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ORIGINAL ARTICLE

Prooxidant-antioxidant balance in the organism of bulls (young cattle) after using cadmium load

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The results of studies of the effect of Cadmium influence on the state of the enzyme and nonenzyme system of antioxidant protection of young cattle organism, namely on the activity of superoxide dismutase, catalase, glutathione peroxidase, level of reduced glutathione, Selenium, vitamins A and E. It was determined that the feeding of young bulls with cadmium chloride in a dose of 0.04 mg / kg of body weight contributed to a decrease both, enzyme and non enzyme level of the system of antioxidant protection (superoxide dismutase by 22%, catalase - by 12%, renewed glutathione by 11%, glutathione peroxidase by 22 %, Selenium - by 18%, vitamin A - by 23%, vitamin E - by 27%,). The lowest level of the antioxidant protection system in the blood of young cattle was set at the sixteenth and twenty-fourth day of the experiment, which is due to the increased activation of lipoperoxidation processes and a disturbance of the balance between the activity of the antioxidant system and the intensity of peroxidation of lipids. The toxic effect of Cadmium contributes to the change in the stationary concentrations of the radical metabolites O2, ˙OH, NO2, which, in their turn, initiate the processes of peroxide oxidation of lipids, indicating an increase in the level of diene conjugates and malonic dialdehyde. The highest level of intermediate and final products of peroxid oxidation of lipids in the blood of young cattle was determined on the thirtieth day of the experiment, while comparing with the control group, they increased by 31 and 27%, respectively.
Key words: cadmium; superoxide dismutase; catalase; glutathione peroxidase; recovered glutathione; vitamins; selenium

Introduction

The pollution of environment that is caused by cadmium and its negative impact on animals' organism, especially young cattle, is considered to be an acute problem to study (Gutij, 2013). The pathogenesis of cadmium toxicity in farm animals is an enormous and relevant problem that should be researched carefully.

It is widely known that the inflow of Cd2 + is associated with the ecological risk for the organism due to its cumulative toxicity to organs and systems. It clearly leads to a decrease in the rate of growth and productivity of animals (Chaney et al., 2001; Kabata–Pendias, 2004; Liu et al., 2008; Al-Azemi et al., 2010; Al-Attar, 2011). The Accumulation of heavy metals in the components of the natural environment, that has been already mentioned, increases the risk of supplies into the body and poses a growing problem for human and animal health (Antonio et al., 1998; El-Refaiy and Eissa, 2012; Peng et al., 2015). In fact, it negatively affects the efficiency of the livestock sector. That is why the profound research of pharmaco-toxicological and biochemical processes that lie on the basis of metabolic and vital functions disorders of the animals' organisms caused by Cadmium should be conducted.

Mechanisms of cadmium exposure in the antioxidant defense system of laboratory animals have been recently and intensively studied (Hutiy, 2012), however, the processes that are considered as a basis for the development of cadmium toxicity in young cattle, have not been found yet. The literature data shows that the relationship between cadmium-induced damage to the liver cells as well as the activity of lipid peroxidation are often contradictory. The species differences in antioxidant defense system reaction to the action of metal, the peculiarities of enzymatic and non-enzymatic metabolic responses, their links to the continuous flow of Cd^{2+} in low and high concentrations have not been studied but the following research is still relevant and essential. The study of these processes will allow revealing some features of metabolic processes in cattle under cadmium loading conditions that are still unknown.

The purpose of research is to find out the impact of cadmium load on prooxidant -antioxidant balance of the young cattle's organisms.

Materials and methods

The research was conducted on the farm called Ivanivci, Zhydachiv district, Lviv region. The research was made on ten calves that were six months old, Ukrainian black and white dairy breed, were formed into two groups of five animals each:

Group 1- control (C), the bulls were on the standard diet;

Group 2 – experimental (E), calves were fed with food that had a dose of 00,4 mg of cadmium chloride per kg of animals' body weight;

The essential rules were followed when the research was conducted, they were required in order to implement zootechnical experiments, selection and maintenance of similar animals in unique groups, the technology of procurement, use and accounting the consumed forage. The diet of the animals was balanced in nutrients and minerals that ensure their basic need for nutrition. The research lasted 30 days. Blood for analysis was taken from the jugular vein on the first, tenth, fifteenth, twenty-fifth and thirtieth day of the experiment. Glutathione peroxidase activity (GP) was determined by the speed of oxidation of glutathione in the presence of a tertiary butyl hydroperoxide and glutathione content in the blood (Vlizlo et al., 2012).

