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Research Article

IN SILICO MOLECULAR DOCKING STUDIES OF MULTI-POTENTIAL COMPOUNDS ISOLATED FROM *PREMNA SERRATIFOLIA* L.

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ABSTRACT

Objective: *Premna serratifolia* L. locally called "Munnai" belongs to the family "Verbenaceae." This study was carried out to identify the phyto components present in the ethanol extract of leaves by gas chromatography/mass spectrometry (GC/MS) analysis. Eight compounds were identified, and its mechanism of action was identified through docking analysis. Most of the drugs currently used for the breast cancer treatment produce side effects, and hence, we focused on plant-based compounds, which exhibit the minimum toxic effect.

Methods: Molecular docking, density function theory, pharmacophore modeling, and absorption, distribution, metabolism, excretion, and toxicity studies were performed for those plant compounds to analyze the antibreast cancer activity. Docking experiments were carried out between biocompounds from leaves with the target protein (Breast cancer [3S7S]) using Accelrys Discovery Studio 4.0.

Results: The result consists of eight compounds from leaves identified through GC/MS of which pentadecanoic acid, 13-methyl-methyl ester is considered as the lead compound due to its desirable interaction with the target protein. The Libdock score and binding energy are 62.708 and −17.7087, respectively.

Conclusion: All the compounds can be further explored for structural modification and detailed investigations to arrive at possibly newer potent agents with better therapeutic effects.

Keywords: *Premna serratifolia* L., Biocompounds, Docking, Pharmacophore, Absorption; distribution; metabolism; excretion; and toxicity, Density function theory, Breast cancer.

INTRODUCTION

Premna serratifolia L. (Verbenaceae) is an important woody, medicinal plant, and locally known as Munnai and has been used significantly and consistently in Ayurveda, Siddha, and Unani system of medicines (Fig. 1) [1-3]. The leaves have anticancer, astringent, anti-inflammatory, and antibacterial properties and are used in cardiac disorder, cough, leprosy, skin disease, constipation, fever, diabetes, obesity, stomach ache, and tumor [4-7]. It has cardiotonic, antihypoglycemic properties, anticoagulant, antiarthritis, and cardioprotective effect [8,9].

Classification	
Kingdom	Plantae
Order	Lamiales
Family	Verbenaceae
Genus	*Premna*
Species	*P. serratifolia L.*

P. serratifolia: *Premna serratifolia*

Breast cancer is a serious health concern in India causing the highest mortality rate in females, which occurs due to uncontrolled cell division and can be metastasize to other parts of the human body. The available drugs and treatments are not satisfactory as they do not completely eradicate the cancerous cells from the body. Hence, newer and more effective drugs and treatments against breast cancer are the need of the hour. The plant-like *P. serratifolia* L. has strong structural activity with breast cancer human body cells [10-12]. Molecular docking was utilized to prove that similar compounds can bind to receptor protein treatment of breast cancer using *in silico* approach [13].

METHODS

Plant material

P. serratifolia L. leaves were collected in clean polythene bags from Queen Mary's College, Chennai. The plant was washed in tap water and shade dried for 20 days.

Preparation of extract

The fresh leaves were shade dried, powdered, and extracted (100 g) successively with 150 ml of ethanol (60-75°C) in a Soxhlet extractor for 18-20 hrs. The extracts were filtered, and excess solvent was evaporated using rotary evaporator.

Analysis of active components using gas chromatography/mass spectrometry (GC/MS)

GC/MS is a method that combines the features of gas-liquid chromatography and MS to identify different substances within a test sample. GC/MS can provide meaningful information for components that are volatile, non-ionic, and thermally stable and have relatively low molecular weight. The crude ethanol extract of *P. serratifolia* L. leaves was analyzed by GC/MS. The instrument used for GC/MS analysis is "JEOL GCMATE II GC/MS" with data system which is a high resolution, double focusing instrument giving maximum resolution: 6000 and maximum calibrated mass: 1500 Daltons. The results obtained through GC/MS analysis is shown in Fig. 2.

Molecular docking studies

Docking software: Discovery Studio 4.0

Discovery Studio 4.0 is highly dynamic, and user-friendly software used for homology modeling, molecular dynamics, pharmacophore modeling, density function theory (DFT), molecular docking, and drug designing.

Protein preparation

The molecule taken is X-ray crystal structure of "human breast cancer protein," Protein Data Bank (PDB) ID-3S7S, with resolution of 1.60 Å. The ligand and crystallographic water molecules are removed from the protein, and the chemistry of the protein was corrected for missing hydrogen by the software.

