SYNTHESIS AND IN VITRO EVALUATION OF N-ALKYL-7-METHOXYTACRINE HYDROCHLORIDES AS POTENTIAL ANTI-ALZHEIMER’S DISEASE AGENTS

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All drugs approved for Alzheimer’s disease (AD) in clinical practice ameliorate the symptoms of the disease. Among them, acetylcholinesterase inhibitors (AChEIs) are used to increase the cholinergic activity [1]. Among them, tacrine was found to be the most toxic and due to this it was withdrawn from the market. On the contrary, tacrine low-toxic derivative called 7-MEOTA (9-amino-7-methoxy-1,2,3,4-tetrahydroacridine) was found to be appropriate candidate for human use [2].

Thanks to this, series of 7-MEOTA analogues (N-alkyl-7-methoxytacrine) were synthesized using standard synthetic approaches within last few years. Afterwards, their ability to inhibit cholinesterases (AChE and BuChE) was evaluated on recombinant human acetylcholinesterase (hAChE) and plasmatic human butryrycholinesterase (hBChE).

Three novel 7-MEOTA derivatives showed promising results towards hAChE if compared with standards - tacrine or 7-MEOTA. Three other compounds resulted as potent inhibitors of hBChE. According to structure-activity relationship study, C⁶-C⁷ N-alkyl chains exert the highest cholinesterase inhibition [3,4].

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