

ABSTRACT

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Title of diploma thesis: Synthesis and biological evaluation of novel uncharged cholinesterase reactivator against nerve agent intoxication

Nerve agents (NPL) and pesticides are strongly toxic organophosphorus compounds with high affinity to acetylcholinesterase (AChE) enzyme. This enzyme is present in CNS and neuromuscular synapses. The intoxication leads into an acute cholinergic crisis, which can ultimately result into death. The therapy must be quick and includes application of atropine, reactivators of AChE and diazepam. Among the commonly used AChE reactivators, mono- or bis- quaternary aldoximes can be found. These compounds are permanently charged, so their penetration through the blood-brain barrier (HEB) is very limited (up to 10 %, often only 1-3 %).

Within the diploma thesis, a non quaternary AChE reactivator has been developed by multiple-steps synthesis approach. This compound, denoted as **K1396**, would exert high ability to penetrate through HEB. *In vitro* assessments of his capability to reactivate AChE has been carried out by method of Ellman. Under *in vitro* conditions, AChE was initially exposed either to different NPL (sarin, tabun and VX) or various pesticides (dichlorvos, paraoxon). The efficiency of reactivation has been validated using two different concentrations – 10 and 100 μ M. The activity of the new non-quaternary reactivator was compared with standard AChE oxime reactivators – obidoxim and pralidoxim.

To conclude, **K1396** achieved better reactivation AChE ability for dichlorvos, sarine and the VX agent compared to obidoxim and pralidoxim.