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In Silico Screening and Molecular Dynamics Analysis of *Ficus palmata* Metabolites as Potential Butyrylcholinesterase Inhibitors

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Abstract Targeting important proteins could help regulate the complicated pathophysiological mechanism of Alzheimer's disease. Thus, in this work, molecular docking and dynamic simulation studies have been used to determine the mechanistic involvement of secondary metabolites predicted in *Ficus palmata* leaf, fruit, and aerial parts for their specific butyrylcholinesterase inhibitory capacity. According to virtual screening, the compounds' binding energy with butyrylcholinesterase ranges from -5.2 to -10.9 Kcal/mol. Quercetin-3-O-rutinoside-7-O-glucoside among all the compounds shown to be the most effective key protein's inhibitory potential with higher binding of energy than all other compounds and reference inhibitors. Consequently, the MDS study conducted for a 100 ns simulation time of this best hit and protein complex revealed that RMSD and RMSF data confirm the least fluctuations and higher stability. Meanwhile, RG values confirm that the compound maintained a stable conformation inside the active site of the enzyme with the least fluctuations of the complex. These findings suggest that the Quercetin-3-O-rutinoside-7-O-glucoside compound of *Ficus palmata* has significant butyrylcholinesterase inhibition potential. This study opens the door for metabolites of *Ficus palmata* as a candidate for further experimental investigation for the management of neuro- disorders.

Key Words *Ficus palmata*, Butyrylcholinesterase, Molecular Dynamics Simulation

INTRODUCTION

The worldwide mortality rate from Alzheimer's disease (AD) and related dementias (ADRD) has increased by 115% from 1991 to 2021, with an average annual increase of 1.10%. by 2021, over 24 million people had both AD and dementia, and projections estimate that 152 million people will have ADRD by 2050 [1,2]. Acetylcholine (ACh) is a neurotransmitter essential for various cellular processes, and deficiencies in the cholinesterase pathway caused by degenerating neurons lead to illness such as cognitive decline and memory loss in AD. Enzyme cholinesterase hydrolyzes ACh in the brain and further decreases in ACh exacerbate the condition. Targeting the cholinesterase pathway is a promising approach to managing AD [3]. Butyrylcholinesterase (BuChE), an isoenzyme of acetylcholinesterase, plays a crucial role in degrading acetylcholine and has significant pharmacological applications, including in AD, cocaine addiction, multiple sclerosis, and organophosphorus poisoning [4]. Recent studies indicate its involvement in lipid metabolism, particularly through the hydrolysis of choline esters, influencing lipid homeostasis and potentially leading to disorders like hyperlipidemia. Recognized since the 1950s for its role in hydrolyzing succinylcholine, BuChE is a key target for developing treatments for moderate- to severe Alzheimer's disease, especially given its links to amyloidogenesis and its prevalence in advanced disease stages. Recent patents for selective BuChE inhibitors highlight ongoing research in this area [5,6].

Current progress in computing has led to the extension of cheminformatics methods for screening and optimizing bioactive compounds through enzyme inhibition [7-9]. Moreover, natural resources, such as the *Ficus palmata* plant from the Moraceae family, show promise in providing therapeutic compounds for conditions like hyperlipidemia, gastrointestinal issues, tumors, and fungal infections [10-14]. Its leaf extracts are rich in polyphenols and flavonoids, showing antiglycation and antioxidant properties [14] while fruit extracts contain Eutin and luteolin, demonstrating strong antioxidant and anticancer activities [16]. The aerial

parts of the plant also possess significant antimicrobial, antidiabetic, analgesic, anticancer, anti-inflammatory, and thrombolytic effects [17-19].

There have been no reports on this plant's ability to treat AD by targeting butyrylcholinesterase, even though various parts of *Ficus palmata* have several beneficial chemicals. Thus, using molecular docking and molecular dynamics, the mechanistic insight and inhibitory potential of all the previously predicted compounds in *Ficus palmata* fruits, leaves, and aerial parts against butyrylcholinesterase (BuChE).

METHODS

The complex's molecular interactions were visualized through BIOVIA Discovery studio visualizer [20]. Workstation utilized in this study has following configuration, 12-GB Nvidia GPU [GTX4070Ti], 2TB SSD, 64GB of RAM, and an Intel core i9 14th edition CPU.

Molecular Interaction Research and In-Silico Screening

Molecular docking has made drug development easier. In this investigation, we employed the crystal structure of the 2018 release of butyrylcholinesterase, expressed in CHO cells in association with a rivastigmine analogue (PDB-ID: 6EYF), having a resolution of 2.60 Å and zero mutations [21]. The grid box dimension was set at 25x25x25 Å, with active site coordinates finalized at x: 42.88, y: 19.88, z: -23.44. The protein was prepared by removing the native ligand, including other heteroatoms, crystallographic water molecules, ions, and cofactors, and adding polar hydrogens only, whereas missing residues were addressed using Swiss PDB-Viewer [22]. Moreover, 3D structures of 57 secondary metabolites experimentally reported in *Ficus palmata* were downloaded from the PubChem database [16,17,23,24]. PyRx version 0.8 is based on AutoDock Vina version 4 and facilitated molecular docking after minimizing and converting the target protein and ligands to the '.pdbqt' format; exhaustiveness was set at 8 [25]. The protocol was initially validated by docking the co-crystallized native ligand and evaluating the RMSD to ensure it remained within the acceptable limit of 2Å, with binding affinity (Ki) and Gibbs free energy of binding (ΔG) reported to illustrate findings.

