ABSTRACT:

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Title of Diploma Thesis: Synthesis of novel acetylcholinesterase reactivators of isoquinolinic type

Organophosphates are worldwide the most common cause of poisoning, whether in the field of agriculture, attempted suicide, accidental contact or abuse as organophosphorus nerve agents. They can be absorbed by all paths - inhaled, ingest or by transdermal penetration. For over 50 years the only causal antidotes on the market have been acetylcholinesterase reactivators. However, bioavailability is inadequate, therapy is ineffective, and there is no broad-spectrum reactivator able to efficiently restore AChE activity after intoxication by different types of organophosphates.

All available reactivators are charged oximes with one or two pyridinium rings. These are pralidoxime, methoxime, trimedoxime, obidoxime, HI-6 and Hlö-7. Effective structure require functional oxime group (R-CH = NOH) which is able to bind the organophosphate agent from enzyme and restore its function.

In this thesis, we focused on preparation, identifying structure and specifying physical and chemical properties of new analogues to pyridinium oximes. These structures are monoquaternary isoquinoline salt, C_3-C_{12} bis-quaternary isoquinoline salts, C_3-C_5 bis-quaternary isoquinoline-isonicotinamide salts and the bis-quaternary isoquinoline salt with oxapropyl chain. These compounds are supposed to be potential new reactive acetylcholinesterase.