Ligand preparation

The compounds 2(1H)-benzocycloctenone, decahydro-10a-methyl-, trans-, pentadecanoic acid, 13-methyl-, methyl ester, hexadecanoic acid, ethyl ester, phytol, 14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester, cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6,6-dimethyl-2.4 dioxo-, methyl ester, 3',4',5'-trimethoxyacetophenone(2-pyridylcarbonyl)hydrazone, Tetracosapentaene. 2,6,10,15,19,23-hexamethyl obtained from GC/MS analysis results of leaf extract from *P. serratifolia* L. were taken. Hydrogen bonds were added, and the energy was minimized using CHARMm force field using the software.

Fig. 1: *Premna serratifolia* L. plant

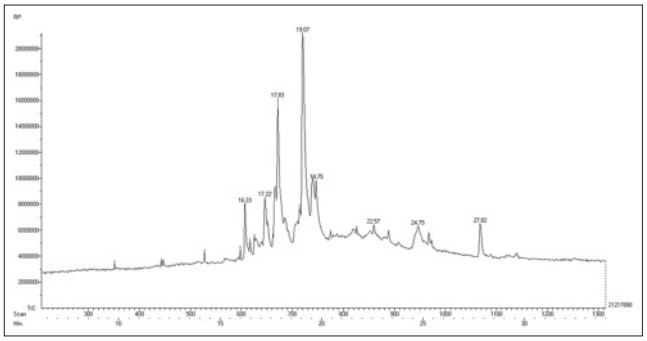


Fig. 2: Gas chromatography-mass spectrometry chromatograph of the leaves of *Premna serratifolia* L.

"Lipinski rule of five" for eight ligand molecules

Using the Discovery Studio 4.0, molecular properties and drug-likeness of the compounds were examined by "Lipinski's Rule of Five," formulated by Christopher. The molecular properties of the compounds are shown in Table 1, which satisfies the "Lipinski's Rule of Five."

RESULTS AND DISCUSSION

Based on the GC/MS analyses, the ethanolic extraction of leaves *P. serratifolia* L. contained numerous phytochemical compounds. The chemical components that had been identified, at various retention time during GC/MS analysis of the plant are summarized in Table 2, and the GC/MS chromatograms are presented in Fig. 3.

Molecular docking

The retrieved crystal structure from PDB (PDB ID 3S7S-Breast Cancer) has the structural weight as 16779.4. This protein has one chain, namely, "A" with 503 amino acid residues in length. Different compounds (ligands) from the plant leaves were docked with the breast cancer protein's target residues (PRO 78, ASN 79, VAL 80, ASP 81, ARG 85, ILE 86, CYS 87, LEU 121, ALA 122, ASN 123) out of which pentadecanoic acid, 13-methyl-, methyl ester showed the best interaction with the active site receptors shown in Table 3. Docked pose of the different compounds with protein is presented in Table 3. Hydrogen, hydrophobic, and favorable interaction histograms of eight compounds with docked residues is shown in Fig. 4. The values of the compounds include Vander Waals energy, Cdocker Energy, Lig score 1 and 2, piecewise linear potential (PLP) - PLP1 and PLP2, Jain, potential of mean force presented in Table 4. The Libdock score, binding energy, hydrogen bond interaction and distance obtained using the ligand Fit protocol of Discovery Studio 4.0 are presented in Table 5.

The ligand (pentadecanoic acid, 13-methyl-, methyl ester) from leaves showed the highest dock score and hydrogen bond interaction with breast cancer protein target when compared to other ligands.

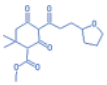
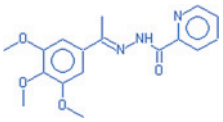
To ensure that the ligand orientation obtained from the docking studies was likely to represent valid and reasonable binding modes, the ligand fit program docking parameters had to be first validated for the crystal structure's active site. Protein utilities and health protocol of Discovery Studio was used to find out if the active site containing amino acids such as PRO 78, ASN 79, VAL 80, ASP 81, ARG 85, ILE 86, CYS 87, LEU 121, ALA 122, and ASN 123. Results of docking showed that the compound binds to the active site residue, which indicates that these compounds can inhibit the breast cancer protein. Further clinical trials on *P. serratifolia* L. plant extracts are required to validate these compounds.

