Abstract

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Title of diploma thesis: Measurement of the efficacy of new acetylcholinesterase inhibitors using the Ellman method

Cholinesterases (ChEs) belong to an important group of enzymes in our body. The best known acetylcholinesterase and butyrylcholinesterase play an important role in the treatment of many diseases, including Alzheimer's disease (AD). It is a neurodegenerative disease that occurs mainly in the elderly. It is one of the most common forms of dementia and its incidence is still increasing. To date, no effective therapy for AD has been developed, only symptomatic treatment is available. It is therefore necessary to look for therapeutics that would be able to stop or cure this serious disease.

The aim of this work was to determine the inhibitory contraction of newly synthesized potential drugs AD against both ChEs. A total of 27 tacrine derivatives were tested, which were enriched with substituents ensuring lower toxicity and better penetration into the brain. The inhibitory potential of the test substances was determined spectrophotometrically using the Ellman method.

The results of inhibitory activity were influenced by both, the number and the type of functional groups attached. However, most of the test substances did not show a higher inhibitory potential compared to the corresponding standard. The best inhibitory results were

obtained by chlorine-substituted derivatives in position 5 of the aminoquinoline skeleton. Increasing the number of chlorine atoms in the molecule reduces the inhibitory potential.

The most suitable candidate for further testing in the search for an effective potential drug for AD appears to be LG 624, which showed the highest inhibitory activity against AChE (IC_{50} = 34 nM) and against BChE (IC_{50} = 62 nM) of all tested substances.