

## MEETING ABSTRACTS

***IN SILICO* AND *IN VITRO* EVALUATION OF TWO NOVEL  
OXIMES K456 AND K733 AGAINST PARAOXON INHIBITED  
HUMAN ACETYLCHOLINESTERASE AND  
BUTYRYLCHOLINESTERASE**

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Organophosphorus compounds (OPs) irreversibly inhibit cholinesterases: acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). There is wide variety of applications of OP compounds including warfare chemicals and pesticides. Oxime-type reactivators are used to reactivate the OP inhibited AChE and BChE. Present study was aimed to evaluate the reactivation potency of two novel oximes K456 and K733 against organophosphate inhibited AChE and BChE. Efficacy was compared with K27 and pralidoxime (2-PAM). Molecular mechanism of reactivation by the oximes is predicted by *In silico* method. Intrinsic toxicity of novel oximes in term of IC<sub>50</sub> and 50 % reactivation of inhibited enzymes (R<sub>50</sub>) were evaluated by *in vitro* methods using human RBC-AChE and plasma BChE. *In silico* study revealed lower free binding energies, but novel oximes did not bind with catalytic anionic site of enzymes. *In vitro* studies showed higher intrinsic toxicity by K456 and K733 than K27 and pralidoxime. R50 for human RBC-AChE were K456=203.59µM±66.96; K733= 405.55µM±67.36; K27=2.68µM±0.98 and pralidoxime 30.71µM±5.10 (mean±SEM) respectively. No substantial reactivation in BChE was noted by tested concentration of novel oximes. The study concludes that oximes with peripheral binding/far from catalytic anionic site are ineffective reactivators. K27 with central (inside the active gorge) binding was superior to all tested oximes.

**Keywords:** Paraoxon; oxime; molecular docking; K456; K733; K27; pralidoxime