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Some Aspects Of The Toxic Effect Of Karate Pyrethroide On Rat Liver Metabolism And Ways Of Their Correction

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Annotation: The activity of alkaline phosphatase, a secretory enzyme synthesized in the liver, has been studied. The research results showed that the activity of alkaline phosphatase increases in comparison with the norm by 2-3 times. According to the accepted identification of clinical diagnostics, such activity is inherent in the liver, in which the parenchyma is inflamed or affected, as a result of which the membranes are also affected. This, in turn, leads to the release of organolytic enzymes into the blood. Apparently, in these experiments, pyrethroid karate destroys the membrane structures of cells, and those isomers of alkaline phosphatase that are contained in organelles do not leak into the blood. Therefore, it can be assumed that this is the reason for the invariably high activity, which is found on the 30th and 50th days of poisoning of karate rats. After the introduction of the antioxidant RAF to poisoned rats, the activity is gradually restored. On the 50th day, the activity of alkaline phosphatase is restored.

Keywords: insecticides, pyrethroids, karate, liver, blood, intoxication, enzymes, phosphatases, alkaline phosphatase, antioxidant, plant antioxidant factor **(**RAF**).**

As you know, today pesticides are widely used in the world, despite the fact that their use violates the microbial balance of the soil, pollutes the atmosphere and water systems. The most famous pesticide DDT, widely used in the 20th century, whose residual concentrations still contaminate the soil, is highly resistant to degradation. No physical factors can strongly influence the degradation process of DDT. Currently, DDT is prohibited for use [1], however, its long-term use on an ever-increasing scale has led to a significant accumulation in the external environment, soil, and water.

Pesticides are chemical and biological agents used to combat pests and diseases of plants, weeds, pests of grain and grain products, wood, wool, leather, cotton products, with ectoparasites of domestic animals, with vectors of human and animal diseases. Plant growth regulators, defoliants and desiccants also belong to pesticides [7,8,11,15].

According to the US National Academy of Sciences, 90% of fungicides, 60% of herbicides, and 30% of insecticides can cause cancer. Of the 400 pesticides used in global agriculture, 262 are mutagenic to varying degrees. Over the past 5 years, the contamination of food with nitrates and their decay products has increased 5 times. Such poisonings are not so common, but, nevertheless, you need to know about them. An estimated one to five million cases of pesticide poisoning occur each year, resulting in several thousand deaths. Children are at a higher risk of pesticide poisoning because their bodies are more susceptible to chemicals [13]. Symptoms suggestive of acute poisoning range from fatigue, dizziness, nausea and vomiting to respiratory and neurological disorders that can be life-threatening. Chronic (even non-intensive) exposure to pesticides leads to an increased risk of cancer, birth defects, damage to the nervous system and disorders of the endocrine system of the human body [37].

Diseases are increasingly common in communities where pesticides are used nearby. This is mainly toxic hepatitis, disorders of the nervous, cardiovascular systems, etc. [6,12,16,20].

All tissues and organs are exposed to pesticide intoxication, but the liver is most affected [1,2,3,19,27,29].

The use of insecticides in agriculture increases every year, the most promising class of insecticides are pyrethroids [7,11,15]. It is believed that when used correctly, pyrethroids do not have a direct toxic effect on humans and animals [16]; moreover, the safety requirements for these drugs have been tightened recently, and a comprehensive assessment of their toxicity has been introduced [6].

To combat harmful plants and representatives of the animal world (insects, pathogens, etc.) in agriculture and in everyday life, a large number of organic and inorganic chemical compounds are used. In relation to these substances, the common name is pesticides (pesticides) [7, 11, 14].

Pesticides show their toxic effect regardless of the route of entry into the body (through the mouth, skin or respiratory system) [15, 18].

