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In silico screening of natural compounds and discovery of novel acetylcholinesterase inhibitors

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Alzheimer's disease (AD) is a widespread neurodegenerative disease that is currently treated symptomatically by inhibiting the acetylcholinesterase (AChE) enzyme. This enzyme is responsible for breaking down the neurotransmitter acetylcholine into acetate and choline at the synaptic cleft. However, the search for more effective AChE inhibitors (AChEIs) with fewer side effects has intensified in recent years, as the number of affected people has increased dramatically.

Natural compounds (NCs) are considered safer and less toxic than synthetic drugs, and therefore, we virtually screened 150,000 NCs via molecular docking. As a result, we discovered thirty-two new molecules from twenty-three structural groups. To estimate the stability of the complexes with AChE, molecular dynamic simulations were performed. Ten compounds formed stable complexes with the enzyme, and these were experimentally tested for AChE and antioxidant activity.

Five compounds exhibited moderate AChE inhibitory activity, and three of them exhibited potent antioxidant activity. These findings suggest that these natural compounds could potentially be developed into effective and safe AChEIs for the treatment of AD, as well as potential antioxidant therapies for other neurodegenerative diseases.

The results are published and are freely accessible at:
`http://www.ddg-pharmfac.net/`.

Keywords: molecular docking, molecular dynamics, drug design, structure-based in silico methods, acetylcholinesterase inhibitors, Alzheimer's disease, multitarget agents