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In silico docking of anti-Alzheimer's molecules from plant derivatives

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Abstract

Alzheimer's disease is a progressive neurodegenerative disease and most often associated with memory deficits and cognitive decline. This study pertains to the development of plant based molecules that can help treating the Alzheimer's conditions. Plant based molecules usually render no side effects, compared to the Allopathic drugs. Also, this study is based on the novel approach of Computer aided drug design. The molecules selected for study are screened for drug likeness property using DruLiTo software. The molecules are also screened for presence of carcinogenicity and mutagenicity using T.E.S.T software. The molecule is then docked with the receptor using the Molegro software. The best pose is selected and results are tabulated and concluded. Any molecule can be considered as 'well-bound' or 'well-docked' if it expresses a fairly negative docking score. The H-bond energy is also a parameter to be considered. Negative H-bond energy is correlated with strong H-bond interaction between the amino acid residues and the molecule. Out of the 3 compounds, Compound 1 [Punicic acid] docked with Acetylcholine Esterase Receptor[1ACJ] displayed the highest negative moldock score [-156.709] and is very well bound to the receptor, followed by compound 2 [Ferrulic acid] and compound 3[Caeffic acd]. These plant based molecules can be further tested to evaluate the extent of their anti-Alzheimer's activity through pre-clinical and clinical testing and may also be incorporated in Ayurvedic medicine for treating Alzheimer's disease.

Keywords: Alzheimer's disease; Computer Aided Drug Design; Drug likeness property; Acetylcholine esterase receptor

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disease most often associated with memory deficits and cognitive decline [1]. The cardinal pathological features of the disease have been known for more than one hundred years, and today the presence of these amyloid plaques and neuro fibrillary tangles are still required for a pathological diagnosis [2][4]. There is no effective treatment option for the great majority of patients, and the primary causes of the disease are unknown except in a small number of familial cases driven by genetic mutations [2][3].

At the cellular level, AD is characterized by a progressive loss of cortical neurons, especially pyramidal cells, that mediate higher cognitive functions [1]. Substantial evidence also suggests that AD causes synaptic dysfunction early in the disease process, disrupting communication within neural circuits important for memory and other cognitive functions. AD-related degeneration begins in the medial temporal lobe, specifically in the entorhinal cortex and hippocampus [5][6]. Damage to these brain structures results in memory and learning deficits that are classically observed with early clinical manifestations of AD [2]. The degeneration then spreads throughout the temporal association cortex and to parietal areas. As the disease progresses, degeneration can be seen in the frontal cortex and eventually throughout most of the remaining neocortex [3].

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Previous Literature studies have proved that the plant molecules could help fight Alzheimer's by reducing inflammation in specific brain cells called microglia [11],[13]. Inflammation in microglia leads to destruction of other brain cells which can make symptoms worse for people with Alzheimer's or dementia [2][3]. The present study involves molecular docking to identify potential plant based anti-Alzheimer's molecules. This plant based study was envisioned to limit the future occurrences of drastic side effects caused by allopathic anti-alzheimer's drugs. After a thorough research, the molecules to be docked were finalised and the receptors were chosen. The present study has showed that these plant molecules can be further used for finding potent combination therapy in the treatment of Alzheimer's disease.