Molecular Dynamics Simulation Analysis

The study of molecular interactions and stability under physiological conditions of the best hits identified through molecular docking was evaluated through molecular dynamics simulation using Desmond software version 2019.4 [26,27]. The complexes were simulated in an orthorhombic box of 10 $Å^3$, neutralized with 0.15 M Na^+ or Cl^- counterions. Energy consumption was minimized using OPLS-2005, and a 100 ns simulation was carried out under NPT conditions (300 K, 1 bar), with a water solvent model.

RESULTS

Virtual Screening of *Ficus palmata* Compounds against Butyrylcholinesterase

The computational screening of *Ficus palmata* metabolites to assess their possible effectiveness against cholinergic enzymes is the focus of this work. It seeks to find substances that might block this enzyme, which is essential for neurodegenerative disease and synaptic transmission. To verify the procedure, initially the native ligand was re-docked into the predetermined location of its corresponding protein. It was noticed that the re-docked native ligand [RDNL] bound to similar residues of the active site, which are usually involved in stabilizing the co-crystallized native ligand (NL). In addition, the redocked native ligand superimposition image demonstrated that it stabilizes with similar residues involved in stabilizing the co-crystallized native ligand (Figure 1). The RMSD value between co-crystallized native ligand and redocked native ligand of butyrylcholinesterase were found to be approximately 1.8 angstrom, which was within the acceptable limit of RMSD of 2 angstroms.

As shown in Table 1, out of 57 secondary metabolites, only 13 metabolites exhibited better binding energy in the range between -10.9 and -10 kcal/mol against the target protein compared with the reference inhibitors like Donepezil (ΔG; -10 kcal/mol), tacrine (ΔG; -8.9 kcal/mol), and rivastigmine (ΔG; -7.6 kcal/mol). It has been noticed that out of these 13 compounds, eight compounds are reported in

Table 1: Binding Energy of the Best 13 Hits of *Ficus palmata* with Buche

S.No.	Code*	Compound Id	Compound Name	Part	ΔG [Kcal/mol]
1	FP1	10190763	Quercetin-3-O-rutinoside-7-O-glucoside	Fruit	-10.9
2	FP2	5280794	Stigmasterol	aerial	-10.8
3	FP3	115250	Taraxasterol	aerial	-10.7
4	FP4	222284	Stigmasterol, 22,23-dihydro-	aerial	-10.6
5	FP5	5280805	Rutin (Quercetin-3-O-rutinoside)	Fruit	-10.6
6	FP6	5318767	Kaempferol-3-O-rutinoside (Nicotiflorin)	Fruit	-10.5
7	FP7	5280804	Isoquercitrin (Quercetin-3-O-glucoside)	Fruit	-10.4
8	FP8	13644663	Vicenin-1 (Apigenin-8-C-glucoside-6-C-xyloside)	Fruit	-10.3
9	FP9	5282102	Astragalin (Kaempferol-3-O-glucoside)	Fruit	-10.2
10	FP10	162350	Isovitexin (Apigenin-6-C-glucoside)	Fruit	-10.1
11	FP11	259846	Lupeol	aerial	-10.1
12	FP12	442021	Brucine	aerial	-10.1
13	FP13	600671	Aegelinol, also known as Decursinol	Fruit	-10
14	RL1	donepezil	Reference inhibitor	-	-10
15	RL2	Tacrine	Reference inhibitor	-	-8.9
16	RL3	rivastigmine	Reference inhibitor and also native ligand	-	-7.6

