RESEARCH PAPER

Molecular Docking Analysis of Elaeocarpidine Phytochemical Compound against BDNF Receptor: Potential Insights for Alzheimer's disease Therapy

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ABSTRACT

Alzheimer's disease (AD) is a debilitating neurodegenerative disorder characterized by the progressive decline of cognitive functions. Current treatments offer symptomatic relief, but no cure exists. In this study, we explored the potential of Elaeocarpidine, a compound from *Elaeocarpus ganitrus*, in targeting the brain-derived neurotrophic factor (BDNF) receptor, implicated in AD. Employing in silico techniques, we performed molecular docking simulations, assessing the binding affinity of Elaeocarpidine with the BDNF receptor. The analysis revealed a strong interaction (binding energy score: -6.4), suggesting Elaeocarpidine's potential as a therapeutic agent for AD. Visualization tools aided in understanding the molecular mechanisms underlying this interaction. These findings provide valuable insights into Elaeocarpidine's efficacy in BDNF receptor-mediated pathways, indicating its promise as a potential treatment for Alzheimer's disease. Further research is warranted to validate its therapeutic applicability.

Keywords: Alzheimer's disease, Elaeocarpidine, BDNF receptor, molecular docking, neurodegenerative disorders, neurotrophic factors, *Elaeocarpus ganitrus*.

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1. INTRODUCTION

Alzheimer's disease (AD) is a neurological condition that slowly destroys brain cells and causes shrinkage. AD is the most frequent cause of dementia, which reduces a person's capacity for independent functioning and is characterized by a progressive decline in mental, behavioural, and social abilities. Although these cases, the individual might still feel as though they are experiencing memory loss, such as forgetting where they put familiar words or where certain objects are located [1]. At this point, symptoms may not be readily apparent, but family members and close friends may notice something, and a doctor would be able to recognize symptoms using specific diagnostic tools. loss of something struggle to find the right words, constantly ask the same questions, and forget the names of things and places. Decision-making skills deteriorate, bad judgment is displayed, and openness to change decreases**.** Cognitive symptoms include mental decline, difficulty understanding and thinking, confusion at night, delusion, disorientation, forgetfulness, making up stories, mental confusion, trouble concentrating, an inability to create new memories, and performance issues such as the inability to recognize common objects or basic mathematical operations [2]. Aggression, agitation, difficulties taking care of oneself, irritation, needless repetition of one's own words, personality changes, and restlessness, a lack of self-control, or roaming and getting lost are examples of behaviours that are problematic. Other typical symptoms include trouble coordinating your movements, slurred speech, general unhappiness, loneliness, and feelings of hostility, apathy, or psychological mood swings including paranoia, sorrow, or hallucinations [3].

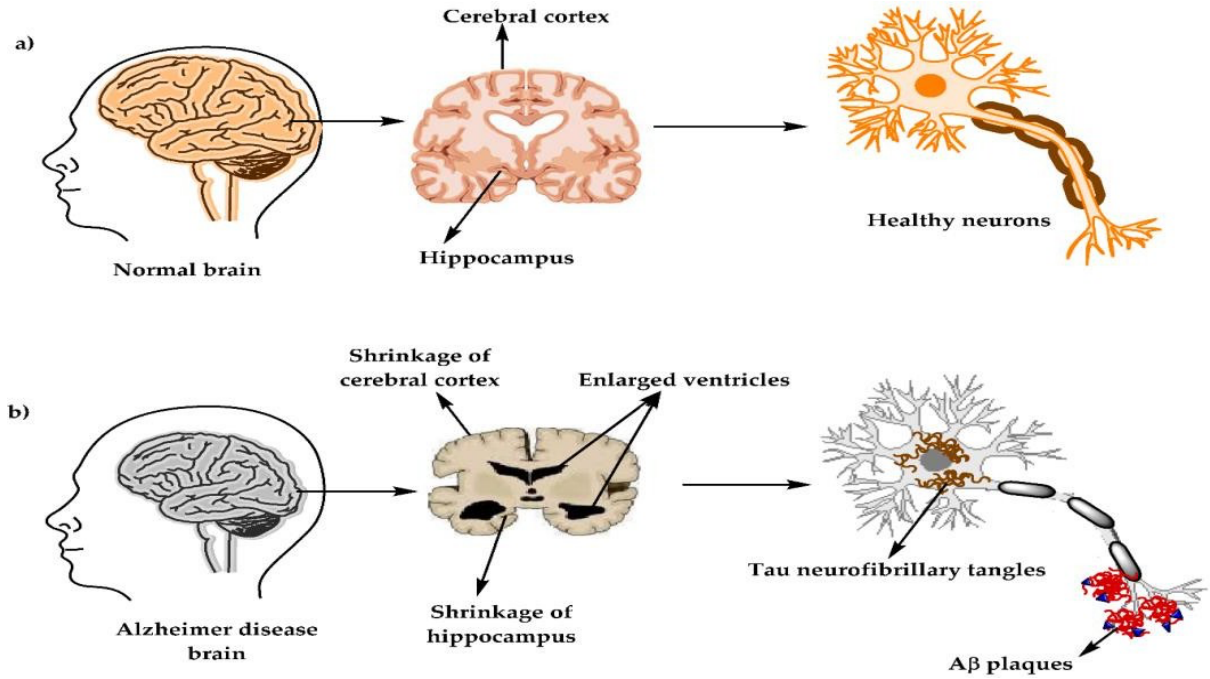


Figure 1: Alzheimer's disease hypothesis a) Healthy brain and b) AD affected brain.

