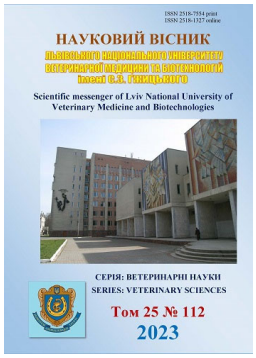

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Effect of milk thistle and silimevit on the functional state and protein synthesizing-function of the liver of laying hens under conditions of cadmium load

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The purpose of the work was to study the effect of Cadmium on liver function disorders and to develop practical recommendations for using silimevit and milk thistle to reduce the toxic effect of Cadmium on chickens. To achieve the set goal in experiments on chickens under cadmium load, it was necessary to solve the following tasks: to study the effect of Cadmium on the protein synthesis function of the liver of laying hens; to study the effect of Cadmium on the functional state of the liver of laying hens; to investigate the effect of silimevit and the fruits of milk thistle on the functional state of the liver of laying hens under cadmium load; to investigate the effect of silimevit and milk thistle fruits on the protein synthesis function of the liver of laying hens under cadmium load and to justify the use of silimevit and milk thistle to prevent cadmium toxicosis in chickens. Drinking cadmium sulfate to laying hens violates the liver's functional state and protein-synthesizing function. A decrease in total protein and albumin content in their blood was established ($P < 0.001$). An increase in alanine and aspartate aminotransferase activity was detected ($P < 0.001$). Silimevit and milk thistle positively affect the functional state of the liver of laying hens under cadmium load, as evidenced by a decrease in the activity of aminotransferases in their blood serum. Silimevit and spotted thistle, under the cadmium load of laying hens, positively affect the liver's protein-synthesizing function, evidenced by an increase in total protein and albumin fraction. Feeding laying hens under cadmium load with slime feed contributed to a better-normalizing effect on the activity of aminotransferases and protein-synthesizing function of the chickens' liver than milk thistle.

Key words: *Cadmium, toxicology, liver, laying hens, aminotransferases, proteins.*

Introduction

As you know, all environmental factors and conditions affect the health of animals and birds. Today, the natural environment is changing faster than the adaptability of animals, which hurts their health. The anthropogenic burden of urban and rural areas today is characterized by multi-component chemical pollution of the environment (atmospheric air, natural waters, and soils) (Bashchenko et al., 2020).

Cadmium compounds deserve special attention from researchers, as this element belongs to the first class of environmental hazards. It is considered a dangerous pollutant of the environment since its toxic effect can lead to various disorders in the functioning of animal and bird organisms. With small doses, this element is deposited in

organs and tissues for a long time, causing the possibility of developing toxicosis and violations of biochemical processes, structure, and functions of cells (Gutyj et al., 2022, 2023).

The toxicity of the metal to the body depends on the penetration method, the total dose, and the duration of poisoning. In addition, the reaction to the action of the toxin varies depending on the species, age, sex of the animal, and the general condition of the body. It is impossible to ensure the uniformity of all these factors. Therefore, conclusions about the mechanism of action, the danger of accumulation in animal tissues and organs, and the impact on the quality of livestock products have certain deviations, and therefore, the establishment of acceptable concentrations in the environment is essential (Kolosova & Shatorna, 2022).

The distribution and accumulation of Cd^{2+} depend on its orientation to various structures, biochemical components of tissues and organs, the strength of the formed complexes, and the speed of their removal. Due to the high permeability of Cadmium, its introduction causes a systematic increase in the metal content in the body. Thus, the concentration of Cadmium in the kidneys of clinically healthy animals, especially with an increased toxin content in the environment, can increase significantly (Kolosova et al., 2021).

Research has established that the kidneys, liver, bone marrow, tubular bones, testicles, and spleen become the main target organs for cadmium intoxication. The effect of Cd^{2}+ on the body of animals manifests itself through chronic and acute toxicoses, which are accompanied by a violation of metabolism, body functions and a decrease in resistance, productivity, and reproductive capacity (Nazaruk et al., 2021).

Clinical manifestations of chronic Cd^{2}+ poisoning in animals are not always easy to detect. Still, they are usually accompanied by a sharp decrease in appetite, growth of chickens and laying hens, loss of body weight, problems with kidney function, proteinuria, impaired liver function, anemia, and increased mortality among newborn animals with congenital disabilities (Nefodova et al., 2021).

Experiments with exposure to cadmium sulfate in chickens have shown that it can lead to metabolic acidosis in their blood. It is noted that under the influence of Cadmium ions, disorders occur in the body's acid-alkaline balance system: a shift in the pH level to the acidic side, a decrease in the blood saturation of CO_2, a decrease in the concentration of HCO_3, the total amount of carbon dioxide and blood oxygen saturation (Ostapiuk et al., 2018).

