

ABSTRACT

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Organophosphorus compounds are chemically organophosphates or organophosphonates. They have been widely used as pesticides but because of their high toxicity and relatively cheap and easy synthesis they can be easily misused as chemical weapons – nerve paralytic compounds. Toxic effect of these compounds is based on irreversible inhibition of the enzyme acetylcholinesterase (AChE).

In case of intoxication by these compounds anticholinergic drugs (atropin) and reactivators of AChE are usually used as antidots. The effect of the reactivators is based on splitting the complex enzyme-inhibitor. Pralidoxim, trimedoxim, obidoxim and asoxim (HI-6) are still the most often used reactivators all over the world. They are the compounds which contain oxime group and one or two quaternary nitrogens in their molecule, what ensures that their affinity to AChE will be strong enough.

Screening and synthesis of new more effective broad-spectrum reactivators of AChE with lower side effects is still very actual and discussed theme. Strategy of the development of new AChE reactivators includes several steps: description of mechanism of intoxication by organophosphorus inhibitors at molecular level (molecular design), prediction of new structures of AChE reactivators by artificial neural networks (ANN), their synthesis, verification of their effectiveness *in vitro* and finally *in vivo* tests.

According to my publications, the best reactivator for cyclosarin was oxime K033 and in case of AChE inhibited by chlorpyrifos the oximes trimedoxime and obidoxime. According to some new articles published by Faculty of Military Health Sciences, University of Defence the most effective reactivator was oxime HI-6. Unfortunately oxime HI-6 is not able to reactivate AChE inhibited by tabun and pesticides. In case of intoxications by tabun the most effective reactivators were oximes K027 and K048. Oxime K027 seems to be even one of the promising candidates for treatment of intoxications caused by a wide spectrum of organophosphates.

Recently, some combinations of two oximes together (HI-6 + trimedoxime, HI-6 + K-203) have been tested as well. However, future tests are needed, and there is also a question concerning toxicity of using two oximes together.