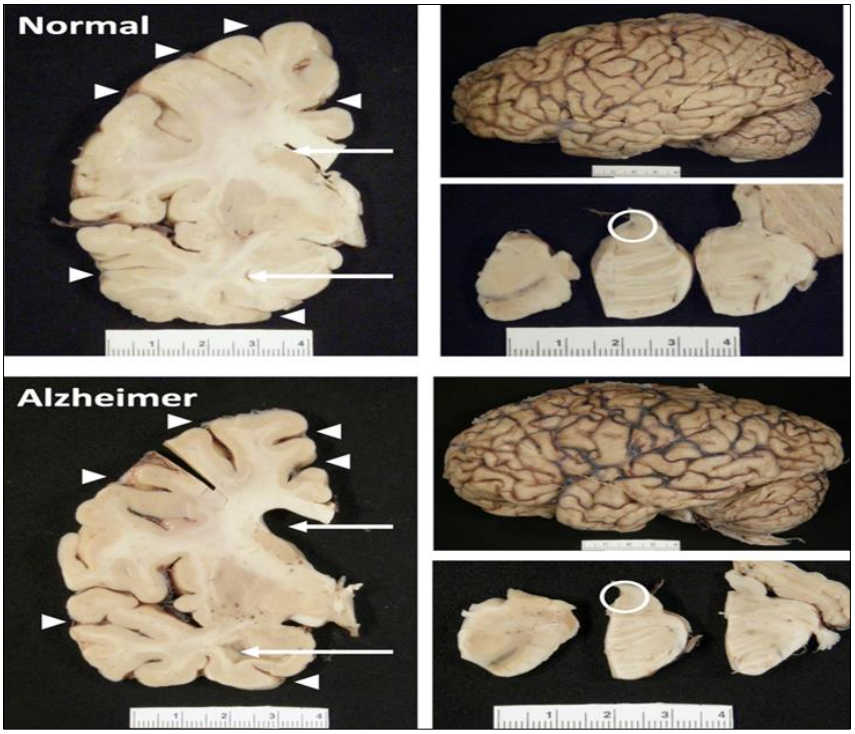


Figure 1 Enlargement of the frontal and temporal horns of the lateral ventricles of the brain in Alzheimer's disease

The U.S. Food and Drug Administration (FDA) has approved two types of medications— cholinesterase inhibitors (Aricept®, Exelon®, Razadyne®) and memantine (Namenda®) — to treat the cognitive symptoms (memory loss, confusion, and problems with thinking and reasoning) of Alzheimer's disease[8][9]. As Alzheimer's progresses, brain cells die and connections among cells are lost, causing cognitive symptoms to worsen. While current medications cannot stop the damage, Alzheimer's affects brain cells, they may help lessen or stabilize symptoms for a limited time by affecting certain chemicals involved in carrying messages among the brain's nerve cells[10].

1.1. CADD

Computer Aided Drug Design (CADD) often referred to as rational drug design, is the inventive process of finding new medications based on the knowledge of the biological target [7]. Molecular docking is the computational modelling of the structure of complexes formed by two or more interacting molecules. The goal of molecular docking is the prediction of the three dimensional structure. The aim of molecular docking is to achieve an optimized conformation for both the protein and ligand and relative orientation between protein and ligand so that the free energy of the overall system is minimized. Molecular recognition plays a key role in promoting fundamental biomolecular events such as enzyme-substrate, drug-protein and drug-nucleic acid interaction[12].

2. Materials and methods

2.1. Databases

- Dr. Duke's ethnobotanical database.
- Pub Chem.
- RCSB PDB.

2.2. Softwares

- Molegro virtual Docker, version 6.0.
- T.E.S.T.
- DruLiTo

2.3. Plan of work

- A thorough literature study to find suitable receptors expressed on Neuronal tissue.
- A thorough literature study to find suitable plant based molecules with anti-Alzheimer's activity.
- The molecules selected for study are screened for drug likeness property using DruLiTo software.
- The molecules are also screened for presence of carcinogenicity and mutagenicity using T.E.S.T software.
- The researched receptor and ligands are downloaded in suitable formats eg.PDB, SDF etc.
- The molecule is now docked with the receptor using the Molegro software. The best pose is selected and results will be tabulated and concluded

