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Impact of lipointersil and closaverm A on the antioxidant status of cows with fasciolosis

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One of the most prevalent and dangerous helminth infections in large and small ruminants is fasciolosis, which causes significant economic losses in animal husbandry, including reduced milk and meat productivity, deterioration in product quality, and costs associated with treatment and prevention measures. According to the literature, various adverse factors, including fasciolosis, significantly enhance cell reactive oxygen species (ROS) reactions through oxidative stress mechanisms. The study aimed to investigate the impact of the liposomal antioxidants Lipointersil and Clozaverm A on the antioxidant status of cows with experimental fasciolosis. Fifteen 4–5-year-old Black-and-White dairy cows were selected and divided into three groups of five animals each. The cows in the control and experimental groups were experimentally infected with *adolescariae*. In the first experimental group, cows received intra-muscular injections of Clozaverm A at 0.5 ml per 10 kg of body weight after experimental fasciolosis induction. The second experimental group received the same dose of Clozaverm A along with Lipointersil at a dose of 6 ml per animal. Based on the research conducted, it was found that fasciolosis suppresses the activity of antioxidant defense enzymes in the host liver, evidenced by decreased catalase and superoxide dismutase activity and increased levels of lipid hydroperoxides and TBK-active products in their blood. The administration of Lipointersil and Clozaverm A to cows with experimental fasciolosis improved their antioxidant status. This was accompanied by a 46.7 % increase in superoxide dismutase activity ($P < 0.001$) and a 30.2% increase in catalase activity ($P < 0.001$) in their blood. Furthermore, there was a suppression of lipid peroxidation processes indicated by a 31.3 % decrease in lipid hydroperoxide levels ($P < 0.001$) and an 18.8 % decrease in TBC-active products ($P < 0.001$).

Key words: large ruminants, fasciolosis, Lipointersil, Clozaverm A, antioxidants.

Вплив ліпоінтерсилу та клозаверму А на антиоксидантний статус організму корів за фасціольозу

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Одним з найбільш поширених і небезпечних гельмінтозів великої та дрібної рогатої худоби є фасціольоз, який завдає значних економічних збитків тваринництву: зниження молочної та м'ясної продуктивності, погіршення якості продуктів, витрати коштів на проведення лікувально-профілактичних заходів. Згідно даних літератури відомо, що за дії на організм різних негативних факторів, в тому числі за фасціольозу, реакції вільнорадикального окиснення у клітинах різко посилюються. Саме тому метою

роботи було дослідити вплив ліпосомального антиоксидантного препарату “Ліпоінтерсил” та “Клозаверму А” на антиоксидантний статус організму корів за експериментального фасціольозу. Для дослідів було відібрано 15 корів 4–5-річного віку, чорно-рябої породи, з яких сформовано 3 групи, по п'ять тварин у кожній. Тварини контрольної та обох дослідних груп були експериментально заражені адолескаріями. Коровам першої дослідної групи за експериментального фасціольозу внутрішньом'язово вводили клозаверм А у дозі 0,5 мл препарату на 10 кг маси тіла тварини. Тваринам другої дослідної групи, за експериментального фасціольозу внутрішньом'язово вводили клозаверм А у дозі 0,5 мл препарату на 10 кг маси тіла тварини та ліпоінтерсил у дозі 6 мл препарату на тварину. На основі проведених досліджень встановлено, що фасціоли пригнічують активність ензимів системи антиоксидантного захисту у печінці хазяїв, на що вказує зниження активності каталази та супероксиддисмутази, а також зростання рівня гідроперексидів ліпідів і ТБК-продуктів у їх крові. Застосування ліпоінтерсилу та клозаверму А коровам за експериментального фасціольозу сприяло підвищенню антиоксидантного статусу їх організму, що супроводжувалось підвищенням у їх крові активності супероксиддисмутази на 46,7 % ($P < 0,001$) та каталази на 30,2 % ($P < 0,001$), а також пригніченням інтенсивності процесів перексидного окиснення ліпідів, зниженням рівня гідроперексидів ліпідів на 31,3 % ($P < 0,001$), ТБК-активних продуктів на 18,8 % ($P < 0,001$).

