MMSL
Military Medical
Science Letters
Since 1925

Mil. Med. Sci. Lett. (Voj. Zdrav. Listy) 2018, 87(supplementum 1)
ISSN 2571-113X (Online)

MEETING ABSTRACTS

IN VITRO EVALUATION OF QUINUCLIDINIUM OXIMES AS REACTIVATORS OF HUMAN CHOLINESTERASES INHIBITED BY ORGANOPHOSPHORUS COMPOUNDS

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This study focused on the evaluation of the use of quinuclidinium oximes as potential antidotes in organophosphorus compound (OPs) poisoning. We determined the reversible inhibition of human red blood cell acetylcholinesterase (AChE) and human plasma butyrylcholinesterase (BChE) by 14 quinuclidinium oximes as well as the reactivation of tabun-, VX-, paraoxon-, sarin- and cyclosarin-inhibited enzymes. Reversible inhibition constants were within 3 μM to 4 mM, depending on the oxime structure. The highest inhibition was observed for Q5, which has a long aliphatic chain on the quinuclidinium ring quaternary nitrogen. It seems that AChE is selective toward oximes that have groups in *meta* position on the benzene ring and BChE to those with a group in *para* position. Quinuclidinium potency to reactivate organophosphorus-inhibited cholinesterases *in vitro* proved promising in restoring cholinesterase activity. VX- and paraoxon-inhibited AChE was reactivated by several candidates at up to 90 - 100 % within 1-4 hours. Oximes with a group *in para* position showed reactivation potency for cyclosarin-inhibited BChE with reactivation up to 90-100 %. Furthermore, at the very beginning of antidote development, we investigated if quinuclidinium oximes are cytotoxic to selected cell lines. As results indicate, quinuclidinium oximes did not show cytotoxic profiles up to 800 μM. An exception was observed only for Q5, an oxime with a long aliphatic chain in the structure, influencing cell vitality at concentrations significant for reactivation of cholinesterases.

Keywords: quinuclidinium; organophosphorus; oximes; reactivation

Acknowledgement

This work was supported by the Croatian Science Foundation grant no. 4307 and UIP-2017-05-7260.