UDC 577

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MECHANOKINETICS OF INHIBITING THE DYNAMICS OF FROG *M. TIBIALIS* ANTERIOR CONTRACTION DUE TO THE EFFECT OF PIRIMIPHOSMETHYL

Acute organophosphorus pesticides poisoning is a significant clinical problem and causes thousands of death cases eachyear. Toxicity of these pesticidesis thought to be caused by irreversible inhibition of acetyl cholinesterase that leads to acetylcholine accumulation and abnormal activation of cholinergic receptors.

Organophosphate pesticides are widely used in the world, and the problem of poisoning with these agents is rather urgent for public health care, especially in developing countries (1, 2, 3, 4, 5). The toxicokinetics of organophosphate poisoning changes both with the exposure time and half-life of organophosphates (1, 2). Taking into consideration different half-lives of the pesticide for different organs and tissues, it is difficult to estimate the exposure period for a specific organ or the whole organism (2, 4).

The traditional treatment involves the reactivation of acetylcholinesterase and restoration of the biochemical effects of acetylcholine with atropine (1, 2, 3). At the

same time the non-cholinergic effects of the organophosphate activity have not been studied in great detail. Toxicity of this pesticides thought to be caused by irreversible inhibition of acetylcholinesterase that leads to acetylcholine accumulation and abnormal activation of cholinergic receptors. Experimental data analysis gives reason to believe that irreversible inhibition of acetylcholinesterase is not an only one mechanism of organophosphorus pesticides toxicity. This noncholinergic effects so far stays almost unknown. Research was conducted on single muscle fibers which was stimulated by electrical impulses. This technique allowed to explore exactly noncholinergic effects of used pesticide.

The results of the strain (change in strength and length) studies of the effect of the organophosphorus insecticide pirimiphosmethil on the dynamics of the contraction of skeletal muscle fibers m. tibialis anterior frog Rana temporaria. Pirimiphosmethyl concentration range was 10^{-8} - 10^{-5} mol/l. At concentrations pirimiphosmethyl 10^{-8} mol/l effects are absent, and the concentration of 10^{-5} mol/l, after nine minutes of exposure completely inhibited the activity of muscle preparations. Experimental data indicate that the inhibitory properties of solutions of all used concentrations of pirimiphosmethil amplified both with the concentration of the substance, and by increasing the time of action.

The results of our studies demonstrated that the direct effect of pirimiphosmethyl on the fascicles of skeletal muscles leads to considerable inhibition of their contractive activity. Thus, the impairment of contractive ability of skeletal muscles due to the effect of this insecticide was revealed. The effect of pirimiphosmethyl on the level of force and the change in contraction length did not differ much in percentage terms within the investigated concentration range.

The determination of the change in the contraction dynamics at the non-cholinergic effect of organophosphate insecticides may facilitate the improvement of therapeutic approaches and prevention of destructive effect of these substances on muscle cells with poisoning.

The results may contribute to improving therapeutic approaches for the prevention of the destructive action of organophosphates in poisoning.

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