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Exploration of Marine Bioactive Compounds Against Alzheimer's Disease: An in Silico Molecular Docking Approach Targeting Human Acetylcholinesterase

[1] Suryawanshi Hanumant Shankar, [2] Gulwe Ashish Bhiwajirao

[1, 2] School of Technology, Swami Ramanand Teerth Marathwada University, Sub Campus Latur – 413531, Maharashtra, India

Corresponding Author: **Suryawanshi Hanumant Shankar**

Abstract

Alzheimer's disease (AD) is a progressive neurological disorder characterized by gradual cognitive decline and memory loss. A reduction in acetylcholine levels in the head region is one of its most important pathological signs. This is mostly caused by acetylcholinesterase (AChE) being more active. Current therapeutic agents offer merely symptomatic relief and are frequently accompanied by adverse effects. Therefore, there is vital requirement to explore safer and more effective alternatives. Marine bioactive compounds have emerged as promising candidates due to their structural diversity and pharmacological potential. This study aims to evaluate the inhibitory potential of selected marine -derived bioactive compounds against human AChE using an in silico molecular docking approach. The docking results revealed that several marine compounds exhibited strong binding affinities, in some cases outperforming standard synthetic drugs. These results underscore the promise of marine-derived metabolites as safer and more efficacious alternatives to synthetic agents for the treatment of Alzheimer's disease.

Keywords: Alzheimer's Disease, Marine Bioactive Compounds, Molecular Docking, Human Acetylcholinesterase, Superiority Over Synthetic Compounds

1. Introduction

Alzheimer's disease (AD) accounts more than 65% of dementia cases worldwide and represents a major global health challenge [1]. The disease is characterized by progressive neuronal degeneration, leading to memory impairment, cognitive dysfunction, and behavioural changes. One of the hallmark features of AD is the reduction of acetylcholine (ACh) levels in the brain, which plays a crucial role in learning and memory. Acetylcholinesterase (AChE) is the enzyme require for the hydrolysis of acetylcholine. Inhibition of AChE is a well-established therapeutic strategy for improving cholinergic transmission in AD patients. Currently available synthetic drugs such as donepezil, rivastigmine, and galantamine are widely used; however, they provide only indicative relief and may cause adverse side effects. Natural bioactive compounds, particularly those obtained from marine habitat, offer an alternative structural diversity, and reduced toxicity. Marine metabolites have demonstrated significant pharmacological activities, including neuroprotective, antioxidant, and enzyme inhibitory properties [2]. Furthermore, these compounds frequently demonstrate improved safety profiles compared to synthetic drugs, highlighting their potential advantage.

2. Materials and Methods

2.1 Target Protein Preparation

The three-dimensional structure of human acetylcholinesterase (AChE) was obtained and prepared from the Protein Data Bank (PDB ID: 4EY7). The protein structure was prepared by removing water molecules and co-crystallized ligands. Energy reduction was performed using appropriate force field parameters to stabilize the structure [3].

2.2 Ligand Preparation

A library of Marine bioactive compounds was compiled from literature and public databases. The structures were obtained in SDF format and changed into PDB format. Energy reduction and geometry optimization were carried out prior to docking [4].

2.3 Molecular Docking

Molecular docking process was performed using AutoDock Vina to evaluate the binding empathy of the selected compounds

with AChE [3]. The active site of the enzyme was defined based on the coordinates of the co-crystallized ligand. Binding energies and interaction profiles were analyzed.

2.4 ADMET Analysis

Pharmacokinetic criteria are mandatory for drug development process includes Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET)—were assessed using computational tools such as SwissADME to evaluate drug-likeness and safety profiles [6].