Synthetic pyrethroids (SP) - analogs of natural pyrethrins contained in flowers of dolmat chamomile (pyrethrum) - are widely used as insecticides for the treatment of potatoes, fruit and vegetable crops, to combat exoparasites of farm animals, and pests of food supplies in everyday life. Currently, a significant number of synthetic pyrethroids, which are derivatives of cyclopropanecarboxylic acids, in particular, chrysanthemum and monocarboxylic acids, have been synthesized and studied [26,32]. Low consumption rates of synthetic pyrethroids (tens or hundreds of grams per hectare), the ability to rapidly biodegrade in the environment, and low volatility have led to an increase in the use of synthetic pyrethroids in agriculture and in everyday life. According to the mechanism of toxic action, all synthetic pyrethroids are divided into 2 types. Type I includes SPs that do not contain a cyano group (allethrin, bifenthrin, pyrethrin, permethrin, etc.). When exposed to animals, synthetic pyrethroids of this group cause hyperactivity, agitation or even aggressive behavior, generalized tremor, and muscle contractures [26, 32]. The peculiarities of the toxic effect of type II synthetic pyrethroid -

cyanopyrethroids (cypermethrin, alpha-cypermethrin, betta-cypermethrin, deltamethrin, sumi-alpha, etc.) - are hypersalivation, convulsions and recurrent seizures, choreathetosis, hyperkinesis [22, 26]. Experimental electrophysiological studies indicate that synthetic pyrethroids cause functional changes in the postsynaptic neuronal membrane. They act on chemically excitable ion channels, have a fairly high affinity for nicotinic acetylcholine receptors [7,17]. Cyano-containing synthetic pyrethroids interact with gamma-aminobutyric acid (GABA) receptors in brain synaptosomes, causing disturbances in the functioning of the extrapyramidal system and spinal intermediate neurons [7]. Considering the ability of synthetic pyrethroids to interact with GABA receptors, in the treatment of poisoning with synthetic pyrethroids, the use of substances acting as GABA ergists and as antagonists of the excitatory glutamate and aspartatergic systems is justified [17]. Thus, the main manifestations of the toxic effects of synthetic pyrethroids are characterized mainly by dysfunctions of the central nervous system (CNS). It has been shown that the neurotoxic effect of synthetic pyrethroids is due to a disturbance in the generation and propagation of excitation along the nerve in the form of an increase in the negative trace action potential and multiple discharges of the nerve to a single stimulus with manifestations of blocking neuromuscular transmission [7,17]. At the same time, other researchers do not find significant morphological changes in peripheral nerves when exposed to synthetic pyrethroids [17,26,32]. The studies of Kokshareva and co-authors, carried out on the most sensitive to neuropathy type of animals - chickens, showed that synthetic pyrethroids do not cause degeneration of the nerve fiber and the development of paresis and paralysis in the long term [17]. In the mechanism of toxicity of synthetic pyrethroids, activation of lipid peroxidation is of great importance [3,4]. Activation of lipid peroxidation (POL) processes was observed in workers in poultry farms in contact with low doses of synthetic pyrethroids during work [21, 24].

The experiment also revealed the hepatotoxic effect of synthetic pyrethroids, which is more pronounced in cyanopyrethroids [20,26,31]. Strict adherence to hygienic regulations and work rules ensures the safety of the use of synthetic pyrethroids, however, if the rules for their use are violated or as a result of accidental ingestion, acute poisoning develops [24,31,33]. In clinical practice, in acute poisoning with synthetic pyrethroids, the predominance of neurotoxic effects has been noted [26, 32]. A large number of observations of acute poisoning with synthetic pyrethroids (1580 cases from 1983 to 1997) are described by Chinese researchers [34,35]. The authors report that poisoning was more often recorded when using deltamethrin, fenvalerate, cypermethrin. The main clinical manifestations of intoxication were headache, dizziness, general weakness, burning and itching of the facial skin, an increase in body temperature in the first 2-3 days to 38-39 ° C, muscle fasciculations, in severe cases convulsive syndrome, pulmonary edema, coma were noted. In case of cymbush poisoning [21], the development of toxic encephalopathy with a predominant lesion of the cerebellar system, toxic hepatitis and secondary hypochromic anemia was noted. American researchers report a fairly high prevalence of poisoning with synthetic pyrethroids [30,37,38]. Poisoning with synthetic pyrethroids