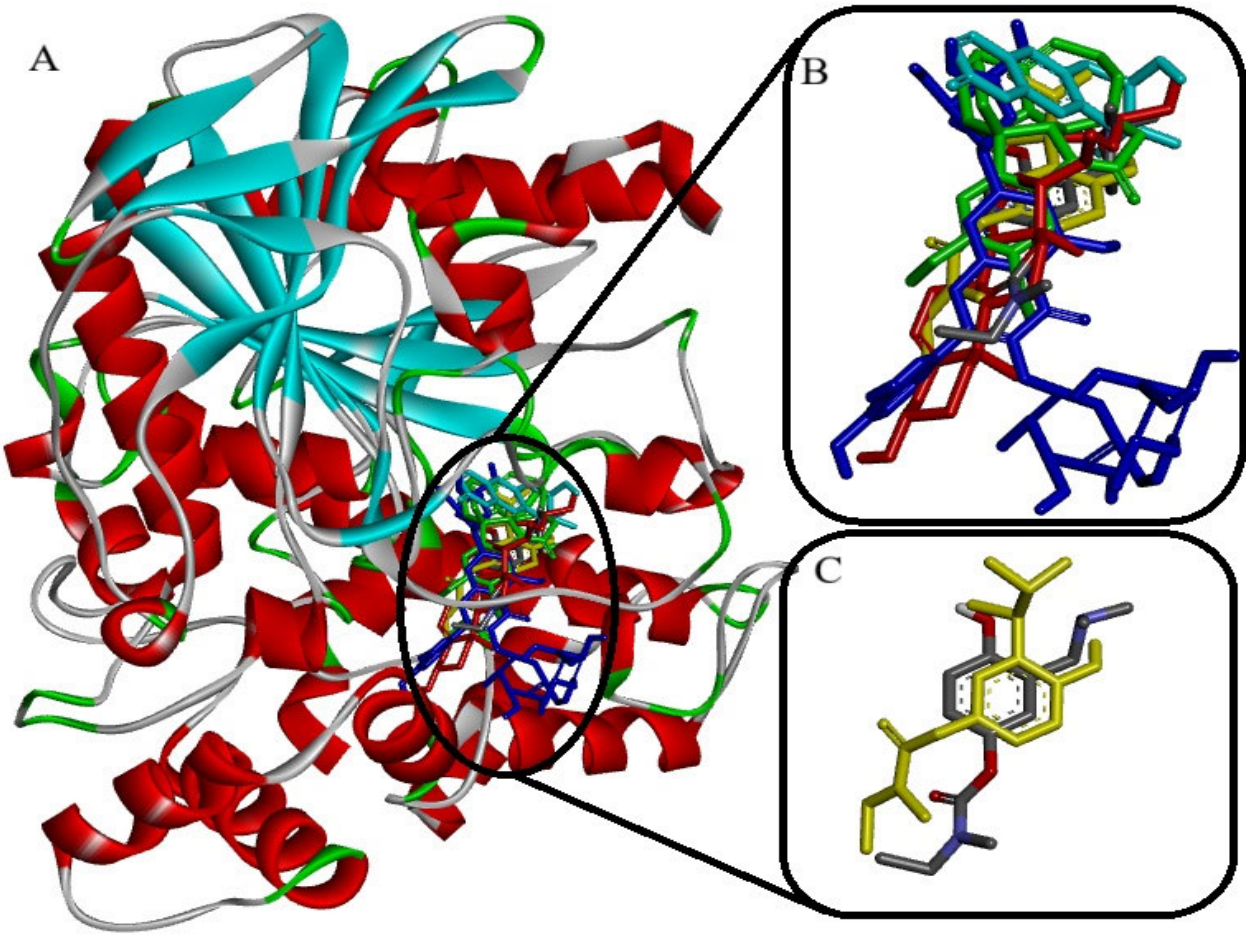


Figure 1: Molecular Docking Image. (A) Overall Image of *Ficus palmata* Best Hit and Native Ligand in Buche Pocket, (B) Co-Crystallized Native Ligand, Redocked Ligand, and *Ficus palmata* Best Hit in Buche Pocket, (C) Co-Crystallized Native Ligand (Grey Color), Redocked Ligand (Yellow Color)

fruit extract, and 5 compounds are reported in aerial part extract, whereas no metabolite of the leaf part exhibited better binding affinity.

Molecular Interaction Analysis

It has been illustrated that 13 compounds exhibited better binding affinity towards the target protein, and the best two hits are Quercetin-3-O-rutinoside-7-O-glucoside (FP1) and Stigmasterol (FP2). Further, it has been observed that out of these 13 best hits, only two compounds [Brucine (FP12), and Aegelinol (FP13)] are blood-brain barrier permeable, as illustrated through the SWISSADME web-based tool. Therefore, in this study, these four compounds were chosen for additional study. It has been observed that TRP82 and PRO285 are the key residues that interact with the co-crystallized native ligand and are present in re-docked native ligand stabilization (Figure 2 A, B). Molecular interaction analysis illustrated that the Quercetin-3-O-rutinoside-7-O-glucoside and protein complex is stabilized with four conventional hydrogen bonds (GLY283, GLU276, HIS438), two carbon hydrogen bonds (GLY116, BXT198), and two pi-alkyl interactions (PRO285) (Figure 2C). The stigmasterol-protein complex is stabilized by one carbon hydrogen bond (ALA277), three alkyl interactions with PRO285, ALA328, MET437, and five pi-alkyl interactions with TRP82, TRP430, TYR440 (Figure 2D). The brucine-protein complex is stabilized by one conventional hydrogen bond (TYR332), three carbon hydrogen bonds (GLU197, HIS438, PRO285), one alkyl interaction with PRO285, and four pi-alkyl interactions with TRP82, HIS438, and PRO285 (Figure 2E). The aegelinol-protein complex has been stabilized by four pi-pi stacking interactions with TRP82 (Figure 2F). Our results are in correspondence with previous reports where residues, namely SER79, TRP82, TYR128, ALA199, TRP231, PRO285, LEU286, VAL288, ALA328, PHE329, TYR332, PHE398, TRP430, MET437, AND HIS438, are involved in stabilizing the reference ligands [28,29].

Molecular Dynamics Simulation Study

Molecular dynamics simulations (MDS) model atomic movement in proteins and molecular systems, predicting biomolecular processes like conformational shifts, ligand binding, and protein folding at femtosecond resolution. They reveal atomic positions and how biomolecules respond to perturbations such as mutations or ligand changes [30].

