decrease in calcium and phosphorus concentrations. To a greater extent, a 7.9–18.1% decrease of calcium content in the blood at different stages of the reproductive cycle was noticeable, indicating a deterioration of renal function.

Low selenium content in agrobiocenoses of biogeochemical provinces leads to low selenium content in feed sources and animal bodies. Hypoelimentosis leads to disruption of lipid bilayer integrity and cell membrane functions, cell proliferation and apoptosis processes, amino and keto acid metabolism, accumulation of calcium inside cells, disruption of DNA synthesis, fertilization, and embryo implantation (Ashenbrenner and Khaperskiy, 2020; Combs, 2015; Mehdi et al., 2013).

The study results indicated that a significant effect of micronutrient biogenic selenium deficiency was observed in agrobiocenosis. In Figure 1, the data on the main indicators of LPO-AOS in pregnant cows are presented in the form of a comparative diagram, clearly demonstrating a decrease in the efficiency of antioxidant protection under deficiency of the micronutrient.

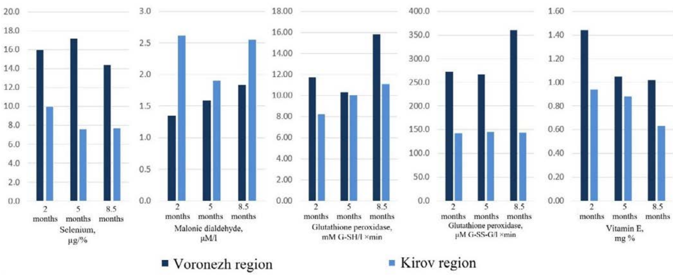

Figure 1: Selenium, MDA, vitamin E, and AOS glutathione content in the blood of cows from various biogeochemical provinces.

The relative availability of selenium in the Kirov region ranged from 44.2% to 81.9% compared to the Voronezh region. Hence, the lipid peroxidation processes under selenium deficiency are significantly more intense in all cows at different pregnancy terms, which is confirmed by quite high MDA levels in the blood. However, a decline in glutathione peroxidase and glutathione reductase activity, which are used to restore the oxidized forms of glutathione, was consistently detected in each group. In other words, given any physiological condition of animals, low selenium level results in high oxidative stress. Free radicals are known to cause direct damages to cells and tissues. Moreover, they trigger the mechanism for migrating and accumulating leukocytes in the affected areas, provoking, thus, further mediated destruction due to the activity of neutrophils (Randjelovic et al., 2012).

Complementing the LPO-AOS analysis with data of biochemical blood composition, it can be concluded that selenium deficiency against the background of reduced antioxidant vitamins and mineral metabolism disorders was found to predispose the development of multiple organ pathology. Primarily, low levels of selenium affect the liver and organs of the excretory system. Furthermore, increased aspartate aminotransferase activity and reduced calcium concentration may indicate myocardiopathy progression (Anurieva et al., 2019). The following may be regarded as evidence for pathological changes. The blood enzymatic system indices used in diagnostic studies differ significantly in cows during different physiological periods, and the activity growth may be associated with the final stage of pregnancy and calving (Stojević et al., 2005). However, selenium deficiency is characterized by intense ALAT, AsAT, and GGT activity in different periods of pregnancy and ordinary or pathological postpartum periods. Some biochemical blood parameters for cows in the Kirov and Voronezh regions are compared in Figure 2.

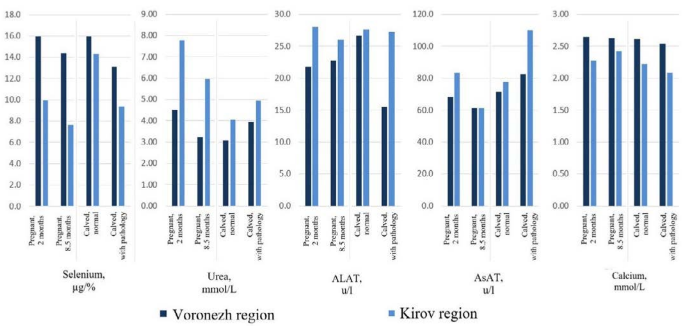

Figure 2: Selenium, urea, ALAT, AsAT, and calcium content in the blood of pregnant and calved cows in various biogeochemical provinces.

CONCLUSIONS AND RECOMMENDATIONS

It has been established that the organism of cows is more exposed to oxidative stress in the selenium-deficient biogeochemical provinces (the Kirov region) due to intense LPO processes. They are expressed in a higher accumulation of MDA in the blood of animals. At the same time, a decrease in the activity of GPx and GR constituting the glutathione chain within AOS is explained by the lack of microelements necessary for the construction of an active GPx center.

The limitation of LPO responses is supported by the coordinated functioning of the enzyme and non-enzyme mechanisms of the AOS system. Thus, the reduced activity of enzyme components was partially offset by the increased intake of antioxidant vitamins A, E, and carotin.

Based on the results obtained, it is strongly recommended to monitor selenium content in animals and feed used for dietary supplements in order to ensure its adequate levels in cattle and prevent pathology associated with hypoelimentosis.

NOVELTY STATEMENT

The present study continues the topic development on the influence of selenium availability in animals on the balance of lipid peroxidation, antioxidant defense system, and homeostasis.

AUTHOR'S CONTRIBUTION

All authors contributed to the study conception and design.

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Conflict of interest

This authors have declared no conflict of interest.

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