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MEETING ABSTRACTS

IN SILICO SCREENING OF NOVEL BChE-REACTIVATORS

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Several years, there are ideas how to use reactivators of BChE in prophylaxis of OP-poisoning. They could be applied in combination with human BChE as a pseudo-catalytic scavenging system. However, the effective hBChE reactivator is still missing.

The aim of this project is to find highly active and plausibly universal reactivator of hBChE. In the first phase, a database of about 6 mil. structures (ZINC Lead Like) was screened by rigid molecular docking. The receptor (hBChE) was found in the PDB database (pdb code 3DJY, hBChE inhibited by tabun) and prepared for docking. For the second phase, over one hundred molecules were selected. These structures were docked to hBChE with flexible residues within the active site. After manual inspection, over twenty molecules were chosen. Such molecules were modified (e.g. addition of oxime moiety, pKa optimization) and redocked to hBChE with flexible residues. Finally, two novel compounds were recommended for synthesis. The newly designed compounds will be further synthesized and evaluated on the model of OP-inhibited hBChE and hAChE. They could be used for development of new series of hBChE reactivators.

Keywords: butyrylcholinesterase; BChE; oxime; reactivator; pseudo-catalytic scavenger

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