O-Pentyne and Morpholine/Piperidine Ethyl Substituted Pyrimidines as Anti-Alzheimer’s Agents

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ABSTRACT: Alzheimer’s disease (AD) is an irreversible neurodegenerative disorder. It is characterized by the impairment in memory and cognitive dysfunctioning. The neuropathological hallmarks of AD are decreased acetylcholine (Ach) levels in brain, increased reactive oxygen species (ROS) and deposition of amyloid beta. The exact pathogenesis of AD is still not clear. In AD there is hyperactivity of acetylcholinesterase (AchE) and monoamine oxidase –B (MAO-B), which leads to decreased Ach and increased ROS levels respectively. So, AchE and MAO-B are the potential therapeutic targets for the treatment of AD. Simultaneous inhibition of these target enzymes with a single molecule can be a beneficial therapeutic strategy. A total of 9 multi-targeted compounds are designed and synthesized using hybrid molecular approach and two pharmacophores are incorporated on the pyrimidine nucleus. The in-silico studies of these compounds revealed that the compound DEV-28 possess potent AchE and MAO-B inhibitory properties. © 2019 iGlobal Research and Publishing Foundation. All rights reserved.