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MEETING ABSTRACTS

7-MEOTA-DONEPEZIL HYBRIDS: POTENTIAL CHOLINESTERASE INHIBITORS FOR THE TREATMENT OF ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is a devastating neurodegenerative disorder characterized by a severe, progressive loss of memory. Currently, AD therapy is limited on the administration of cholinesterase inhibitors (ChEIs) and the N-methyl-D-aspartate (NMDA) antagonist, memantine. Tacrine as the first registered acetylcholinesterase (AChE, E.C. 3.1.1.7) inhibitor was withdraw due to its adverse effects. 7-Methoxytacrine (7-MEOTA) was prepared as a pharmacologically equal active compound with lower toxicity compared to THA. Donepezil as a highly selective inhibitor for AChE was connected with 7-MEOTA scaffold due to the ability to interact within calatytic anionic site (CAS) as well as peripheral anionic site (PAS) regions of AChE [1].

Recent research has been focused on studying the association between the intracellular amyloid beta (Aβ) cascade and the dysfunction of subcellular organelles, especially mitochondria. Mitochondrial enzyme amyloid beta binding alcohol dehydrogenase (ABAD) might contribute to the neuronal dysfunction associated with AD by interacting with intracellular Aβ [2].

These derivatives embodying 7-MEOTA and donepezil moieties [3] could be effective in the treatment of AD with the respect of their ability to interact with the multiple targets. Within our contribution, synthesis, *in vitro* biological evaluation including cholinesterase inhibitory activity and effects on mitochondrial function of 7-MEOTA-donepezil series will be reported.

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