Discovery of potential inhibitor against human Asparagine Endopeptidase

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Abstract

Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative condition of the central nervous system among old people. AD is characterized by two neuropathological hallmarks: Extracellular senile plaque deposits, composed of amyloid beta (Aβ), and Intracellular neurofibrillary tangles (NFTs), made of truncated and hyperphosphorylated tau. Previous studies suggest that Asparagine Endopeptidase (AEP), a lysosomal cysteine proteinase, is activated during aging process. It proteolytically degrades tau and abolishes its microtubule assembly function, induces tau aggregation and triggers neurodegeneration.

Methods and Results: Therefore, AEP is an attractive target of drug discovery against AD. In this study, we investigated the important pharmacophore feature required for inhibitors of AEP by generating a structure-based pharmacophore model followed by virtual screening and subsequent validation by molecular docking. The computational findings discussed in our study provide initial information of inhibitory effects of ligand, (ZINC3979524), over AEP.

Conclusions: VS of the ZINC database against AEP led to select some good inhibitors for the treatment of Alzheimer's disease. Therefore, this study can be a good starting point for in vitro and in vivo experimental studies and can establish as a novel therapeutic agent against AD

Key words: Alzheimer's disease, Virtual screening, Asparagine Endopeptidase (AEP), molecular docking