German physician Alois Alzheimer initially identified a case of AD in 1907. In 1901, he had his first encounter with the 51-year-old Auguste Deter. Mechanism of Alzheimer's disease is the amygdala, substantia nigra, striatum, hypothalamus, thalamus, locus ceruleus, and areas of the cerebral cortex are all impacted by AD. Depending on how neurotransmitters, neuromodulators, and neuropeptides are expressed, different types of neuronal cells are affected spatially in different ways. Treatment though AD has no known cure, a variety of medications have been shown to both slow the disease's progression and treat its symptoms. Prevention strategies for Alzheimer's disease a healthy, balanced diet that includes at least servings of fruit and vegetables each day, limiting alcohol intake, quitting smoking, and sustaining these lifestyle choices are all effective approaches to enhance your health [4].

Acetyl cholinesterase is an enzyme that rapidly breaks down acetylcholine into acetic acid and choline, blocking impulse transmission. The patient's cholinergic systems degenerate significantly in AD, which affects the function of cholinergic neurons and reduces endogenous levels of acetylcholine. AChE inhibitors are therefore given as a means of reducing these effects and increasing synaptic levels of acetylcholine. Only three AChE inhibitors donepezil, rivastigmine, and galantamine are now employed in AD therapy; however, they largely treat mild to severe dementia and only provide symptomatic relief. As a result, AChE inhibitors must be improved and updated [5].

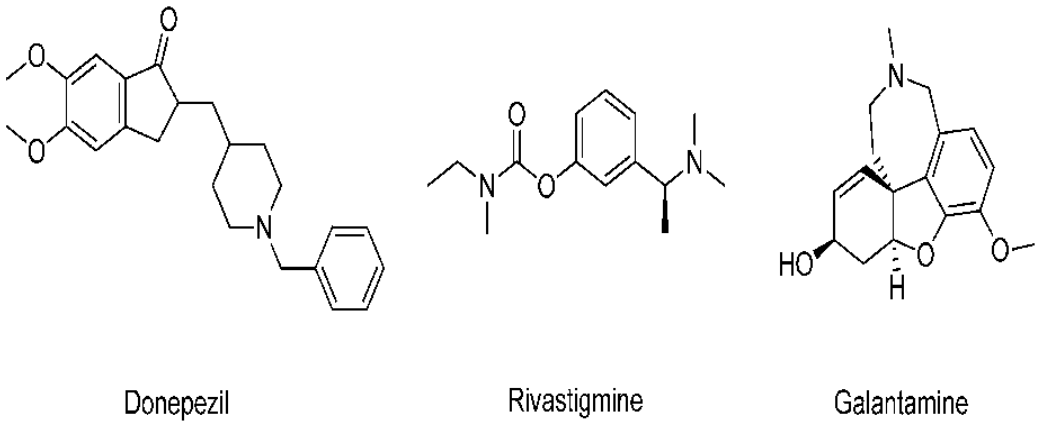


Figure 2: Structures of donepezil, rivastigmine, and galantamine drugs approved for AD.

The primary proteins and enzymes in the amyloid hypothesis of AD are BNDF (brain-derived neurotropic factor). BDNF is a crucial chemical in dementia and neurodegenerative diseases because of its basic involvement in cognition, learning, and memory formation through modifying synaptic plasticity. Therefore, the enzymes were chosen for the in-silico inhibition studies to dock the screened phytocompounds against the above-

mentioned protein, which plays a very crucial part in memory and cognition activities. the three-dimensional BDNF, PDB ID is like 1B8M [6].

Elaeocarpus ganitrus, also referred to as Rudraksha in India, is a member of the Elaeocarpaceae family and is found in the Himalayas. Greek literature is where the word "Elaeocarpus" originated. Both the Greek terms elaeo, which means "olive," and carpus, which means "fruit" (referring to the olive-like fruits produced by the genus), mean "fruit." About 360 species of the elaeocarpus type are found in Australia, East Asia, Malaysia, and the Pacific Islands. About 25 of the 120 species of this genus may be found in Indialaone [7]. They are all from various regions of Asia. Rudraksha beads have significant religious, spiritual, and materialistic connotations according to Hindu mythology. In Hindu mythology, the rudraksha symbolises the connection between earth and heaven. It is thought to hold all the data required to unravel the whole evolutionary history of the cosmos. It is used in traditional medicine to treat conditions like hypertension, arthritis, migraines, stress, anxiety, depression, palpitations, nerve pain, and liver illnesses. It is also used to treat various illnesses, including epilepsy. The heart, nerves, and neurological system benefit from wearing Rudraksha, according to Ayurvedic medicine. Wearing Rudraksha beads, according to the Ayurvedic medical system, reduces stress, anxiety, loss of focus, insomnia, depression, hypertension, palpitations, infertility, rheumatism, and asthma [8]. It has anti-aging properties as well. After screening of numerous medicinal plants, it was shown that the extracts of E. ganitrus were efficient against biological targets and had a variety of pharmacological actions. Many literature papers discuss a variety of pharmacological activities, such as analgesic and anti-inflammatory properties, CNS effects, hypnosis potentiation, sedative, antiasthmatic effects, hydrocholeretic, anti-diabetic benefits, anti-hypertensive effects, and cardiostimulant effects. Carbon, nitrogen, hydrogen, oxygen, and trace elements are among the elements found in rudraksha beads. The proportion of gases present in rudraksha beads [9].

Rudraksha offers a wide range of Ayurvedic benefits that are widely covered with regard to boosting body constitutions. The rudraksha's beads, bark, and leaves are all used in the treatment of a variety of illnesses, including mental disorders, headaches, fevers, and skin conditions. Rudrakshas can be worn on many parts of the body, such as the arm, wrist, and other places [10]. Rudraksha is a potent memory booster when mixed with milk. Rudraksha can effectively heal all types of brain illnesses, including brain fever and others. Rudraksha should be used as a blood purifier to heal blood impurities since it strengthens the body's tissues. Rudraksha has antibacterial qualities that make it useful for treating burns and scars (Prof Philip Scheltens MD et *al*., 2016). Additionally, coughs and respiratory issues can be treated with it [11].