Determination of catalase activity was done as described (Koroljuk et al. 1988). The principle of the following method is based on the ability of hydrogen peroxide to form stable color complexes with molybdate salts.

Determination of superoxide dismutase (SOD) was done as described (Dubinina et al., 1983). The method consists in the restoration of nigrosine tetrazolium by superoxide radicals, which are formed in the reaction between phenazine methosulfate and the reduced form of nicotinamide diene in dinucleotide.

The method of determination of Selenium (Se) content lies in acidic mineralization sample by the mixture of nitric and perchloric acids, the recovery of hexavalent selenium to Se^{+4} and the formation of selenium acid with 2,3- diaminophthalene-piazoselenol so that the magnitude of fluorescence was proportional to the content of selenium in the sample (Vlizlo et al., 2012). The concentration of A and E vitamins was designated by the high-performance liquid chromatography method (Vlizlo et al., 2012).

All manipulations with animals were conducted in accordance with the European Convention for the Protection of Vertebrate Animals used for Experimental and Scientific Purposes (Strasbourg, 1986). The mathematical processing of research results was statistically analyzed using the Statistica 6.0 software package. The results of middle indices were considered as statistically credible at * - $P < 0.05$ (ANOVA).

Results and discussion

The initial stage of free radical oxidation is controlled by enzyme superoxide dismutase, which neutralizes superoxide radical and therefore reduces the overall toxic effects of reactive oxygen forms (Bielenichev et al., 2002; Vucic et al., 2006; Martyshuk et al., 2016; Khariv et al., 2016). Table 1 shows the effect of cadmium load on superoxide dismutase activity in the bull's blood.

Table 1. Effect of cadmium chloride on superoxide dismutase activity in the blood of the bulls; c. u. / mg protein (M. ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	0.58 ± 0.009	0.59 ± 0.012
First day	0.59 ± 0.010	0.66 ± 0.014 *
Tenth day	0.62 ± 0.009	0.54 ± 0.009 *
Fifteenth day	0.61 ± 0.009	0.48 ± 0.009 *
Twenty-fifth day	0.60 ± 0.011	0.47 ± 0.010 *
Thirtieth day	0.61 ± 0.010	0.49 ± 0.010 *

At the beginning, the activity of superoxide dismutase in the blood of control and experimental groups was within the values of 0.58 ± 0.009 – 0.59 ± 0.012 c.u. / mg of protein. After feeding the animals with cadmium chloride at a dose of 0.04 mg/ kg per body weight, blood superoxide dismutase activity in the experimental group was significantly increased by 12% on the first day of the experiment in comparison to the control group. On the tenth day of the experiment, the decrease in the enzyme activity was established. On the fifteenth and twenty-fifth day of the experiment, the superoxide dismutase activity in the blood of experimental group was lower by 13 and 21% compared to the control group of animals. On the twenty-fifth day of the experiment, the enzyme activity in the blood of experimental group was the lowest, 0.47 ± 0.010 c.u. / mg of protein. On the thirtieth day of the experiment the superoxide dismutase activity began to rise slightly, but still, it remained at a low level.

It is required to note that the superoxide dismutase activity is closely connected with the catalase activity, which protects the organism from highly toxic oxygen radicals. What is more, the sharp increase in the superoxide dismutase activity, without proper activation in catalase is cytotoxic. Catalase catalyzes the splitting of hydrogen peroxide with the formation of water and oxygen (Pereira et al., 1998; Bielenichev et al., 2002; Gutyj et al., 2017). The change of catalase activity in the conditions of feeding bulls with food cadmium chloride is given in the table 2.

It is established that under the influence of cadmium chloride at a dose of 0.04 mg/kg per body weight happens a decrease in enzyme activity, compared to control value, namely, on the tenth day - 4.9%, on the fifteenth day - 11, 7%, on the twenty-fifth day - 12.2 %, on the thirtieth day - 8%.

