

Abstract

Theoretical Study of Anti-Alzheimer's Disease Using Molecular Modeling Methods [†]

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Neurodegenerative diseases damage the nervous system and lead to a variety of complex progressive chronic issues. Alzheimer's disease (AD) is one such case. The most common form of dementia is a degenerative disorder of the brain that leads to memory loss, confusion, and behavioral changes. The main drug classes currently used to treat AD are acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitors. In this study, we investigated the inhibitory effects of a series of newly synthesized compounds of 2-hydroxy-N-phenylbenzamide derivatives on AChE and BChE, using molecular modeling approaches such as molecular dynamics and bioisosteric replacement to treat or reduce Alzheimer's disease.

The best docking complexes, L18 and L6', were used as simulation inputs to evaluate the stability of the complex (protein–ligand), using potential energy as a function of time. These results were verified using molecular dynamics simulations, demonstrating the strength of both complexes.

Furthermore, we found that the bioisosteric replacement method successfully proposed two novel analogs of each compound (L18 and L6') with low energy scores and similar biological activity by replacing molecular substructures with similar chemical groups.

All these methods allow us to identify new inhibitors that have potential against this disease and can be suggested as new drugs against Alzheimer's disease.

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