Ключові слова: велика рогата худоба, фасціольоз, ліпоінтерсил, клозаверм А, антиоксиданти.

Introduction

Fasciolosis is among the prevalent parasitic diseases affecting various animals, predominantly sheep, goats, cattle, and occasionally pigs, deer, rabbits, and horses (Sliusarenko et al., 2010; Hud & Dovhii, 2021; Gröning et al., 2023; Hecker et al., 2024). The adult stage of the helminth localizes in the liver and gallbladder, while the larvae are found in the lungs. Parasitizing in the host's body, fasciolids release metabolic products and toxic substances that damage biological cell membranes, inhibit cellular energy mechanisms membrane-dependent enzyme activity, and disrupt substance transport processes through membranes (Stybel et al., 2014).

Given the intense epizootic situation regarding fasciolosis in cattle in Ukraine and its significant economic and social impact, further study is necessary to explore the distribution characteristics of the invasion, determine the pathogenic influence of helminths on animals, improve lifelong diagnostics, and develop effective control measures (Koval, 2015).

Fasciolosis, as one of the dangerous helminth infections, causes considerable economic losses to farms. Under these conditions, dairy cow productivity and calf weight gain decrease, negatively impacting herd reproduction. A critical issue is the development of parasite resistance to anthelmintics (Avramenko et al., 2019). This underscores the relevance of studying different treatment regimens, particularly comprehensive therapies for this invasion.

Researchers have recently focused on studying lipid membrane oxidative stress as a regulator of physiological processes (Calabrese et al., 2005). According to modern concepts, excessive intensification of lipid peroxidation processes and membrane damage are universal types of cell damage leading to the death of various organs' cells. Excessive activation of lipid peroxidation causes conformational disturbances and increased permeability of biological membranes, leakage of enzymes from mitochondria and lysosomes, inactivation of aerobic oxidation enzymes, disruption of oxidative phosphorylation, and DNA mutations (Stybel et al., 2021; Martyshuk et al., 2021).

According to the literature, the actions of various negative factors significantly enhance free radical oxidative reactions in cells (Kausar et al., 2018; Cunha-Oliveira et al., 2020). Free radical peroxidation results in the formation of several products at practically all stages, which are the outcome of interactions between free radicals themselves and biological macromolecules (Martyshuk et

al., 2019; Grymak et al., 2020; Varkholiak et al., 2021). It is crucial to emphasize that the heightened formation of primary free radicals is a byproduct of increased biochemical reaction intensity in response to extreme factors (Gutyj et al., 2017; Slivinska et al., 2020; Nazaruk et al., 2021; Martyshuk et al., 2021).

Based on previous research, we have determined that during experimental fasciolosis in cows, parasites release metabolites that contribute to forming free radicals, thereby intensifying the initiation of lipid peroxidation processes. This is evidenced by increased lipid peroxidation products such as diene conjugates, lipid hydroperoxides, and TBC-active products (Kulyaba et al., 2016; 2017; 2019; Kuljaba et al., 2022).

The aim of the study

The work aimed to investigate the effect of closaverm A and lipointersil on the antioxidant status of cows with experimental fasciolosis.

Material and methods

For the experiments, 15 4-5-year-old Holstein cows were selected and divided into three groups of five animals each. The control group (C) was experimentally infected with adolascariae. Cows in the first experimental group (E₁) received intramuscular injections of clozaverm A at a dose of 0.5 ml per 10 kg body weight to induce experimental fascioliasis. Cows in the second experimental group (E₂) received intramuscular injections of clozaverm A at the same dose, along with lipointercil at a dose of 6 ml per animal.

