

## MEETING ABSTRACTS

# REACTIVATION OF ACETYLCHOLINESTERASE INHIBITED BY NOVICHOK AGENTS – A COMPUTATIONAL STUDY

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Novichoks are a set of militarily abused substances from the group of nerve agents. The mechanism of their action is the covalent binding to Ser203 of acetylcholinesterase and inhibition of acetylcholine degradation. Any *in vitro* or *in vivo* experimental studies of novice-inhibited acetylcholinesterase reactivation have not been published yet (1). However, the possibilities of reactivation can also be investigated computationally. For this study, we used the methods of molecular docking in combination with molecular dynamics.

We hypothesized that reactivation of novichok-inhibited acetylcholinesterase is not possible for steric reasons. In the molecular modeling study, we investigated whether the oxime group of reactivators can get close enough to the active site to make the nucleophilic attack. Calculations were performed for commercial oximes (HI6, obidoxime, pralidoxime etc.) and also for new experimental ones, in total 60 reactivators.

We have found out that some of the reactivators can adopt a position close to the active site and the nucleophilic attack is possible. Our original hypothesis was refuted.

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*Keywords: acetylcholinesterase; in silico; nerve agent; novichok; oximes*

## References

1. Santos MC, Botelho FD, Gonçalves AS, Kuca K, Nepovimova E, Cavalcante SFA, et al. Theoretical assessment of the performances of commercial oximes on the reactivation of acetylcholinesterase inhibited by the nerve agent A-242 (Novichok). Food and Chemical Toxicology. 2022;165:113084.