The term "*in silico*" work is used in the text to describe computational analyses and simulations done on a computer as opposed to in a real-world laboratory setting. In this situation, scientists would screen and find candidate quorum sensing Ligands that might interact with BDNF using computational approaches. A computer method called molecular docking would be used to forecast how these Ligands may bind to BDNF. Molecular dynamics simulations and modeling might also aid in evaluating the dynamics and stability of BDNF interactions throughout time. This novel method offers a viable route for creating fresh treatments or interventions by fusing knowledge of bacterial communication systems with our comprehension of neurodegenerative diseases. Before potentially moving on to experimental studies, computational studies [12].

Figure 3. *Elaeocarpus ganitrus* medicinal plant.

1. Materials and methods

1.1. Protein preparation

The Protein Data Bank (PDB), a database of protein structural information, made the three-dimensional BDNF, PDB IDs like 1B8M that were necessary for the in-silico analysis accessible. The Pymol software was used to clean the water molecules present in the protein (Fig 4) This protein was further subjected to validation [13].

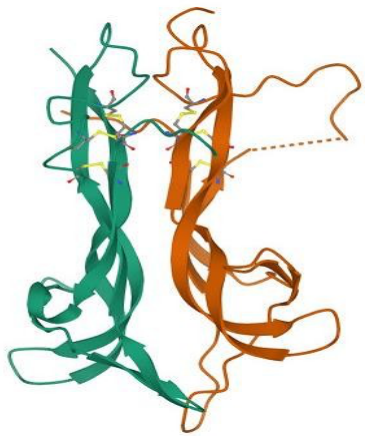


Figure 4. 3D structure of BDNF protein.

1.2. Protein validation

Protein purification is a technique used to separate significant amounts of physiologically significant proteins for in-depth study in both industrial and scientific settings. To extract or purify a target protein from the mixture of proteins to determine its function, experimental approaches were needed. The PROCHECK module of the PDBSum server [https://servicesn.mbi.ucla.edu/PROCHECK/], which employs several protein quality-based parameters, such as the proportion of residues lying in preferred and allowed regions, the quantity of glycine and proline residues, was used to further confirm the stereochemical stability of the predicted models [14].

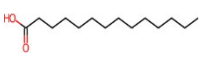
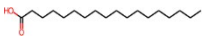
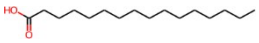
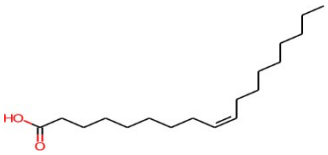
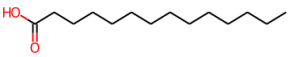
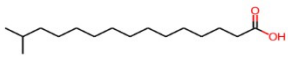
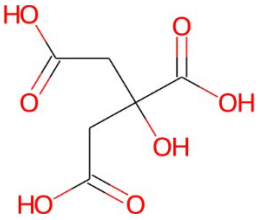
1.3. Active site prediction

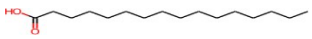
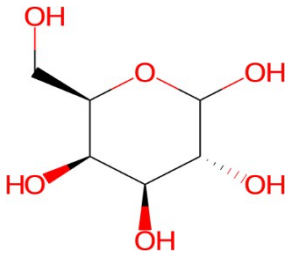
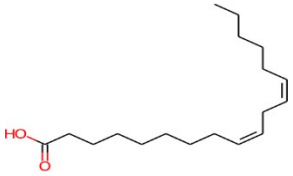
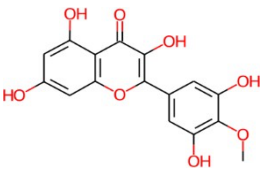
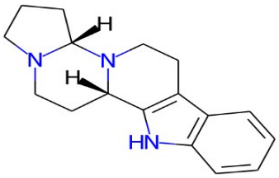
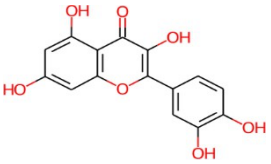
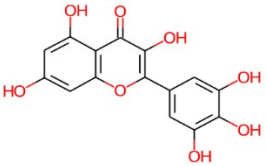
After protein production, predictions about the protein's active site should be generated. If present, water molecules and heteroatoms are predominantly removed. The binding sites of a protein are the amino acid residues that make contact with the ligand. The CASTp 3.0 server (http://sts.bioe.uic.edu/castp/index.html?4jii) was utilised to anticipate this binding location. The abbreviation for this is Computed Atlas of Surface Topography of Proteins. The server uses the protein model to determine which amino acids are crucial for binding interactions [15].

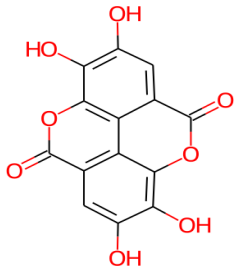
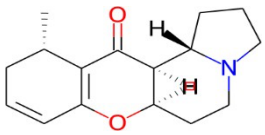
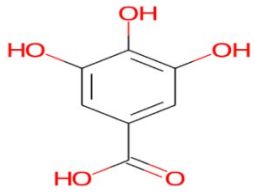
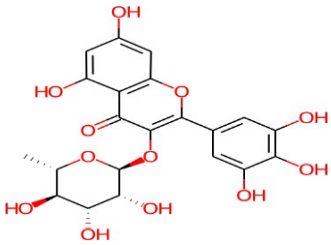
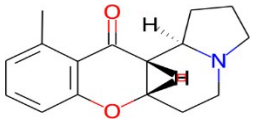
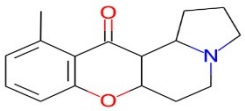
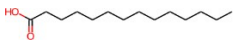
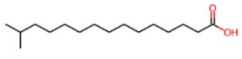
1.4. Ligand preparation