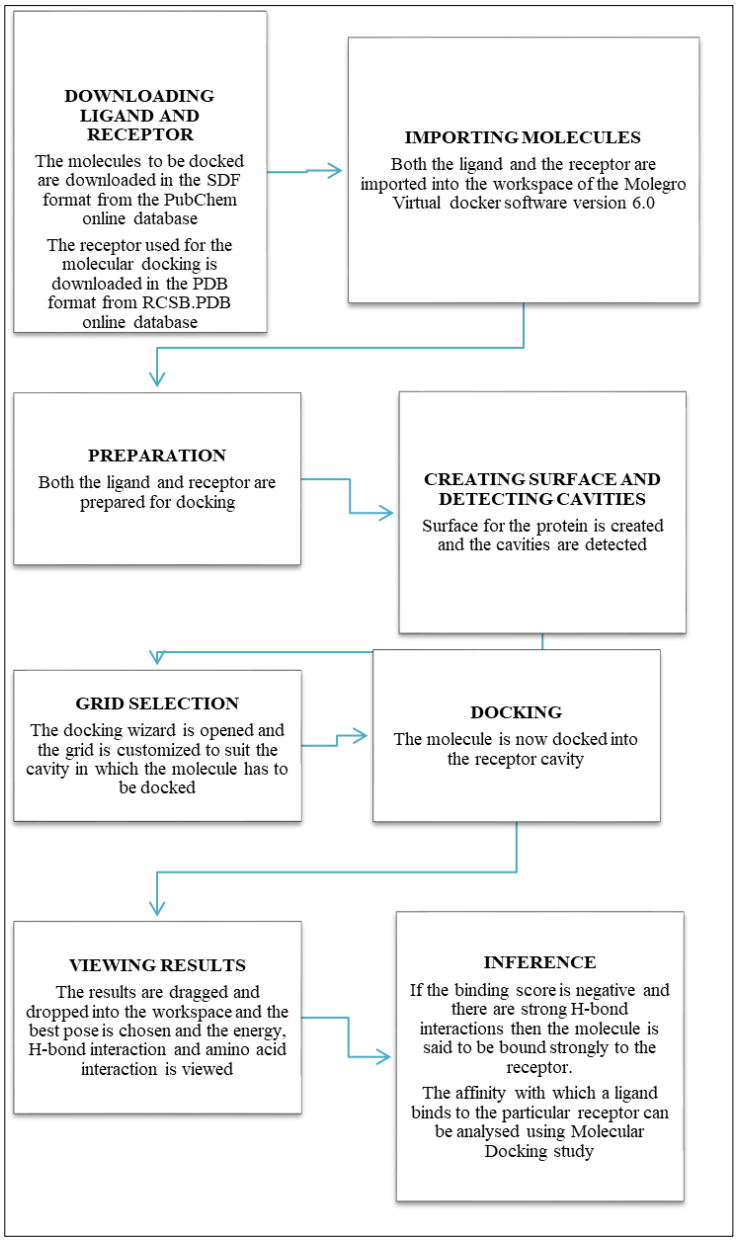


Figure 2 Plan of Work

2.4. Compound 1 : Punicic acid

Punicic acid (PA) (also known as trichosanic acid, helps in treating senile plaques and neuritic plaques and also reduces inflammatory response in the neuronal cells[13].

Researchers believe that this pomegranate compound could help fight Alzheimer's by reducing inflammation in specific brain cells called microglia. Inflammation in microglia leads to destruction of other brain cells which can make symptoms worse for people with Alzheimer's or dementia. The recent study proves the positive effects of pomegranate extract on brain health.

Figure 3 Pomegranate-Source of Punic acid

2.4.1. Drug likeness testing

DruLiTo was used to test the drug likeness property of the molecule, the results are tabulated as follows;

Table 1 Drug Likeness Testing of Compound 1

Selected Filters	Total Number of Molecule Filter	Total Number of Molecule Violated the Rule
Lipinskie's Rule of Five	0	1
Ghose_Filter	0	1
CMC-50 Like Rule	0	1
Vebers Rule	0	1
MDDR Like Rule	0	1
BBB Likeness Rule	0	1
Unweighted QED	1	0
Weighted QED	1	0
All Selected Filters	0	1

2.4.2. Docking

Observation and tabulation

Different poses with energy

Table 2 Different poses with energy – Compound 1

Name	Ligand	Mol Dock Score	Rerank Score	H Bond
[00]4871	4871	-156.709	-66.2479	-0.207288
[01]4871	4871	-156.385	-74.7764	-1.58843
[02]4871	4871	-150.908	-74.8905	4.20898
[03]4871	4871	-147.478	-5.41793	-1.02086
[04]4871	4871	-144.909	-31.3886	-1.7092

The pose [00]4871 was evaluated in detail

Ligand atoms and their energy

Table 3 Pose [00]4871

ID	Name	Total	E Pair	E Intra
0	O	-5.96559	-7.63774	1.67215
1	O	-5.27661	-5.97054	0.693922
2	O	1.79334	-4.41236	6.2057
3	O	-2.2749	-4.7783	2.5034
4	O	-6.53273	-7.17305	0.640321
5	O	0.642305	-0.2827	0.925005
6	C	-10.4226	-10.6459	0.223324
7	C	-5.83859	-7.33765	1.49906
8	C	-7.09092	-8.11481	1.02389
9	C	-7.93113	-7.09522	-0.83592
10	C	-6.10685	-7.11785	1.011
11	C	-5.50787	-6.02812	0.52025
12	C	-4.05364	-5.38868	1.33503
13	C	-8.70222	-9.8657	1.16348
14	C	-4.24197	-5.64463	1.40266
15	C	-4.79415	-3.84711	-0.94704
16	C	-2.83072	-1.81292	-1.0178
17	C	-6.46486	-8.65149	2.18664
18	C	-4.33571	-5.29213	0.956423
19	C	-6.84406	-6.47651	-0.36755
20	C	-8.06729	-8.42025	0.352968
21	C	-6.15762	-6.26021	0.102595
22	C	-5.73425	-7.23978	1.50553
23	C	-8.48308	-8.25195	-0.23113
24	C	-1.3637	-2.04671	0.683007

25	C	-7.70527	-8.32156	0.616287
26	C	-1.96974	-1.26098	-0.70877
27	C	-5.26744	-6.45879	1.19135
28	C	-7.9707	-8.73555	0.764849
29	C	-3.2699	-3.85725	0.587358

Target protein with the amino acid residues involved in the interaction and their energy

