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Yours sincerely,

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PROSPECTIVE METHODS OF PREVENTING POISONING BY PHOSPHORORGANIC COMPOUNDS USING COMPOUNDS OF NATURAL ORIGIN

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Today, the topic of organophosphorus (OP) poisoning is becoming more relevant due to their easy availability and large-scale use not only in agriculture, but also in the chemical and pharmaceutical industries. Poisoning by these compounds actually ranks first among other exogenous poisonings not only in frequency but also in severity [1].

The main pathogenetic mechanism of action of organophosphorus compounds based on the inhibition of cholinesterase enzyme, which hydrolyzes acetylcholine and plays an important role in the process of synaptic transmission of nerve impulses in cholinergic formations [2]. As a result, in the case of organophosphorus poisoning, there is a significant decrease in serum butyrylcholinesterase (BCHE) activity and accumulation of acetylcholine in cholinergic synapses with excessive stimulation of cholinergic receptors, which in turn leads to "cholinergic syndrome" [3]. All this makes the task of finding a new way to treat or prevent poisoning very important.

A promising method of preventing OP poisoning is the use of flavonoids, compounds of natural origin that have a broad therapeutic effect and are also low-toxic. In this paper, a biologically active substance of flavonoid nature diosmin considered as a preventive against OP poisoning.

Evaluation of the premedical properties of diosmin were performed by determining the activity of butyrylcholinesterase in human serum, using a modified Ellman method. This method based on the ability of thiocholine, the reaction product, to reduce potassium hexacyanoferrate (III), which has a yellow color, to transparent potassium hexacyanoferrate (II). The use of potassium hexacyanoferrate (III) allows the analysis of serum butyrylcholinesterase in a wide linear range without prior dilution of samples. The advantage of the method is that it is possible to use liquid reagents that are quite stable over a long period of storage.

The study was performed spectrophotometrically. Kinetics was studied at $\lambda = 405$ nm. The rate of decrease in the absorbance of the reaction solution is directly proportional to the activity of BCHE serum. Ouragan-Forte, in which glyphosate, diluted to 10 mM, was the active ingredient, was selected as the model organophosphorus pesticide. At this concentration, glyphosate can inhibit the activity of the enzyme BCHE 1.7 times. Instead, pre-addition of diosmin to the reaction mixture reduced the negative effect of glyphosate on human serum BHE activity.

It has been found that diosmin at a concentration of 200 μM is able to reduce the inhibition of BCHE by glyphosate by approximately 15-20%. The results of the study show that the higher the concentration of diosmin, the more pronounced the effect of preventing the inhibition of BCHE by glyphosate. Diosmin acts as a reversible inhibitor - it binds to the active site of the enzyme without leaving spot for glyphosate. After a period of time, diosmin leaves the active site of the BCHE, as a result of which the activity of the enzyme is restored.

It concluded that diosmin can be a promising substance to prevent intoxication with organophosphorus compounds and can be used as an active pharmaceutical ingredient in the development of drugs to prevent OP poisoning.

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