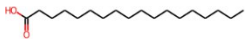
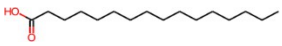
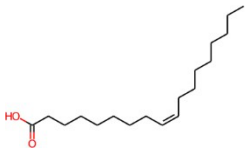
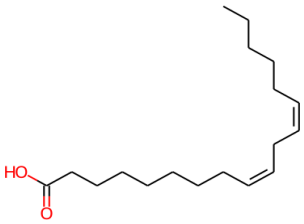
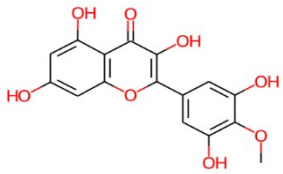
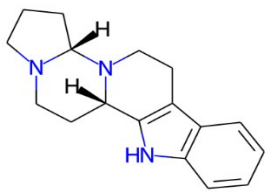
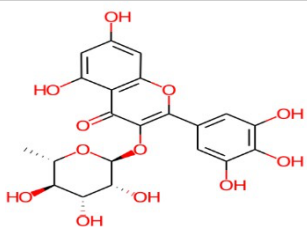
Thirty ligands were identified from the plant Elaeocarpus ganitrus. The Indian medicinal plant phytochemistry and treatments (IMPPAT) database was used for the ligand retrieval. These ligands were chosen to interact with the target proteins. The 3D structures of these ligands were downloaded for analysis and docking [16].

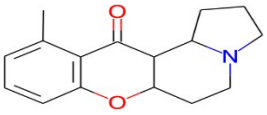
Table 1: Represents the library of phytocompounds of *Elaeocarpus ganitrus* taken from IMPPAT database.

SI.NO	LIGANDS	PARTS USED		2D STRUCTURE
1	Myristic acid	bark	Molecular weight:228.38 Hydrogen bond acceptor:1 Hydrogen bond donors:1	
2	Stearic acid	bark	Molecular weight:284.48 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
3	Palmitic acid	bark	Molecular weight:256.43 Hydrogen bond acceptosr:1 Hydrogen bond donars:1	
4	Oleic acid	bark	Molecular weight:282.47 Hydrogen bond acceptors:1 Hydrogen bond donars:1	
5	Myristic acid	fruit	Molecular weight:228.38 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
6	14-methyipentadecanoic acid	fruit	Molecular weight:256.43 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
7	Citric acid	fruit	Molecular weight:192.12 Hydrogen bond acceptors:4 Hydrogen bond donars:4	

8	Palmitic acid	fruit	Molecular weight:256.43 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
9	d-galactose	fruit	Molecular weight:180.16 Hydrogen bond acceptors:6 Hydrogen bond donors:5	
10	**Linoleic acid**	**fruit**	**Molecular weight:280.45 Hydrogen bond acceptors:1 Hydrogen bond donors:1**	
11	Mearnsetin	leaf	Molecular weight:332.26 Hydrogen bond acceptors:8 Hydrogen bond donors:5	
12	Elaeocarpidine	leaf	Molecular weight:267.38 Hydrogen bond acceptors:2 Hydrogen bond donors:1	
13	Quercetin	leaf	Molecular weight:302.24 Hydrogen bond acceptors:7 Hydrogen bond donors:5	
14	Myricetin	leaf	Molecular weight:318.24 Hydrogen bond acceptors:8 Hydrogen bond donors:6	

15	Ellagic acid	leaf	Molecular weight:302.19 Hydrogen bond acceptors:8 Hydrogen bond donors:4	
16	(-) isoelaeocarpiline	leaf	Molecular weight:259.35 Hydrogen bond acceptors:3 Hydrogen bond donors:0	
17	Gallic acid	leaf	Molecular weight:170.12 Hydrogen bond acceptors:4 Hydrogen bond donors:4	
18	Myricitrin	leaf	Molecular weight:464.38 Hydrogen bond acceptors:12 Hydrogen bond donors:8	
19	Isoelaeocarpine	leaf	Molecular weight:257.33 Hydrogen bond acceptors:3 Hydrogen bond donors:0	
20	**Isoeleocarpine**	**leaf**	**Molecular weight:257.33 Hydrogen bond acceptors:3 Hydrogen bond donors:0**	
21	Myristic acid	seed	Molecular weight:228.38 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
22	14-Methylpentadecanoic acid	seed	Molecular weight:256.43 Hydrogen bond acceptors:1 Hydrogen bond donors:1	

23	Stearic acid	seed	Molecular weight:284.48 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
24	Palmitic acid	seed	Molecular weight:256.43 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
25	Oleic acid	seed	Molecular weight:284.47 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
26	Linoleic acid	seed	Molecular weight:280.45 Hydrogen bond acceptors:1 Hydrogen bond donors:1	
27	Mearnsetin		Molecular weight:332.26 Hydrogen bond acceptors:8 Hydrogen bond donors:5	
28	Elaeocarpidine		Molecular weight:267.38 Hydrogen bond acceptors:2 Hydrogen bond donors:1	
29	**Myricitrin**		**Molecular weight:464.38** **Hydrogen bond acceptors:12** **Hydrogen bond donors:8**	

30	Isoeleocarpine	Molecular weight:257.33 Hydrogen bond acceptors:3 Hydrogen bond donors:0	

2. RESULT AND DISCUSSION

2.1. Protein preparation

Protein Data Bank (PDB), a protein structural database, provided the three-dimensional structures of BDNF PDB IDs like 1B8M that were necessary for the in-silico studies. The Pymol software was used to clean the water molecules present in the protein (Fig 4) This protein was further subjected to validation [17].