Table 1: Lipinski's Rule of five for compound obtained from GC/MS analysis

S. No.	Name	Num_H_Donors_ Lipinski	Num_H_Acceptors_ Lipinski	Molecular weight	A Log P
1	2(1H)-benzocycloctenone, decahydro-10a-methyl-, trans-	0	1	194.313	3.477
2	Pentadecanoic acid, 13-methyl-, methyl ester	0	2	270.451	6.414
3	Hexadecanoic acid, ethyl ester	0	2	284.477	6.967
4	Phytol	1	1	296.531	7.337
5	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester	1	3	312.487	5.921
6	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester	0	6	322.353	1.394
7	3',4',5'-trimethoxyacetophenone (2-pyridylcarbonyl) hydrazone	1	7	329.35	1.892
8	Tetracosapentaene 2,6,10,15,19,23-hexamethyl	0	0	412.734	11.581

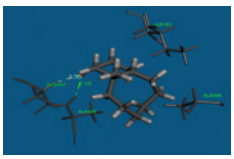
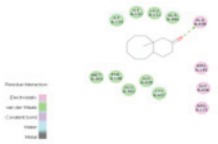
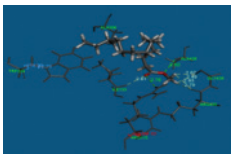
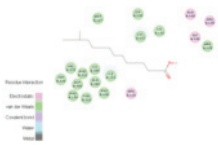
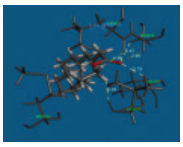
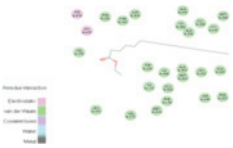
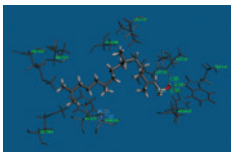
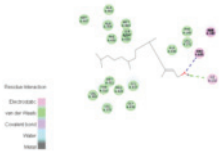
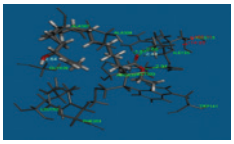
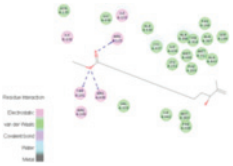
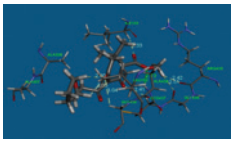
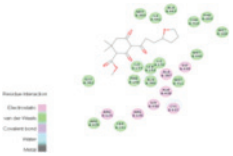
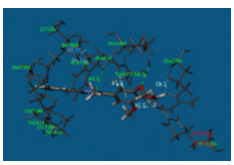
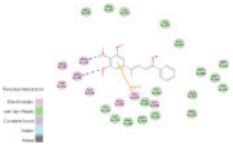
GC/MS: Gas chromatography/mass spectrometry

Table 2: Phyto components identified in ethanolic extraction of the leaves of *P. serratifolia* L.

Peak	Reaction time	Compound identified	Structure
1	16.23	2(1H)-benzocycloctenone, decahydro-10a-methyl-, trans-	
2	17.22	Pentadecanoic acid, 13-methyl-, methyl ester	
3	17.83	Hexadecanoic acid, ethyl ester	
4	19.07	Phytol	
5	18.75	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester	
6	22.57	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester	
7	24.75	3',4',5'-Trimethoxyacetophenone(2-pyridylcarbonyl)hydrazone	
8	27.82	Tetracosapentaene 2,6,10,15,19,23-hexamethyl	

P. serratifolia: *Premna serratifolia*

Table 3: Hydrogen bond interaction with breast cancer protein of plant leaves compounds

S.No	Name	Hydrogen bond interaction	2D diagram
1	2(1H)-benzocycloctenone, decahydro-10a-methyl-, trans-		
2	Pentadecanoic acid, 13-methyl-, methyl ester		
3	Hexadecanoic acid, ethyl ester		
4	Phytol		
5	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester		
6	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester		
7	3',4',5'-trimethoxyacetophenone (2-pyridylcarbonyl) hydrazone		
8	Tetracosapentaene 2,6,10,15,19,23-hexamethyl	-	-