The experiments adhered to the rules regarding animal selection and housing. The cows' diets were balanced in terms of nutrients and minerals.

Plasma lipid hydroperoxides and TBC-active products were determined according to Vlizlo (2012). Serum catalase activity (K.E. 1.11.1.6) was assessed using the method of M.A. Korolyuk (1988), and superoxide dismutase activity (K.E. 1.15.1.1) was measured following the method of E.E. Dubinina (Vlizlo, 2012). Blood samples were collected from the jugular vein before infection and on days 7, 14, 21, and 28 of the experiment.

The experimental procedures were conducted following the Law of Ukraine “On the Protection of Animals from Cruelty” dated March 28, 2006, and the rules of the European Convention for the Protection of Vertebrate

Animals Used for Experimental and Other Scientific Purposes dated November 13, 1987.

Statistical analysis of the results was performed using the Statistica 6.0 software package. Statistical significance was assessed using the Student's t-test. Mean values were considered statistically significant at * – $P < 0.05$, ** – $P < 0.001$ (ANOVA).

Results and discussion

Based on the conducted research, it was established that in cows of the control group with experimental fasciolosis, lipid peroxidation processes intensified in the blood, indicated by increased lipid hydroperoxides and TBC-active products (Fig. 1, 2). By the 14th day of the study, the level of lipid hydroperoxides in the blood of cows in the control group increased by 29 %, and TBC-active products increased by 15.9 % compared to the pre-infection period. By the 21st day of the study, the level of

lipid hydroperoxides reached 2.56 ± 0.03 AU E/mL, and TBC-active products reached 6.98 ± 0.10 nmol/mL. It is worth noting that the highest values of these indicators were observed on the 28th day of the study, where they increased by 45.6 % and 22.9 %, respectively, compared to the beginning of the study.

After administering closantel-A to treat cows with experimental fasciolosis, a reduction in the intensity of lipid peroxidation processes was observed. On the 14th day of the study, a decrease in the level of lipid hydroperoxides by 11.5 % and TBC-active products by 9.1 % compared to the control group was found. Subsequently, the level of lipid peroxidation products in the blood of the first experimental group continued to decrease. By the 28th day of the study, the levels were 2.09 ± 0.05 unit E/mL for lipid hydroperoxides and 6.06 ± 0.13 nmol/mL for TBC-active products, whereas, in the control group, these indicators were 2.64 ± 0.04 unit E/mL and 7.14 ± 0.11 nmol/mL, respectively.

