

Design, synthesis, and evaluation of 3-(benzylpyridinium-4-yl-methylene) oxindole derivatives as AChE inhibitor

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Background and Aims: Alzheimer's disease (AD) is one of the most severe health problems of the aged which is a progressive neurodegenerative disease characterized by a loss of cognitive function and behavioral abnormalities. Decrease of acetylcholine level in the hippocampus and cortex is the one of the most important causes of AD, therefore some of acetylcholinesterase inhibitors (AChEI) are effective agents for treatment of AD's symptoms. AChE inhibitors are the first and the most developed group of drugs approved for AD symptomatic treatment, such as tacrine, donepezil, rivastigmine, huperzine, pyrimidines, and galanthamine. In this work, we have focused on designing compounds with potential ability of interaction towards both binding sites on AChE.

Methods: In an attempt to find novel series of AChEI, a series of oxindole derivatives with benzylpyridinium moiety have been synthesized as novel and potent compounds for this purpose. At the first step for synthesis of these derivatives, oxindole and pyridine-4-carbaldehyde in the presence of p-toluenesulfonic acid (PTSA) was refluxed to obtain 3-(pyridine-4-yl-methylene)oxindole derivatives. In the second step, the latter compounds reacted with benzyl chloride derivatives in toluene under reflux for 8-12 hours. They were tested for their inhibitory activity toward acetylcholinesterase using colorimetric Ellman's method.

Results and Conclusions: In this study some new derivatives of the oxindole were synthesized and tested for their inhibitory activity toward acetylcholinesterase. It was revealed that some synthesized compounds exhibited high anticholinesterase activity.

Keywords: Alzheimer's disease; Cholinesterase inhibitor; Oxindole; Pyridine-4-carbaldehyde