2D: Two-dimensional

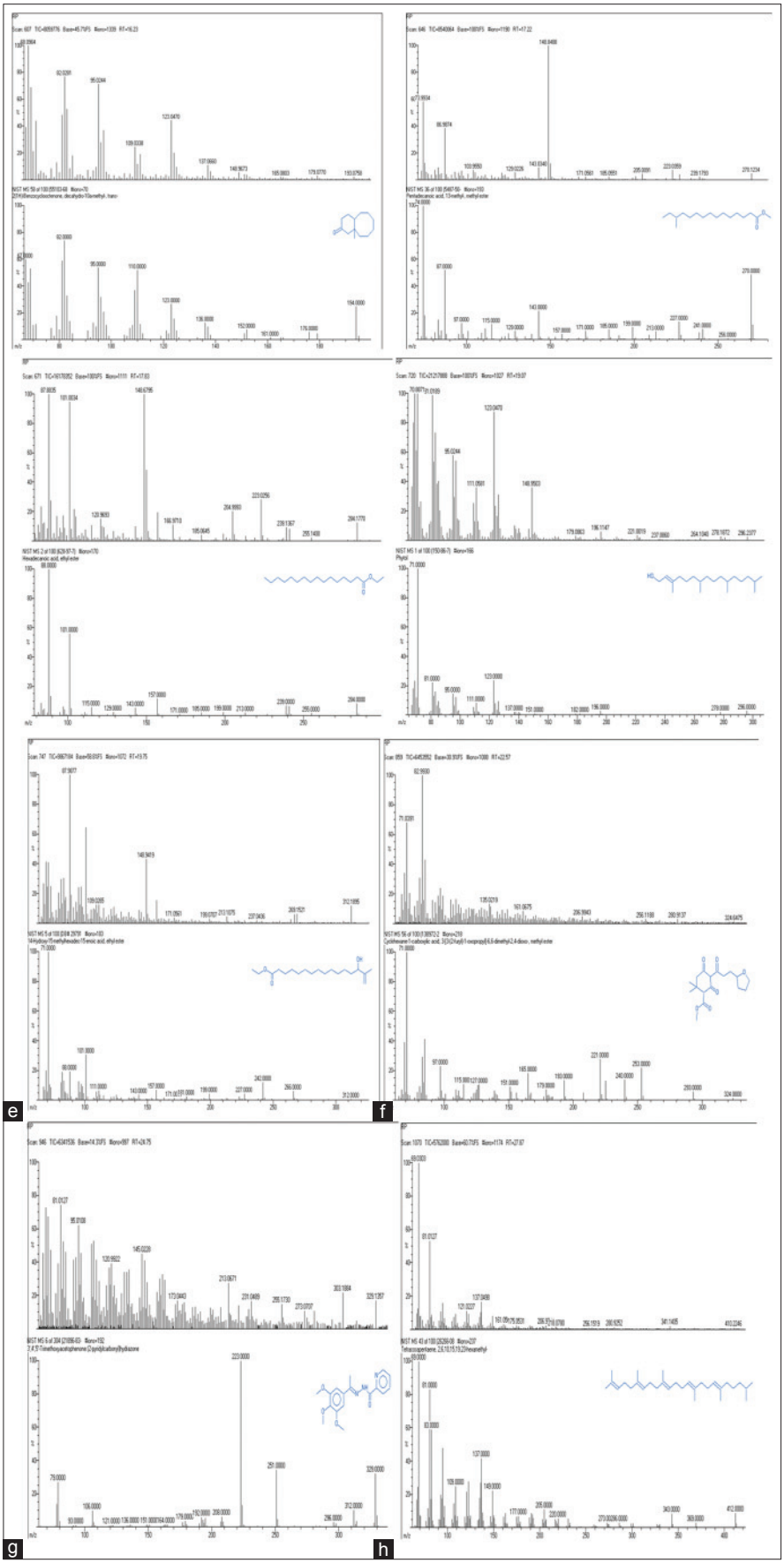


Fig. 3: Phytocomponents identified in ethanolic extraction of the leaves of *Premna serratifolia* L. Gas chromatography-mass spectrometry peak report (a-h)

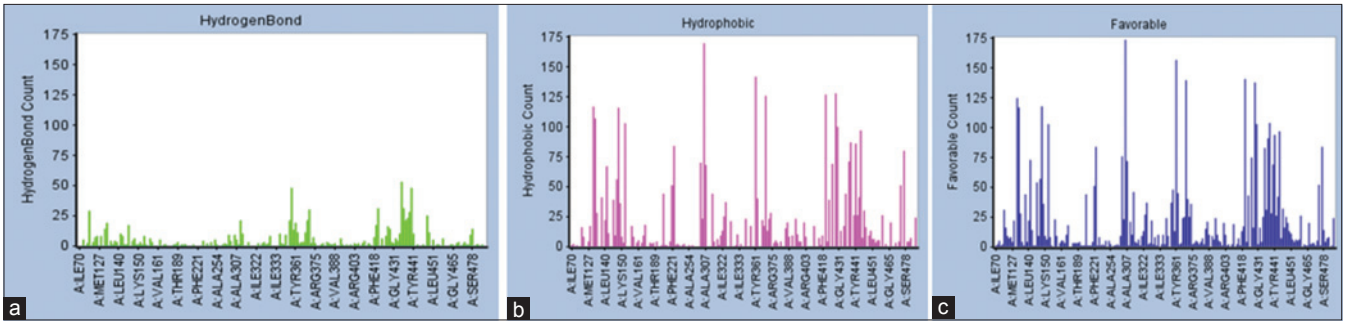


Fig. 4: Histogram showing residue interaction with the eight compounds, (a) Hydrogen bond, (b) hydrophobic interactions, (c) favorable interactions