(39%) was most often noted, less often with organophosphorus compounds (28%) and other drugs (33%). In the state of California from 1998 to 2000. out of 844 registered cases of poisoning, 134 (15.9%) were caused by the effects of synthetic pyrethroids (more often type II - cyanopyrethroids) [30]. Most authors, with prolonged exposure to low doses of synthetic pyrethroids, note a violation of the sensitivity of the facial skin, the appearance of symptoms of irritation of the upper respiratory tract [38], indicating the involvement of peripheral axons in the pathological process. These phenomena are especially pronounced in patients with acute poisoning with synthetic pyrethroids [37]. The victims note not only tingling, burning, itching, but also severe painful paresthesias in the area of open areas of the body. In the works of Balan and others, an analysis of the clinical manifestations of 6 cases of acute poisoning with synthetic pyrethroids during treatment and follow-up for 3 years was carried out. The program of examination of patients, along with general clinical studies, included biochemical tests according to the generally accepted method (activity of ALT, AST, ALP, thymol, formol tests, Veltman reaction, protein fractions, cholesterol, bilirubin). Along with this, the study of serum and erythrocyte XE according to S. Hestrin was carried out [36]. To assess endotoxicosis, we determined the average molecular weight peptides [10]. All 6 victims suffered acute poisoning with cyano-containing synthetic pyrethroids (two with deltamethrin, one with karate, one with cypermethrin and two with sumicidin) due to gross violations of the hygienic rules of their use. A patient with karate poisoning developed astheno-vegetative syndrome, stage II. with a pronounced neurotic component (frequent headache against a background of depressed mood, irritability, tearfulness, insomnia). Dynamic observation for 3 years revealed a certain persistence of neurological syndromes, with a decrease in their severity. This is apparently associated with both exogenous and metabolic endogenous intoxication. In patients with poisoning with sumicidin and karate, astheno-vegetative syndrome of mild severity was preserved. Thus, acute poisoning with synthetic pyrethroids is accompanied by a predominant lesion of the central nervous system, damage to the lungs, kidneys, and very often the liver. These data indicated to us the need to investigate the effect of karate on certain aspects of the metabolism of hepatocytes.

Phosphatases are enzymes of the hydrolase class that catalyze the hydrolysis of phosphoric acid monoesters.

A large number of phosphatases are represented by nonspecific enzymes capable of cleaving various compounds (monoesters of phosphoric and thiophosphoric acids, phosphamides and polyphosphates). Some F., for example, glucose-6-phosphatase and fructose-bis-phosphatase, exhibit selective specificity to the substrate.

Nonspecific phosphatases, depending on the pH of the medium in which their maximum enzymatic activity is manifested, are divided into alkaline (optimum action at pH 8-10) and acidic (pH 4-6). Alkaline phosphatase (ALP) is found in almost all tissues of the human body. Its greatest amount is concentrated in bone tissue, intestinal mucosa, liver and kidneys. [43]. Alkaline phosphatase is found in animal tissues (intestinal mucosa, placenta, kidneys, bones, and others), blood serum, milk, bacteria,

and fungi. but not in plants. Acid phosphatases are found in the tissues of the prostate gland, spleen, in higher plants, bacteria, yeast. The difference between the two groups of phosphatases is also observed when they act on sulfur-containing substrates: alkaline phosphatase hydrolyzes S-esters, and acidic phosphatase - O-esters of thiophosphoric acid. [eleven].

The most well studied is the alkaline phosphatase of Escherichia coli. Its primary structure and spatial structure are known. The enzyme (molecular weight 94 thousand) consists of two identical subunits, each of which has an active center, but in itself is inactive. [28].

The function of phosphatases in the body is to maintain the concentration of phosphate required for various biochemical processes and, possibly, for the transport of phosphate into the cell [25].

Determination of the activity of acid and alkaline phosphatases is important in the diagnosis of certain diseases accompanied by changes in their concentration (for example, an increase in the concentration of acid phosphatase in prostate cancer and alkaline phosphatase in liver disease and bone metabolism disorders) [5,6].

Alkaline phosphatase is an enzyme found in the cells of the liver and biliary tract and is a catalyst for certain biochemical reactions in these cells. When these cells are destroyed, their contents enter the bloodstream. Normally, some of the cells are renewed, so a certain amount of alkaline phosphatase is found in the blood. If many cells die, the level can rise very significantly. Alkaline phosphatase levels increase dramatically when bile flow is obstructed, such as stones in the bile duct. This stagnation of bile is called cholestasis. In bones, alkaline phosphatase is formed in special cells called osteoblasts, which play an important role in the formation and renewal of bone tissue. The higher the activity of osteoblasts, the higher the level of alkaline phosphatase in the blood, therefore, in children and persons who have had bone fractures, the level of alkaline phosphatase is high. Alkaline phosphatase is also found in intestinal and placental cells.

Alkaline phosphatase is involved in the exchange of phosphoric acid, breaking it down from organic compounds and facilitating the transport of phosphorus in the body. The highest levels of alkaline phosphatase are found in bone tissue, intestinal mucosa, placenta and mammary gland during lactation.

