Abstract

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This work focuses on the preparation of peripherally acting AChE inhibitors as a potential treatment of myasthenia gravis. These compounds could also be used as a pre-treatment of poisoning by organophosphorus AChE inhibitors. They can occupy the active site of an enzyme making it inaccessible for irreversible inhibitors. Compounds used in this indication should fulfill these requirements: inhibit efficiently AChE (standards currently used in the treatment were chosen for the comparison of the inhibitory efficacy), have selective effect on AChE and not to cross the blood-brain barrier in order to lower the possible side effects.

Six series of bisquaternary compounds were prepared. Their inhibitory ability was determined *in vitro* against human erythrocyte or recombinant AChE and human plasmatic BChE. According to inhibitory ability values acquired, a structure - activity relationships were investigated in every series. A few compounds with significant affinity towards AChE were found. These most promising compounds were further examined in kinetic tests and a non-competitive type of inhibition was confirmed. In the docking studies, many interactions of the compounds and amino acid residues in the active site of the enzyme were observed. Three compounds were also chosen for *in vivo* determination of the acute toxicity and the ability to work as a pre-treatment against soman poisoning. Compared to prophylactic efficacy of pyridostigmine, these compounds however showed no significant tendency to protect AChE against organophosphorus inhibitor. No influence on the efficacy of the subsequent antidote treatment was either observed.