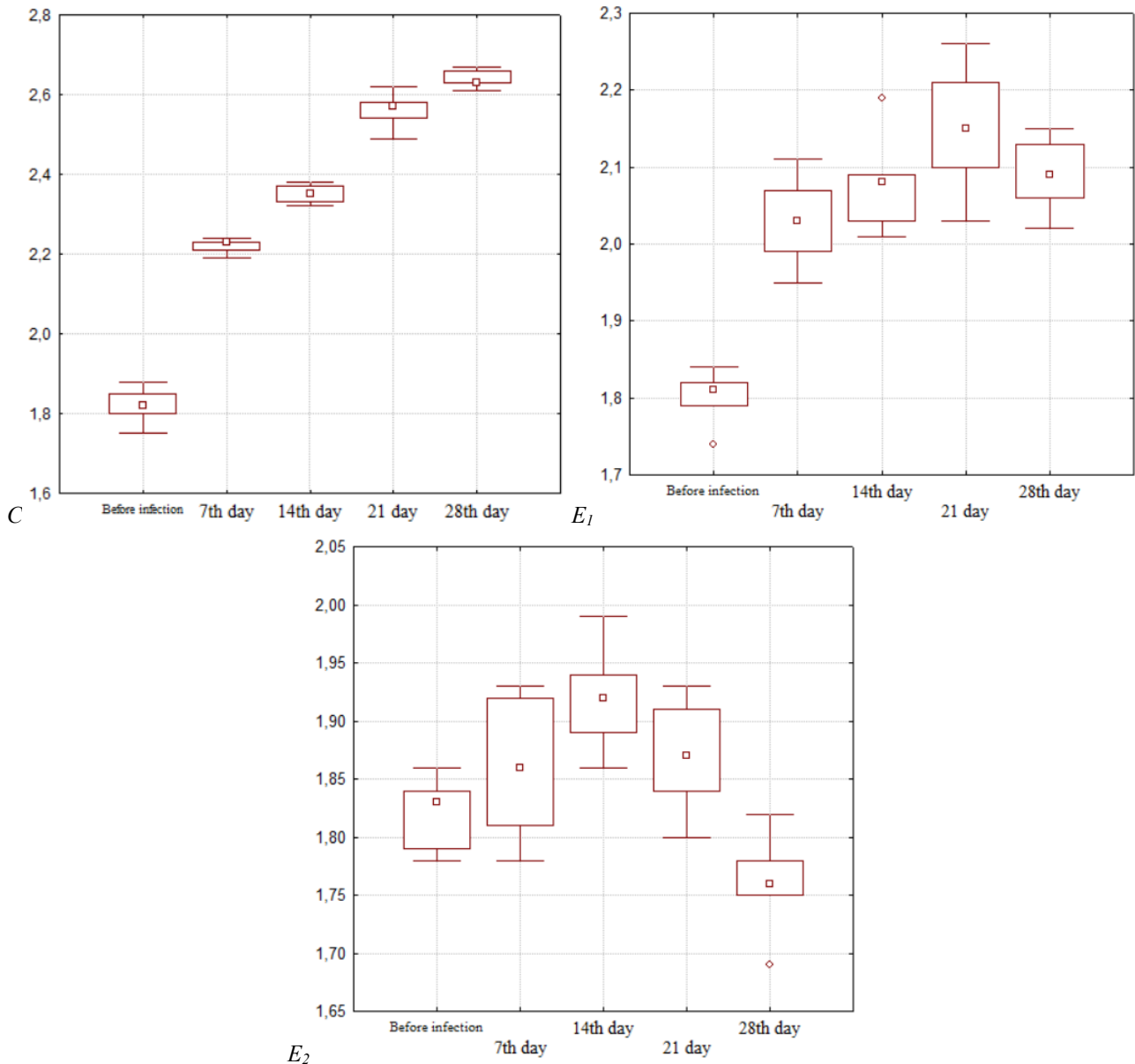


Fig. 1. The effect of closaverm A and lipointersil on the level of lipid hydroperoxides in the blood of cows with experimental fasciolosis, unit E/ml ($M \pm m$; $n = 5$)