2.1.1. Protein validation

The PROCHECK module of the PDB Sum server [https://servicesn.mbi.ucla.edu/PROCHECK/], which uses a number of protein quality-based parameters, such as the percentage of residues lying in preferred and allowed regions, the amount of glycine and proline residues, was used to further confirm the stereochemical stability of the predicted models [18].

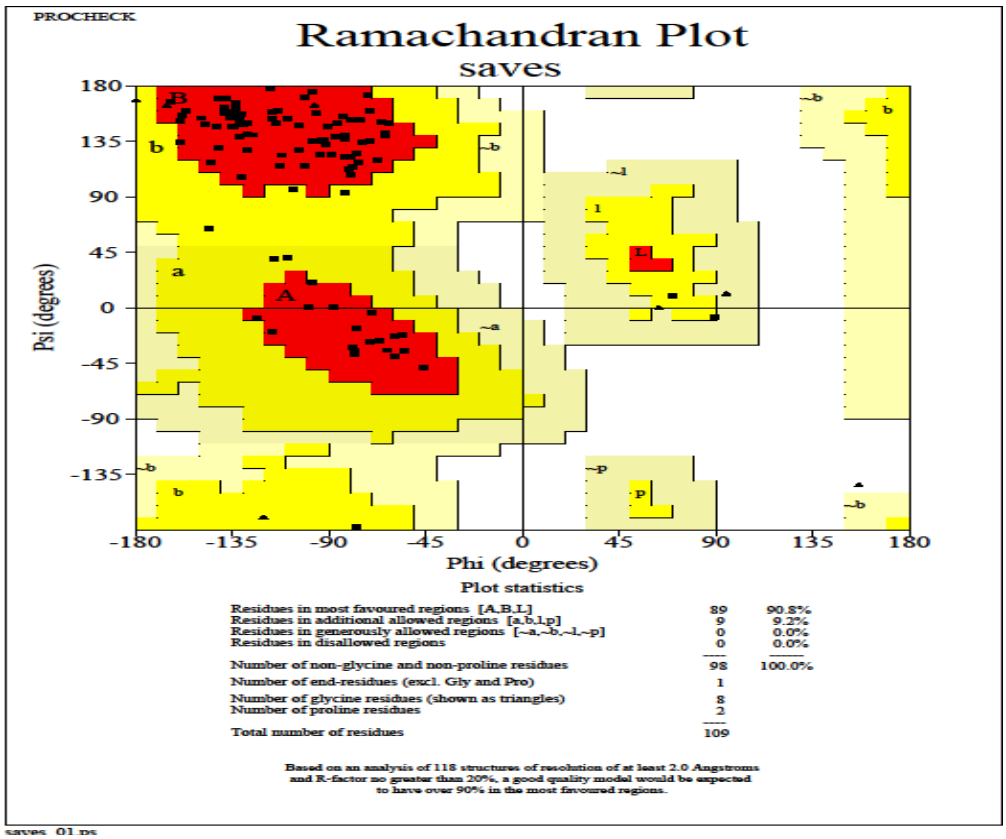


Figure 5. Protein validation Ramachandran Plot

2.2. Molecular docking

The interactions are looked at while the protein is docked with the ligand. The scoring function assigns a score based on the best docked ligand complex that is chosen. The molecular steps that target proteins go through when they bind can be studied using MD. It is a tool used frequently

in the production of medications. We performed molecular docking using PyRx 0.8, a virtual screening programme [https://pyrx.sourceforge.io] [19].

The preferred orientation of the receptor (a protein) for the ligand to bind is established using the molecular docking procedure in order to create a stable molecule. Based on the preferred orientation, it is feasible to forecast the strength of the bond or binding affinity between the ligand and the protein using scoring methods. In order to estimate a drug's affinities and activities, docking is frequently utilized to forecast the orientation in which drug candidates would attach to protein targets. Therefore, docking plays a key role in the process of developing innovative drugs. To achieve an optimal conformation and reduce the free energy of the entire system, molecular docking tries to computationally replicate the molecular identification process. The process of developing a new medicine is tough. The primary goals of molecular docking are to achieve optimal conformation, lower the

overall system's free energy, and simulate the molecular identification process computationally. The process of creating a brand-new drug is challenging [20].

Table 2: Represents the binding energy details of top five phytocompounds.

SI.NO	LIGAND	BINDING AFFINITY
1	Elaeocarpidine	-6.4
2	Myricitrin	-6.3
3	Quercetin	-6.3
4	Mearnsetin	-6
5	Isoelaeocarpiline	-5.8

Modern drug development is mostly based on *in-silico,* chemical, and biological methods. The use of computer-aided techniques in the process of developing new drugs is growing in popularity. The MD data were assessed for bonded and non-bonded interactions using the visualization programme Discovery Studio 3.1 (Accelrys, San Diego, United States) [21].

2.3. Visualization

Protein and ligand's affinity for each other reveals how firmly they bind. The docking score was used to determine the ideal docking conformation. By comparing binding energy scores for complexes with known 3D structures, it is possible to determine the binding affinity of a protein-ligand complex. The binding energy includes consideration of Van der Waals interactions, hydrophobic effects, and hydrogen bonds. Using the visualization programme Discovery Studio 3.1, all the complexes' 3D and 2D interactions were examined (22,23).

A protein-ligand complex's binding affinity to a known 3D structure is measured using the binding energy score. Hydrogen bonds, van der Waals interactions, and hydrophobic effects are some of the factors that the binding energy considers. By calculating the binding energy, it is possible to put a number on how strong the interaction is between the protein and the ligand. To better understand the interactions inside protein-ligand complexes, cutting-edge visualization techniques are employed. Discovery Studio 3.1 is one such programme that permits the analysis of both the 3D and 2D interactions within the complexes. This visualization system makes it easy to identify key molecular interactions, like hydrogen bonds and hydrophobic interactions, between the protein and its ligand (24).

