MMSL
Military Medical
Science Letters
Since 1925

Mil. Med. Sci. Lett. (Voj. Zdrav. Listy) 2018, 87(supplementum 1)
ISSN 2571-113X (Online)

MEETING ABSTRACTS

PHENYL VALERATE ESTERASE ACTIVITY OF HUMAN CHOLINESTERASES

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The toxicity of organophosphorus compounds (OPs) cannot be explained only by action on acetylcholinesterase or neuropathy target esterase (NTE). A fraction of the membrane bound phenylvalerate esterase activity (PVase) is associated to NTE, the key initiating molecular event in the OP-induced delayed neuropathy (OPIDN). An enzymatic fraction in chicken brain soluble PVase has been reported to be due to a butyrylcholinesterase protein, and we suggested that this enzymatic fraction could be related to the mode of action of the potentiation/promotion phenomenon of the OPIDN. We showed that human butyrylcholinesterase (hBuChE) shows PVase activity. Mipafox, iso-OMPA or PMSF inhibited both activities with similar kinetic constants for both activities. Moreover, the substrates acethylthiocholine and phenyl valerate showed competition in their activities. The results suggest that both activities are related to the same active center.

This work studies in depth the kinetic interactions between phenyl valerate and acetylthiocholine in human butyrylcholinesterase, showing that the interactions are different to the competitive model of substrates according to the Michaelis-Menten reaction. The approach introduced in this work suggests that other site could be involved in the interaction with phenyl valerate.

In addition, we have observed that human acetylcholinesterase has also phenyl valerate esterase activity, but with lower activity than human butyrylcholinesterase. The level of phenylvalerate esterase activity in cholinesterases depends on the species and the type of cholinesterase. Further evaluation of the molecular interactions is under study.