

MEETING ABSTRACTS

***IN VITRO* EVALUATION OF STANDARD ACETYLCHOLINESTERASE REACTIVATORS AS REACTIVATORS OF HUMAN PLASMA BUTYRYLCHOLINESTERASE**

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Bioscavengers are considered to be a promising approach in the prophylaxis or treatment of poisoning by organophosphorus inhibitors (OPI; nerve agents and organophosphate pesticides). They can efficiently neutralize diverse OPIs in the bloodstream before they reach their natural targets - cholinesterases. Antidotal efficacy of administered butyrylcholinesterase (BChE; EC 3.1.1.8), one of the possible bioscavengers, could be further increased when it is co-administered with an oxime reactivator of a sufficient reactivation potency. Therefore, the activity of BChE, inhibited by OPI, could be continuously renewed (pseudo-catalytic bioscavenger).

In this study, we evaluated the ability of standard reactivators (pralidoxime, obidoxime, HI-6, methoxime and trimedoxime) and newly developed ones (K027, K048 and K203) to reactivate human plasma BChE inhibited by nerve agents (sarin, cyclosarin, VX and tabun) and dimethoxy and diethoxy pesticide (dichlorvos and paraoxon). Overall reactivation potency was decreased as follows: cyclosarin > sarin > VX > paraoxon > dichlorvos > tabun. HI-6 was the most efficient reactivator of cyclosarin- and sarin-inhibited BChE, whereas pralidoxime achieved highest potency for VX. Obidoxime was the most active in the case of pesticide inhibited enzyme. Reactivation of tabun-inhibited BChE was negligible for all tested compounds. Generally, reactivation ability of examined standard reactivators was deficient and uneven as they were designed for the reactivation of acetylcholinesterase. Therefore, there is a need for development of both more balanced and potent reactivators, suitable for pseudo-catalytic bioscavengers. Assayed oximes will serve for further standardization of our in vitro testing method and subsequent evaluation of newly synthesized BChE reactivators.

Keywords: bioscavengers; butyrylcholinesterase; nerve agents; organophosphates; oxime reactivators

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