Table 4: *P. serratifolia* L. leaves results for protein-ligand interaction

S.No	Name	VDW energy	Cdocker energy	Cdocker interaction energy	Lig score 1	Lig score 2	-PLP1	-PLP2	Jain	-PMF
1	2(1H)-benzocycloctenone, decahydro-10a-methyl-, trans-	−3754.47	1.047	29.192	2.48	4.53	47.89	45.93	2.32	49.89
2	Pentadecanoic acid, 13-methyl-, methyl ester	−3754.47	36.553	42.055	3.16	5.39	56.68	48.12	1.42	78.53
3	Hexadecanoic acid, ethyl ester	−3754.47	48.28	49.22	2.07	5.18	70.04	64.65	3.19	69.95
4	Phytol	−3754.47	14.949	46.572	4.2	5.6	81.41	80.06	2.84	84.3
5	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester	−3754.47	32.048	52.967	4.04	6.3	92.19	84.92	2.64	85.62
6	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester	−3754.47	2.389	39.481	2.78	5	72.3	64.28	2.48	54.17
7	3',4',5'-trimethoxyacetophenone (2-pyridylcarbonyl) hydrazone	−3754.47	28.614	47.944	4.47	6.16	91.47	86.04	1.81	70.07
8	Tetracosapentaene 2,6,10,15,19,23-hexamethyl	-	-	-	-	-	-	-	-	-

VWE: Vander Waals Energy, PLP: Piecewise linear potential, PMF: Potential of mean force, *P. serratifolia*: *Premna serratifolia*

Table 5: Hydrogen bond interaction between bioactive compounds and breast cancer protein

