



The State of the Antioxidant System of White Rats under Acute Exposure to Dorilin

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Annotation: The problems of ensuring environmental safety in the Republic of Uzbekistan are one of the most important national tasks. The mechanisms of the biological action of the toxicant allow us to come close to the development of pathogenetic justification for the prevention, diagnosis and treatment of intoxication. The latter makes relevant research devoted to the study of the mechanisms of biological action of new chemicals intended for use in agriculture. At the present time, a new plant growth stimulator Dorilin is being proposed for the practice of agriculture.

Keywords: experimental animals, clinical picture, catalase activity.

To determine the parameters of acute toxicity of Doriline during intragastric exposure, studies were conducted on 3 types of experimental animals: white mice, white rats and rabbits. The following results were obtained: average lethal doses for rats - 3700 (4133÷3266), for mice - 3275 (3499÷3051) mg/kg and for rabbits - 3200 mg/ kg. The species sensitivity coefficient equal to 1.1 showed that the drug does not have species sensitivity. The clinical picture of poisoning was the same in different types of experimental animals and was characterized by inhibition of motor activity, lack of appetite, drowsiness, salivation. The death of animals from toxic doses was observed on 2-4 days.

In order to study the state of the antioxidant system under the influence of Dorilin on the body of experimental animals, an acute experiment was conducted on white rats. The animals were divided into 4 groups: the 1st group received intragastric Dorilin once at a dose of 1000 mg / kg; the 2nd group -100.0 mg / kg; the 3rd group – 10.0 mg / kg; the 4th group served as a control. In animals, the activity of catalase and superoxide dismutase (SOD) enzymes was determined in whole blood after 2 hours, 24 hours, 48 hours, 72 hours, 7 and 14 days.

The most pronounced changes in the activity of catalase and SOD enzymes were detected in the 1st group of animals. Thus, catalase activity in the blood of experimental white rats was inhibited more than 2 times 24, 48 and 72 hours after administration of Dorilin ($p < 0.001$). After 7 days, catalase activity acquires a sensitive tendency to recovery, however, even after 14 days after the seed, the indicators did not normalize.

Indicators of the toxicity of the drug were: the activity of catalase, SOD, lactate dehydrogenase (LDH) enzymes, the content of pyruvic (PVC) and lactic (MK) acids, the content of SMP 280 nm, SMP 254 nm and a paramecium test in the blood of experimental animals.

The activity of catalase in the blood of white rats is presented in Table 4.9, from which it is clearly seen that our acute experiment revealed a significant decrease in catalase activity 2 hours after administration of 1000 mg / kg of Dorilin. The most significant changes in catalase activity were detected 2 days after administration of the drug - 8.14 ± 0.37 mcat / ml., with a control of 19.38 ± 0.61 mcat / ml ($P < 0.001$), i.e. the decrease in catalase activity was almost 2.4 times.



It should be noted that observations of the catalase activity index in group 1 animals for 2 weeks did not reveal a restoration of its activity, although the trend towards normalization was clearly traced. So, on day 14, the level of catalase activity was reduced by 1.2 times compared to the control ($P < 0.001$). In animals of the 2nd group, catalase activity also decreased, but the decrease in its activity was less pronounced and persisted for 7 days. Thus, we have established that the antioxidant system plays an important role in protecting cells from the damaging effects of lipid peroxidation products. Changes in the activity of its enzymes leads to a violation of cellular homeostasis, an increase in the aggressiveness of molecular oxygen and hydroperoxides formed during metabolism. The degree of inhibition of catalase and SOD activity in the body depends on the administered dose of Dorilin and the timing of the study. The obtained data will form the basis for the development of pathophysiological mechanisms of biological action of Dorilin, a new plant growth stimulator proposed for introduction into agricultural production of the Republic of Uzbekistan. To determine the parameters of acute toxicity of Doriline during intragastric exposure, studies were conducted on 3 types of experimental animals: white mice, white rats and rabbits. The following results were obtained: average lethal doses for rats - 3700 (4133÷3266), for mice - 3275 (3499÷3051) mg/kg and for rabbits - 3200 mg/kg. The coefficient of species sensitivity, equal to 1.1, showed that the drug does not have species sensitivity. The clinical picture of poisoning was the same in different types of experimental animals and was characterized by inhibition of motor activity, lack of appetite, drowsiness, salivation. The death of animals from toxic doses was observed on 2-4 days.

In order to study some aspects of the mechanism of biological action of Dorilin on white rats, the following doses were studied: 1000.0; 500.0 and 50.0 mg/kg. Indicators of the toxicity of the drug were: the activity of catalase, SOD, lactate dehydrogenase (LDH) enzymes, the content of pyruvic (PVC) and lactic (MK) acids, the content of SMP 280 nm, SMP 254 nm and a paramecium test in the blood of experimental animals.

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Catalase activity in the blood of white rats with acute intragastric administration of Dorilin (mccat / ml), M= m

Terms of research	Animal groups			
	1	2	3	4
Background	21,01±0,54	19,04±1,0	21,12±0,47	20,75±0,76
2 hours	14,74±0,82***	19,16±0,88	19,92±0,86	21,07±0,40
24 hours	10,21±0,38***	15,62±0,58**	21,19±0,37	21,14±0,39
48 hours	8,14±0,37***	13,7±0,43***	20,01±0,75	19,38±0,61
72 hours	9,74±0,49***	17,7±0,86	20,03±1,01	19,97±0,51
7 days	15,21±0,54***	18,94±0,50	19,72±0,54	20,17±0,44
14 days	16,82±0,46***	19,96±0,70	20,74±0,65	21,02±0,43



Note: * - significantly compared to background data (* - $P < 0.05$, ** - $P < 0.01$, *** - $P < 0.001$)

The state of activity of the SOD enzyme in the blood of experimental animals is presented in Table 4.10.

