Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

New pantacyclic tacrines as potent acetylcholinesterase inhibitors

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Background and Aims: Importance of cholinesterase inhibition as a promising strategy for the treatment of Alzheimer, senile dementia, ataxia, and Parkinson's disease has spurred the development of numerous structural classes of compounds. Tacrine, a potent and reversible AChE inhibitor, was the first drug approved in the USA for the palliative treatment of AD; however, it exhibited side effects like hepatotoxicity. Current research is focused on developing new AChE inhibitors with improved activity and reduced adverse side effects of Tacrine.
Methods: In this context, we designed and synthesized new series of pantacyclic derivatives which could be easily prepared by the AlCl3 promoted Friedla¨nder reaction between the corresponding, known dihydropyrano[c]chromenes and cyclohexanone. Corresponding 2-amino-3-cyano dihydropyrano[c]chromenes were easily prepared with simple treatment of 4-hydroxycoumarin with malononitrile and various benzyl halides.
Results: The anticholinesterase activity of synthesized compounds was measured using colorimetric Ellman's method. A significant AChE inhibitory activity was observed for most of these synthesized compounds.
Conclusions: In this work we've synthesized a new series of pyrannocumarin fused to tacrine as pantacyclic heterocyclic as novel acetylcholinesterase inhibitors. Assuming biological data showed high inhibitory activity against acetyl cholinesterase enzyme with IC50 values within pico and nano molar ranges.

Keywords: Acetylcholinesterase inhibitors; Pyrannocumarin; Tacrine; Ellman's method