The most significant antioxidant in glutathione system of the antioxidant protection is glutathione that performs many functions in animals' organism, one of which is to protect against free radicals, to support the functions of membranes, the participation in the metabolism of xenobiotics and the impact on the activity of enzymes (Ferreira et al., 1999; Bielenichev et al., 2002; Gutyj et al., 2016). Glutathione has a direct antioxidant effect. Reduced glutathione acts as a donor of electrons to neutralize the active forms of oxygen.

Table 2. Effect of cadmium chloride on catalase activity in the bulls' blood serum; units (M ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	6.48 ± 0.13	6.50 ± 0.14
First day	6.56 ± 0.12	6.47 ± 0.13
Tenth day	6, 53 ± 0,14	6.21 ± 0,10
Fifteenth day	6.57 ± 0.13	5.80 ± 0,10 *
Twenty-fifth day	6.49 ± 0.11	5.70 ± 0,12 *
Thirtieth day	6.50 ± 0.14	5.98 ± 0,10 *

Effect of cadmium chloride on the level of reduced glutathione in the blood serum of bulls is shown in table 3. On the first day of the experiment, the level of reduced glutathione in the blood of animals of the experimental group that were fed with cadmium chloride at a dose of 0.04 mg/kg per body weight increased by 5.7%, and accordingly it presented 34.19 ± 0.54 mg%. Starting from the tenth day of the experiment, the blood in experimental group of animals marked the decrease of reduced glutathione, which on the fifteenth day of the experiment decreased by 7.6%, and on the twenty-fifth day of the experiment – by 11.3%. On the thirtieth day of the experiment, the increase in the level of reduced glutathione in the experimental group of animals was noted.

Table 3. Effect of cadmium chloride on the activity of reduced glutathione in the blood serum of bulls; mg % (M ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	31.72 ± 0.52	32.10 ± 0.52
First day	32.35 ± 0.50	34.19 ± 0.54 *
Tenth day	31.96 ± 0.49	31.10 ± 0.64
Fifteenth day	32.15 ± 0.44	29.71 ± 0.53 *
Twenty-fifth day	32.82 ± 0.61	29.10 ± 0.64 *
Thirtieth day	32.13 ± 0.59	30.51 ± 0.65

An increase in the level of reduced glutathione on the first day of the experiment is believed to be due to the arrival of toxic elements that trigger the formation of free radicals and the enhancement of lipid peroxidation processes. Later on, the reduction of the level of reduced glutathione can be explained as depletion of the glutathione system for the formation of large amounts of free radicals and lipid peroxidation products.

As a result of our research, we found that, before the cadmium chloride was fed, the activity of glutathione reductase and glutathione peroxidase was within the limits of physiological quantities.

After feeding cadmium chloride at doses of 0.04 mg/kg per animal's body weight the activity of glutathione peroxidase and glutathione reductase on the first day of the experiment increased by 5.3 and 9.3% accordingly (Table. 4 and 5).

Table 4. Effect of cadmium chloride on glutathione peroxidant activity in the blood serum of bulls; nmol NADPH / min per 1 mg of protein (M ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	36.1 ± 1.19	36.3 ± 1.21
First day	36.0 ± 1.17	37.9 ± 1.24
Tenth day	36.2 ± 1.18	31.6 ± 1.11 *
Fifteenth day	36.3 ± 1.20	30.1 ± 1.13 *
Twenty-fifth day	36.1 ± 1.21	28.3 ± 1.19 *
Thirtieth day	36.4 ± 1.24	31.8 ± 1.14 *

Subsequently, the activity of the enzymes in the glutathione system of the antioxidant protection of the young cattle's organism was gradually decreased. It was established that on the fifteenth and twenty-fifth day of the experiment, the activity of glutathione peroxidase had decreased by 14.4% and 21.6%, in accordance with the control.

Similar changes are observed in the study of glutathione reductase activity, which had decreased in the blood of the experimental group of animals by 13.9 and 26.1% in the above-mentioned periods.

On the thirtieth day of the experiment slightly increased the activity of glutathione peroxidase and glutathione reductase can be noted, but if it is compared to the control group, it still remains at a low level.