Table 4 Energy of Target proteins with the amino acid residues – Compound 1

Target Atoms: Molecule	Residue	ID	Total	E Pair
1ACJ [A]	Asn	85	-10.3503	-10.3503
1ACJ [A]	Asp	72	-11.3307	-11.3307
1ACJ [A]	Gln	69	-10.4715	-10.4715
1ACJ [A]	Glu	199	1.04866	1.04866
1ACJ [A]	Gly	80	-4.24283	-4.24283
1ACJ [A]	Gly	117	-0.3037	-0.3037
1ACJ [A]	Gly	118	-1.40209	-1.40209
1ACJ [A]	Gly	123	-0.68634	-0.68634
1ACJ [A]	Gly	441	-5.41925	-5.41925
1ACJ [A]	His	440	-12.8899	-12.8899
1ACJ [A]	Ile	439	-4.16394	-4.16394
1ACJ [A]	Ile	444	-1.00882	-1.00882
1ACJ [A]	Met	436	-1.01059	-1.01059
1ACJ [A]	Phe	330	-26.2693	-26.2693
1ACJ [A]	Pro	86	-2.27029	-2.27029
1ACJ [A]	Ser	81	-8.48673	-8.48673
1ACJ [A]	Ser	122	-9.98267	-9.98267
1ACJ [A]	Ser	200	-1.52353	-1.52353
1ACJ [A]	Trp	84	-52.0879	-52.0879
1ACJ [A]	Trp	432	-8.56228	-8.56228
1ACJ [A]	Tyr	70	11.9315	11.9315
1ACJ [A]	Tyr	121	-5.8244	-5.8244
1ACJ [A]	Tyr	130	-0.5977	-0.5977
1ACJ [A]	Tyr	334	-8.08975	-8.08975
1ACJ [A]	Tyr	442	-2.41497	-2.41497
1ACJ [A]	Val	71	-7.1409	-7.1409

Score and h-bond energy

Table 5 Docking Score – Compound 1

Energy overview: Descriptors	Value	Mol Dock Score	Rerank Weight	Rerank Score
Total Energy		-156.709		-70.24
External Ligand interactions		-189.428		-89.398
Protein - Ligand interactions		-189.428		-89.398
Hydrogen bonds	-5.235	-5.235	0.792	-4.146

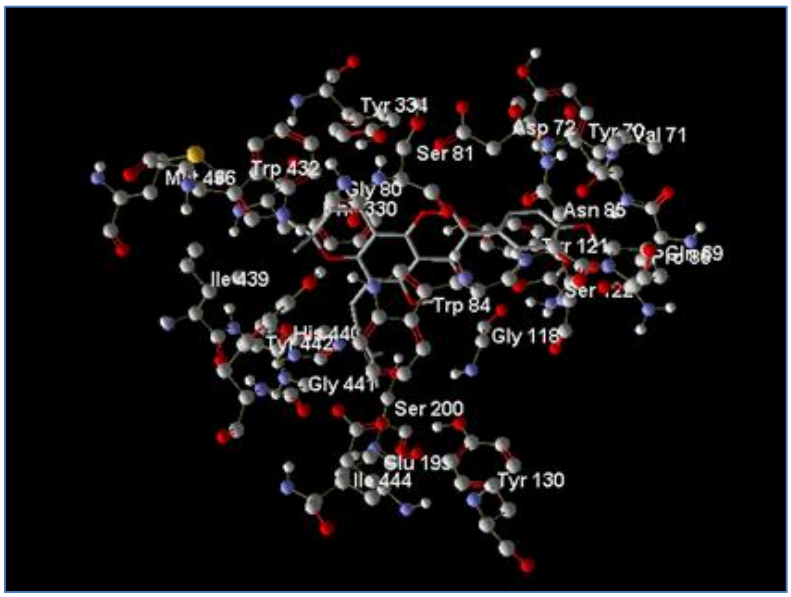


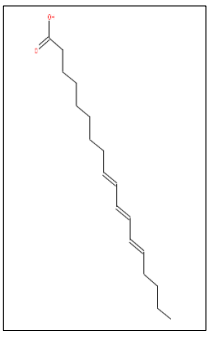
Figure 4 The amino acid interaction involving Punicic acid

2.5. Mutagenicity and oral rat ld50 testing

T.E.S.T. software was used determine the mutagenicity and oral rat LD50

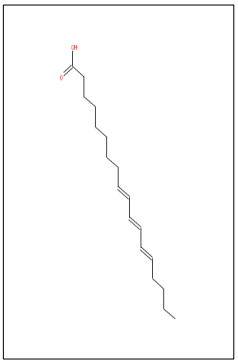
Predictions for consensus method for mutagenicity

Table 6 Results of Mutagenicity Testing – Compound 1

ID	Structure	Experimental Value	Predicted Value	Experimental Result	Predicted Result
C0_1558714463410		0.00	0.20	Mutagenicity Negative	Mutagenicity Negative