By examining interactions within protein-ligand complexes and visualizing molecular docking poses, researchers can get crucial knowledge about the binding affinities and specific molecular mechanisms that contribute to the strength of the protein-ligand interaction. Understanding the potential efficacy and usefulness of a particular ligand as a therapeutic agent or drug candidate requires this knowledge.

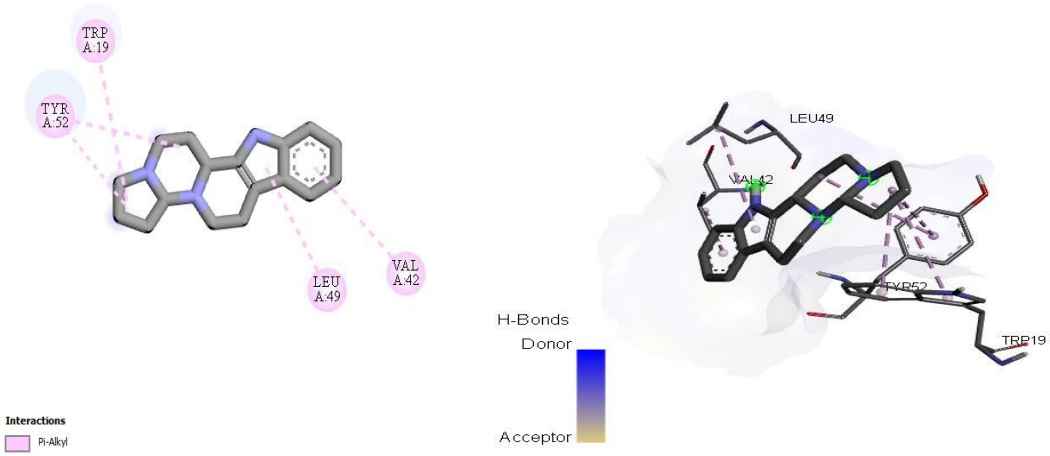


Figure 6: Visualization of protein Elaeocarpidine A) 2D Interaction B) 3D Interaction.

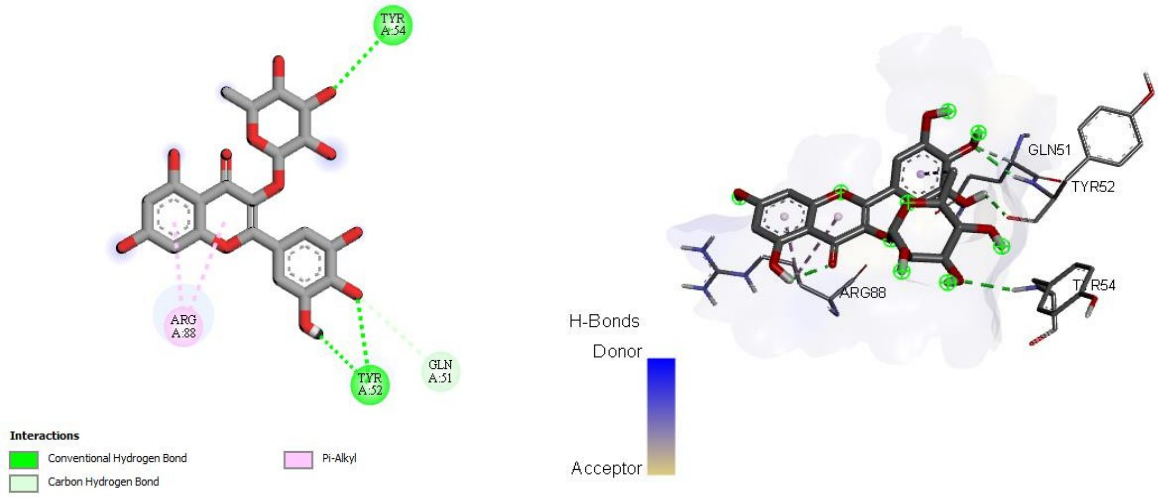


Figure 7: Visualization of protein. Myricitrin A) 2D Interaction B) 3D Interaction.