Selenium is one of the important elements of antioxidant protection of animal's organism. The antioxidant effect is caused by neutralizing dangerous free and aggressive radicals (Bielenichev et al., 2002).

Table 5. Effect of cadmium chloride on the glutathione reductase activity in the blood serum of bulls; nmol NADPH / min per 1 mg of protein (M ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	1.59 ± 0.033	1.62 ± 0.043
First day	1.61 ± 0.038	1.76 ± 0.039*
Tenth day	1.59 ± 0.036	1.52 ± 0.037
Fifteenth day	1.58 ± 0.040	1.36 ± 0.054 *
Twenty-fifth day	1.60 ± 0.043	1.30 ± 0.023**
Thirtieth day	1.59 ± 0.034	1.38 ± 0.039*

The content of selenium in the blood of the bull for the cadmium load is shown in the table 6. Starting from the first day of the experiment the content of selenium in the blood of experimental bulls had gradually decreased. On the fifteenth day of the experiment, it was noticed that selenium content in the blood of animals which were fed with food cadmium chloride at a dose of 0.04 mg/kg body weight had significantly decreased by 8.1%

On the twenty-fifth day of the experiment, the content of selenium in the blood of the bulls of the experimental group was the lowest, and, accordingly, it was: 40.7 ± 0.80 mkg/l. On the thirtieth day of the experiment, the content of selenium began to increase gradually, however, compared to the control group, the content of selenium was lower by 9.3%.

Table 6. Effect of cadmium chloride on selenium content in the blood of bulls; Mkg / l (M ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	46.7 ± 0.94	47.0 ± 0.89
First day	49.0 ± 0.83	45.2 ± 0.80
Tenth day	47.2 ± 0.84	44.0 ± 0.91
Fifteenth day	46.7 ± 0.77	42.9 ± 0.90*
Twenty-fifth day	49.8 ± 0.83	40.7 ± 0.80*
Thirtieth day	48.0 ± 0.64	43.5 ± 0.95*

Reducing the content of selenium in the animals' bodies after cadmium loading as a whole indicates an inhibition of the antioxidant system in the body of animals.

The intensity of the formation of free radicals in the body of animals depends on the concentration of oxygen in the tissues, as well as the activity of the enzyme and non enzyme systems. Important antioxidants that belong to non enzyme systems of antioxidant protection are vitamins A and E. The mechanism of antioxidant action of these compounds is based on reducing the amount of available oxygen in the cells and increasing the activity of oxidation and phosphorylation (Bielenichev et al. 2002). At the beginning of the experiment the content of vitamin A in the bulls' blood, control and experimental groups as within values of 0.81 ± 00,23 – 0,82 ± 0,028 Mcmol/l.

Table 7. Effect of cadmium chloride on the content of vitamin A in the blood of bulls; Mcmol/l (M ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	0.81 ± 0.023	0.82 ± 0.028
First day	0.80 ± 0.026	0.78 ± 0.016
Tenth day	0.83 ± 0.024	0.73 ± 0.019*
Fifteenth day	0.79 ± 0.019	0.68 ± 0.014*
Twenty-fifth day	0.81 ± 0.025	0.62 ± 0.019*
Thirtieth day	0.82 ± 0.021	0.67 ± 0.019*

After feeding the animals with cadmium chloride, the content of vitamin A in the blood of the bull's research group began to decrease, moreover, in comparison with the control group, on the tenth and fifteenth day of the experiment it fell by 12.0 and 13.9% respectively in the control group of animals that were not after cadmium load. On the twenty-fifth day of the experiment, the vitamin A in the blood of the bull's research group was the lowest, where accordingly to the control it decreased by 23.4%.

Table 8 shows the effect of cadmium chloride on the content of vitamin E in the blood of the bulls.Furthermore, it is known that this vitamin is related to endogenous antioxidants that protect cell membrane from free radical attack. The content of vitamin E in the blood of bulls after cadmium load, throughout the experiment, had decreased. The possible reduction of vitamin E was found on the tenth day of the experiment. In fact, calves were fed with cadmium chloride at the dose of 0.04 mg/kg per body

weight, the content of vitamin E in their blood was 3.5 ± 0.11 Mcmol/l. On the fifteenth and twenty-fifth day of the experiment, the vitamin E in the blood of an experimental group of animals decreased by 15.4 and 26.8% compared to the control group.