Predictions for consensus method for oral rat LD50

Table 7 Results of Oral Rat LD50 Testing – Compound 1

ID	Structure	Experimental Value -Log10(mol/kg)	Predicted Value - Log10(mol/kg)	Experimental Value mg/kg	Predicted Value mg/kg
C0_1558714463410		N/A	1.44	N/A	10023.62

2.6. Compound 2: Ferrulic acid

Ferulic acid (FA) (4-hydroxy-3-methoxycinnamic acid) is the most abundant hydroxycinnamic acid found in plant cell walls forming covalent ester linkages to polysaccharides and ether or ester linkages to lignin. It is reported to have antioxidant, antimicrobial, anti-inflammatory, cholesterol-lowering and anticancer activities, as well as ability to prevent thrombosis and atherosclerosis[11].

Figure 5 Sources of Ferrulic acid-Corn

Molecular Formula: $C_{10}H_{10}O_4$; PUBCHEM CID: 445858

Structure

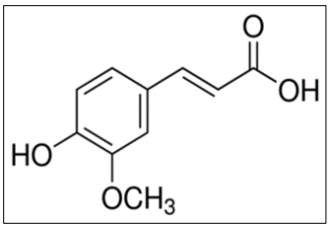


Figure 6 Chemical Structure of Ferrulic acid

2.6.1. Drug likeness testing

DruLiTo was used to test the drug likeness property of the molecule, the results are tabulated as follows;

Table 8 Drug Likeness Testing of Compound 2

Selected Filters	Total Number of Molecule Filter	Total Number of Molecule Violated the Rule
Lipinskies Rule of Five	1	0
Ghose_Filter	1	0
CMC-50 Like Rule	0	1
Vebers Rule	1	0
MDDR Like Rule	0	1
BBB Likeness Rule	0	1
Unweighted QED	1	0

2.6.2. Docking

Observation and tabulation

Different poses with energy

Table 9 Different poses with energy – Compound 2

Name[poses]	Ligand	Mol Dock Score	Rerank Score	H Bond
[00]445858	445858	-105.806	-91.191	-9.20023
[02]445858	445858	-101.683	-87.0293	-5.56349
[01]445858	445858	-100.788	-86.6516	-10.8428
[04]445858	445858	-100.223	-86.6558	-7.91425
[03]445858	445858	-99.4504	-86.1993	-5.13655

The pose [00]445858 was evaluated in detail

Ligand atoms and their energy

Table 10 Pose [00]445858

ID	Name	Total	E Pair	EIntra
0	O	-4.17355	-4.97107	0.797521
1	O	-5.81754	-6.54248	0.724945
2	O	-11.9915	-13.0123	1.02081
3	O	-10.029	-9.64584	-0.38313
4	C	-8.55634	-8.94148	0.385144
5	C	-4.84363	-6.01922	1.17559
6	C	-4.02118	-5.86999	1.84881
7	C	-7.14872	-7.97852	0.8298
8	C	-6.21678	-7.35077	1.13399
9	C	-7.78922	-8.54658	0.757359
10	C	-7.93984	-8.41276	0.472917
11	C	-9.75988	-9.35369	-0.40618
12	C	-6.39244	-6.43163	0.039195
13	C	-11.1581	-10.594	-0.56418

Target protein with the amino acid residues involved in the interaction and their energy;

Table 11 Energy of Target proteins with the amino acid residues – Compound 2

Target Atoms: Molecule	Residue	ID	Total	E Pair
1ACJ [A]	Glu	199	-7.29523	-7.29523
1ACJ [A]	Gly	80	-2.87149	-2.87149
1ACJ [A]	Gly	117	-1.16423	-1.16423
1ACJ [A]	Gly	118	-3.79823	-3.79823
1ACJ [A]	Gly	119	-0.84135	-0.84135
1ACJ [A]	Gly	441	-5.33598	-5.33598
1ACJ [A]	His	440	-17.3869	-17.3869
1ACJ [A]	Ile	439	-3.61033	-3.61033
1ACJ [A]	Ile	444	-0.41303	-0.41303
1ACJ [A]	Met	436	-0.60353	-0.60353
1ACJ [A]	Phe	330	-20.3547	-20.3547
1ACJ [A]	Phe	331	-1.26882	-1.26882
1ACJ [A]	Ser	81	-0.30148	-0.30148
1ACJ [A]	Ser	122	-0.32386	-0.32386
1ACJ [A]	Ser	200	-2.81166	-2.81166
1ACJ [A]	Trp	84	-22.0726	-22.0726
1ACJ [A]	Trp	432	-9.03428	-9.03428
1ACJ [A]	Tyr	121	-0.72124	-0.72124
1ACJ [A]	Tyr	334	-0.477	-0.477
1ACJ [A]	Tyr	442	-9.8041	-9.8041

