

Comparison of Index pI_{50} of New Cholinesterase Inhibitors with Rivastigmine and Galanthamine

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The aim of the research was to find a suitable inhibitor decreasing the concentration and/or activity of acetylcholine esterase (ACHE) and/or butyrylcholinesterase (BCHE) and to compare its inhibiting power with the drugs for Alzheimer disease (AD) treatment already in use.

The inhibiting power of chosen carbamates and carbazates owing to the hydrolysis of acetylthiocholine by butyrylcholinesterase or acetylcholinesterase was tested. The force of every substance (I) inhibiting an enzyme can be approximately evaluated by its index pI_{50} , i.e. the negative logarithm of the concentration of I producing the 50% inhibition (pI_{50}) of the enzyme activity under given conditions. For determination of pI_{50} the spectrophotometric Ellman's method was used.

Recently only four remedies for AD treatment with different inhibiting action are worldwide allowed, the most important of whom, rivastigmine (Exelon®), is the cholinesterase carbamate inhibitor with dual effect on brain ACHE and brain BCHE. According to this knowledge we have focused our study to the N'-monoalkyl- of 3-N,N-diethylaminophenol (carbamates) and chlorine derivates of 2-phenoxy-carbonyl-2-methylhydrazinium-chloride and 2-phenoxy-carbonyl-1,2-dimethylhydrazinium-chloride (carbazates), which showed similar inhibiting action as rivastigmine.

All tested substances showed anticholinesterase activity. The determined values of pI_{50} of the tested substances were compared with pI_{50} of the commercially used drugs for the Alzheimer disease treatment – rivastigmine and galanthamine. According to the pI_{50} indices, the tested carbamates are equally or more effective inhibitors of the used esterases in comparison with the currently used drugs. But their pI_{50} values are not dramatically greater than pI_{50} of the compared drugs. The tested carbazates appeared, according to the same criteria, as less effective inhibitors of the used esterases than these drugs.

The most active substances have inhibiting coefficient pI_{50} for ACHE in an interval 4.8 – 6.2 and 5.5 – 6.9 for BCHE. The value of pI_{50} for rivastigmine is 3.70 for ACHE and 4.75 for BCHE.