Kinetics of 13 New Cholinesterase Inhibitors

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Kinetics of hydrolysis of acetylcholine and acetylthiocholine by two types of acetylcholinesterase and butyrylcholinesterase inhibited by 13 new inhibitors (5 carbamates and 8 carbazates – hydrazinium derivatives) was measured *in vitro* in a batch reactor at 25 °C, pH 8, ionic strength 0.11 M and enzyme activity 3.5 U by four nondependent analytical methods. Sevin®, rivastigmin (Exelon®) and galantamin (Reminyl®) served as comparative inhibiting standards. Kinetics of hydrolyses inhibited by all studied carbamates, sevin, carbazates (with exceptions) and rivastigmin (with exceptions) can be simulated by the competitive inhibition model with irreversible reaction between enzyme and inhibitor. Galantamin does not fulfil this model. In positive simulations, the value of inhibition (carbamoylation) rate constant k_3 was calculated, describing the reaction velocity between the given enzyme and inhibitor. Physiologically important hydrolyses of acetylcholine catalyzed by acetylcholinesterase from electric eel or bovine erythrocytes and butyrylcholinesterase from horse plasma can be most quickly inhibited by carbamoylation of the mentioned enzymes by the 3-*N,N*-diethylaminophenyl-*N′*-(1-alkyl) carbamates **4** and **5**. Probably this is due to a long enough hydrocarbon aliphatic substituent (hexyl and octyl) on the amidic nitrogen atom. The tested carbazates failed as inhibitors of cholinesterases. The regeneration ability of the inhibited enzymes was not measured.

Key words: Cholinesterases, Inhibition, Kinetics