Score and h-bond energy

Table 12 Docking Score – Compound 2

Energy overview: Descriptors	Value	Mol Dock Score	Rerank Weight	Rerank Score
Total Energy		-105.806		-91.191
External Ligand interactions		-113.67		-96.831
Protein - Ligand interactions		-113.67		-96.831
Hydrogen bonds	-9.2	-9.2	0.792	-7.287

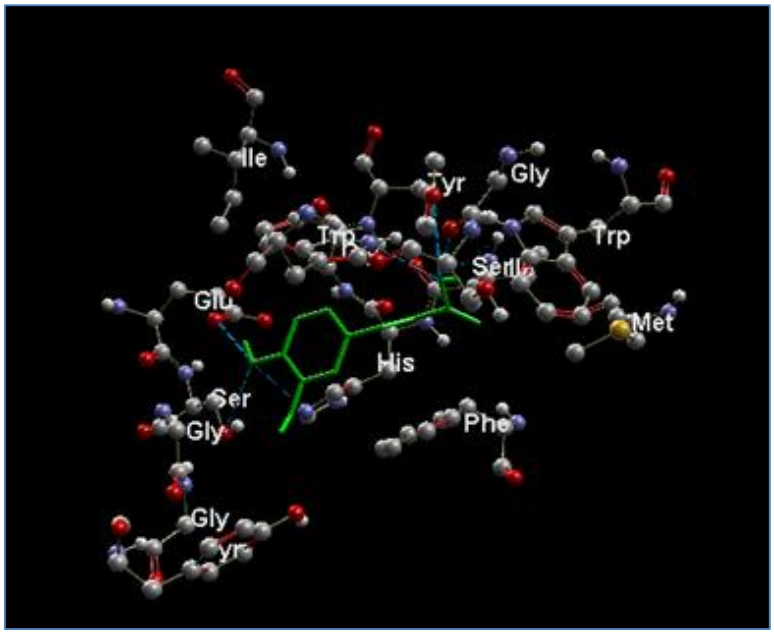


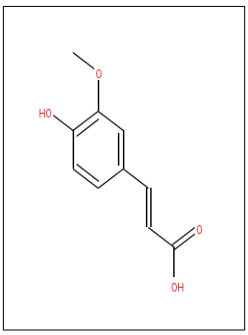
Figure 7 The amino acid interaction involving Ferrulic acid

2.7. Mutagenicity and oral rat ld50 testing

T.E.S.T. software was used determine the mutagenicity and oral rat LD50

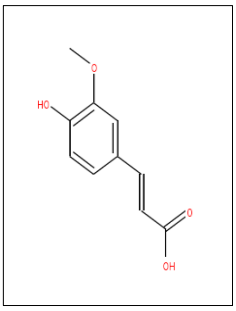
Predictions for consensus method for mutagenicity

Table 13 Results of Mutagenicity Testing – Compound 1

ID	Structure	Experimental Value	Predicted Value	Experimental Result	Predicted Result
C0_1558704706532		0.00	0.22	Mutagenicity Negative	Mutagenicity Negative

Predictions for consensus method for oral rat LD50

Table 14 Results of Oral Rat LD50 Testing – Compound 2

ID	Structure	Experimental Value-Log10(mol/kg)	Predicted Value -Log10(mol/kg)	Experimental Value mg/kg	Predicted Value mg/kg
C0_1558713442611		N/A	1.61	N/A	4742.73

2.8. COMPOUND 3 : CAEFFIC ACID

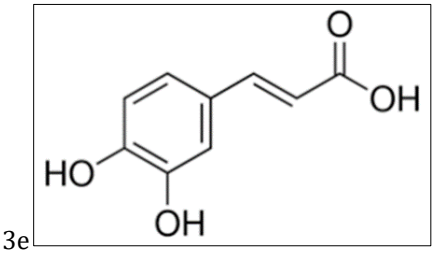
Caffeic acid (3,4-dihydroxy cinnamic acid) (CA) is naturally found in fruits, vegetables, olive oil, and coffee. caffeic Acid is an orally bioavailable, hydroxycinnamic acid derivative and polyphenol, with potential anti-oxidant, anti-inflammatory, and antineoplastic activities. Upon administration, caffeic acid acts as an antioxidant and prevents oxidative stress, thereby preventing DNA damage induced by free radicals.

