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### TITLE

#### Identification of Acetylcholinesterase Targeted Novel Alkaloids as Potential Therapeutic Agents for Alzheimer's Disease: An in silico Approach

**Huma Naaz, Swati Singh, Veda P. Pandey,  
Priyanka Singh, Upendra N. Dwivedi**

University of Lucknow, India

Alzheimer's disease (AD) is a progressive neurodegenerative disorder with many cognitive and neuropsychiatric symptoms including dementia. Biochemically, development of AD has been related to a significant decrease in the brain neurotransmitter acetylcholine (ACh). Therefore, augmentation of the central cholinergic function by the inhibition of acetylcholinesterase (AChE) is, the major effective approach, clinically, for the treatment of Alzheimer's disease. Currently used drugs, such as tacrine (Cognex) and rivastigmine (Exelon), having AChE inhibitory action, are reported to have several side effects. Therefore, there is a great need to identify and develop novel drugs, coming from natural sources, which are safe without any side effects. Alkaloids, derived from plants, have also been reported to possess neuroprotective properties, by virtue of their interaction with the receptors at the nerve endings. Many alkaloids have been reported to act as AChE inhibitors. Alkaloid galanthamine, a competitive inhibitor of AChE, has been used to treat AD in many European countries. In the present study, thirteen alkaloids from three plants namely *Polyalthia longifolia*, *Pleiocarpa mutica* and *Hunteria zeylanica* were analyzed for their anticholinergic potential using acetylcholinesterase as target through docking. The alkaloid pleiocarpine was found to be the best among all these alkaloids. Theoretical improvement of the pleiocarpine by making an amino derivative revealed about six folds higher anticholinergic potential for this as compared to that of pleiocarpine. A comparison of pleiocarpine and its amino derivative with those of commonly used drugs Cognex and Exelon, for their anticholinergic potentials, revealed pleiocarpine and its amino derivative as much better inhibitors of acetylcholinesterase, suggesting these novel molecules having great potential for their therapeutic application.

#### Biography

Huma Naaz: M.Sc. Bioinformatics, Research Fellow, Centre of excellence in bioinformatics, Department of Biochemistry, University of Lucknow, Lucknow-226007, U.P., India. Email: [naaz.hh786@gmail.com](mailto:naaz.hh786@gmail.com)