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# Discovery of non-oxime reactivators using an *in silico* pharmacophore model of oxime reactivators for tabun-inhibited acetylcholinesterase

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We earlier reported an in silico pharmacophore model for reactivation of oximes to tabun-inhibited AChE. Since DFP (diisopropylfluorophosphate) like tabun is a G-agent simulator, we utilized the model as a rational strategy for discovery of OP-inhibited reactivators and present here a discovery of twelve non-oxime reactivators of DFP (diisopropylfluorophosphate)-inhibited acetylcholinesterase (AChE). The non-oximes were obtained through virtual screening of an in-house database that showed rate constant (kr) efficacy values within ten-fold of pralidoxime (2-PAM) in an in vitro assay and one of them showed in vivo efficacy comparable to 2-PAM against brain symptoms for DFP-induced neuropathology in guinea pigs. Short listing of the identified compounds were performed on the basis of fit score to the pharmacophore model, conformational energy requirement for the fit, and in silico evaluations for favorable blood brain barrier penetrability, octanol-water partition (log P), toxicity (rat oral LD 50) and binding affinity to the active site of the crystal structure of inhibited AChE.

**Keywords:** *In silico* pharmacophore model, Virtual screening, WRAIR-CIS database, Non-oxime reactivators, DFP-inhibited AChE.

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