https://africanjournalofbiomedicalresearch.com/index.php/AJBR
Afr. J. Biomed. Res. Vol. 28(2s) (January 2025); 387-415
Research Article

Pharmacognostic Characterization, GC-MS Profiling of *Lumnitzera Racemosa* Willd: Molecular Docking and ADMET Studies Of Its Bioactive Compounds Against Target Proteins of Potential Menopausal Symptoms (PMS)

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Abstract
Background: The present study focuses on exploration of the phytochemical composition, GC-MS profiling, to conduct in silico molecular docking studies, and evaluate ADMET properties of the selected compounds to understand their bioactivity.
Methods: The compounds that are present in the methanolic extract are subjected for molecular docking studies that exhibited good binding affinity for the targeted proteins. GC-MS analysis identified some of the compounds.
Results: PyRx software was used to conduct Molecular docking studies on 39 compounds as ligands, targeting 3-Dimensional structures of eestrogen receptors α (1x7e,1x7r) and estrogen β receptors (1U9e,1x7b,1x7j,1x76,1x78), osteoporosis target proteins like TNFSF 11:1s55,TRAF 3 IP2:2eqo, Hot flashes associated with Serotonin-5HT 2A receptors target 8dpf, Depression targets CREB1:2lxt, CASP3:7rn7, TP53:8swj, GABA A:5osc,1bnd (brain derived neurotrophic factor) CaMKIV:2w4o,Egr-1:4x9j, CREB:5zko, Sleep disturbances associated targets HIF-1a:1h2n, CAMP:5k8s, Toll like receptor:7nt7, Schizophrenia target SYNII: 6uFP, Bipolar disorders target Catechol-o-aminotransferase, brain derived neurotrophic factor, Voltage dependent Ca+2 channel α-1 subunit: 6COA. All the compounds exhibited binding capacities between -5 kcal /mol and 11 kcal /mol.
Conclusion: The research provided valuable insights into the chemical composition of the *L. racemosa* extract and validated their bioactive potential through in silico analysis. Castalagin has good binding affinity with most of the targeted proteins. This emphasizes the potential therapeutic applications of the *L. racemosa* extract. The results uptrained enhance the understanding of therapeutic potential of *L. racemosa* and opens avenues for future research in natural products and drug discovery.

Key words: CAMP, GABA, ADMET

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Received - 02/10/2024 Acceptance - 11/10/2024

DOI: https://doi.org/10.53555/AJBR.v28i2S.6836

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Introduction

The family Combretaceae comprises various plant species, among which *L. racemosa*, is a white-flowered black mangrove (Fig. 1) is included. This species can be found not only in several locations within the western Indo-Pacific region but also along the eastern coast of Africa. Traditionally it is used to treat skin disorders, Herpes simplex infections, scabies, pruritus (itchy skin), wound healing thrush of fungal infections, snake bites, to purify blood, to control asthmatic attacks, leprotic sores, as anti-fertility agent, anti-diabetic and treat renal calculi [1-5].

Present study provides information about pharmacognostic parameters, gas chromatography-Mass Spectrometry (GC-MS) profiling and molecular docking studies of bioactive compounds against target proteins of Potential Menopausal symptoms (PMS). Microscopic and Macroscopic evaluation plays important role in the pharmacognostic study of plant [6]. GC-MS employed for the detection of all the important phytochemicals substances in the plant extract [7,8]. Docking studies are employed to study the interaction between target protein and chemical constituents.

Additionally, by combining various analytical methods, *L. racemosa* may be thoroughly characterized, providing insight into its safety profile, possible pharmacological actions, and chemical makeup. With the growing popularity of herbal remedies and dietary supplements, thorough characterizations are essential to guaranteeing the efficacy, safety, and quality of these products. Based on the previously indicated rationale, the objective of this study is to contribute the current body of knowledge regarding *L. racemosa*. This will enable more investigation into its potential for therapeutic benefit and encourage the use of *L. racemosa* in both conventional and modern healthcare systems.



Fig 1: *Lumnitzera racemosa* willd

Materials

L. *racemosa* was collected from Koringa Mangrove Forest, Kakinada, Andhra Pradesh, India. A particular gas chromatograph, mass spectrometer, and column were used for GC-MS profiling. After wet digestion, atomic absorption spectrophotometry was utilized for elemental analysis. SRM institute of science and technology, Chennai, TamilNadu, used GCMS-QP2010 Plus Shimadzu equipment to do GC-MS analysis. The NIST14.lib Program and the Wiley 8.0 library were used for component identification.

Methods

Collection of plant material and authenticity

Lumnitzera racemosa was collected from 16º-30' to 17º-00' N latitudes and 82º-14' to 82º-23' E longitudes of Koringa Magroove forest located in Kakinda, Andhra Pradesh, India. Plant material was

Authenticated in Botany department of Krishna University, Andhra Pradesh. Voucher samples were kept in the herbarium for further reference.

Preliminary phytochemical analysis, pharmacognostic and physicochemical evaluation

The *L. racemosa* Leaves were washed thoroughly with water, shade dried and grounded into fine powder. Macroscopic and Mmicroscopic analyses were performed to evaluate morphological characteristics and cellular architecture. Physicochemical analysis, which included extractive values, moisture content, and ash value according to the procedures prescribed in the previous research. Extraction of the plant was done with water, ethanol, methanol, ethyl acetate and petroleum ether by using the Soxhlet apparatus. Rotary Flash evaporator was used for concentration of the extracts obtained. Several tests used in preliminary phytochemical screening were cited in earlier studies [9,10].