Figure 8 Source of Caeffic acid – Coffee

Moolecular Formula : $C_9H_8O_4$

PUBCHEM : 689043

Structure:



3e

Figure 9 Chemical structure of Caeffic acid

2.8.1. Drug likeness testing

DruLiTo was used to test the drug likeness property of the molecule, the results are tabulated as follows;

Table 15 Drug Likeness Testing of Compound 3

Selected Filters	Total Number of Molecule Filter	Total Number of Molecule Violated the Rule
Lipinskies Rule of Five	1	0
Ghose_Filter	1	0
CMC-50 Like Rule	0	1
Vebers Rule	1	0
MDDR Like Rule	0	1
BBB Likeness Rule	0	1
Unweighted QED	1	0
Weighted QED	1	0
All Selected Filters	0	1

2.8.2. Docking: observation and tabulation

Different poses with energy

Table 16 Different poses with energy – Compound 1

Name	Ligand	Mol Dock Score	Rerank Score	H Bond
[00]689043	689043	-100.577	-87.0337	-10.2958
[01]689043	689043	-99.1529	-84.9387	-11.3375
[02]689043	689043	-97.7868	-84.0279	-11.2002
[03]689043	689043	-94.8294	-83.0289	-7.04706
[04]689043	689043	-93.0178	-80.684	-3.69993

The pose[00]689043 was evaluated in detail

Ligand atoms and their energy

Table 17 Pose [00]689043

ID	Name	Total	E Pair	E Intra
0	O	-6.24811	-7.04669	0.798576
1	O	-6.67426	-7.60289	0.928627
2	O	-14.5198	-14.1893	0.330424
3	O	-8.90157	-9.22381	-0.330424
4	C	-8.51971	-9.07159	0.55188
5	C	-6.97747	-7.87203	0.894567
6	C	-5.19815	-6.4	1.20185
7	C	-7.36702	-8.53785	1.17083
8	C	-6.18915	-7.41407	1.22492
9	C	-5.11776	-6.04772	0.929963
10	C	-8.45336	-8.40682	0.0465424

11	C	-8.40164	-8.22096	-0.18066
12	C	-10.8962	-10.3121	-0.584137

Target protein with the amino acid residues involved in the interaction and their energy;

Table 18 Energy of Target proteins with the amino acid residues – Compound 3

Target Atoms: Molecule	Residue	ID	Total	E Pair
1ACJ [A]	Glu	199	-10.0695	-10.0695
1ACJ [A]	Gly	80	-4.56251	-4.56251
1ACJ [A]	Gly	117	-1.40504	-1.40504
1ACJ [A]	Gly	118	-2.06653	-2.06653
1ACJ [A]	Gly	441	-6.19694	-6.19694
1ACJ [A]	His	440	-14.5193	-14.5193
1ACJ [A]	Ile	439	-2.21006	-2.21006
1ACJ [A]	Ile	444	-1.16576	-1.16576
1ACJ [A]	Met	436	-0.44702	-0.44702
1ACJ [A]	Phe	330	-16.7322	-16.7322
1ACJ [A]	Phe	331	-0.34353	-0.34353
1ACJ [A]	Ser	81	-0.50063	-0.50063
1ACJ [A]	Ser	200	-3.89757	-3.89757
1ACJ [A]	Trp	84	-23.6633	-23.6633
1ACJ [A]	Trp	432	-8.33573	-8.33573
1ACJ [A]	Tyr	334	-0.48767	-0.48767

Score and h-bond energy

Table 19 Docking Score – Compound 3

Energy overview: Descriptors	Value	Mol Dock Score	Rerank Weight	Rerank Score
Total Energy		-100.577		-89.32
External Ligand interactions		-110.346		-94.2
Protein - Ligand interactions		-110.346		-94.2
Hydrogen bonds	-13.182	-13.182	0.792	-10.44

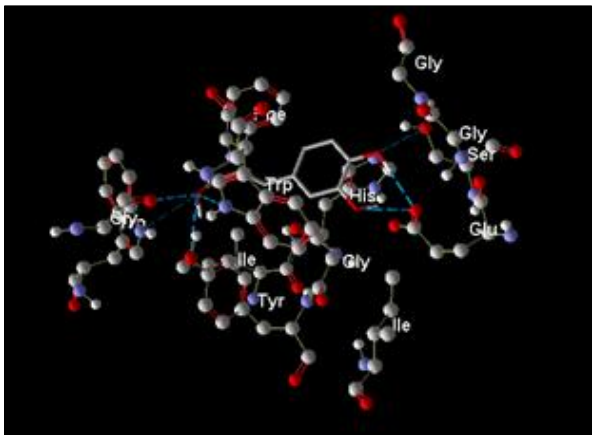


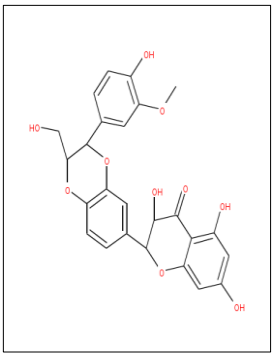
Figure10 The amino acid interaction involving Caeffic acid