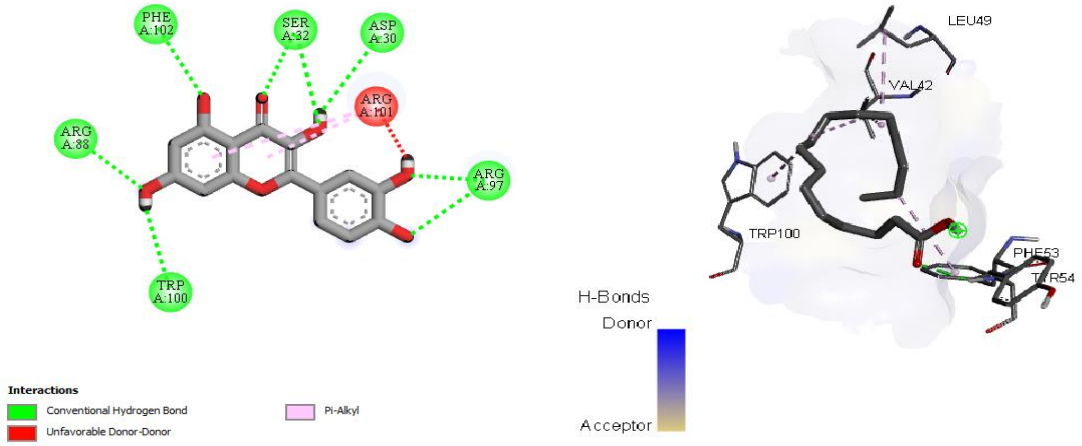


Figure 8: Visualization of protein Quercetin A) 2D Interaction B) 3D Interaction

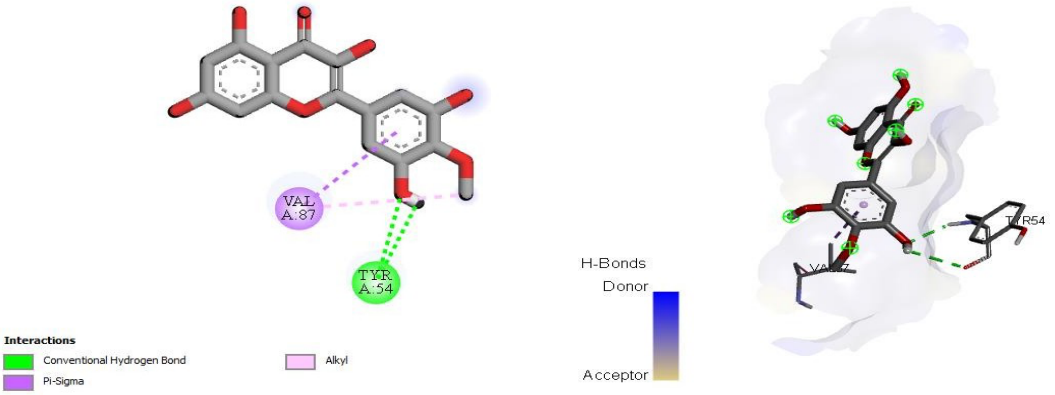


Figure 9: Visualization of protein Mearnsetin A) 2D Interaction B) 3D Interaction.

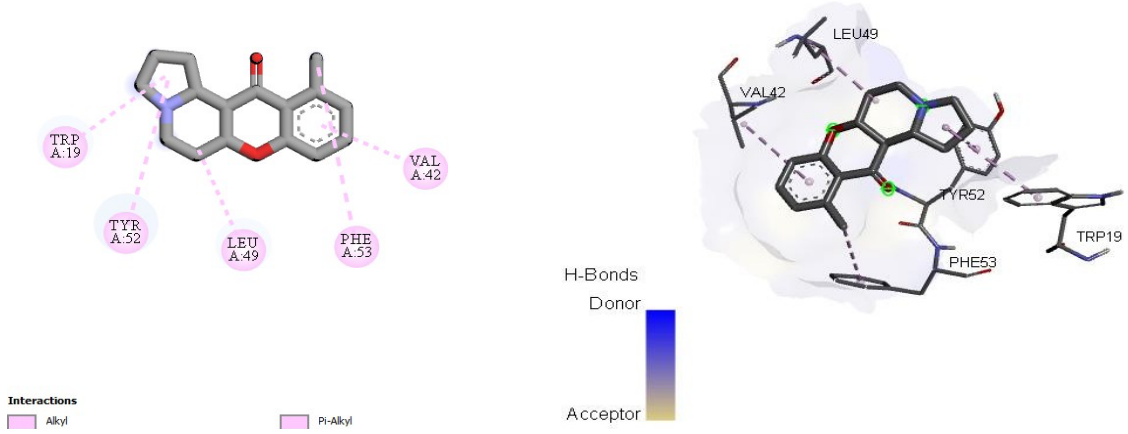


Figure10: Visualization of protein Isoelaeocarpiline A) 2D Interaction B) 3D Interaction.

3. CONCLUSION

The analysis and visualisation of molecular docking poses between the Elaeocarpidine phytocompound from Elaeocarpus ganitrus and the brain-derived neurotrophic factor (BDNF) receptor, which is involved in Alzheimer's disease, have given important insights into their binding affinity. The binding energy score of -6.4 for elaeocarpidine indicates that it interacts strongly with the BDNF receptor and may be effective in treating Alzheimer's disease. By validating the docking process and identifying the optimal ligand-protein orientations using the docking score, the results are made credible. By considering factors such as hydrogen bonds, van der Waals interactions, and hydrophobic effects, the binding energy score evaluates the strength of the protein-ligand interaction and indicates a favourable binding affinity. Visualisation tools like Discovery Studio 3.1 enable knowledge of the precise chemical mechanisms behind the interaction between the BDNF receptor and elaeocarpidine by evaluating both 3D and 2D interactions. Our understanding of the potential therapeutic application of elaeocarpidine in BDNF receptor-mediated signaling pathways related to Alzheimer's disease is now better thanks to the information provided. More study is needed to determine the efficacy and suitability of elaeocarpidine as a potential treatment for Alzheimer's disease in light of its high affinity for the BDNF receptor.

Compliance with ethical guidelines: Not Applicable

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REFERENCE

1. A.P.Porsteinsson, R.S.Isaacson, Sean Knox, M.N.Sabbagh and I.Rubino (2021). Diagnosis of Early Alzheimer's disease. *National library of medicine National center for biotechnology information*, 371-386.
2. Anderson LA, McConnell SR. (2007). Cognitive health: an emerging health issues. *Alzheimer's and Dementia*. 2007; 3(S1):S70-S73.
3. Catterall WA, Goldin AL, Waxman SG. International Union of Pharmacology XLVII Nomenclature and structure-function relationships of voltage-gated sodium channels. *Pharmacol Rev*. 2005; 57:397–409. [PubMed] [Google Scholar].
4. Chengxuan Qiu, Miia Kivipelto and Eva Von Strauss (2022). Epidemiology of Alzheimer's disease occurrence, determinants, and strategies toward intervention 111-128.
5. Davies, P. (1999). Challenging the Cholinergic Hypothesis in Alzheimer Disease. *JAMA* 281, 1433. doi:10.1001/jama.281.15.1433.
6. Day KL, McGuire LC, Anderson LA, 2009. Disease control and preventions healthy brain initiative. 33(1); 11-17.
7. Goedert M, Spillantini M G, and Crowther R A. (1991). Tau Proteins and Neurofibrillary Degeneration. *Brain Pathol*. 1, 279–286.
8. Lang JE, Moore MJ, Harris AC, Anderson LA 2005. Healthy aging: priorities and programs of the centers for Disease control and Prevention.; 29(2):24-29.
9. Maciej Dulewicz, Agnieszka Kulczy, Piotr Mroczko, Johannes Kornhuber, Piotr Lewczuk and Barbara Mroczko. Biomarkers for the Diagnosis of Alzheimer's disease in Clinical Practice: *International journal of molecular science*. 221-250.
10. Padeep S, Prabhuswaminath SC, Reddy P, Srinivasa SM, Shati AA, Alfaifi MY, Eldin I. Elbehairi S, Achar RR, Silina E, Stupin V, Manturova N, Glossman-Mitnik D, Shivamallu C and Kollur SP (2022) Anticholinesterase activity of *Areca Catechu*: *In Vitro* and *in silico* green synthesis approach in search for therapeutic agents against AD. *Front. Pharmacol.* 13:1044248. doi: 10.3389/fphar.2022.1044248
11. Pradeep, S., Jain, A. S., Dharmashekara, C., Prasad, S. K., Akshatha, N., Pruthvish, R., ... &

