Abstract

Toward an Innovative Treatment of Alzheimer’s Disease: Design of MTDLs Targeting Acetylcholinesterase and α-7 Nicotinic Receptors †

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Abstract: Alzheimer’s disease (AD) is a complex and progressive neurodegenerative disorder. The available therapy is limited to symptomatic treatment, and its efficacy remains unsatisfactory. In view of the prevalence and expected increase in the incidence of AD, the development of an effective therapy is crucial for public health. Since the therapeutic paradigm “one compound–one-target” has shown its limits in the treatment of AD, new strategies are emerging to overcome the lack of efficiency of the current pharmacotherapy in the past decade. The most promising is the multitarget-directed ligands (MTDLs) strategy. This project consists of the development of new multifunctional agents, which will act simultaneously on the different players in AD pathology by combining an AChE inhibitory activity based on the structures of a well-known AChE inhibitor (Rivastigmine) with an α-7 nAChR activation. Indeed, nAChRs were recently put forward as potential targets for the treatment of central nervous system (CNS) diseases, such as AD. Because of their distribution and abundance in the CNS, the α-7 subtypes are potential therapeutic targets for this disorder.

Keywords: Alzheimer’s disease; Multitarget-Directed Ligand; AChE inhibitor; α-7 nAChR agonist

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