3. Results and Discussion

Table 1: Top Marine Bioactive Compounds with its Docking Scores

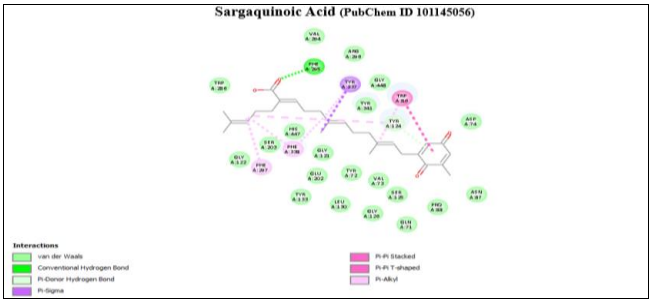
S. No	Compound Name	Source	Compound CID	Binding Energy (Kcal/mol)
1	Sargaquinoic Acid	*Sargassum serratifolium*	101145056	-10.2
2	Caulerpin	*Caulerpa racemosa.*	5326018	-8.8
3	Gracilin A	*Spongionella gracilis*	23425244	-7.4
4	Aaptamine	*Aaptos aaptos*	163192233	-8.6
5	Sargachromenol	*Sargassum macrocarpum*	51003424	-9.6
6	Manzamine A	*Micromonospora sp.*	6509753	14.6
7	Manoalide	*Luffariella variabilis*	6437368	-7.9
8	Barettin	*Geodia barretti*	1177588	-9.6
9	Brassicasterol	*Gonyaulax polygramma*	5281327	-8.1
10	Donepezil* (Control)	Synthetic	3152	-9.3

Table 2: ADMET and Drug Likeness Features of Selected Marine Compounds

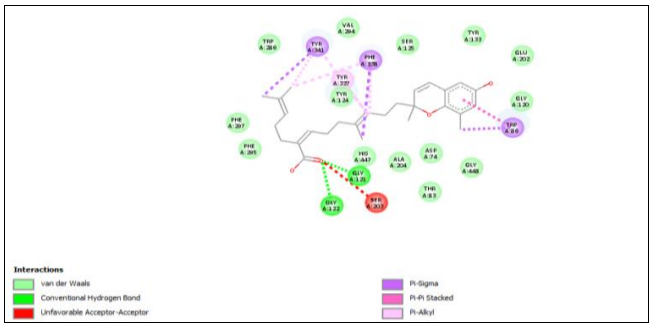
S. No	Compound Name	Lipinski Compliance	BBB	GI Absorption
1	Sargaquinoic Acid	Yes	Moderate	High
2	Caulerpin	Yes	High	High
3	Gracilin A	No	Moderate	Moderate
4	Aaptamine	Yes	High	High
5	Sargachromenol	Yes	Moderate	High
6	Manzamine A	Yes (1 Violates)	High	Moderate
7	Manoalide	Moderate	Low	Moderate
8	Barettin	Yes	High	High
9	Brassicasterol	No	Low	High
10	Donepezil* (Control)	Yes	High	High

Table 3: 2D Structures of Highly Rated Marine Compounds

Sargaquinoic Acid (PubChem ID 101145056)



Sargachromenol (PubChem ID 51003424)



Barettin (PubChem ID 11177588)

