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MEETING ABSTRACTS

NEAR ATTACK CONFORMATION APPROACH FOR MOLECULAR MODELING STUDIES UPON THE PROPHYLACTIC AGENT 7-METHOXYTACRINE-4-PYRIDINEALDOXIME HYBRID COMPARED WITH OTHER REACTIVATORS OF VX-INHIBITED *Hss*AChE

Jorge Alberto Valle da Silva [1], Eugenie Nepovimova [2], Kamil Kuča [3], Teodorico Castro Ramalho [3,4], Tanos Celmar Costa França [1, 3]
Presenting author: Tanos Celmar Costa França [1,3]

[1] Laboratory of Molecular Modeling Applied to the Chemical and Biological Defense (LMCBD), Military Institute of Engineering, Rio de Janeiro/RJ, Brazil;
[2] Biomedical Research Centre, University Hospital Hradec Kralove, Czech Republic;
[3] Center for Basic and Applied Research, Faculty of Informatics and Management, University of Hradec Kralove, Hradec Kralove, Czech Republic.
[4] Laboratory of Molecular Modeling, Chemistry Department, Federal University of Lavras, Lavras, MG, Brazil

The novel 7-methoxytacrine-4-pyridinealdoxime agent, named hybrid 5C, is a hybrid compound comprised of a linkage between 7-methoxytacrine (7-MEOTA-4-PA) and reactivator 4-pyridinealdoxime (4-PA) moieties through a 5-carbon length-spacer. This compound was formerly designed as a prophylactic agent for intoxication by organophosphates (OP), able to form a complex with acetylcholinesterase (AChE) and reactivate this enzyme in case of OP inhibition. In order to check if the 5 carbons spacer is the ideal to maximize the interactions of this compound inside AChE, we performed in this work docking, molecular dynamics and mmpbsa studies on a series of analogues of hybrid 5C, varying the spacer-length from 1 to 10 carbons long. Our results helped to elucidate the interactions of these compounds with the different binding sites inside human AChE (*Hss*AChE) and pointed to the 4 and 5 carbons long as the best spacers for optimizing these interactions.

Keywords: Acetylcholinesterase; molecular modeling; aldoxime; 7-MEOTA-4-PA

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