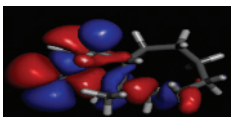
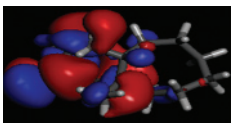
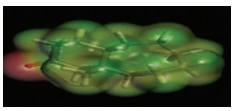
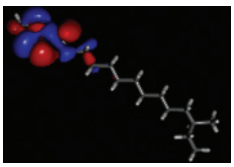
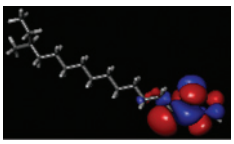
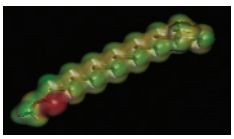
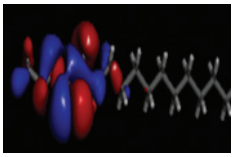
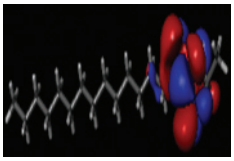
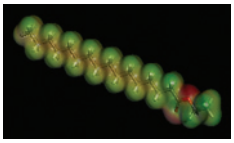
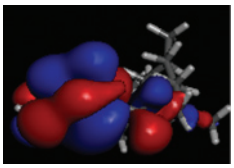
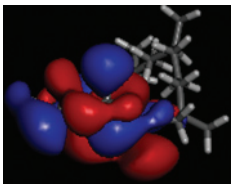
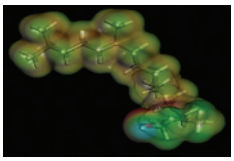
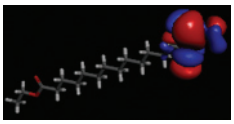
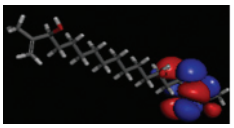
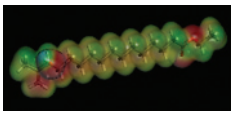
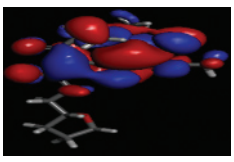
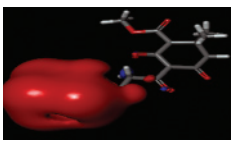
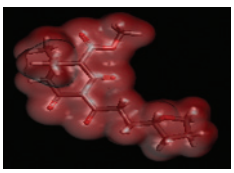
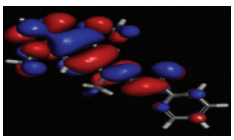
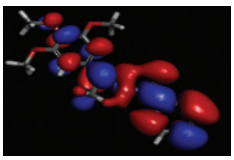
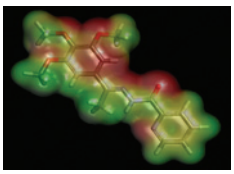
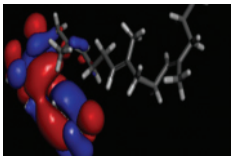
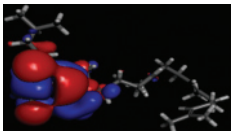
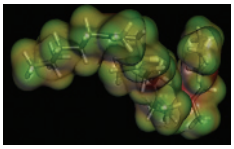
S.No	Name	Libdock score	Binding energy	Ligand energy	Protein energy	Hydrogen bond interaction	Distance (Å)
1	2(1H)-benzocycloctenone, decahydro-10a-methyl-, trans-	50.418	−42.816	26.0418	−18146.1	ALA 438 C-H...O CYS 437 C-H...O	2.15 2.50
2	Pentadecanoic acid, 13-methyl-, methyl ester	62.708	−17.7087	−10.8196	−18114.3	ARG 115 C-H...O ILE 133 C-H...O ALA 438 C-H...O C-H.O GLY 436 C-H.O GLY 436 ARG 435 C-H...O ARG 435 C-H...O	2.76 2.61 2.62 2.67 2.49 2.93 2.79
3	Hexadecanoic acid, ethyl ester	63.092	−48.9938	−14.5986	−18150.3	C-H.O LEU 372 VAL 370 C-H...O SER 478 C-H...O SER 478 C-H...O C-H...O LEU 477	2.38 2.79 2.6 2.47 2.46
4	Phytol	69.248	−68.2018	31.7219	−18124.2	C-H...O ILE 133 C-H...O ILE 132 ARG 435 C-H...O TRP 141 C-H...O	3.01 1.99 1.39 2.00
5	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester	77.174	−85.6638	0.6432	−18035.6	ARG 435 C-H...O ILE 133 C-H...O ARG 115 C-H...O ARG 115 C-H...O GLY 439 C-H...O	2.51 2.44 2.66 1.67 2.64
6	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester	50.862	−13.4619	46.6613	−18070.3	ILE 133 C-H....O C-H...O ARG 435 C-H...O GLY436 ALA438 C-H...O CYS 437 C-H...O GLY 439 C-H...O	2.33 2.42 2.51 2.73 2.41 3.04
7	3',4',5'-Trimethoxyacetophenone (2-pyridylcarbonyl) hydrazone	45.795	−78.2676	18.8429	−18132.7	GLU 439 C-H...N ALA438 C-H...O ARG 145 C-H...O C-H...O ARG 435	3.04 2.74 2.49 2.43
8	Tetracosapentaene 2,6,10,15,19,23-hexamethyl	-	-	-	-	-	-

Table 6: Molecular orbital calculations of eight compounds from DFT

S.No	Name	Total energy (kcal/mol)	Binding energy (kcal/mol)	HOMO energy (kcal/mol)	LUMO[b] energy (kcal/mol)	Dipole Magnetic function
1	2(1H)-Benzocycloctenone, decahydro-10a-methyl-, trans-	−578.55928519	−6.55532286	−0.18610409	−0.05201516	1.55676472
2	Pentadecanoic acid, 13-methyl-, methyl ester	−811.33717859	−9.24629928	−0.22871376	−0.03231323	0.51444295
3	Hexadecanoicacid, ethyl ester	−850.28218855	−9.77688051	−0.22617830	−0.03014546	0.62677913
4	Phytol	−853.40325194	−10.59188187	−0.18768254	−0.00133012	0.88125210
5	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester	−962.71137806	−10.22204917	−0.20313798	−0.02904795	1.03587724
6	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester	−1103.04933836	−8.58649718	0.15291521	0.22139433	6.24029275
7	3',4',5'-trimethoxyacetophenone(2-pyridylcarbonyl) hydrazone	−1114.78437723	−8.40308616	−0.15336818	−0.09008000	2.62677957
8	Tetracosapentaene 2,6,10,15,19,23-hexamethyl	−1163.30385239	−14.68380366	−0.17608521	−0.00060306	0.17139820

HOMO: Highest occupied molecular orbital, LUMO: Lowest unoccupied molecular orbitals, DFT: Density function theory