The toxic effect of Cadmium on the bodies of animals leads to a reduction in their lifespan and a violation of the dynamics of changes in weight indicators. High concentrations of Cadmium contribute to the damage of the central nervous and cardiovascular systems and also have an embryotoxic and mutagenic effect (Ostapyuk et al., 2021, 2023).

It should be noted that the circulatory system is the most sensitive to the influence of environmental factors on the animal body; it is one of the first to respond to changes in animal feeding, and even more so to changes in the macro-, microelement, and vitamin supply of the body. Among the changes that occur in the peripheral blood of animals, the first and most convenient for detecting the toxic effect of heavy metals are changes in their morphological and biochemical composition (Slobodian et al., 2019, 2020, 2021, 2022).

In the literature, Something needs to sufficiently elucidate the regularities of changes in the functional state and protein-synthesizing function of the liver of laying hens under cadmium load. The study of these processes will allow us to reveal hitherto unknown features of metabolic processes in chickens under the conditions of the development of cadmium toxicosis. Conducting research in this aspect is relevant.

The aim of the study

The purpose of the work was to study the effect of Cadmium on liver function disorders and to develop practical recommendations for using silimevit and milk thistle to reduce the toxic effect of Cadmium on chickens.

Material and methods

24 laying hens of the Highsex white cross, with an average live weight of 1.5 kg and age of 78 weeks, were selected for research. These chickens were divided into three groups: control (C) and two experimental (E_1, E_2), taking into account their age and weight. Chickens of the control group (C) and experimental groups were given cadmium sulfate at 4 mg per kilogram of body weight. The hens of group E_1 were fed milk thistle fruits at a dose of 2.0 g per kilogram of feed once a day for 30 days. Chickens of group E_2 received silimevit at a dose of 0.36 g per kilogram of feed once a day for 30 days.

The conditions of keeping the chickens of all experimental groups the control group, and the microclimate parameters in the room were similar. During the experiment, the amount of feed and water consumed was recorded.

When performing experimental research on laying hens, all bioethical standards concerning animals were observed, which meet the requirements of the Law of Ukraine No. 3447-4 “On the Protection of Animals from Cruelty Treatment”, the provisions of the European Convention on the Protection of Vertebrate Animals Used in Experimental and Other Scientific Research purposes (Strasbourg, 1986) and the regulation on the use of vertebrate animals for research and other scientific purposes at the Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies, Lviv, Ukraine.

The blood of laying hens was collected from the sub pterygoid vein in the following periods: before the administration of the experimental drugs and the toxicant, on the first, seventh, fourteenth, twenty-first, and thirtieth days of the experiment.

The following drugs were used in the experiments:

Cadmium sulfate is an inorganic compound with the chemical formula $CdSO_4$. Cadmium sulfate is well soluble in water; therefore, it is well absorbed into the blood in the digestive tract and is known for its toxic effects on living organisms.

Spotted thistle – Silybum marianum is a family of complex flowers. In its wild form, it grows on wastelands, along roads, on abandoned fields, and in medicinal gardens. The fruits of the spotted thistle are used for treatment. They contain protein 17–18 %, fats 10–11 %, flavonolignans 2–3 %, essential oil 0.08 %, vitamins A, E, and K, biogenic amines, and quartzetin.

Silimevit is a feed additive which includes milk thistle fruits, selenium, metiphene, and vitamins A, E, and C.

We determine doses of drugs for experimental studies following the literature data and technical conditions.

In blood serum, the activity of aspartate aminotransferase (AsAT; K.E. 2.6.1.1) and alanine aminotransferase (AlAT; K.E. 2.6.1.2) was studied – according to the method of Reitman and Frenkel as modified by K. G. Kapetanaki (1962) (Vlizlo et al., 2012).

The protein synthesis function of the liver of laying hens was determined by the level of total protein (biuret reaction) and protein fractions (polyacrylamide gel electrophoresis) in blood serum.

The data of hematological and biochemical studies were processed statistically with the calculation of average arithmetic values (M), mean squared error (m), and the degree of probability of difference (P) between indicators. Statistical processing of research results was carried out according to the method described by I. A. Oivin (1960), using the statistical software package Statistica 6.0 for Windows. The degree of probability, compared to the control group's data, was – $P < 0.05$ – *, $P < 0.01$ – **, $P < 0.001$ – ***.

Results and discussion

The condition of the liver in laying hens was analyzed by determining the activity of aminotransferase enzymes in blood serum, particularly aspartate and alanine aminotransferase. It was found that in those laying hens that did not receive the experimental drugs, the activity of alanine aminotransferase increased throughout the experiment, reaching the highest value on the 21st day of the experiment, where it was 0.47 ± 0.008 mmol/g/l, respectively (Table 1).