The norm of alkaline phosphatase in the blood of a woman is up to 240 U / l, in a man - up to 270 U / l. Alkaline phosphatase affects bone growth, which is why its content is higher in children than in adults.

A biochemical blood test for alkaline phosphatase is performed to diagnose diseases of the skeletal system, liver, biliary tract and kidneys.

An increase in alkaline phosphatase occurs in the last trimester of pregnancy, after menopause, with a lack of calcium and phosphate in food, from an overdose of vitamin C and as a result of taking certain medications (oral contraceptives containing estrogen and progesterone, antibiotics, and others).

The level of alkaline phosphatase is reduced in hypothyroidism, bone growth disorders, lack of zinc, magnesium, vitamin B12 or C (scurvy) in food, anemia (anemia). Taking medications can also cause a decrease in alkaline phosphatase in the blood. During pregnancy, a decrease in alkaline phosphatase activity occurs when the placenta fails to develop.

During pregnancy, the normal level of alkaline phosphatase is increased, since it is contained in the placenta. A temporary increase in alkaline phosphatase is noted after fractures. Children and adolescents have higher alkaline phosphatase levels than adults as they grow bone. Aspirin, paracetamol, allopurinol, antibiotics, and a number of other drugs can increase alkaline phosphatase levels. Taking oral contraceptives sometimes decreases alkaline phosphatase levels. Alkaline phosphatase levels may be elevated if blood has cooled after collection. The level of alkaline phosphatase sometimes increases in healthy individuals, this does not necessarily indicate any pathology. To correctly interpret the change in the level of alkaline phosphatase, a comprehensive assessment of the results of other analyzes, as well as other medical data, is needed [6,9].

Any condition that is associated with bone growth or increased bone cell activity increases alkaline phosphatase activity. Therefore, the analysis for alkaline phosphatase can be used, for example, in order to determine that the tumor has spread beyond the primary focus - in the bone.

Determination of the activity of alkaline phosphatase is of diagnostic value in violation of a number of metabolic processes due to severe pathologies and diseases with an unfavorable prognosis, therefore, the importance of correctly determining the boundaries of normal values for the activity of this enzyme can hardly be overestimated.

Alkaline phosphatase activity in vivo undergoes significant changes with age. In newborns and children up to adolescence, the levels of this enzyme exceed the "adult" values by 3-5 times. This is due to the fact that the enzyme is actively involved in the formation of the skeleton. A sign of pathology for children is a decrease in the level of alkaline phosphatase. In contrast, elevated alkaline phosphatase levels are considered unfavorable in adults. Sex differences also affect the level of the enzyme, and in adolescence it is much more pronounced than in adults (the activity of alkaline phosphatase in the serum of boys from 13 to 17 years is 2-2.5 times higher than in girls of the same age, while the difference in activity in adult men and women is 10-17%). [6.9].

Determination of the activity of alkaline phosphatase is of diagnostic value in a number of diseases accompanied by impaired phosphate metabolism [9].

An increase in the activity of alkaline phosphatase by 3-7 times or more is observed in bone tissue pathologies associated with an increase in the number of osteoblasts, as well as in bone tissue breakdown: hyperparathyroidism, Paget's disease (deforming osteitis), osteosarcoma, bone carcinoma, tumor metastases in the bone, Beck's sarcoidosis, lymphogranulomatosis with bone lesions, myeloma, ossifying myositis, Gaucher disease with bone resorption.

A decrease in the activity of alkaline phosphatase occurs when osteoblastic processes are weakened [45]. Revealed the inhibitory effect of mercury acetate on the activity of alkaline phosphatase. Moreover, this effect is observed both in high (10-3 mol / l) and low (10-6 mol / l) concentrations of the tested ecotoxicant, the differences are in the degree of inhibition, as well as the time of the appearance of the effect [43].

An increase in the activity of alkaline phosphatase in urine occurs in patients with chronic renal failure, including those caused by kidney injury or due to diseases of other organs (for example, with tumor uricemia) [44].

An increase in serum alkaline phosphatase activity accompanies the normal course of pregnancy. The maximum values are reached at the time of delivery. The placental isoenzyme of alkaline phosphatase, produced by microvilli of the trophoblastic membrane, is present in the blood. The test for total alkaline phosphatase and the relative content of the placental isoenzyme is used to monitor the state of the placenta during pregnancy [46].

