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Edited by:
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***Correspondence:**
Malarvili Selvaraja
malarvili@ucsiuniversity.edu.my
Yadu Nandan Dey
yadunandan132@gmail.com

†These authors have contributed equally to this work and share first authorship

‡ORCID:
Pukar Khanal
https://orcid.org/0000-0002-8187-2120
Farshid Zargari
https://orcid.org/0000-0002-0287-0013
Yadu Nandan Dey
https://orcid.org/0000-0003-4016-4379

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Integration of System Biology Tools to Investigate Huperzine A as an Anti-Alzheimer Agent

***Pukar Khanal*[1†‡], *Farshid Zargari*[2,3†‡], *Bahareh Farasati Far*[4], *Dharmendra Kumar*[5], *Mogana R*[6], *Yasir K. Mahdi*[6], *Najwan K. Jubair*[6], *Shailendra K. Saraf*[7], *Parveen Bansal*[8], *Ranjit Singh*[9], *Malarvili Selvaraja*[6*] *and Yadu Nandan Dey*[10*‡]**

[1]Department of Pharmacology and Toxicology, KLE College of Pharmacy Belagavi, KLE Academy of Higher Education and Research (KAHER), Belagavi, India, [2]Pharmacology Research Center, Zahedan University of Medical Sciences, Zahedan, Iran, [3]Department of Chemistry, Faculty of Science, University of Sistan and Baluchestan, Zahedan, Iran, [4]Department of Chemistry, Iran University of Science and Technology, Tehran, Iran, [5]Department of Pharmaceutical Chemistry, Laureate Institute of Pharmacy, Kangra, India, [6]Faculty of Pharmaceutical Sciences, UCSI University, Kuala Lumpur, Malaysia, [7]Faculty of Pharmacy, BBDNIIT, Lucknow, India, [8]University Centre of Excellence in Research, Baba Farid University of Health Sciences, Faridkot, India, [9]AVIPS, Shobhit University, Saharanpur, India, [10]Department of Pharmacology, Dr. B.C. Roy College of Pharmacy and Allied Health Sciences, Durgapur, India

Aim: The present study aimed to investigate huperzine A as an anti-Alzheimer agent based on the principle that a single compound can regulate multiple proteins and associated pathways, using system biology tools.

Methodology: The simplified molecular-input line-entry system of huperzine A was retrieved from the PubChem database, and its targets were predicted using SwissTargetPrediction. These targets were matched with the proteins deposited in DisGeNET for Alzheimer disease and enriched in STRING to identify the probably regulated pathways, cellular components, biological processes, and molecular function. Furthermore, huperzine A was docked against acetylcholinesterase using AutoDock Vina, and simulations were performed with the Gromacs package to take into account the dynamics of the system and its effect on the stability and function of the ligands.

Results: A total of 100 targets were predicted to be targeted by huperzine A, of which 42 were regulated at a minimum probability of 0.05. Similarly, 101 Kyoto Encyclopedia of Genes and Genomes pathways were triggered, in which neuroactive ligand–receptor interactions scored the least false discovery rate. Also, huperzine A was predicted to modulate 54 cellular components, 120 molecular functions, and 873 biological processes. Furthermore, huperzine A possessed a binding affinity of −8.7 kcal/mol with AChE and interacted within the active site of AChE *via* H-bonds and hydrophobic interactions.

Keywords: Alzheimer's disease, huperzine A, system biology, donepezil, ligand–receptor interactions