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Project Title: Designed and synthesis of ascorbic derivatives as multi-target lead compounds for Alzheimer's disease

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Abstract

The number of older with Alzheimer's disease, a common neurodegenerative disorder, will reach to 152 million people in 2050 (1). Not only patient suffers from this disease but also care giver will effect for this disease. There are only five drugs that are currently approved by FDA for AD treatment namely donepezil, rivastigmine, galantamine and memantine (2). However, these drugs are only managing to alleviate the symptoms. Thus, this research focused on discovery of novel lead compounds with multi-target activity to inhibit etiopathology of the disease on amyloid cascade such as inhibition of β-secretase enzyme, amyloid aggregation and free radical (3-5). Ascorbic acid was selected to be a core structure due to its effective antioxidant, amyloid aggregation inhibition and ability of transportation to the brain and neuron (6,7). Ten proposed ascorbic derivatives were synthesized by using copper (I) catalyzed azide-alkyne cycloaddition reaction or click chemistry. Compounds vak2e and vak5e, possessed multifunctional activities as BACE1 inhibitor, amyloid aggregation inhibitor, antioxidant and neuroprotective agent. These compounds were suitable for lead optimization further.

Keywords: Multi-target drug, Amyloid β, Alzheimer's disease, Ascorbic derivatives