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MEETING ABSTRACTS

THEORETICAL ASSESSMENT OF THE PERFORMANCES OF COMMERCIAL OXIMES ON THE REACTIVATION OF ACETYLCHOLINESTERASE INHIBITED BY THE NERVE AGENT A-242

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The nerve agents of the A-series are relatively recent chemical weapons with no antidote available yet (1). Once inside the human body, those chemicals act similarly to the classic nerve agents, by binding to the catalytic residue Serine 203 (Ser203) of human acetylcholinesterase (*Hss*AChE) and thus preventing the proper function of this enzyme. However, there is no experimental evidence yet if the current antidotes for intoxication by nerve agents are also capable of restoring AChE inhibited by the nerve agents of the A-series. In order to launch some light on this issue, we used computational techniques (molecular docking, molecular dynamics and MM-PBSA interaction energy calculations) to assess the performances of the four currently available commercial oximes (2-PAM, HI-6, obidoxime and trimedoxime) when in contact with *Hss*AChE inhibited by the agent A-242 (2). Based on the near-attack conformation (NAC) criterion, our results suggest that the commercial oximes would have limited efficacy to reactivate the enzyme since they are not able to properly approach the adduct Ser203-A-242. Among those oximes, trimedoxime seems to be the most promising, since it showed lower values of energy in the MM-PBSA calculations, a higher stability inside the catalytic anionic center (CAS) of HssAChE and was able to adopt a position closer to the NAC that could enable the reactivation mechanism.

Keywords: A-series nerve agents; A-242; Commercial oximes; Near-attack conformation

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