ABSTRACT

Alzheimer's disease is a severe neurodegenerative disorder connected with neuronal death, brain tissue loss and functional disruption of the cholinergic system. Pathophysiological changes are manifested especially as deterioration of memory and other cognitive functions. Current treatment consists mainly of pro-cognitive drugs – acetylcholinesterase inhibitors (previously - tacrine, today - donepezil, rivastigmine and galantamine) and NMDA (N-methyl-D-aspartate) antagonist memantine which can delay the disease progression. The aim of this study was to evaluate the therapeutic effect of three selected acetylcholinesterase inhibitors - tacrine, rivastigmine and donapezil on pharmacologically induced cognitive disorder in rats. As an amnesic drug, 3-quinuclidinyl benzilate was used and the effect of selected inhibitors was investigated using two different behavioral methods - water maze and passive avoidance test. The method of the water maze was focused on the study of spatial orientation, while the passive avoidance test belong to the methods of emotional learning. Selected tests were based on different principles and target structures of the brain so their combination allowed us more comprehensive investigation. Best results were achieved with rivastigmine which was effective in both tests probably due to its properties such as dual
inhibition effect (inhibition of acetylcholinesterase and butyrylcholinesterase) which favorize rivastigmine against both other drugs. Weakest effect showed tacrine which acts primarily in the periphery than in the central nervous system (especially higher affinity to butyrylcholinesterase). Donepezil showed promising activity in the water maze, but there was no significant effect in the passive avoidance test (higher affinity to acetylcholinesterase).