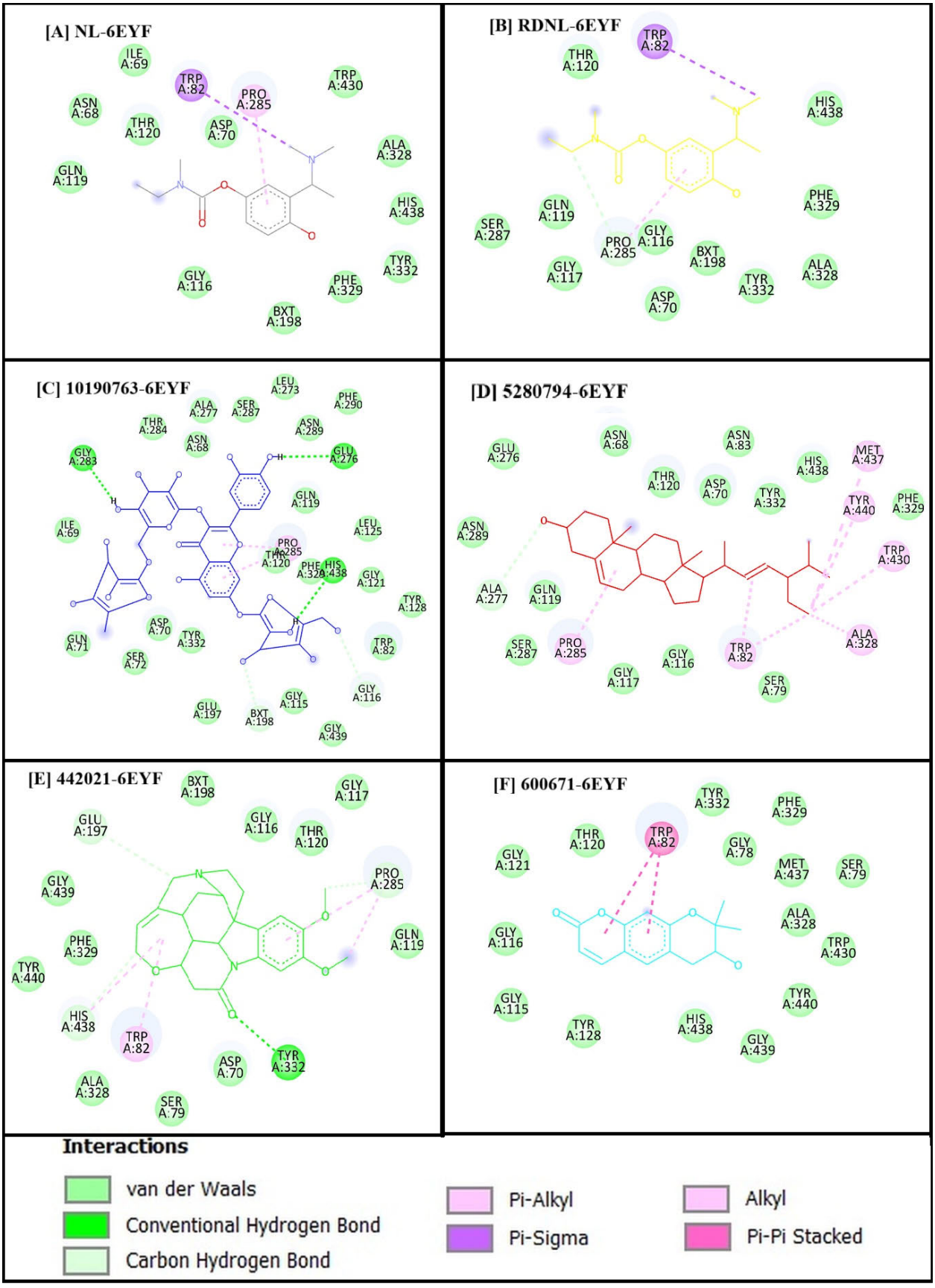


Figure 2: Molecular Interactions of [A] Native Ligand, [B] Redocked-Native Ligand, [C] Quercetin-3-O-Rutinoside-7-O-Glucoside, [D] Stigmasterol, [E] Brucine, and [F] Aegelinol in Complex with Butyrylcholinesterase Enzyme