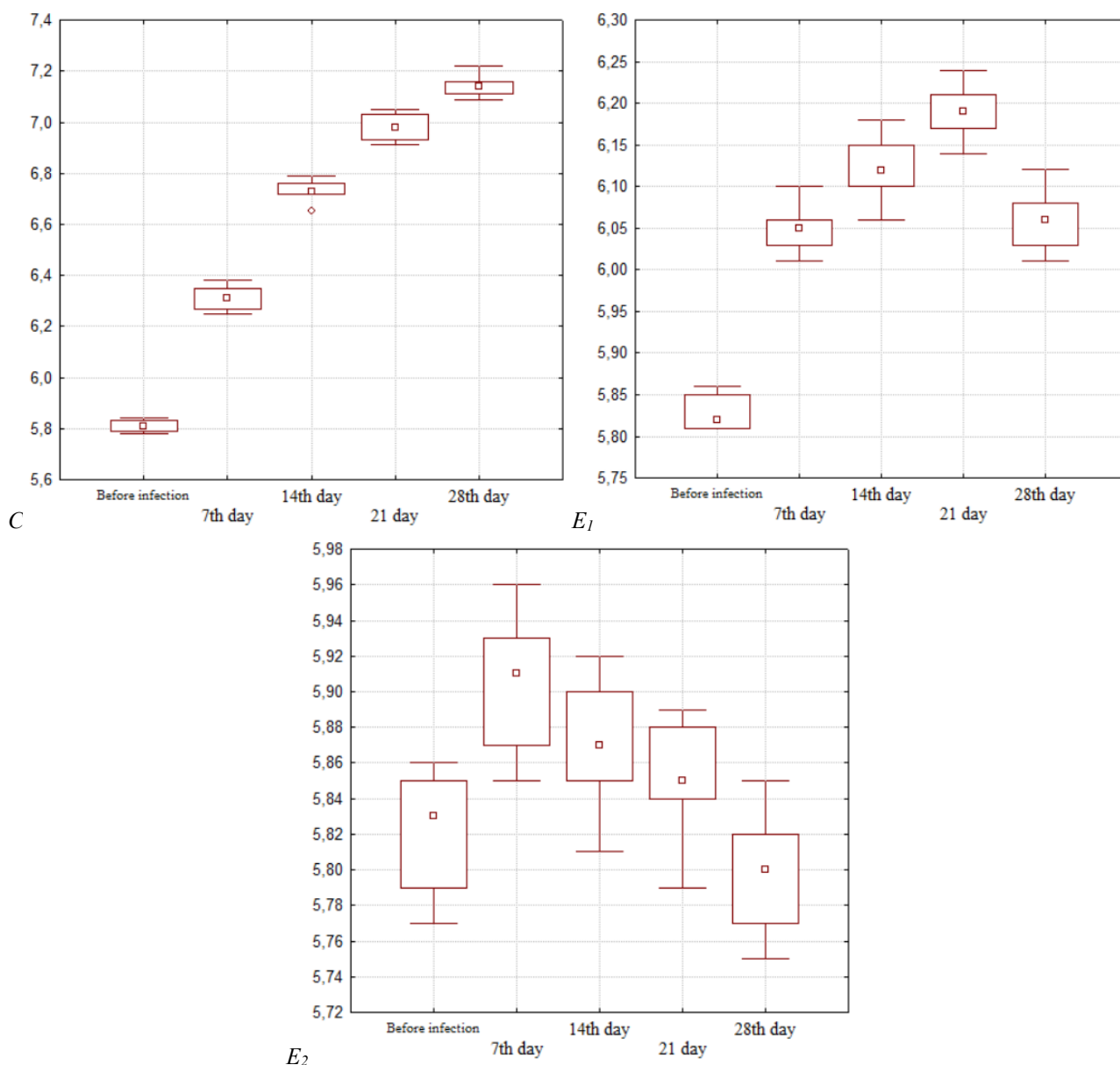


Fig. 2. The influence of closaverm A and lipointersil on the level of TBC-active proproducts in the blood of cows with experimental fasciolosis, nmol/mL ($M \pm m$; $n = 5$)

In the second experimental group of animals, a significant reduction in intermediate and final products of lipid peroxidation in their blood compared to the first experimental group was observed. The application of lipoicintersil to the experimental cows allowed for a substantial decrease in the intensity of lipid peroxidation processes in their bodies. A significant decrease in the levels of lipid hydroperoxides and TBC-active products was observed as early as day 7 of the study, where they decreased by 16.2 % and 6.5 %, respectively, compared to the control group. By the 14th day of the study, the levels of lipid hydroperoxides and TBC-active products decreased to 1.92 ± 0.04 unit E/mL and 5.87 ± 0.16 nmol/mL, respectively. On the 21st day of the study, a decrease in the level of lipid hydroperoxides by 27 % and TBC-active products by 16.2 % relative to the control was observed in the blood of cows in the second experimental group. By the 28th day of the study, the levels of lipid hydroperoxides and TBC-active products reached physiological levels.

The obtained data indicate that under the influence of Clozaverm A and Lipointersil in the bodies of experimental cows with experimental fasciolosis, redox processes are normalized, and the level of lipid peroxidation products decreases, thereby reducing organism intoxication.

