

MEETING ABSTRACTS

IN VITRO CHARACTERIZATION OF THE STANDARD ACETYLCHOLINESTERASE REACTIVATORS

Muckova L. & Hepnarova V., Misik J, Jun D, Soukup O

Department of Toxicology and Military Pharmacy, Faculty of Military Health Sciences, University of Defense, Hradec Kralove, Czech Republic

Acetylcholinesterase (AChE; 3.1.1.7) reactivators play a key role in the treatment of organophosphate poisoning. The main mechanism of reactivators is disruption of the covalent bond between organophosphorus compounds and AChE and restore the physiological function of this enzyme. On the other hand, there are some evidence, other mechanisms not related to reactivation, which may lead to survival.

Thus, their effect on muscarinic (M1 subtype), nicotinic (α 7 subtype) and N-methyl-D-aspartat (NMDA; 2B subtype) receptor was studied. They are able to significantly modulate the receptors at higher concentration (100 μ M) and for this reason, their toxicities were tested. Cytotoxicity of standard oximes was evaluated using neuroblastoma cell line SH-SY5Y. MTT assay and real-time cell viability assay were used to measure cytotoxicity of selected compounds.

The tested reactivators showed different cytotoxicity. Methoxime was the most and K027 was the least toxic. Reactivators had no influence on NMDA receptor in tested concertation. The nicotinic receptor was the most inhibit by K027. However, trimedoxime and obidoxime showed the highest inhibition of muscarinic receptor.

Keywords: reactivator; cytotoxicity; muscarinic receptor; nicotinic receptor; NMDA receptor

Acknowledgement

This work was supported by the Ministry of Education, Youth, and Sport, Czech Republic - SV/FVZ201508 and by the Long-term organization development plan Medical Aspects of Weapons of Mass Destruction of the Faculty of Military Health Sciences, University of Defence.