HPLC STUDY OF BLOOD-BRAIN BARRIER PENETRATION OF TWO ACETYLCHOLINESTERASE INHIBITORS - TACRINE AND 7-MEOTA AFTER ORAL ADMINISTRATION IN RATS

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The Alzheimer disease is a slowly progressive neuropsychiatric illness of unknown etiology. This illness is characterized by a progressive loss of cognitive ability and other intellectual functions. The most surveyed neurochemical imbalance is a deficit of enzyme choline acetyltransferase (EC 2.3.1.6) in brain, enzyme malfunction leads to impairment of acetylcholine synthesis, an important neurotransmitter. The lower level of acetylcholine in synapses may be increased by inhibition of enzyme acetylcholinesterase (AChE; EC 3.1.1.7). The AChE inhibitors remain the key drugs in the treatment of Alzheimer disease.

In the present study, basic information about two AChE inhibitors, tacrine and its derivate 7-MEOTA (7-methoxytacrine) was characterized. 7-MEOTA is a potent, centrally active cholinesterase inhibitor with severalfold lower acute toxicity when compared to tacrine. 7-MEOTA also does not influence cognitive functions of treated animals.

Both tested AChE inhibitors were applied orally in equimolar doses. These doses correspond with therapeutic dose (5 % LD₅₀) of tacrine. 7-MEOTA was also applied in its therapeutic dose (37.65 mg/kg). Following oral administration of tacrine equimolar doses (5.15 mg/kg) and 7-MEOTA (5.01 mg/kg) the distribution thru the blood-brain barrier was different. Tacrine brain concentration was relatively high (57.13 ± 23.03 ng/ml), but the 7-MEOTA brain concentration after application of equimolar dose was significantly lower (5.56 ± 2.46 ng/ml). Levels of both AChE inhibitors in the brain tissue were comparable only if the 7-MEOTA was applied in its therapeutic dose. The brain concentration of 7-MEOTA was 52.59 ±16.80 ng/ml.