In the investigation of the enzymatic components of the antioxidant defense system in the animals' bodies, it was found that during experimental fasciolosis, the activity of catalase and superoxide dismutase decreased in the blood of cows in the control group (Fig. 3, 4). Specifically, on the 14th day of the study, a decrease in catalase activity by 18 % and superoxide dismutase activity by 15.8 % relative to the initial values was observed. The lowest activity of these enzymes in the blood of cows in the control group was recorded on the 21st day of the study, with catalase activity at 45.28 ± 1.12 μ kat/L and superoxide dismutase activity at 0.92 ± 0.03 units/mg protein.

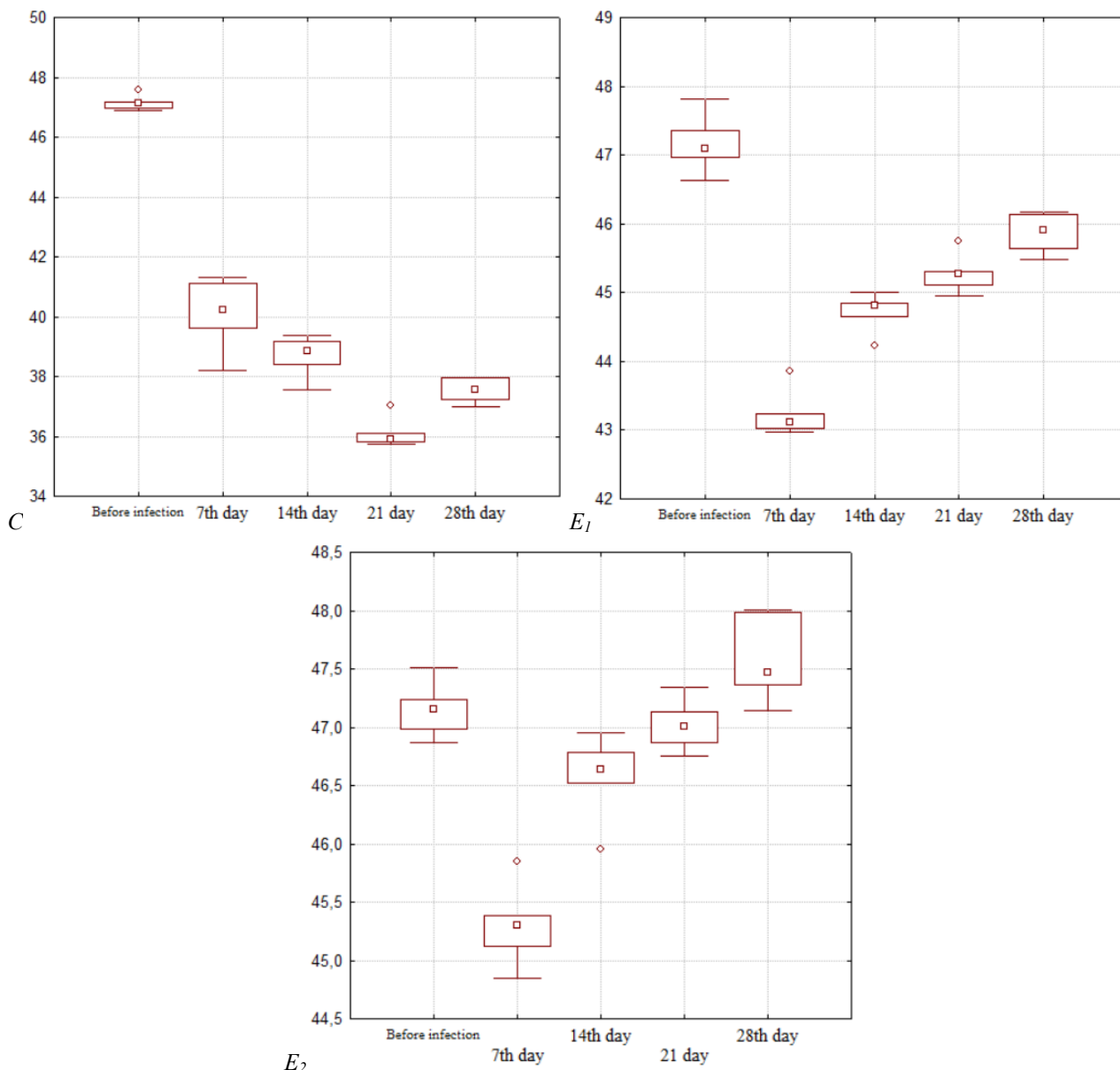


Fig. 3. The effect of closaverm A and lipointersil on the activity of catalase in the blood of cows with experimental fasciolosis, µkat/L ($M \pm m$; $n = 5$)

After treatment of cows with experimental fasciolosis using Clozaverm A, normalization of enzyme activity in serum was noted from the 14th day of the study. On the 21st day of the study, catalase activity in the serum of the first experimental group increased by 25.4 %, and by the 28th day of the study, it increased by 22.1 % compared to the values in the control group of cows.