An increase in the activity of alkaline phosphatase in practically healthy people can be caused by taking anti-inflammatory drugs. An increase in the activity of the enzyme can also be caused by the use of drugs, the effect of which on the liver or cholestasis is not expressed clinically. Among these drugs are such common anti-inflammatory and antibacterial drugs as aspirin, indomethacin, sulfonamides, most antibiotics (gentamicin, erythromycin, ampicillin, tetracycline, lincomycin, etc.), which are periodically used by almost all age groups of practically healthy people for the treatment of ARVI or local inflammation [40, 42, 43, 47, 48].

Thus, from the above literature data it follows that alkaline phosphatase is a secretory enzyme, and the study of its activity in blood serum will enable us to evaluate the toxic effect of karate pyrethroid.

With lesions of liver cells, in particular their membranes, it can be assumed that the study we are planning will be of great importance for elucidating the mechanism of the damaging action of pyrethroid - karate. The study of the effect of the plant antioxidant factor (RAF) against pesticide intoxication, in particular karate, will contribute to the disclosure of the mechanism of its action and the prevention of pathological conditions of the body.

The aim of this research was to study the effect of synthetic pyrethroid karate, in combination with RAF, on the activity of the enzyme alkaline phosphatase [ALP].

In connection with the above, we were faced with the following tasks:

- to investigate the effect of the synthetic pyrethroid pesticide karate on the activity of alkaline phosphatase (ALP) in the blood serum of rats.

- to study the effect of the plant antioxidant factor (RAF) on the change in the activity of alkaline phosphatase (ALP) in poisoned karate rats.

Research materials. The material for the study was male Wistar rats weighing 100-120 grams. The karate pesticide preparation is administered orally in the form of an aqueous suspension through a tube at a dose of 1／10 LD50 in an amount of 1.18 mg, once. The second group of experimental rats was injected with the same amount of pesticide and, after 30 minutes, plant antioxidant factor (RAF) in an amount of 1 ml. RAF is a 5% alcohol-based plant extract. After inoculation, the rats were kept on the usual diet of the vivarium. On days 1, 5, 30, 50, both control and experimental rats were sacrificed for experiments to determine the activity of alkaline phosphatase. The object of the study was the liver homogenate and blood serum of rats.

Karate pesticide is the full chemical name-L-cyanophenoxybenzyl 3- (2-chloro-3,3,3-trifluoroprol-1-ethyl) -2,2-dimethylcyclopropanecarboxylate [41]. In the study, an SF-46 spectrophotometer and a K-24 centrifuge (Germaniya) were used.

Research methods. Blood sampling. After decapitation, blood was immediately drawn from the carotid artery into a centrifuge tube. The blood was left at room temperature for 30-40 minutes. Then the blood was centrifuged at 2000 - 2500 rpm for 10 minutes. Serum was used to determine the activity of alkaline phosphatase and protein concentration to calculate the specific activity of the enzyme.

Determination of protein concentration by the method of Lowry et al [23].

Determination of the activity of alkaline phosphatase was carried out by the optimized micromethod with the substrate p-nitrophenyl phosphate described [9].

Determination of the activity of alkaline phosphatase is important in the diagnosis of certain diseases accompanied by a change in their concentration, for example, with various liver lesions. Determination of the activity of alkaline phosphatase is of diagnostic value in a number of diseases accompanied by impaired phosphate metabolism.

Alkaline phosphatase is synthesized primarily in the liver. Under physiological conditions, these enzymes are mainly excreted in the bile. The mechanisms regulating the flow of these enzymes into the bile capillaries have not yet been fully elucidated. In many pathological processes, the secretion of excretory enzymes in the bile is impaired, and the activity in the blood plasma decreases [5].

Alkaline phosphatase is localized on the cell membrane, where it apparently takes part in the processes of phosphate transport. Due to the fact that the liver is the source of the main component of alkaline phosphatase in blood serum, we studied the effect of karate on this indicator.

On the 1st, 5th, 30th, 50th days after karate poisoning, the determination of the alkaline phosphatase activity was carried out in the blood serum and liver homogenate of experimental rats. The animals were divided into three groups: group I consisted of intact rats; Group II - rats poisoned by karate (karate); Group III consisted of animals fed with RAF, 30 minutes after poisoning with karate (karate + RAF).