Glossman-Mitnik, D. (2021). Synthesis, Computational Pharmacokinetics Report, Conceptual DFT-Based Calculations and Anti-Acetylcholinesterase Activity of Hydroxyapatite Nanoparticles Derived from Acorus Calamus Plant Extract. *Frontiers in Chemistry*, 9, 741037.

12. Pradeep, S., Patil, S. M., Dharmashekara, C., Jain, A. S., Ramu, R., Shirahatti, P. S., ... & Kollur, S. P. (2022). Molecular insights into the in-silico discovery of corilagin from Terminalia chebula as a potential dual inhibitor of SARS-CoV-2 structural proteins. *Journal of Biomolecular Structure & Dynamics*, 1-19.
13. Marcos Vinicius Ferreia Silva, Cristina de Mello Gomide Loures, Luan Carlos Vieira Alves, Leonardo Cruz de Souza, Maria das Gracas Carvalho (2019). Alzheimer's disease risk factors and potentially protective measures. *Journal of Biomedical Science* 26, 33.
14. Mark W Bondi, Emily C.Edmonds, David P.Salmon(2017).Directions and predictions for dementia J In Neuropsychology Soc; 23(9-10): 818–831.
15. Mathew Schrag, Claudius Mueller, Udochukwu Oyoyo, and Wolff M., Kirsch Prog Neurobiol (2011). A quantitative meta-analysis. Some insight on the influence of citation bias on scientific opinion 94(3): 296-306.
16. Satish, A. M., Dakshinamurthy, V., Chakith, M. R. S., Ashwini, P., Raju, G. Y., Pradeep, S., Kollur, S. P., & Shivamallu, C. (2023). Evaluation of anti-inflammatory activity of cilnidipine in albino Wistar rats. *Eur Chem Bull*, 12(S2), 2519-2532.
17. Reddy Pruthvish, Pradeep Sushma, S. M. Gopinath, Dharmashekar Chandan, G. Disha, M. R. Sai Chakith, Srinivasa Chandrashekar, Shati Ali A., Alfaifi Mohammad Y., Elbehairi Serag Eldin I., Achar Raghu Ram, Silina Ekaterina, Stupin Victor, Manturova Natalia, Shivamallu Chandan, Kollur Shiva Prasad (2023). Cell cycle arrest and apoptotic studies of Terminalia chebula against MCF-7 breast cancer cell line: an in vitro and in silico approach. *Frontiers in Oncology* – 13. DOI=10.3389/fonc.2023.1221275
18. McGuire LC, Strine TW, Vachirasudlekha S, Mokdad AH, Anderson, LA (2008). The prevalence of depression in older U.S Women, Behavioural Risk Factor Surveillance System. *Journal of Women's health* 501-507.
19. Prof Philip Scheltens MD, Prof Kaj Blennow MD, Prof Monique MB Breteler MD, Prof Bart de Stopper MD, Prof Giovanni B Frisoni MD, Prof Stephen Salloway MD, (2016). Alzheimers Disease. *Ntional Library of Medicine.Volume* 388, Issue 10043, 505-517.
20. Shivalingaiah, T., Thoyojaksha, T., Pallavi, K., Shekar, P. K., Sushma Pradeep, S. P., Sai Chakith, M. R., ... Chandan Shivamallu, C. S. (2022). Computational approach in search of therapeutics for Colorectal Cancer. *International Journal of Food and Nutritional Sciences*, 9(3), 37-41.
21. Shivalingaiah, T., Thoyojaksha, T., Sai Chakith, M. R., Sushma Pradeep, P. K., Pallavi, K. S., Kavana, C. P., ... Chandan Shivamallu, C. S. (2022). In-Silico Evaluation of Anti-acne Property of Syzygium (S.) aromaticum. *International Journal of Food and Nutritional Sciences,* 9(2), 31-36.
22. Shailja Choudhary and Hemlata Kaurav (2021). Elaeocarpus ganitrus (Rudraksha): A Drug with Spiritual and Medicinal Properties. *International Journal of Pharmacy and Biological Sciences-IJPBSTM* 11 (3):242-253
23. Stefan Teipal, Deborah Gustafson, Rik Ossenkoppele, Oskal Hansson, Claudio Babiloni, Michael Wagner, Steffi G. Riedel-Heller, Ingo Kilimann and Yi Tang (2023). Standard of Diagnosis, Treatment, Care and Prevention. *Nuclear medicine* 63(7) 981-985.
24. Zeinab Breijyeh, Rafik Karaman, 2020 Comprehensive Review of Alzheimer's disease *Molecules*, *25*(24), 5789;