Using Novel Benzimidazole Sulfonate Derivatives for Inhibitory Activity on Enzymes Associated with Alzheimer's Disease

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Alzheimer's disease is a widespread neurodegenerative disorder characterized by abnormal protein accumulation in the brain. From 1990 to 2019, the global burden of Alzheimer's disease and other forms of dementia significantly increased, going from 9.66 million to 25.28 million disability-adjusted life years (DALYs). Studies predict that by the year 2050, the number of individuals with Alzheimer's is expected to reach a staggering 152 million. This research aims to identify and synthesize new derivatives for benzimidazole sulfonate. Then, assess their effectiveness against the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), which are responsible for Alzheimer's disease. The synthesis process involved the utilization of 15 different agents to create sulfonate samples, which were subsequently analyzed using various techniques such as FT-IR, H-NMR, C-NMR, and MS. Afterwards, the synthesized compounds underwent biological assays to evaluate their inhibitory activity. Among the tested analogs, six displayed excellent inhibitory activities compared to the standard drug donepezil, exhibiting IC50 values of 0.016 uM ± 0.01 for AChE and 0.30 uM ± 0.010 for BuChE. Compounds containing fluoro and trifluoro groups demonstrated the most promising activity, likely due to the high electronegativity of the fluorine atom, enabling effective interaction with the enzymes. Molecular docking was then employed to confirm these findings by identifying the precise binding sites of the derivatives with the enzymes. This study is a promising beginning for further investigations to be conducted for the development of a novel drug for the treatment of Alzheimer's disease.