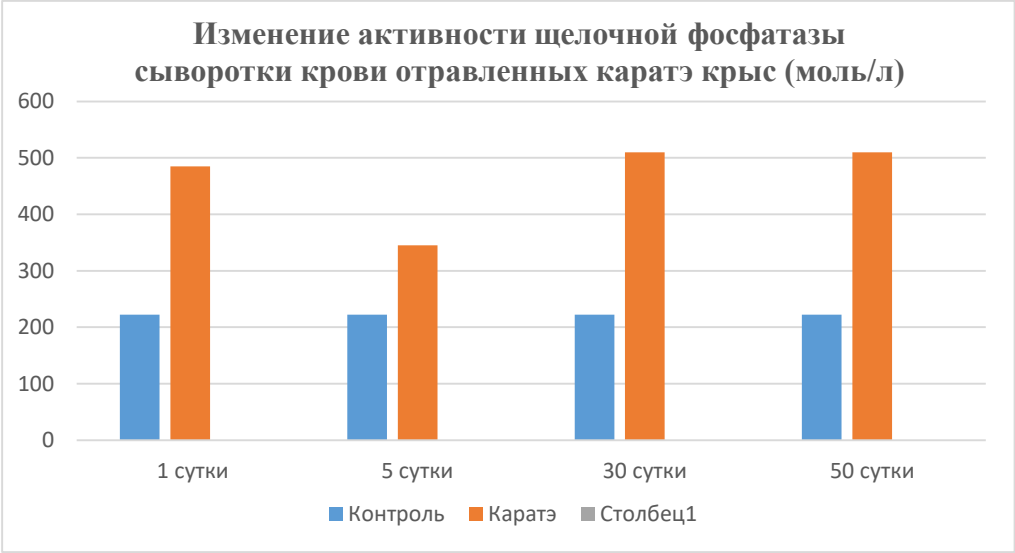
The results of determining the activity of alkaline phosphatase in blood serum are shown in Table 1 and Figure 1. As can be seen from the table, the activity of alkaline phosphatase in intact animals

averages 222.0 ± 7 mmol / L. After poisoning with pyrethroid karate, apparently, noticeable changes occur in the liver. This is evidenced by the results of determination of alkaline phosphatase in rats poisoned by karate. The data given in table 1 show that one day after poisoning, an intensification of alkaline phosphatase is observed by more than 2 times. On the fifth day after the poisoning, the initial activity decreases slightly. In the rest of the experiment, that is, on the 30th and 50th days, the activity is kept at the same high level. In comparison with the norm, this indicator exceeds the norm by almost 2.3 times. An analysis of these figures makes it possible to assume that an intense detoxification begins in the liver tissue initially affected by the action of karate. Therefore, on the 5th day, the activity of alkaline phosphatase decreases slightly. But on the following days of the experiment, the activity of alkaline phosphatase increases by 230% and does not change until 50 days.

Table 1 Changes in the activity of alkaline phosphatase in blood serum of poisoned karate rats (mol / l)

Variants	Time after poisoning (days)			
	1	5	30	50
Control	222 ± 7,6	222 ± 7,6	222 ± 7,6	222 ± 7,6
Karate	485 ± 11,0	345 ± 10,2	510 ± 12,0	510 ± 11,9

As you know, antioxidant systems during this period are strongly activated, which was shown in [2,3]. But in the days following poisoning, alkaline phosphatase is kept at a high level.



Picture 1. Changes in alkaline phosphatase activity blood serum of poisoned karate rats (mol / l)