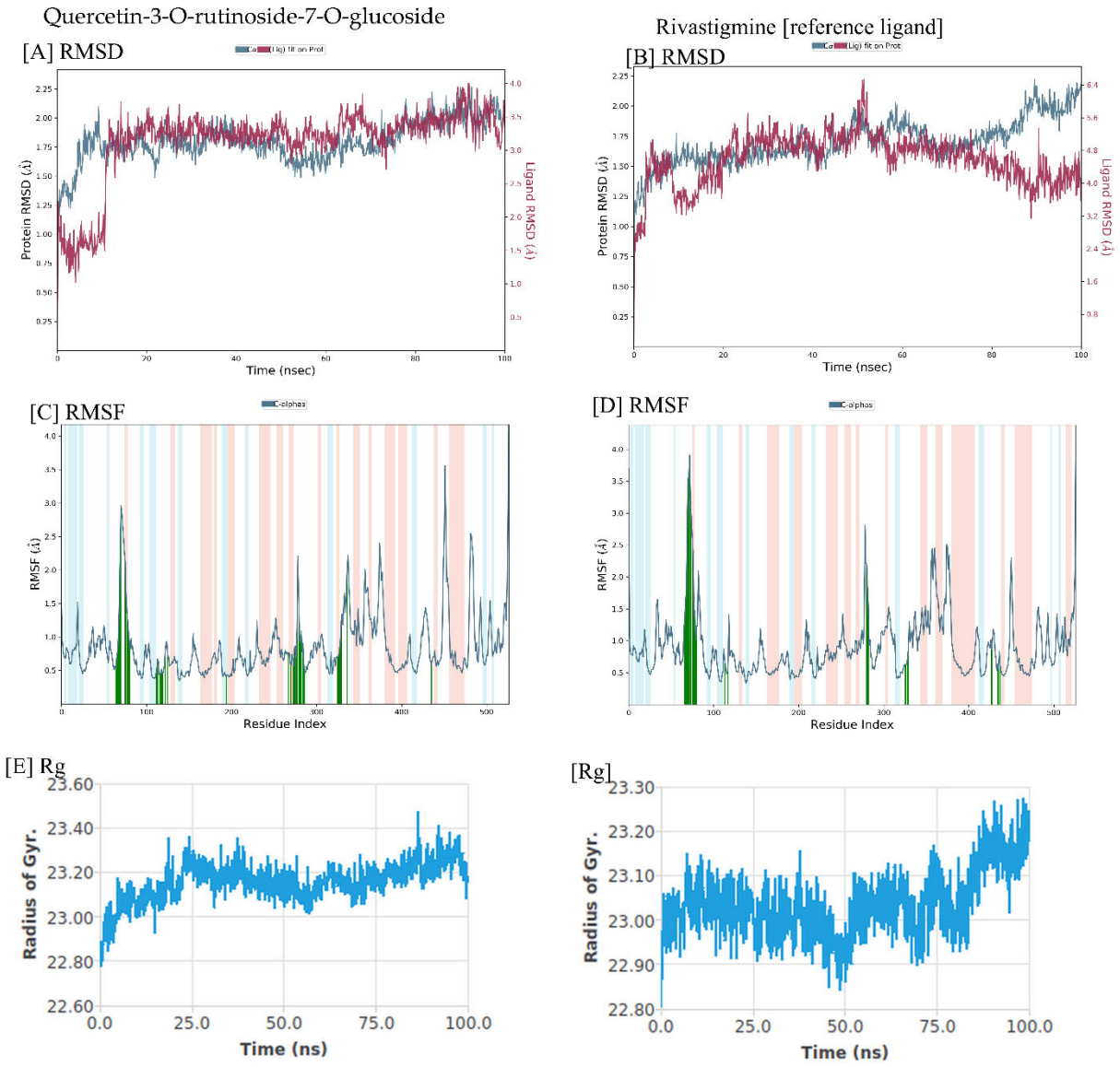


Figure 3: Molecular Dynamics Simulation Parameters of Fp1 And Rivastigmine in Complex with Butyrylcholinesterase Enzyme

Computational drug discovery methods utilize molecular docking and thermodynamic-based molecular dynamics simulation to analyze protein-ligand interactions virtually. MD simulations complement docking techniques, enhancing the *In Silico* drug discovery process. Molecular dynamics simulation research relies heavily on the examination of molecular interactions and metrics like root mean square deviation (RMSD), root mean square fluctuation (RMSF), and radius of gyration (RG) [31].

In this study, the FP1-BuChE complex has been selected for further MDS study due to its strong binding potential and interaction with key residues. During the 100 ns simulation, we evaluated the RMSD value of the target protein (BuChE) using the chemical FP1. Furthermore, the examination of RMSF values offers important information about the dynamics, stability, and flexibility of protein-ligand complexes. A stronger and more stable contact between the ligand and the protein is shown by a lower RMSF value, which implies less shift or fluctuation at the binding site residues [32]. To identify local conformational changes in the protein's side chain structure brought on by ligand interaction, RMSF must be continually monitored [33]. In this regard, the RMSF for BuChE was also evaluated in the Presence of the ligand Quercetin-3-O-rutinoside-7-O-glucoside. Our findings show how the RMSD values for C-alpha atoms of the ligand-bound protein changed during the course of the simulation. Throughout the simulation, the protein in the BuChE-FP1 complex remained in the active site location and demonstrated significant stability, fluctuating within the permissible overall range of 3 angstroms (Figure 3 A). In relation to the protein in the complex of BuChE-FP1 the average RMSD value of