Table 4.10. Activity of SOD in the blood of white rats with acute intragastric administration of Dorilin (CU / ml), M = m

Terms of research	Animals group			
	1	11	111	1Y
Background	19,82±1,02	18,61±1,27	20,02±0,22	20,25±0,25
2 hours	15,56±0,43***	17,82 ±0,74	20,12±0,27	19,16±1,00
24 hours	10,15±0,57***	14,42±0,22**	17,94±0,16***	18,72±0,74
48 hours	7,52±0,24***	15,42±0,44*	20,92±0,27*	21,14±0,37
72 hours	9,51±0,46***	17,11±0,29	20,08±0,24	19,54±0,93
7 days	15,44±0,26***	20,08±0,24	21,05±0,75	20,14±0,70
14 days	16,72±0,75*	19,54±0,93	20,14±0,29	19,15±0,37*

Note: * - significantly compared to background data (* - $P < 0.05$, ** - $P < 0.01$, *** - $P < 0.001$)

The effect of Dorilin on the state of carbohydrate metabolism in the body was studied by the activity of lactate dehydrogenase and the content of metabolites of carbohydrate metabolism – pyruvic (PVC) and lactic (MK) acids in blood serum.

It was found that the activity of LDH, which catalyzes the reaction of lactate to pyruvate and back in the body, significantly changed from exposure to Dorilin at doses of 1000 mg / kg and 500 mg/mg after a single intragastric administration of the drug. The results of the study of LDH activity in animal blood serum are shown in Fig. 4.14.

In group 1 animals, LDH activity increased significantly 2 hours after Dorilin administration - up to 498±6.4 IU/l, with a control of 435±3.62 IU/l ($P < 0.001$). After 24 and 48 hours, LDH activity continued to increase and amounted to 745± 4.35 IU/l and 781±5.5 IU/l, respectively. However, during all remaining observation periods (72 hours, 7 and 14 days) the activity of the enzyme decreased, but it did not recover to normal values. In group 2 animals treated with Dorilin at a dose of 500 mg/kg, LDH activity was high only during the observation period of 24, 48 and 72 hours. A one-week period (7 days) was sufficient to normalize the indicator in animals of the 2nd group.

The results of studies of metabolites of carbohydrate metabolism of pyruvic and lactic acids are presented in Tables 4.11 and 4.12.

A decrease in the content of PVC and an increase in the content of lactic acid in the blood serum of animals of the first 2 experimental groups were revealed. The level of PVK in the blood serum after 48 hours decreased in animals of the 1st group by almost 4 times, and in the 2nd - by 2.1 times compared with the control. The lactic acid content for the same observation period in group 1 animals increased by 2 times. and in animals of the 2nd group - 2.6 times in relation to the control levels ($P < 0.001$).

Consequently, it has been established that Dorilin in large doses leads to changes in the blood metabolites of carbohydrate metabolism - pyruvic and lactic acids, which indicates an increase in glycolysis, and naturally, a relative lack of oxygen in the respiratory chain. Oxygen deficiency contributed to the activation of the lactate dehydrogenase reaction.



The degree of endogenous intoxication in the body of animals was studied on the basis of studies of the content of medium molecular peptides (SMP) at a wavelength of 254 nm and 280 nm and according to the indications of a paramecium test.

Table 4.11. The content of pyruvic acid (PVC) in the blood serum of white rats with acute intragastric administration of Dorilin (mmol / l), $M \pm m$

Terms of research	Animal groups			
	1	2	3	4
Background	0,076±0,006	0,084±0,006	0,091±0,002	0,082±0,004
2 hours	0,061±0,006	0,087±0,007	0,093±0,004	0,097±0,004*
24 hours	0,042±0,003***	0,074±0,003	0,092±0,003	0,088±0,003
48 hours	0,280±0,003***	0,052±0,004***	0,106±0,002***	0,111±0,003***
72 hours	0,036±0,004***	0,074±0,001	0,102±0,002***	0,094±0,004*
7 days	0,048±0,004***	0,095±0,003	0,098±0,005	0,113±0,007***
14 days	0,064±0,004	0,085±0,006	0,079±0,004*	0,084±0,006

Note: * - significantly compared to background data (* - $P < 0.05$, ** - $P < 0.01$, *** - $P < 0.001$)

Summing up the toxicological studies on the study of toxicity parameters and the effect of growth stimulants on some functions and systems of the body, the following conclusions can be drawn:

According to the parameters of acute intragastric toxicity, Dorilin belongs to the 4th hazard class. The mechanism of the toxic effect of the drug consists of a sharp inhibition of AOS enzymes, leading to the phenomena of hypoxia and aggravated by the development of endogenous intoxication of the body. The dose of Dorilin 50 mg / kg with a single intragastric injection was established as "inactive"

The results of the conducted research are the basis for scientific substantiation and development of hygienic standards in environmental objects - regulations for the use of Rostbisol, Oxyhumate, Bahor and Dorilin in agricultural production of the Republic of Uzbekistan

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