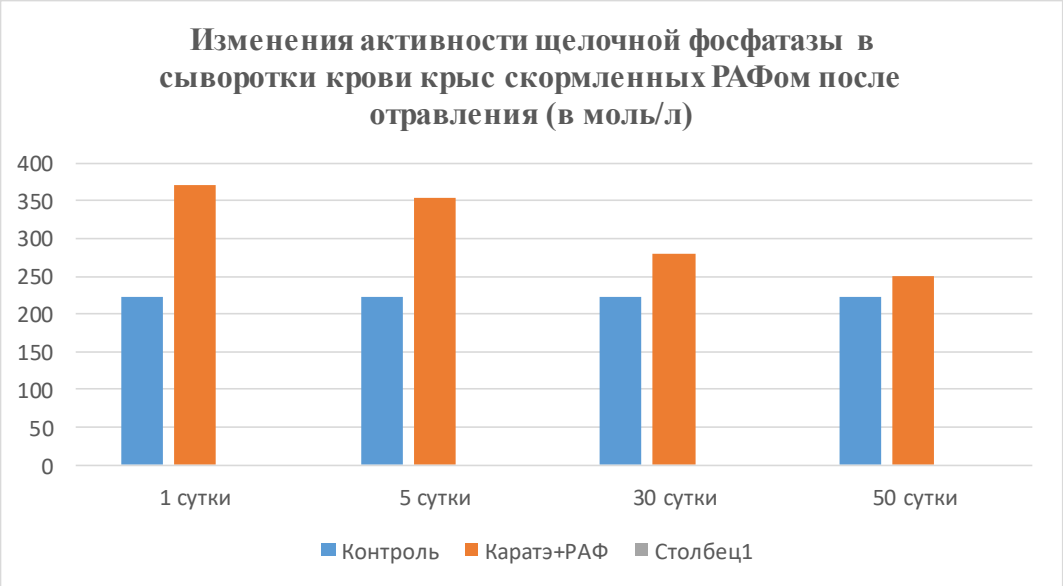
Hepatotoxic disorders lead to various changes in metabolic processes, including phosphate metabolism. It is known that alkaline phosphatase is involved in maintaining the concentration of phosphate required

for various biochemical processes, and, possibly, in the transport of phosphate into the cell. This enzyme is activated 2-3 times under the action of pyrethroid pesticides [25].

Due to the fact that the determination of the degree of increase in the level of alkaline phosphatase is used for differential diagnosis, we studied the changes in the activity of the enzyme under the influence of RAF in rats poisoned with karate. The activity of alkaline phosphatase in the blood serum of poisoned karate rats, after taking RAF, are shown in Table 2 and Figure 2.

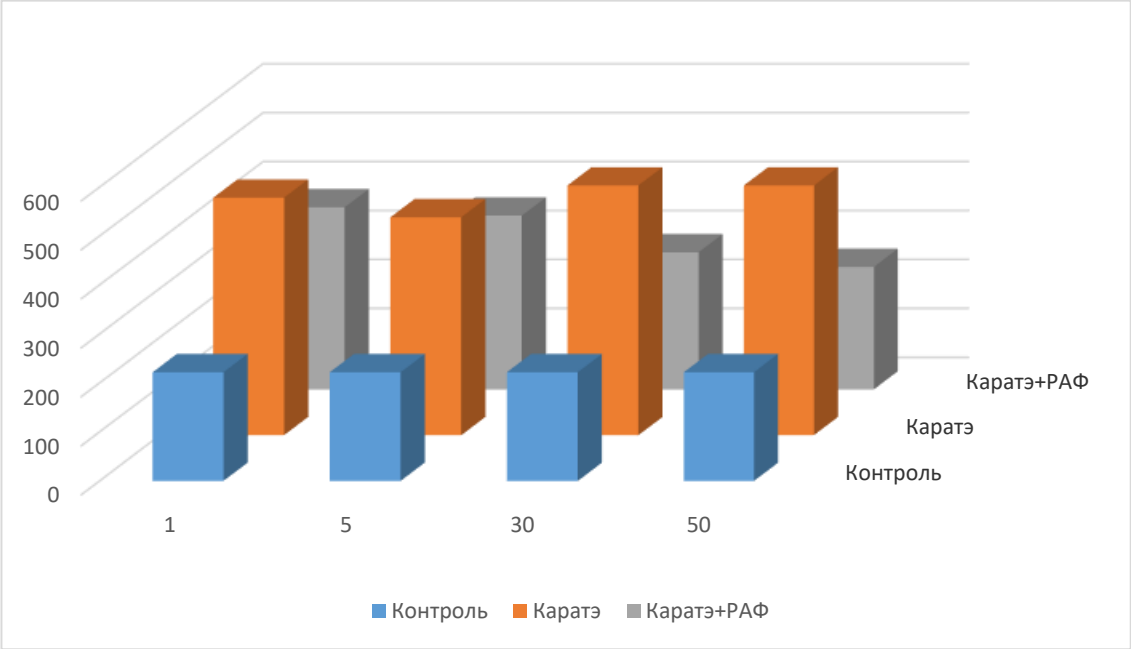
Table 2 Changes in the activity of alkaline phosphatase in the blood serum of rats fed with RAF **after poisoning (in mol / l)**