Based on the data obtained, the application of Lipointersil to the animals in the second experimental group led to a quicker increase in catalase activity, starting from the 7th day of the study. By the 21st and 28th days of the study, catalase activity in their blood ranged within physiological values, precisely 47.02 ± 1.14 and 47.59 ± 1.13 µkat/L, respectively.

Simultaneously, there is a correlation between the intensity of redox processes in the tissues of animals and the activity of superoxide dismutase (SOD), a key enzyme in the antioxidant defense system. The decrease in SOD

activity in cows in the control group with experimental fasciolosis, influenced by various factors, can lead to an increase in lipid peroxide content due to the activation of free radical oxidation processes.

Initially and at the end of the study, SOD activity fluctuated within the range of 1.33 ± 0.01 to 0.92 ± 0.04 unit/mg protein. The administration of Clozaverm A and Lipointersil to the experimental groups of cows promoted the activation of SOD activity in their serum. By the 14th day of the study, SOD activity increased by 2.7 % in the first experimental group and by 16.1% in the second experimental group compared to the control group. On the 21st day of the study, a significant increase in SOD activity was observed in both experimental groups, reaching 1.17 ± 0.02 and 1.35 ± 0.04 units/mg protein, respectively. In contrast, this indicator was 0.92 ± 0.04 units/mg protein in the control group.