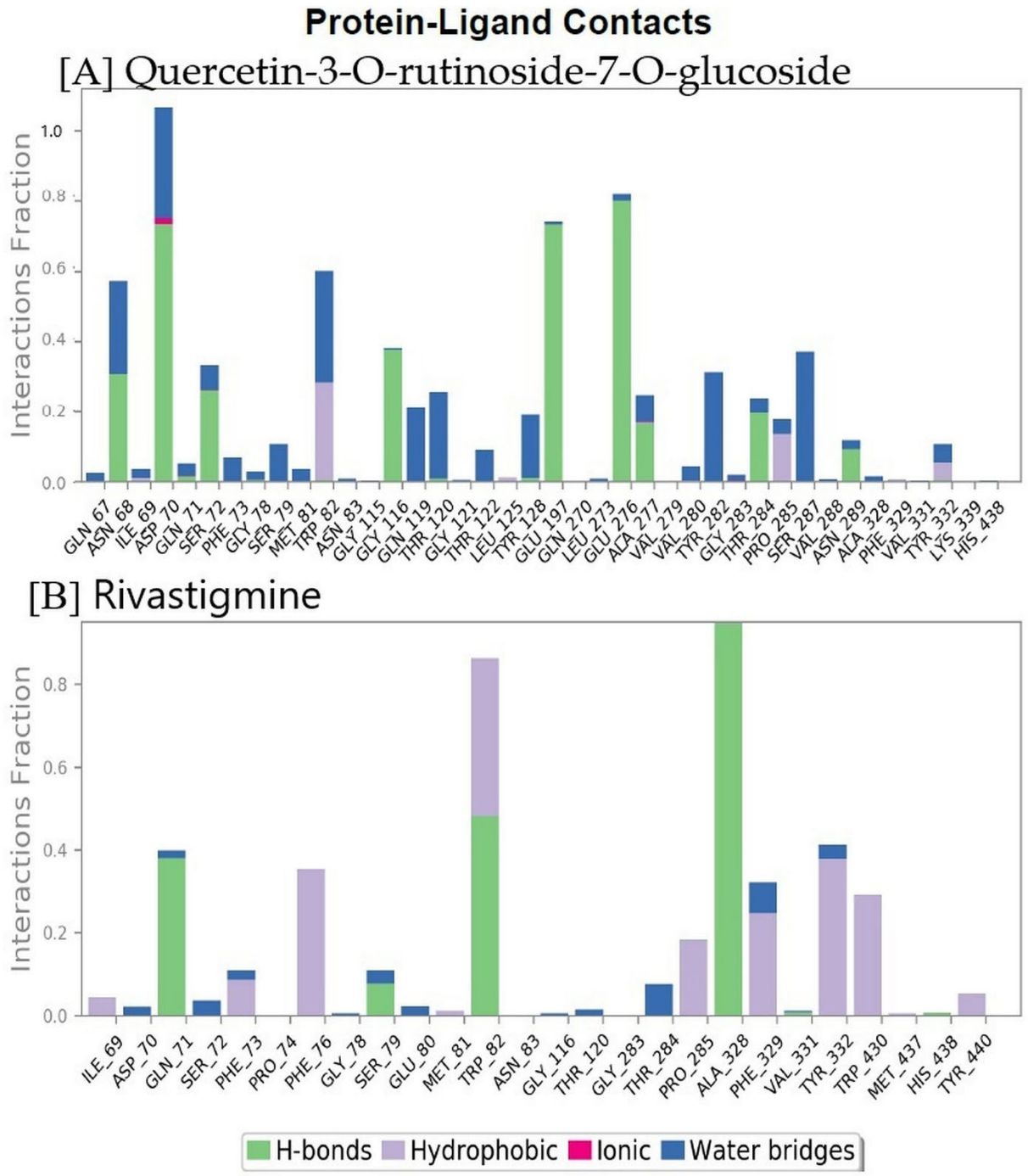


Figure 4: (A) Intermolecular Interactions of FP1 with Buche Enzyme, (B) Intermolecular Interactions of Rivastigmine with Buche Enzyme

protein's C-alpha and ligand were determined to be 1.80±0.17 Å and 3.13±0.40 Å, respectively. In contrast, the average RMSD values of the ligand and protein C-alpha in the complex of BuChE-rivastigmine (redocked-native ligand) were 1.70±0.19 Å, and 4.58±0.60 Å, respectively (Figure 3 B). Here we noticed that FP1 is more stable than rivastigmine.

The average RMSF value of protein C-alpha in complex with FP1 and redocked native ligand, rivastigmine were 0.92±0.53 Å, and 0.93±0.60 Å, respectively. Except for few additional residues (GLN67, ASN68, GLY115, GLN119, GLY121, THR122, LEU125, TYR128, GLU197, GLN270, LEU273, GLU276, ALA277, VAL279, VAL280, TYR282, SER287, VAL288, ASN289,LYS339) the residues involved in stabilizing the BuChE- FP1 complex were largely similar to those involved in stabilizing its native ligand (ILE_69, ASP_70, GLN_71, SER_72, PHE_73, GLY_78, SER_79, MET_81, TRP_82, ASN_83, GLY_116, THR_120,

GLY_283, THR_284, PRO_285, ALA_328, PHE_329, VAL_331, TYR_332, HIS_438) (Figure 3 C, D). The correlation between simulation duration and a compound's radius of gyration (Rg) sheds light on how a ligand moves inside the binding pocket of an enzyme [34]. The stability of the protein-ligand bond during the simulation is reflected in the degree of compactness of the protein-ligand complex, as shown by Rg [33]. Our findings show that the Rg of the protein-ligand interaction varies during the course of the simulation. The average Rg value for BuChE in complex with FP1 and rivastigmine is recorded as follows: 23.15±0.09 Å and 23.04±0.07 Å, respectively (Figure 3 E, F).

The study found substantial hydrogen bonding and hydrophobic interactions while evaluating the molecule FP1's interaction pattern with BuChE. FP1 demonstrated a hydrogen bond with GLN67, ASP70, SER72, GLY116, GLU197, GLU276, THR284, and ASN289 throughout a significant simulation period, as well as hydrophobic contacts with residues TRP82, THR285, and TYR332, for over 20% of the total interaction time over 100 ns of simulation (Figure 4A, B). All things considered, these interactions show that FP1 stayed inside the target protein's binding pocket and formed a stable protein-ligand complex. According to the histogram bar chart, connections that were maintained for 100% of the simulation period during the trajectory are represented by a value of 1.0.

Drug design is a laborious and costly process; thus, the pharmaceutical industry greatly benefits from techniques that help cut costs and development time. Affinity prediction techniques play a major role in structure-based drug design, and computational rules greatly facilitate drug design and molecular docking by facilitating quick analysis and reducing cost in comparison to experimental methods. Brucine has known toxicological concerns. The relatively large molecular size and polarity of FP1 have potential implications for passive transport across the blood–brain barrier. However, these techniques have significant limitations, especially as they only assess energy affinity once and do not consider drug metabolism, underscoring the necessity of molecular dynamics for thorough analysis of interactions. Limitations also include selecting compounds from previously reported phytochemical profiles without experimentally confirming their presence and concentrations in the plant material used in this study. In this study, a limitation is that no enzyme inhibition assay, cytotoxicity assessment, pharmacokinetic evaluation, or animal study was conducted. For future studies, it identifies in vitro BuChE inhibition assays, selectivity testing against AChE, cytotoxicity and safety evaluation, experimental BBB-permeability assessment, and subsequent pharmacokinetic studies as necessary next steps before any preclinical or therapeutic claims can be considered. While in vitro and in vivo investigations can be speed up by computer studies or *In Silico* studies, they are not a substitute for them; rather, they are used to anticipate the molecular interaction sites in a particular protein-ligand complex [35,36].

CONCLUSIONS

Few metabolites of *Ficus palmata* inhibit the target protein more efficiently than the reference inhibitor of its corresponding protein according to this computational screening and interaction analysis of *Ficus palmata*, secondary metabolites predicted in earlier studies against the protein of cholinergic pathway (BuChE), out of all the compounds found in *Ficus palmata* it has been noticed that FP1 (PubChem ID-10190763) was the most prevalent and demonstrated the best binding energy (ΔG: -10.9 Kcal/mol), against the target protein as well as comparatively greater potency than its native ligand (ΔG: -7.6 Kcal/mol). Additionally, detailed information regarding the behavior of compounds in a physiological environment has been obtained by a molecular dynamics modelling study. FP1 demonstrated the most favourable predicted docking score among the screened metabolites and maintained a comparatively stable simulated interaction with BuChE under the reported computational conditions. Here, according to this investigation, FP1 is predicted to be an effective therapeutic medication for the treatment of neurological disorders and Alzheimer disease. It has been explicitly emphasized that biochemical, cellular, pharmacokinetic and appropriate in vivo investigations are required before therapeutic or clinical conclusions can be drawn. However, experimental validation is required before any therapeutic or clinical conclusions can be drawn, and more research is needed to approve FP1 for use in human consumption in the treatment of neurological disorders.

