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MEETING ABSTRACTS

NOVEL MODIFIED PRALIDOXIME DERIVATES AS POTENTIAL REACTIVATORS OF ORGANOPHOSPHATE-INHIBITED CHOLINESTERASES

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Acetylcholinesterase (AChE) oxime reactivators are used as antidotes to organophosphate (OP) poisoning, while butyrylcholinesterase (BChE) reactivators are suitable for pseudocatalytic uptake of OP. OP acts as irreversible inhibitors of AChE. Due to the inhibition of AChE OPs cause impairment of cholinergic functions, which can lead to the death of the organism (1). The modification of the already known structure of pralidoxime aims primarily at overcoming the problems associated with physicochemical properties. The disadvantage of quaternary pyridinium oximes, which have a permanently positive charge, is poor penetration across the blood-brain barrier (BBB), which makes them ineffective in the central nervous system (2). Introducing a substituent that could contribute to increased lipophilicity, may thus provide better penetration into BBB. At the same time, a substituent in a suitable position relative to the oxime group on the pyridinium ring can reduce its pK_a value and thus lead to easier formation of the oximate anion, which is important for the ability to reactivate inhibited cholinesterase (3). The aim of this work is to synthesize oxime reactivators derived from the structure of pralidoxime, determine their stability and pK_a values. Finally, the new derivatives will be measured *in vitro* for their ability to reactivate OP-inhibited cholinesterases.

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Keywords: pralidoxime; acetylcholinesterase; butyrylcholinesterase; organophosphate

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