Table 8. Effect of cadmium chloride on the content of vitamin E in the blood of bulls; Mcmol/l (M ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	3.9 ± 0.13	4.1 ± 0.12
First day	3.9 ± 0.12	3.8 ± 0.14
Tenth day	4.0 ± 0.10	3.5 ± 0.11*
Fifteenth day	3.9 ± 0.11	3.3 ± 0.12*
Twenty-fifth day	4.1 ± 0,11	3.0 ± 0.13*
Thirtieth day	3.9 ± 0.10	3.3 ± 0.13*

The literature data, as well as our own research, clearly shows that a significant reduction of vitamins A and E indicates not only a pathological condition of the liver but also enhance of oxidative processes associated with decreased activity of antioxidant enzymes system (Bielenichev et al., 2002). Cadmium compounds with high biological activity may easily form complex compounds with proteins, nucleic acids, that is why it is easier for them to inactivate series of enzymes. Inhibition of antioxidant enzymes system activity leads to the accumulation of a large number of lipid peroxidation products, which in turn destroy the membranes of cells, tissues, and organs.

Obviously, the decrease in the activity of the enzyme and the non enzyme level of the antioxidant protection system after cadmium load is due to the fact that cadmium contributes to the enhanced formation of free radicals and active forms of oxygen, which results in a disturbance of the balance between products of peroxidation and antioxidants.

Reducing the enzymatic antioxidant level in the blood of calves under conditions of cadmium load is caused by activation of free-radical oxidative process, indicated by the results of table 9 and 10.

After feeding calves cadmium chloride at a dose of 0.04 mg / kg per body weight on the first day of the experiment, the level of peroxidation products in the control group increased, malondialdehyde by 3.4% and diene conjugates by 4.7 % On the tenth day of the experiment, the level of malondialdehyde was below 0.265 ± 0.009 mcmol / l, that was 12.3% higher than in the control group of animals, while the level of diene conjugates was 6.91 ± 0.21 mcmol / l, actually it increased by 20.4% in relation to the control group. On the fifteenth day, the level of lipid peroxidation products (malondialdehyde and diene conjugates) continued to grow again and it became 0.285 ± 0.010 and 7.24 ± 0.19 mcmol / l.

Table 9. Influence of cadmium chloride on the level of malondialdehyde in the blood serum of bulls; Mcmol / l (M ± m, n = 5)

Time of blood study (days)	Animal groups	
	Control	Experimental
At the beginning of the experiment	0.235 ± 0.006	0.233 ± 0.007
First day	0.234 ± 0.008	0.242 ± 0.009
Tenth day	0.236 ± 0.009	0.265 ± 0.009*
Fifteenth day	0.235 ± 0.009	0.285 ± 0.010*
Twenty-fifth day	0.231 ± 0.007	0.290 ± 0.009*
Thirtieth day	0.236 ± 0.008	0.299 ± 0.009*

On the twenty-fifth day of the experiment, the level of malondialdehyde and diene conjugates was 0.290 ± 0.009 and 7.41 ± 0.21 mcmol / l. On the thirtieth day level of lipid peroxidation of the products was the highest, which was respectively 0.299 ± 0.009 (malondialdehyde) and 7.55 ± 0.24 mcmol / l (diene conjugates).

Table 10. Effect of cadmium chloride on the level of diene conjugates in blood serum of bulls; Mcmol / l (M ± m , n = 5)

Time of blood study (day)	Groups of animals	
	Control	Experimental
At the beginning of the experiment	5.75 ± 0.16	5.73 ± 0.15
The first day	5.78 ± 0.15	6.05 ± 0.20
Tenth day	5.74 ± 0.17	6.91 ± 0.21*
Fifteenth day	5.79 ± 0.15	7.24 ± 0.19*
Twenty-fifth day	5.73 ± 0.16	7.41 ± 0.21*
Thirtieth day	5.76 ± 0.17	7.55 ± 0.24*

Probably the set changes in the level of diene conjugates and malondialdehyde in serum of experimental animals are due to the toxicity of cadmium that promotes a radical change of steady-state concentrations of metabolites $O_2^{\cdot -}$, $^{\cdot}OH$, $HO_2^{\cdot}$, which in turn initiate the lipid peroxidation process. After feeding animals cadmium chloride, the concentration of radical metabolites had increased. Based on the research results, we concluded that the intensity of lipid peroxidation changes from feeding cadmium in different doses but also from the time that was over after feeding experimental bulls with it.