Author Contributions

M.A. contributed to all aspects of manuscript preparation starting from conceptualization till final approval of the manuscript.

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Data Availability Statement

All the data associated with this research have been included in this submitted article. However, if raw data is required, then it can be provided by the corresponding author.

Conflicts of Interest

The author reports no conflicts of interest, and the funders were not involved in any aspect of the study, including design, data handling, manuscript writing, or publication decisions.

AI Disclosure Statement

The authors utilized the Quill Bot online tool to edit the language, enhance grammar, and summarize some text for fluency during the preparation of the manuscript. Authors further reviewed the entire AI-assisted content to ensure accuracy and keep the originality of the concept. The integrity and ultimate content of the manuscript are entirely the author's responsibility.

Consent

The author states that this portion does not apply to this research.

Ethical Approval

The author hereby declare that there are no experiments performed therefore ethical approval is not applicable to this study.

REFERENCES

[1] "Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: An analysis for the Global Burden of Disease Study 2019." *The Lancet Public Health*, https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00249-8/fulltext. Accessed 19 Jan. 2026.

[2] Xiaopeng Z. *et al.* "Global burden of Alzheimer's disease and other dementias in adults aged 65 years and older, 1991–2021: Population-based study." *Frontiers in Public Health*, vol. 13, 2025. https://doi.org/10.3389/fpubh.2025.1585711.

[3] Atatreh N. *et al.* "Discovery of new butyrylcholinesterase inhibitors via structure-based virtual screening." *Journal of Enzyme Inhibition and Medicinal Chemistry*, vol. 34, no. 1, 2019, pp. 1373–79. https://doi.org/10.1080/14756366.2019.1644329.

[4] Sun T. *et al.* "New insights into butyrylcholinesterase: Pharmaceutical applications, selective inhibitors and multitarget-directed ligands." *European Journal of Medicinal Chemistry*, vol. 275, 2024, article 116569. https://doi.org/10.1016/j.ejmech.2024.116569.

[5] Furtado-Alle L. *et al.* "Butyrylcholinesterase and lipid metabolism: Possible dual role in metabolic disorders." *Chemico-Biological Interactions*, vol. 383, 2023, article 110680. https://doi.org/10.1016/j.cbi.2023.110680.

[6] Fernández-Bolaños J.G. and López Ó. "Butyrylcholinesterase inhibitors as potential anti-Alzheimer's agents: An updated patent review (2018–present)." *Expert Opinion on Therapeutic Patents*, vol. 32, no. 8, 2022, pp. 913–32. https://doi.org/10.1080/13543776.2022.2083956.

[7] Iqbal D. *et al.* "Soyasapogenol-B as a potential multitarget therapeutic agent for neurodegenerative disorders: Molecular docking and dynamics study." *Entropy*, vol. 24, no. 5, 2022, article 593. https://doi.org/10.3390/e24050593.

[8] Iqbal D. *et al.* "Pharmacophore-based screening, molecular docking, and dynamic simulation of fungal metabolites as inhibitors of multi-targets in neurodegenerative disorders." *Biomolecules*, vol. 13, no. 11, 2023, article 1613.

[9] Iqbal D. *et al.* "Multitargeted virtual screening and molecular simulation of natural product-like compounds against GSK3β, NMDA-receptor, and BACE-1 for the management of Alzheimer's disease." *Pharmaceuticals*, vol. 16, no. 4, 2023, article 622.

[10] Wang S. *et al.* "Role of natural compounds and target enzymes in the treatment of Alzheimer's disease." *Molecules*, vol. 27, no. 13, 2022, article 4175. https://doi.org/10.3390/molecules27134175.

[11] Andrade S. *et al.* "Natural compounds for Alzheimer's disease therapy: A systematic review of preclinical and clinical studies." *International Journal of Molecular Sciences*, vol. 20, no. 9, 2019, article 2313. https://doi.org/10.3390/ijms20092313.

[12] Khan M.R. *et al.* "Evaluation of the characteristics of native wild Himalayan fig (*Ficus palmata* Forsk.) from Pakistan as a potential species for sustainable fruit production." *Sustainability*, vol. 14, no. 1, 2022, article 468. https://doi.org/10.3390/su14010468.

[13] Iqbal D. *et al.* "In vitro screening for β-hydroxy-β-methylglutaryl-CoA reductase inhibitory and antioxidant activity of sequentially extracted fractions of *Ficus palmata* Forsk." *BioMed Research International*, vol. 2014, 2014, article 762620. https://doi.org/10.1155/2014/762620.

[14] Almalki S.G. *et al.* "Antioxidant, LC-MS analysis, and cholinesterase inhibitory potentials of *Phoenix dactylifera* cultivar Khudari: An in vitro enzyme kinetics and *In Silico* study." *Biomolecules*, vol. 13, no. 10, 2023, article 1474.

[15] Alouffi S. *et al.* "Antiglycation and chemopreventive effects of leaf extracts of *Ficus palmata* Forssk. found in the Hail region of Saudi Arabia." *Biotechnology and Genetic Engineering Reviews*, vol. 40, no. 3, 2024, pp. 1709–25. https://doi.org/10.1080/02648725.2023.2196477.

[16] Tewari D. *et al.* "Phenolic profiling, antioxidants, multivariate, and enzyme inhibitory properties of wild Himalayan fig (*Ficus palmata* Forssk.): A potential candidate for designing innovative nutraceuticals and related products." *Analytical Letters*, vol. 54, no. 9, 2021, pp. 1439–56. https://doi.org/10.1080/00032719.2020.1804395.

