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MEETING ABSTRACTS

COMBINATION OF OXIMES WITH OVERLAPPING REACTIVATION SPECTRA: OBIDOXIME AND HI-6

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Despite extensive oxime research in the last 60 years pralidoxime is still the standard oxime in e.g. United States, British and French forces and obidoxime standard therapy for OP poisoning in several European countries. Oxime research focusses on highly potent oximes with activity against selected nerve agents, broad-spectrum oximes with activity against relevant nerve agents and centrally active (non-)oximes but virtually no compound brought significant improvements compared to the established obidoxime and pralidoxime. In the US MMB-4 is sought to replace pralidoxime and in Germany, France, UK, Canada and other European countries HI-6 is in advanced development for use as nerve agent antidote. Yet, both compounds are not considered as broad-spectrum antidotes and as a mid-term solution combinations of oximes in service with overlapping reactivation potency e.g. obidoxime and HI-6 have been proposed. We here set out to analyze the combination of obidoxime and HI-6 in both a static and dynamic model against poisoning with nerve agents and organophosphorus compound pesticides *in vitro*. In a cuvette based system the combination of HI-6 and obidoxime both 30 µM for sarin-, cyclosarin-, tabun-, VX- and paraoxon-inhibited human AChE did not result in an impaired reactivation compared to the sole use of both oximes but in a broadened spectrum. Similar results were gained with a dynamic model allowing simulation of nerve agent and pesticide toxicokinetics and oxime pharmacokinetics resembling *in vivo* conditions. Additional experiments in species closely related to humans e.g. swine are necessary to analyse a potential benefit *in vivo*.

Keywords: HI-6; obidoxime; reactivation; nerve agents; pesticides