



A Toxidromic Approach for Chemical Medical Countermeasure Development

Chlorinated Oximes for High and Efficient Reactivation of Acetylcholinesterase and Butyrylcholinesterase Inhibited by Sarin and VX

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The cholinesterase reactivators (so called "oximes") are used as causal antidotes in case of organophosphorus intoxications. The oxime moiety in the form of oximate anion is crucial factor for effective reactivation of cholinesterases. Recently, the chlorinated oximes were introduced to increase the formation of oximate formation and thus for effective reactivation [1]. The chlorinated oximes were found to be highly efficient reactivators of phosphorylated acetylcholinesterase when compared to pralidoxime and asoxime (HI-6) [1]. Moreover, the chlorinated oximes were found to be efficient reactivators of phosphorylated butyrylcholinesterase when compared to pralidoxime and asoxime [2]. The best compound K868 was able to reactivate phosphorylated acetylcholinesterase up to 100% in 10 minutes. The same chlorinated oximes was able to reactivate phosphorylated butyrylcholinesterase up to 100% in 10 min. K868 was proved to be able to scavenge various organophosphates in human whole blood samples. The chlorinated oximes seem to be improvement of standard oximes with excellent or high reactivation rate in vitro and are recently subjected to in vivo experiments. [1] Zorbaz, T et al. J. Med. Chem. 2018, 61, 10753. DOI: 10.1021/acs.jmedchem.8b01398 [2] Zorbaz, T. et al. Chem Biol Interact. 2019, 307, 16. DOI: 10.1016/j.cbi.2019.04.020