Variants	**Time after poisoning (days)**			
	1	5	30	50
Control	222 ± 7,6	222 ± 7,6	222 ± 7,6	222 ± 7,6
Karate + RAF	372 ±12,0	355 ±8,0	280 ±15,0	250 ±8,0



Picture 2. Changes in the activity of alkaline phosphatase in the blood serum of rats fed with RAF after poisoning (in mol / l)

It should be noted from Table 2 and Figure 2 that the activity of alkaline phosphatase in the case of those fed with RAF has a slightly different picture. So, on the first day, the activity of this enzyme is overestimated by 167.6% relative to the norm. This indicator tends to gradually decrease on the following days. On the 5th day of the experiment, alkaline phosphatase is activated by more than 1.5 times compared to the control.



Picture 3. The effect of Karate and RAF on the change in the activity of alkaline phosphatase in the blood serum of poisoned karate rats (in mol / l)

On the 30th and 50th days of karate poisoning in rats who took RAF, the activity of alkaline phosphatase again decreases and exceeds the control by 1.26 and 1.12 times, respectively.

In the case of karate poisoning of rats without an antioxidant, the activity was overestimated by 230%. In the experiment with the use of RAF, the activity of alkaline phosphatase constantly decreased and on the 50th day of poisoning, the activity was overestimated by only 12% compared to the control. These data indicate that RAF, when fed 30 minutes after karate poisoning of rats, immediately begins to act, apparently, against the accumulation of toxic radicals formed when hepatocytes are damaged by lipid peroxidation. Prevention of lipid peroxidation by RAF facilitates the function of the liver's own antioxidant systems and, probably, therefore, the activity of the secretory enzyme alkaline phosphatase acquires almost normal values (Figure 3).

The harm caused by pesticides to wildlife cannot be accurately estimated - but it can definitely be said that it is enormous. Two factors are of primary importance here: the fact that all synthetic pesticides are substances alien to living nature and inaccessible to metabolic degradation and the fact that almost all of them are capable of bioaccumulation, that is, they are contained in living organisms in higher concentrations than in the environment.

Analysis of the dependence of the action of pyrethroids and their structure made it possible to establish Yu.S. et al, that cyanide-containing pyrethroids are more toxic to warm-blooded animals than compounds that do not contain a cyano group. The biological activity of pyrethroids depends not only on the presence of certain groups in the molecule, but also on the polarization of molecules, spatial isomerism: cis - forms, as a rule, are more toxic than trans - forms. [13].

According to the literature, it is known that in case of poisoning with synthetic pyrethroid pesticides of the cis-form, there is an increased formation of peroxide products and free radicals. Lipid peroxidation is accompanied by damage to the structural integrity and functional integrity of membranes. If acute pesticide poisoning occurs, then with an increase in lipid peroxidation, antioxidant enzymes (SOD, catalase) are activated [24,39,40]. However, the slow utilization of the pesticide from the liver inhibits the activity of these enzymes. Therefore, the accumulation of lipid peroxidation products negatively affects the tissue membranes and destabilizes the liver metabolic processes, including an increase in the activity of alkaline phosphatase.

Hepatotoxic disorders lead to various changes in metabolic processes, including phosphate metabolism. It is known that alkaline phosphatase is involved in maintaining the concentration of phosphate required for various biochemical processes and, possibly, in the transport of phosphate into the cell. This enzyme is activated 2-3 times under the action of pyrethroid pesticides [25].

To be convinced of the reliability of our assumption, we studied the activity of alkaline phosphatase, a secretory enzyme synthesized in the liver. The results of our research have shown that the activity of alkaline phosphatase increases in comparison with the norm by 2-3 times. According to the accepted identification of clinical diagnostics, such activity is inherent in the liver, in which the parenchyma is inflamed or affected. In this regard, membranes are also affected. This, in turn, leads to the release of organolytic enzymes into the blood. Apparently, in our experiments, pyrethroid karate destroys the membrane structures of cells, and those isomers of alkaline phosphatase that are contained in organelles do not leak into the blood. Therefore, it can be assumed that this is the reason for the invariably high activity, which is found on the 30th and 50th days of poisoning of karate rats.

After the introduction of the antioxidant RAF to poisoned rats, the activity is gradually restored. On the 50th day, the activity of alkaline phosphatase is restored.

Thus, during karate intoxication, the liver of rats undergoes significant changes that lead to metabolic disorders, and which is caused by a violation of the structural and functional state of the membranes. The RAF introduced correlates these changes.

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