When feeding laying hens with milk thistle feed, a decrease in the activity of ALT in the blood serum of birds of the first experimental group was established throughout the experiment. Thus, on the 14th day of the experiment, the enzyme activity in their blood decreased by 14.3 %, and on the 21st day, it decreased by 23.4 % compared to the blood indicators of the control group. On the 30th day, a slight increase in alanine aminotransferase activity was found in the blood serum of the first experimental group compared to the previous day.

Feeding laying hens with silimevit feed contributed to the normalization of alanine aminotransferase activity in the blood serum of the second experimental group starting from the 7th day of the experiment. On the 14th day of the experiment, the activity of AlAT in the blood serum of experimental group D_2 decreased by 23.8 % compared to the indicators of chickens of the control group. On the 21st and 30th days, the enzyme activity in the blood serum of the chickens of this experimental group fluctuated within physiological values. It was 0.33 ± 0.010 and 0.34 ± 0.010 mmol/g/l, respectively, while the activity of this enzyme in the chickens of the control group was significantly higher and was 0.47 ± 0.008 and 0.44 ± 0.006 mmol/g/l, respectively.

Similar changes were also established in the study of aspartate aminotransferase activity in the blood serum of laying hens. Thus, in the control group of chickens, this enzyme's activity increased to 5.72 ± 0.23 mmol/g/l (Table 2).

When feeding laying hens with silimevit under conditions of cadmium load, a better normalization of the activity of aspartate aminotransferase in their blood was established. On the 7th day of the experiment, in the blood serum of the chickens of the second experimental group, a decrease in enzyme activity was established by 5.4 %, and on the 14th day of the experiment – by 15.3 % compared to the control group. A probable decrease in the activity of AsAT in the blood of chickens of experimental group E_2 was established on the 21st day of the experiment, where it was 4.41 ± 0.15 mmol/g/l, while in the control group, this indicator was 5.72 ± 0.23 mmol/g/l.

Table 1

The effect of the spotted thistle Silimevitus on the activity of alanine aminotransferase in the blood serum of laying hens under conditions of cadmium load (M ± m, n = 8)

Blood test time (days)	AlAT (mmol/g/l)		
	Groups of chickens		
	Control	Experimental 1	Experimental 2
At the beginning of the experiment	0.31 ± 0.007	0.32 ± 0.007	0.32 ± 0.006
first day	0.32 ± 0.009	0.33 ± 0.008	0.32 ± 0.011
7th day	0.37 ± 0.009	0.35 ± 0.010	0.34 ± 0.009
14th day	0.42 ± 0.007	0.36 ± 0.009**	0.32 ± 0.008***
21st day	0.47 ± 0.008	0.36 ± 0.012***	0.33 ± 0.010***
30th day	0.44 ± 0.006	0.37 ± 0.007***	0.34 ± 0.010***

Table 2
The effect of the spotted thistle Silimevitus on the activity of aspartate aminotransferase in the blood serum of laying hens under conditions of cadmium loading (M ± m, n = 8)

Blood test time (days)	AsAT (mmol/g/l)		
	Groups of chickens		
	Control	Experimental 1	Experimental 2
At the beginning of the experiment	4,28 ± 0.15	4.32 ± 0.17	4.31 ± 0.20
first day	4.37±0.16	4.34 ± 0.23	4.35 ± 0.12
7th day	4.61 ± 0.20	4.41 ± 0.19	4.36 ± 0.24
14th day	5.17 ± 0.19	4.45 ± 0.17*	4.38 ± 0.19**
21st day	5.72 ± 0.23	4.55 ± 0.25***	4.41 ± 0.15***
30th day	5.56 ± 0.24	4.50 ± 0.22***	4.39 ± 0.21***

In order to understand the influence of silimevit and spotted thistles on the body of laying hens, it is essential to study metabolic processes. Our biochemical studies of the blood of this bird under the conditions of cadmium load show impaired liver function in protein synthesis. As a result of the experiment, we found that the content of total protein and its fractions in the blood plasma of laying hens changes. For example, in laying hens that were given Cadmium, a decrease in the total protein level in the blood of birds of the control group was observed at 39.06 ± 1.21 g/l (Table 3).

The level of total protein in the blood of laying hens of the first experimental group at the beginning of the experiment fluctuated within physiological values. On the 7th day of the experiment, an increase in the level of the studied indicator in their blood was established to 45.23 ± 1.20 g/l, while in the control group, this indicator was 44.64 ± 0.99 g/l. The highest level of total protein in the indicated period of the experiment was in the blood of chickens of the second experimental group, which were fed silimevit.

