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MEETING ABSTRACTS

INHIBITION OF HUMAN ACETYLCHOLINESTERASE AND BUTYRYLCHOLINESTERASE BY METHYLENE VIOLET 3RAX

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Cholinesterases are divided into two classes according to differences in substrate specificity, behaviour in high substrate concentrations, inhibitor sensitivity and tissue distribution: acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). The both enzymes are sensitive to broad spectrum of molecules and may be inhibited by several compounds, such as organophosphate and carbamate pesticides or nerve agents. In a previous study, a phenazine-derived natural product, geranyl-phenazine-diol was shown to inhibit human AChE with IC50 value of 2.62 µM. Phenazines which are naturally produced by bacteria and archaeal *Methanosarcina* species are nitrogen containing tricyclic molecules with antibiotic, antitumor, and antiparasitic activities. Phenazines are used as electron acceptors-donors in wide range of fields including environmental biosensors.

In this study, the inhibitory effect of a synthetic phenazine dye, methylene violet 3RAX (also known as diethyl safranine) was tested on human erythrocyte AChE and human plasma BChE and its inhibitory mechanism on both enzymes was studied in detail. AChE and BChE activities were assayed spectrophotometrically at 25 oC in 50 mM MOPS buffer pH 8, using 0.05-0.4 mM butyrylthiocholine or 0.025-0.4 mM acetylthiocholine as substrate, 0.125 mM DTNB and 0-80 µM dye. Kinetic analyses showed that methylene violet 3RAX acts as a hyperbolic noncompetitive inhibitor of AChE with Ki value of 1.42±0.09 µM; α=1 β=0.11. On the other hand, it caused linear competitive inhibition of BChE with K_i value of 0.46±0.02 µM; $\alpha=\infty$. In conclusion, methylene violet 3RAX with K_i value in the low micromolar range may be a promising lead candidate for the treatment of Alzheimer's disease.

Keywords: Acetylcholinesterase; butyrylcholinesterase; methylene violet 3RAX; cholinesterase inhibition