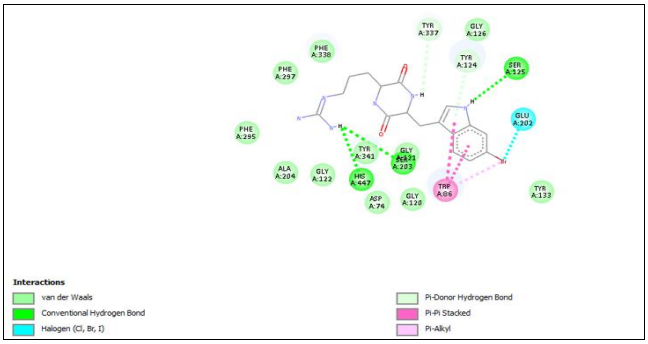
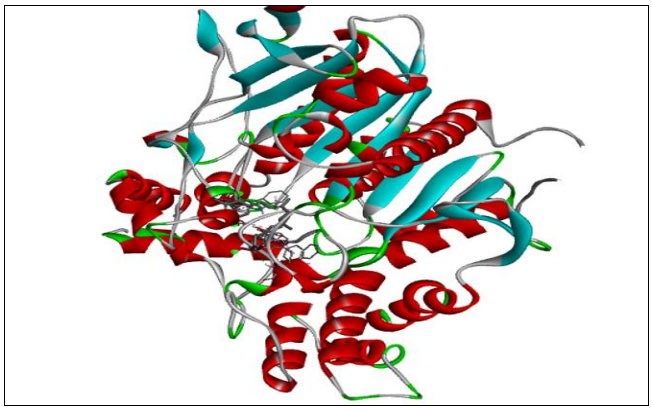
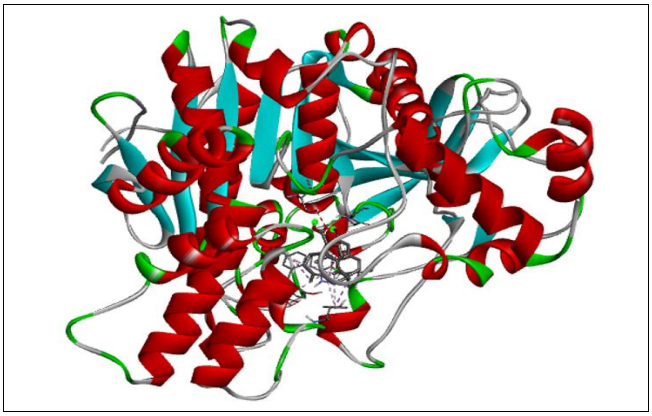


Table 4: 3D Structures of Highly Rated Marine Compounds

Sargaquinoic Acid (PubChem ID 101145056)



Sargachromenol (PubChem ID 51003424)



Barettin (PubChem ID 11177588)

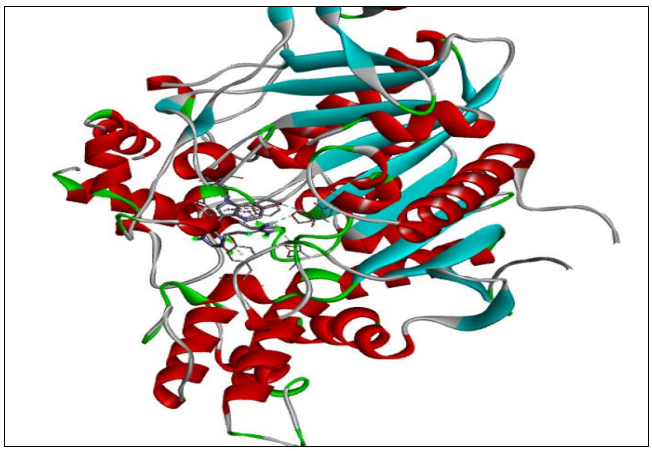


Table 5: Comparative Docking Analysis Table with Human Acetylcholinesterase (PDB ID - 4EY7)

Parameter	Sargaquinoic Acid	Sargachromenol	Barettin
PubChem CID	101145056	51003424	11177588
Binding Mode	Extended (spans gorge)	Extended (CAS + PAS)	Compact
Hydrogen Bonds	PHE295	GLY121, GLY122, SER203	SER125, GLY121, TYR341, HIS447
Catalytic Residue Interaction	HIS447, SER203, GLU202 (vdW)	SER203 (H-bond), HIS447 (vdW)	HIS447 (H-bond), GLU202 (halogen)
π–π Stacking	TRP86, TYR337, PHE297	TRP86, TYR337	TRP86
π–Sigma Interaction	TYR337	PHE338	-
π–Alkyl Interactions	TYR124, VAL73, LEU130	TYR124, PHE297, VAL294	TYR124, PHE338, PHE297
Halogen Interaction	-	-	GLU202 (Br bond)
PAS Binding	TRP286, TYR337	TRP286, TYR341	TRP86, TYR337
van der Waals	GLY121, GLY122, SER203, GLU202, HIS447	GLU202, HIS447, ASP74, THR83, GLY120	ASP74, GLY120, GLY122, ALA204, TYR133
Unfavourable Interaction	None	SER203 clash	None
Binding Stability	High	Moderate–High	Very High
Key Forces	π–π + hydrophobic	π–π + H-bonds	H-bonds + π–π + halogen
CAS Interaction	Yes	Yes	Strong
PAS Interaction	Yes	Yes	Yes
Dual Binding	Yes	Yes	Yes
Overall Potential	Strong Inhibitor	Good Inhibitor	Very Strong Inhibitor