Table 3
The effect of milk thistle and silimevit on the level of total protein in the blood of laying hens under conditions of cadmium load (M ± m, n = 8)

Blood test time (days)	Total protein (g/l)		
	Groups of chickens		
	Control	Experimental 1	Experimental 2
At the beginning of the experiment	46.57 ± 0.91	46.54 ± 1.10	46.49 ± 1.08
first day	45.79 ± 1.13	46.29 ± 1.16	46.35 ± 1.23
7th day	44.64 ± 0.99	45.23 ± 1.20	45.47 ± 1.31
14th day	42.33 ± 1.20	44.98 ± 1.25	45.77 ± 1.20*
21st day	39.06 ± 1.21	45.49 ± 1.21**	46.38 ± 1.24***
30th day	39.67 ± 1.16	45.95 ± 1.22**	46.52 ± 1.33***

It is worth noting that a probable increase in the total protein level in the blood of laying hens of group E_2 was observed on the 14th day of the experiment, where compared to the control group, this indicator increased by 8.1 %. On the 21st day, a probable increase in the total protein level was observed in two experimental groups, where compared to the control, the level of the studied indicator increased by 16.5 % in group E_1 and 18.7 % in group E_2. On the 30th day, the level of total protein in the blood of chickens of the experimental groups was within physiological values.

Similar changes were found in the study of albumin content (Table 4). It was established that the albumin content of intoxicated birds decreased throughout the experiment. The lowest content of the studied indicator was on the 21st day, where, compared to the initial values, it decreased by 5.62 %, respectively.

In experimental groups of laying hens, a gradual increase in the albumin content in their blood was established. So, on the 14th day of the experiment, the albumin content in the blood of the first experimental group increased by 1.63 %. The second experimental group increased by 3.29 % compared to the control group. In the subsequent 21 days of the experiment, the albumin level in the blood of groups E_1 and E_2 increased by 4.61 and 5.5 %, respectively, compared to the control group.

The difference between the birds of the control group and the groups receiving the drugs was detected on the 14th day of the experiment.

When studying the content of globulins in the blood of laying hens, its increase was established only in hens of the control group, which were subjected to cadmium loading. On the 21st day of the experiment, the level of globulins in the blood of this group of chickens increased by 5.62 % compared to the initial values.

Table 4
The effect of milk thistle and silimevit on the level of albumins in the blood of laying hens under conditions of cadmium loading (M ± m, n = 8)

Blood test time (days)	Albumins (%)		
	Groups of chickens		
	Control	Experimental 1	Experimental 2
At the beginning of the experiment	33.80 ± 0.86	33.89 ± 0.81	33.76 ± 0.75
7th day	32.94 ± 0.97	33.25 ± 0.78	33.69 ± 0.85
14th day	31.83 ± 0.78	32.55 ± 0.89	32.85 ± 0.82
21st day	29.64 ± 0.96	31.27 ± 0.95*	32.93 ± 0.91*
30th day	28.18 ± 0.82	32.79 ± 0.82***	33.68 ± 0.76***
7th day	29.36 ± 0.95	33.24 ± 0.85**	33.81 ± 0.82**

Table 5
The effect of milk thistle and silimevit on the level of globulins in the blood of laying hens under conditions of cadmium loading (M ± m, n = 8)

Blood test time (days)	Globulins (%)		
	Groups of chickens		
	Control	Experimental 1	Experimental 2
At the beginning of the experiment	66.20 ± 1.81	66.75 ± 1.62	66.24 ± 1.74
first day	67.06 ± 1.92	66.45 ± 1.73	66.31 ± 1.98
7th day	68.17 ± 2.25	67.45 ± 1.89	67.15 ± 1.81
14th day	70.36 ± 1.90	68.73 ± 1.92	67.07 ± 1.93
21st day	71.82 ± 2.12	67.21 ± 1.90*	66.32 ± 2.07*
30th day	70.64 ± 1.89	66.76 ± 1.84	66.19 ± 2.10*

When feeding the birds of the first experimental group with spotted thistle and the second experimental group with silimevit, a slight increase in the globulin fraction was established on the first and seventh days. On the 14th day, the level of the studied indicator in the blood of groups E_1 and E_2 was 68.73 ± 1.92 and 67.07 ± 1.93 %. In contrast, the level of globulins in the control was significantly higher and was 70.36 ± 1.90 % In the blood of laying hens under conditions of cadmium load, which were fed silimevit, a probable decrease in globulins was established on the 14th day. Similar changes are observed in the first experimental group on the 21st day.

Conclusions

Silimevit and milk thistle positively affect the functional state of the liver of laying hens under cadmium load, as evidenced by a decrease in the activity of aminotransferases in their blood serum.

Silimevit and spotted thistle, under the cadmium load of laying hens, have a positive effect on the liver's protein-synthesizing function, evidenced by an increase in the level of total protein and albumin fraction.

Feeding laying hens under cadmium load with silimevit feed contributed to a better-normalizing effect on the activity of aminotransferases and protein-synthesizing function of the chickens' liver than milk thistle.

Conflict of interest

The authors declare that there is no conflict of interest.

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