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MEETING ABSTRACTS

NERVE AGENT INHIBITED CHOLINESTERASES CAN BE EFFICIENTLY REACTIVATED BY OXIMES WITH ENHANCED NUCLEOPHILICITY

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Organophosphorus compounds (e.g. nerve agents - sarin, VX or tabun) cause deleterious intoxications via inhibition of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) leading to cholinergic crisis or even death of intoxicated person. Their causal treatment is managed by oxime reactivators (e.g. pralidoxime, obidoxime, asoxime), which are primarily restoring function of AChE via nucleophilic oximates and thus safe a life.

Recently, we have proved that nucleophilicity of oxime reactivators may be improved by using other substituents attached to the close proximity of the oxime moiety. Such modifications are leading to the increased formation of oximate nucleophile and thus to the increased reactivation of phosphylated cholinesterases. In particular, the substitution by chlorine atoms led to the powerful and rapid reactivation of sarin, cyclosarin or VX-inhibited AChE *in vitro* (1) or *in vivo* (2). On the other hand, the substitution by fluorine atoms led to even higher nucleophilicity, but also rapid depletion of oximes into isoxazole degradation products (2-3). Interestingly, some further modified reactivators were proved to be effective *in vitro* to simultaneously restore function of AChE and BChE. These promising results make prospects for further detailed investigation of modified oximes nucleophiles for treatment of organophosphorus intoxications. This work was supported by Czech Science Foundation (no. 21-03000S).

Keywords: organophosphate; cholinesterase; reactivator; oxime; nucleophile

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