4. Conclusion

Sargaquinoic acid demonstrates robust binding within the AChE active gorge, forming critical interactions with both catalytic and peripheral residues. The presence of π–π stacking with TRP86 and TYR337, along with hydrogen bonding and hydrophobic contacts, indicates a stable and effective inhibitory profile. Its binding mode suggests comparable behaviour to standard AChE inhibitors, supporting its potential as a promising marine-derived anti-Alzheimer's candidate.

Sargachromenol exhibits strong and stable binding within the active gorge of AChE, supported by π–π interactions with TRP86 and TYR337, along with hydrogen bonding near the catalytic triad (SER203, GLY121, GLY122). The ligand bridges both CAS and PAS regions, suggesting a dual inhibitory mechanism. Despite a minor unfavourable interaction with SER203, the overall binding profile indicates that Sargachromenol is a promising marine-derived acetylcholinesterase inhibitor for Alzheimer's disease.

Barettin demonstrates a robust binding profile within the AChE active gorge, characterized by multiple hydrogen bonds with catalytic residues (HIS447, SER203 region), strong π–π stacking with TRP86, and a unique halogen bond with GLU202. The ligand effectively bridges the catalytic and peripheral sites, indicating a dual inhibitory mechanism. These features, combined with its brominated scaffold, make Barettin a highly promising marine-derived acetylcholinesterase inhibitor for Alzheimer's disease.

5. References

1. Lane RM, Kivipelto M, Greig NH. Acetylcholinesterase and its inhibition in Alzheimer disease. Clinical neuropharmacology, May 1, 2004; 27(3):141-149.
2. Ajay N Ambhore, Ashish B Gulwe, Ebube S Chidera, Awote O Kayode. Molecular Docking Study of Selected Bio-Active Compounds in Alzheimer's Disease Using BACE-1 (PDB ID: 5QCU) as target protein. Journal of Population Therapeutics & Clinical Pharmacology. 2023; 30(3):787-793.
3. Morris GM, Huey R, Olson AJ. Using autodock for ligand-receptor docking. Current Protocols in Bioinformatics, Dec 2008; 24(1):8-14.
4. Kaitwad R, Gulwe A, Dipke C, Suryawanshi H, Murge N, Nalage D. Current and emerging therapies for Parkinson's disease: Advances toward disease modification. Life Res. 2025; 8(4):22.
5. Pradeepkiran JA, Reddy PH. Structure based design and molecular docking studies for phosphorylated tau inhibitors in Alzheimer's disease. Cells, Mar 19, 2019; 8(3):260.
6. Liu T, Cao L, Zhang T, Fu H. Molecular docking studies, anti-Alzheimer's disease, antidiabetic, and anti-acute myeloid leukemia potentials of narcissoside. Archives of Physiology and Biochemistry, Mar 4, 2023; 129(2):405-415.
7. Barai P, Raval N, Acharya S, Borisa A, Bhatt H, Acharya N. Neuroprotective effects of bergenin in Alzheimer's disease: Investigation through molecular docking, *in vitro* and *in vivo* studies. Behavioural Brain Research, Jan 1, 2019; 356:18-40.