[17] Al-Qahtani J. *et al.* "Phytochemical, antimicrobial, antidiabetic, thrombolytic, anticancer activities, and *In Silico* studies of *Ficus palmata* Forssk." *Arabian Journal of Chemistry*, vol. 16, no. 2, 2023, article 104455. https://doi.org/10.1016/j.arabjc.2022.104455.

[18] Al-Qahtani J. *et al.* "Analgesic and anti-inflammatory potential of *Ficus palmata* Forssk.: An in vitro and in vivo approach." *Scientific Reports*, vol. 15, no. 1, 2025, article 37926. https://doi.org/10.1038/s41598-025-25430-5.

[19] Aziz B. *et al.* "In vitro evaluation of the cytotoxic potential of *Ficus palmata* and its combination with chemotherapy and photodynamic therapy." *Laser Physics Letters*, vol. 20, no. 5, 2023, article 055601. https://doi.org/10.1088/1612-202X/acc244.

[20] BIOVIA. *BIOVIA Discovery Studio*. 2021, https://www.3ds.com/products-services/biovia/products/molecular-modeling-simulation/biovia-discovery-studio/. Accessed 1 Oct. 2021.

[21] Dighe S.N. *et al.* "Rivastigmine and metabolite analogues with putative Alzheimer's disease-modifying properties in a *Caenorhabditis elegans* model." *Communications Chemistry*, vol. 2, no. 1, 2019, article 35. https://doi.org/10.1038/s42004-019-0133-4.

[22] Guex N. and Peitsch M.C. "SWISS-MODEL and the Swiss-PdbViewer: An environment for comparative protein modeling." *Electrophoresis*, vol. 18, no. 15, 1997, pp. 2714–23. https://doi.org/10.1002/elps.1150181505.

[23] Alaizari A. *et al.* "Comparative analysis of phytochemical and antioxidant activity in the mother tree and in vitro regenerated fegra fig (*Ficus palmata* Forssk.)." *Applied Ecology and Environmental Research*, vol. 22, 2024. https://doi.org/10.15666/aeer/2206_59655976.

[24] Kim S. *et al.* "PubChem 2025 update." *Nucleic Acids Research*, vol. 53, no. D1, 2025, pp. D1516–25. https://doi.org/10.1093/nar/gkae1059.

[25] Dallakyan S. and Olson A.J. "Small-molecule library screening by docking with PyRx." *Chemical Biology: Methods and Protocols*, edited by J.E. Hempel, C.H. Williams, and C.C. Hong, Springer, 2015, pp. 243–50. *Methods in Molecular Biology*. https://doi.org/10.1007/978-1-4939-2269-7_19.

[26] Iqbal D. *et al.* "Exploring the binding pattern of geraniol with acetylcholinesterase through *In Silico* docking, molecular dynamics simulation, and *in vitro* enzyme inhibition kinetics studies." *Cells*, vol. 10, no. 12, 2021, article 3533. https://doi.org/10.3390/cells10123533.

[27] Filipe H.A.L. and Loura L.M.S. "Molecular dynamics simulations: Advances and applications." *Molecules*, vol. 27, no. 7, 2022, article 2105. https://doi.org/10.3390/molecules27072105.

[28] Sindhu T.J. *et al.* "Mechanistic insights into thiazolidinones as anticholinesterase agents: 3D QSAR pharmacophore modeling, molecular docking, MD simulations, and DFT studies for Alzheimer's therapy." *Journal of Computational Biophysics and Chemistry*, vol. 24, no. 10, 2025, pp. 1415–40. https://doi.org/10.1142/S2737416525500309.

[29] T.J.S. *et al.* "MD simulations, DFT and molecular docking studies of Schiff base-derived heterocycles as potent BuChE inhibitors for Alzheimer's disease." *ChemistrySelect*, vol. 11, no. 1, 2026, article e03914. https://doi.org/10.1002/slct.202503914.

[30] Hollingsworth S.A. and Dror R.O. "Molecular dynamics simulation for all." *Neuron*, vol. 99, no. 6, 2018, pp. 1129–43. https://doi.org/10.1016/j.neuron.2018.08.011.

[31] Singh S. *et al.* "Molecular docking and molecular dynamics simulation." *Bioinformatics Methods and Applications*, Academic Press, 2022, pp. 291–304. https://doi.org/10.1016/B978-0-323-89775-4.00014-6.

[32] aqvi A.A.T. *et al.* "Advancements in docking and molecular dynamics simulations towards ligand-receptor interactions and structure-function relationships." *Current Topics in Medicinal Chemistry*, vol. 18, no. 20, 2018, pp. 1755–68. https://doi.org/10.2174/1568026618666181025114157.

[33] Adelusi T.I. *et al.* "Molecular modeling in drug discovery." *Informatics in Medicine Unlocked*, vol. 29, 2022, article 100880. https://doi.org/10.1016/j.imu.2022.100880.

[34] Ausaf Ali S. *et al.* "A review of methods available to estimate solvent-accessible surface areas of soluble proteins in the folded and unfolded states." *Current Protein and Peptide Science*, vol. 15, no. 5, 2014, pp. 456–76.

[35] Dutkiewicz Z. "Computational methods for calculation of protein-ligand binding affinities in structure-based drug design." *Physical Sciences Reviews*, vol. 7, no. 9, 2022, pp. 933–68. https://doi.org/10.1515/psr-2020-0034.

[36] Agu P.C. *et al.* "Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management." *Scientific Reports*, vol. 13, 2023, article 13398. https://doi.org/10.1038/s41598-023-40160-2.