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"*Insilico* analysis and Molecular docking studies against Acetylcholinesterase - A novel approach to identify Anti-Alzheimer's compounds"

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ABSTRACT

Alzheimer's disease (AD) is a progressive neurodegenerative disorder of the central nervous system (CNS) with deterioration of cognitive functions and behavioral abnormalities such as irritability, anxiety and depression. AD is characterized by the aggregation of amyloid β plaques (Aβ) and formation of Neuro Fibrillary Tangles (NFT's) in brain.Cholinergic hypothesis explains that the decline in cognitive and mental functions associated with AD are related to the loss of cortical cholinergic neurons and elevating Acetylcholinesterase levels.Thus, one of the most promising approaches for treating this disease is to enhance the acetylcholine level in the brain using acetyl cholinesterase (AChE) inhibitors. Hence, it is worthwhile to identify these Acetylcholinesterase inhibitors (AChEI) which can interfere with the progression of Alzheimer's disease (AD). The present study was aimed tofind out new anti-Alzheimer's compounds by performing "Docking studies against Acetylcholinesterase byusing modern docking programmers or software packages. The findings of the study revealed that ligands bind to the target protein at active sites with exact conformation and configuration. Based on literature, 168 ligands were selected and virtually screened to identify the best ligands, out of them compound 3955 & 44428320 showed the best affinity (Docking Score: 11.9 & 10.5) against AChEviz., 1EVE and 4EY4. From this preliminary study, it is suggested that compound 3955 & 44428320 can be used asdrug molecules to enhance the acetylcholine (ACh) levels in the brain of AD patients.

Key words: Alzheimer 's Disease, Acetylcholinesterase, AChEInhibitors, Insilico Screening and Molecular Docking studies.

INTRODUCTION:

For a quarter of a century, the pathogenesis of Alzheimer's disease has been linked to a deficiency in the brain neurotransmitter acetylcholine. This was based on observations that correlated cholinergic system abnormalities with intellectual impairments [1].Subsequently the cholinergic hypothesis of AD gained considerable acceptance. It stated that a serious loss of cholinergic function in the central nervous system contributed to cognitive symptoms. Over the years both evidences for and challenges to the relationship between acetylcholine dysfunction and AD have been put forward [2]. In essence, it has been argued that acetylcholine dysfunction is well known primary pathological cause for AD but rather a consequence of the disease. Hence, in addition to cholinergic dysfunction, a role for β- amyloid deposition, oxidative stress and inflammation have been investigated in the AD, and currently, trials are underway to test