Thus, the increase in growth levels of derivative and final products of lipid peroxidation (diene conjugates and malondialdehyde) was noticed in the blood serum of bulls under the condition of chronic cadmium toxicity.

The effect of cadmium on animals is manifested by chronic and acute intoxication, which are accompanied by metabolic disorders, physiological function, reduced resistance, productivity and ability to reproduce.

The experimental results indicate that cadmium significantly affects the metabolism process in the cells of the liver, therefore, it stimulates the processes of lipid peroxidation and oppresses the enzyme activity of the antioxidant system. It is not a secret that cadmium increases the content of active forms of oxygen in cells by direct and indirect means. The reaction of active forms of oxygen induces lipid peroxidation and other processes that lead to destructive changes in the cells of the liver. Under such conditions, the reduction in antioxidant protection of animals' liver cells intoxicated by cadmium may increase its harmful effects on the body as a whole.

Lipid peroxidation is a form of tissue respiration. As a rule, the following process is characteristic of normal tissues and it usually occurs after the construction of lipid membrane structures, updating them during the biosynthesis of a number of hormones. However, free radical oxidation may be activated in unfavorable environmental conditions, in our case, by cadmium chloride action.

It is known that free radical peroxidation of lipids is an important milestone in the body lesions by heavy metals, and newly formed products of this process (hydroperoxides and organic peroxides substrates) cause a pronounced damaging effect on the cell membrane, activating the lipid peroxidation in them. This leads to violation of the structure and integrity of the membrane and it also causes changes in the acid-base balance of blood, followed by activation of lipid peroxidation, accompanied by changes in the functioning of ion-conveyor systems.

First of all, introduced intravenously or intraperitoneally cadmium damages the liver, and later on the other organs (Hwang and Wang, 2001; Gutij et al., 2004; Massadeh and Al-Safi, 2005). Toxicity of cadmium element is associated with the ability to generate peroxidation reaction of lipid membranes of hepatocytes (Fregoneze et al., 1997; Watjen and Beyersman, 2004; Uetani et al., 2005). In addition, the activity of some enzymes decreases, in particular, glutathione peroxidase, glutathione reductase, glucose-6-phosphatase, that can be a test for early diagnosis of damaged liver tissue (El-Shahat et al., 2009; Hariv and Gutyj, 2016).

The peculiarity of the harmful effects of cadmium is its rapid absorption by the body and slow output, which leads to accumulation of the following metal in the tissues (Salvatori et al., 2004; Kumar and Prasad, 2004; Lu et al., 2005; Darmohray and Gonchar, 2015). Cadmium accumulates mainly in the liver and kidneys and has a long half-life (up to 30 years), mainly, in the aspect of the application it can be assumed that the deposition of cadmium in the animals' bodies is a lifetime.

In the pathogenesis of cadmium toxicity was revealed an imbalance in the system "lipid peroxidation ↔ antioxidant defense system," which is manifested by increasing synthesis of free radicals in the background of exhaustion of compensatory mechanisms in the antioxidant system, which leads to disruption of cellular homeostasis and development of oxidative stress.

Conclusions

Feeding bulls with cadmium chloride in the doses of 0.04 mg/kg per body weight for 30 days, resulted in the development of chronic cadmium toxicity, which was characterized by impaired prooxidant -antioxidant balance. In the blood of bulls that carried the cadmium load, a decrease in activity of the enzyme and nonenzyme parts of antioxidant protection and enhancement of lipid peroxidation was noted. The lowest activity level of nonenzyme and enzyme part of antioxidant defense system in the body of young cattle were observed on the twenty-fifth day of the experiment. The conducted experiments made it possible to uncover deeper the pathogenesis of toxic effect of cadmium on the bulls' organism and use the following data in developing an antidote in case of cadmium intoxication.

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