ABSTRACT

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Alzheimer's disease (AD) is a neurodegenerative disorder of complex etiology, with insidious progression and fatal consequences. Its global incidence rates are very high, rising in line with the aging population. AD is manifested as a progressive decline of cognitive and intellectual functions. Histopathological hallmarks include the presence of β-amyloid neuritic plaques, neurofibrillary tangles composed of hyperphosphorylated τ protein and atrophy of brain tissue. Neurotransmitter levels are decreased in case of acetylcholine (ACh) while glutamate levels are elevated. Nowadays, there are two pharmacological groups employed in the treatment of AD: acetylcholinesterase inhibitors (AChEIs) and antagonist of *N*-methyl-D-aspartate receptors (NMDARs) – memantine. Both groups act only symptomatically, not having disease-modifying effect. The aim of our study was preparation of a series of novel hybrid molecules combining AChEIs, namely tacrine, 7-methoxytacrine and 6-chlorotacrine, with molecule BQCA – positive allosteric modulator of M1 subtype of muscarinic ACh receptors (mAChRs). Inhibitory effectiveness of the newly synthetized compounds against cholinesterases (ChEs) was determined *in vitro* by the Ellman´s colorimetric method and expressed as IC_{50}. The effect on mAChRs was determined by measurement of intracellular calcium concentration using fluorescent indicator. The results proved the ability of newly synthesized molecules to inhibit ChEs in the micromolar and sub-micromolar IC_{50} values, with antagonist activity towards M1 mAChRs.