Mutagenicity and oral rat ld50 testing

T.E.S.T. software was used determine the mutagenicity and oral rat LD50

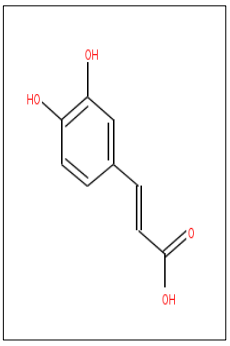
Predictions for consensus method for mutagenicity

Table 20 Results of Mutagenicity Testing – Compound 1

ID	Structure	Experimental Value	Predicted Value	Experimental Result	Predicted Result
C0_1558713867598		N/A	0.41	N/A	Mutagenicity Negative

Predictions for consensus method for oral rat LD50

Table 21 Results of Oral Rat LD50 Testing – Compound 3

ID	Structure	Experimental Value-Log10(mol/kg)	Predicted Value -Log10(mol/kg)	Experimental Value mg/kg	Predicted Value mg/kg
C0_1558688723439		N/A	1.82	N/A	2708.93

3. Results and discussion

The aim of our project is to identify potential anti-Alzheimer's molecules with less side effects. The molecules selected for our study are various plant derivatives. The selection of the molecules was based on literature study of the characteristics and pre-existing activity using "Dr.Dukes ethanobotanical database".

3.1. DruLiTo

All of the following criteria was tested for each molecule individually:

- Lipinskies Rule of Five
- CMC-50 like rule
- Ghose filter
- Vebers rule
- MDDR like rule
- BBB likeness rule
- Unweighted QED
- All selected filters

Among these filters, the 'Lipinski rule' is deemed as the most essential filter a compound has to pass for it to be considered as a 'drug-like' molecule. Of the selected molecules, compound 1 Punic acid violated the Lipinski rule. Compound 2 and 3 obeyed the rule. The remaining criteria were also tested and tabulated.

3.2. Insilico docking

All the 3 compounds were docked using "Molegro Virtual Docker" Version 6.0. Any molecule can be considered as 'well-bound' or 'well-docked' if it expresses a fairly negative docking score. The higher the negativity of the score the stronger the interaction. This negative score is indicative of the energy with which a molecule is bound to its receptor. The H-bond energy is also a parameter to be considered. Negative H-bond energy is correlated with strong H-bond interaction between the amino acid residues and the molecule.

3.3. Mol-dock score

- Compound 1 Punicic acid→ --156.709
- Compound 2 Ferrulic acid→ -105.806
- Compound 3 Caeffic acid→ -100.577

Highly negative mol dock score and H-bond interaction suggests the affinity with which the molecules are bound to the receptor cavity.

T.E.S.T [Toxicity Estimation Software Tool]

T.E.S.T was used to test and eliminate the molecules with a potential to cause Mutagenicity. Oral LD50 values were also calculated using this tool.

Al the 3 compounds showed no mutagenicity and the oral LD50 predicted values were safe.

4. Conclusion

Molecular docking study was performed to identify potential plant based anti-Alzheimer's molecules. This plant based study was envisioned to limit the future occurrences of drastic side effects caused by allopathic anti-alzheimer's drugs. After a thorough research, the molecules to be docked were finalised and the receptors were chosen. Prior to docking, the X-ray crystal structure for receptors were downloaded from RCSB PDB database. The 3-D structure of all the 3 compounds was downloaded from the pubchem database. The compounds docked showed favourable H-Bond interactions and significantly good Molecular Dock scores. Further testing using "DruLiTo" software for "drug likeness" property showed that the compounds 2 and 3 obeyed the Lipinski rule, whereas compound 1 Punicic acid violated the rule. Using the software T.E.S.T, the mutagenicity and Oral LD50 was determined. All the 3 compounds displayed no signs of mutagenicity and the Oral LD50values are given.

Out of these 3 compounds Compound 1[Punicic acid] PUBCHEM ID:5281792 docked with Acetylcholine Esterase Receptor[1ACJ] displayed the highest negative moldock score[-156.709] and is very well bound to the receptor, followed by compounds 2 and 3 in the descending order of their mol dock score. These plant based molecules can be further tested to evaluate the extent of their anti-Alzheimer's activity through pre-clinical and clinical testing. All the above mentioned molecules hold good future potential as Anti-Alzheimer's agents, and if activity is confirmed, can lead to the evolution of new Anti-Alzheimer's drugs. These molecules may also be incorporated in Ayurvedic medicine for treating Alzheimer's disease

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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