Table 7: Eight compounds from DFT molecular interaction

S.No	Name	HOMO interaction	LUMO interaction	MEP
1	2(1H)-benzocycloctenone, decahydro-10a-methyl-, trans-			
2	Pentadecanoic acid, 13-methyl-, methyl ester			
3	Hexadecanoic acid, ethyl ester			
4	Phytol			
5	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester			
6	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester			
7	3',4',5'-trimethoxyacetophenone (2-pyridylcarbonyl) hydrazone			
8	Tetracosapentaene 2,6,10,15,19,23-hexamethyl			

HOMO: Highest occupied molecular orbital, LUMO: Lowest unoccupied molecular orbitals, MEP: Molecular electrostatic potentials

DFT

DFT calculations were performed for eight compounds. Optimized molecular orbital calculations provide a detailed description of orbitals including spatial characteristics, nodal patterns, and individual atom contributions. The highest occupied molecular orbital (HOMO) orbitals are located on the substituted molecule, whereas lowest unoccupied molecular orbital (LUMO) orbitals resemble those obtained for the unsubstituted molecule, and therefore, the substitution has an influence on the electron donation ability, but only a small impact on electron acceptance ability. The orbital energy levels of HOMO and LUMO of eight compounds are listed in Table 6. The energy gaps can be seen between HOMO and LUMO of the compounds. The HOMO and LUMO energy gap explain interaction taking place within the molecules. Selected optimized geometrical parameters have been reported and HOMO, LUMO energies, and structures are elucidated and are shown in Table 7.

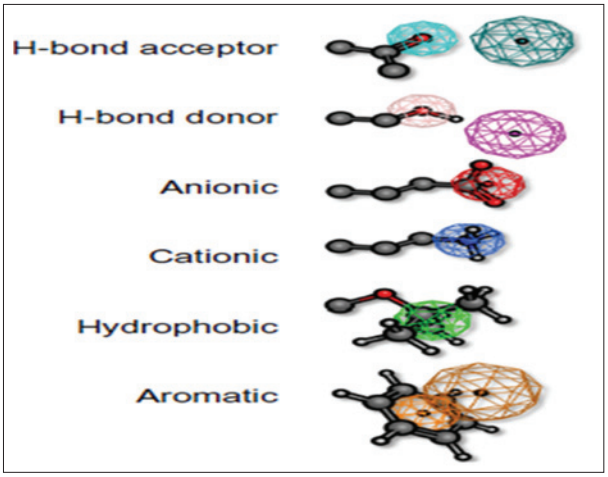


Fig. 5. Pharmacophore query

Pharmacophore modeling

Pharmacophores are the lead compound against the desired target. A pharmacophore is a three-dimensional (3D) arrangement of functional groups within a molecule which are essential for the compounds to bind with a macromolecule's active site. Identification of the pharmacophore is an important step in understanding the interaction between receptor and ligand. The pharmacophore models produced were evaluated qualitatively through visual inspection. A pharmacophore query is comprised of different features representing molecular recognition motifs such as hydrogen bond acceptors or donors, anionic, cationic, hydrophobic, and aromatic groups (Fig. 5). The pharmacophore expresses constraints on the 3D structure of the molecule by specifying relative atom positions that should be maintained to increase the likelihood that the molecule will bind with the receptor site. For all the eight ligands, pharmacophores were generated as shown in Table 8. The content 2 of Table 8 shows pharmacophore model generated for pentadecanoic acid, 13-methyl-, methyl ester which is found to be having the best interactions with breast cancer protein indicating very good antibreast cancer effect. These could be further used for drug designing against breast cancer. The pharmacophore studies have also shown that these compounds are having very fewer side effects and thus can be further investigated through clinical trials.

Absorption, distribution, metabolism, excretion, and toxicity (ADMET)

The ADMET properties of the compounds with results are described in Fig. 6. Computer aided ADME studies have been done using the software (Accelrys Discovery Studio software). These studies are solely based on the chemical structure of the molecule. Some of the parameters that are calculated are Atom based Log P98 (A Log P98), polar surface area, blood brain barrier, and cytochrome P450. The physiochemical properties of novel compounds are shown in Table 9. Hence, there is a high probability that these compounds can be used as drugs to inhibit the desired target once clinically proven.

