

Comparison of Acetylcholinesterase Reactivators Cytotoxicity with Their Structure

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Abstract : The development of acetylcholinesterase reactivators, i.e. antidotes against organophosphorus poisoning, is an important goal of defence research. The aim of this study was to compare cytotoxicity and chemical structure of 5 currently available (pralidoxime, trimedoxime, obidoxime, methoxime, and asoxime) and 4 newly developed compounds (K027, K074, K075, and K203). In oximes, there could be at least four important structural factors affecting their toxicity, including the number of oxime groups in the molecule, the position of oxime group(s) on pyridinium ring, the length of carbon linker, and the substitution by oxygen or insertion of the double bond into the connection chain. The cytotoxicity of tested substances was measured using colorimetric 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide assay (MTT assay) in SH-SY5Y cell line. Toxicity was expressed as toxicological index IC_{50} . The tested compounds showed different cytotoxicity ranging from 1.5 to 27 mM. K027 was the least, and methoxime was the most toxic reactivator. The lowest toxicity was found in a monopyridinium reactivator and bispyridinium reactivators with simple 3C carbon linker. Shortening of connection chain length to 1C, incorporation of oxygen moiety into 3C compounds, elongation of carbon linker to 4C and insertion of a double bond into 4C substances increase AChE reactivators' cytotoxicity. Acknowledgements: This work was supported by a long-term organization development plan Medical Aspects of Weapons of Mass Destruction of the Faculty of Military Health Sciences, University of Defence.

Keywords : acetylcholinesterase, cytotoxicity, organophosphorus poisoning, reactivators of acetylcholinesterase

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