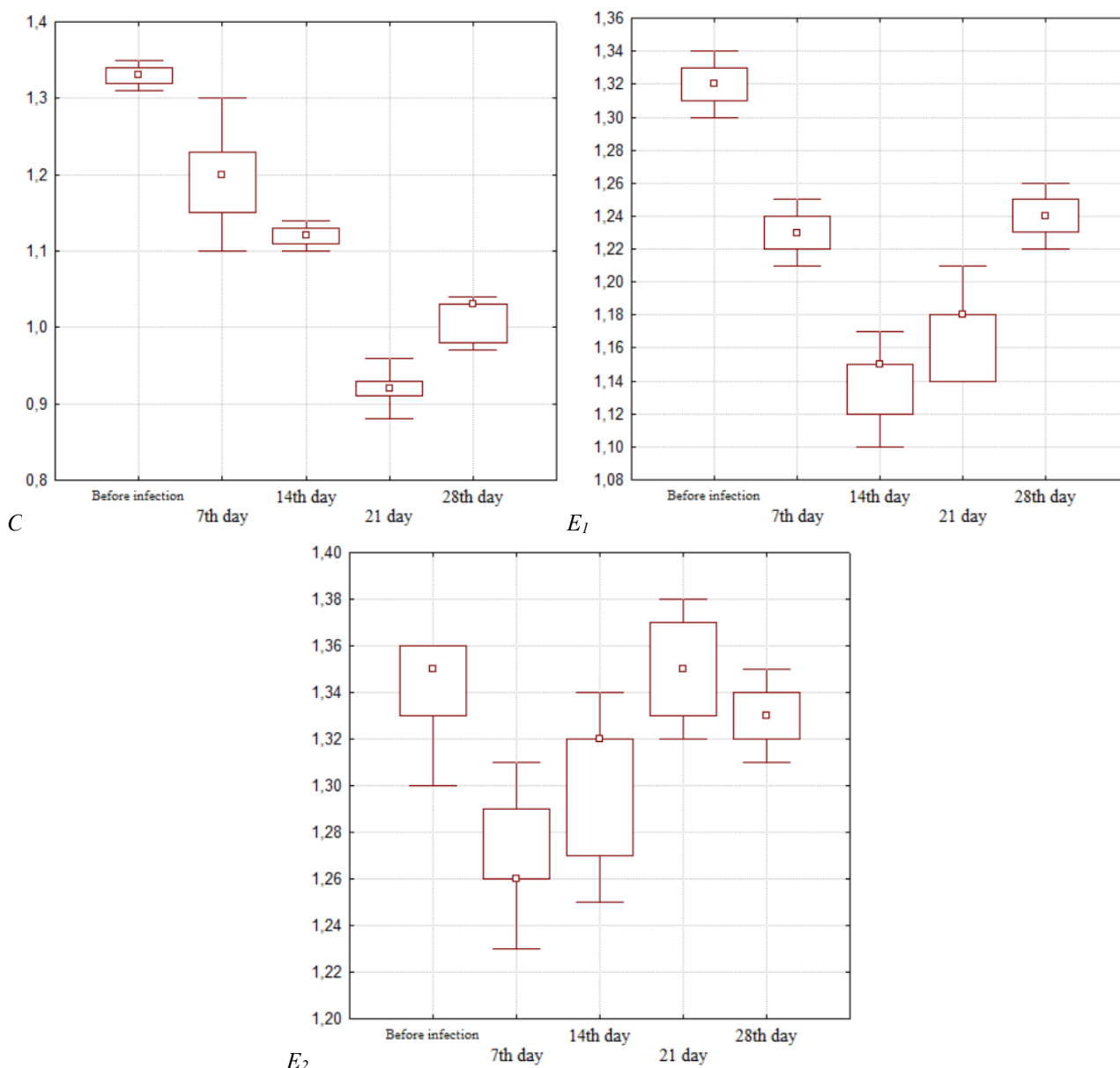


Fig. 4. The effect of closaverm A and lipointersil on the activity of superoxide dismutase in the blood of cows with experimental fasciolosis, unit/mg protein ($M \pm m$; $n = 5$)

The highest SOD activity was recorded in the serum of animals from the second experimental group on the 28th day of the study, where it reached 1.33 ± 0.02 unit/mg protein, which is 31.7 % higher than the control group.

Analysis of the obtained results indicates that the SOD activity in the serum of cows in the experimental groups positively correlates with catalase activity.

Conclusions

Fasciolae suppress the activity of antioxidant defense system enzymes in the hosts' liver, indicated by decreased catalase and superoxide dismutase activity, as well as increased levels of lipid hydroperoxides and TBC (thio-barbituric acid reactive substances) in their blood.

Administration of lipoic acid and closantel to cows with experimental fascioliasis contributed to enhancing their antioxidant status, accompanied by increased activi-

ties of superoxide dismutase by 46.7 % ($P < 0.001$) and catalase by 30.2 % ($P < 0.001$) in their blood. Additionally, it led to suppression of lipid peroxidation processes, reducing lipid hydroperoxide levels by 31.3 % ($P < 0.001$) and TBC by 18.8 % ($P < 0.001$).

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Conflict of interest

The authors declare that there is no conflict of interest.

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