Table 8: Interaction between pharmacophore model of eight ligands with breast cancer protein

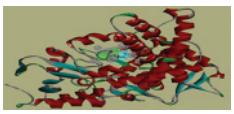
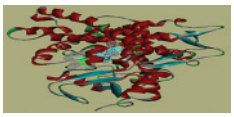
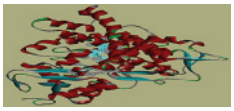
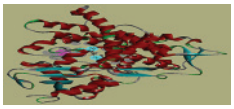
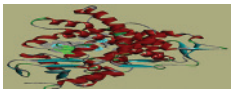
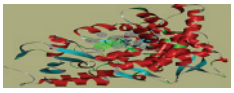
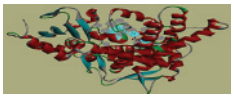
S.No	Name	Pharmacophore modeling
1	2(1H)-benzocyclooctenone, decahydro-10a-methyl-, trans-	
2	Pentadecanoic acid, 13-methyl-, methyl ester	
3	Hexadecanoic acid, ethyl ester	
4	Phytol	
5	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester	
6	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester	
7	3',4',5'-Trimethoxyacetophenone (2- pyridylcarbonyl) hydrazone	
8	Tetracosapentaene 2,6,10,15,19,23-hexamethyl	No interaction

Table 9: Physiochemical properties of compounds identified in *P. serratifolia* L.

S.No	Name	CYP2D6	AlogP98	PSA	BBB
1	2(1H)-benzocycloctenone, decahydro-10a-methyl-, trans-	−3.2955	3.477	17.3	0.647
2	Pentadecanoic acid, 13-methyl-, methyl ester	−2.52335	6.414	26.23	1.413
3	Hexadecanoicacid, ethyl ester	−0.3881	6.967	26.23	1.584
4	Phytol	−1.06037	7.337	20.815	-
5	14-hydroxy-15-methyl hexadec-15-enoic acid, ethyl ester	−1.75497	5.921	47.046	0.932
6	Cyclohexane-1-carboxlyic acid, 3-[3-[2-furyl]-1-oxopropyl]-6, 6-dimethyl-2.4 dioxo-, methyl ester	−3.42607	1.394	87.063	−1.101
7	3',4',5'-trimethoxyacetophenone (2-pyridylcarbonyl) hydrazone	−5.55845	1.892	79.485	−0.827
8	Tetracosapentaene 2,6,10,15,19,23-hexamethyl	−0.01585	11.581	0	-

PSA: Polar surface area, BBB: Blood brain barrier, *P. serratifolia*: *Premna serratifolia*

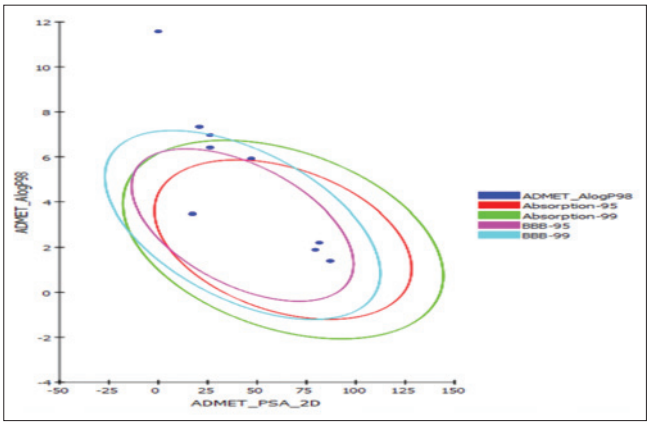


Fig. 6: Absorption, distribution, metabolism, excretion, and toxicity properties of bioactive compounds from *Premna serratifolia* L. leaves

CONCLUSION

The main objective of this study was to identify the chemical constituents from the leaf of *P. serratifolia* L. This work will help to identify the new compounds, which may help to produce important therapeutic products. The protein-ligand interaction plays a key role in structural-based drug designing. In the present work, eight phyto compounds have been identified from ethanol extract of the leaves of *P. serratifolia* L. by GC/MS analysis. The presence of various bioactive compounds justifies the use of the leaves of the plant for various ailments by traditional practitioners. In this study, we have docked the eight bioactive compounds with the active site residues of breast cancer protein. Out of 8 compounds, the pentadecanoic acid, 13-methyl-, methyl ester of *P. serratifolia* L. had maximum hydrogen bond interaction, minimum binding energy value, and maximum dock score. Further *in-vitro* and *in-vivo* approaches are required to elucidate the molecular mechanisms of this compound to find the potentiality of the drug against breast cancer. Molecular docking, DFT, and Pharmacophore modeling and ADME and toxicity profiles of the newly designed compounds were studied and were found to be desirable for therapeutics. These compounds appear to be safer even at high doses as indicated by the computational studies. With these encouraging results, all the compounds can be further explored for structural modification and detailed investigations to arrive at possibly newer potent agents with better therapeutic effects.

ACKNOWLEDGMENTS

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