GC-MS Profiling

Methanolic extract of *L. racemosa* leaves was used for GC-MS analysis. Helium was used as the carrier gas in an injector to make a 2 μL injection [11]. SRM institute of science and technology, Chennai, TamilNadu, India, GC-MS analysis was carried out using GCMS-QP2010 Plus , a Shimadzu GC-MS model and a Rxi-5MS fused silica capillary column. The NIST14.lib Program and the Wiley 8.0 library database were used to identify the compounds by comparing their spectra and peak areas with those of known compounds.

Molecular docking studies:

Nature's living things all have the potential to change. Today's blossom will wither tomorrow, and a leaf that appears green today will drop off. Humans also experience this. Humans go through a number of developmental or transitional turning points throughout their lifespan.

A girl's transitory changes begin when she reaches menarche.

In this manner, a girl became a lady. The woman will eventually enter the stage of menopause, during which time she will experience a variety of physiological and psychological changes. However, the majority of women typically overlook these.

The phases of a woman's existence are structured around what Goddess Cultures referred to as the "blood mysteries": menarche (the first monthly flow of blood), delivery, which is accompanied by blood from birth. A woman may experience anovulatory cycles, which are menstrual cycles without ovulation, when her hormone balance starts to change. She might start to experience menopausal symptoms.

A persistent amenorrhea known as menopause results from the loss of ovarian activity. Menopause can only be diagnosed retroactively after a woman has experienced amenorrhea for a full year. Estrogen-dependent tissue's function gradually declines as ovarian function declines. Menstruation and ovarian activity stop. As people age, the tissue in their vagina, vulvar, and other estrogen-dependent organs such as breasts changes. In addition, fever follicles react to stimulate gonadotropins, which lowers the level of estrogen and causes the symptoms of menopause [32].

The natural onset of menopause typically occurs between the ages of 45 and 52, characterized by the cessation of menstruation. Nearly 85% of postmenopausal women worldwide suffer from symptoms of menopause at a particular point in their lives. By 2060, 59.8% of women will have undergone menopause, an increase from the current percentage of nearly half in 2030 [33].

As a woman matures, her ovarian follicle count gradually declines. As granulosa cells are lost, the production of ovarian estrogen and Inhibin declines. The FSH and LH levels are still high since the ovary is not providing any unfavourable feedback. Because the stromal compartment is spared, androgen synthesis from the ovary continues after menopause. Because of peripheral aromatization of ovarian and adrenal androgens, menopausal women continue to have low amounts of circulating estrogens. Since the principal site of aromatization is adipose tissue, obesity has an impact on numerous menopause side effects. According to theory, the thermoregulatory system resets and narrows in response to fluctuations in estrogens and FSH levels, this causes hot flashes. It is also believed that the emergence of these symptoms may be influenced by the lowered levels of serotonin and increased levels of norepinephrine [56].

An In-silico experimentation is virtual screening methodology where docking of ligands to Protein macromolecules that determines the biological effect of the ligand molecule [29]. In this study the bioactive compounds that are identified from *L. racemosa* extract are docked against the targets for various potential menopausal symptoms like Vulvo vaginal atropy (caused due to estrogen insufficiency), osteoporosis, hot flashes, depression, anxiety, sleep disturbances, schizophrenia and bipolar disorders using PyRx open-source software. The protein macromolecules for these PMS are obtained from RCSB protein data bank. RCSB protein data bank provided 3-Dimensional structures of estrogen receptors α (1x7e,1x7r) and estrogen β receptors (1U9e,1x7b,1x7j,1x76,1x78) [31], osteoporosis target proteins like TNFSF 11:1s55,TRAF 3 IP2:2eqo [30], Hot flashes associated with Serotonin-5HT 2A receptors target 8dpf, Depression targets CREB1:2lxt, CASP3:7rn7, TP53:8swj, GABA A:5osc,1bnd (brain derived neurotrophic factor) CaMKIV:2w4o,Egr-1:4x9j, CREB:5zko, Sleep disturbances associated targets HIF-1a:1h2n, CAMP:5k8s, Toll like receptor:7nt7, Schizophrenia target SYNII: 6uFP, Bipolar disorders target Catechol-o-aminotransferase, brain derived neurotrophic factor, Voltage dependent Ca+2 channel α-1 subunit: 6COA. The 3D structures of the designated proteins were transformed into PDB formats using Biovia Discovery Studio-2021 Client by integrating polar hydrogens, removing water molecules, and using HETATOMS.

Total 40 were chosen for docking experiments. The pertinent structures were obtained in the SDF (structure

data file) format from the PUBCHEM database (https://pubchem.ncbi.nlm.nih.gov/, accessed on 08 November 2023). The selected compounds with various pharmacological actions from previous research are Lumnitzera lactone which is an ellagic acid derivative of Lumnitzera racemosa [37], Zingerone (CID: 31211), Phellingridine (CID: 16109845), Beta stigmastenol (CID: 91692579), Ellagic acid [38] (CID: 5281855), Epigallo catechin (CID: 72277), Isoquercetin (CID: 5281654), Kaempferol (CID:5280863), Luteol (CID: 5280445), Methyl ellagic acid (5281860), Myricetin (CID: 5281672), Quercetin [21] (CID: 5280343), Stigmasterol (CID: 5280794), Adenosine (CID: 60961), Alpha amyrin (CID: 73170), Benzyl Beta arabinosyl (CID: 11253445), Castalagin (CID: 168165), Corilagin (CID: 73568), Dimethoxy xanthone (CID: 10039726), Fridelin (CID: 91472), Galacto pyranosyl glycerol (CID: 129887920), Gallic acid (CID: 370), Ginsenoside (CID: 3086007), Glucopyranoside (CID: 9930064), Hederagenin arabinosyl pyranose (CID: 441928), Icariside (CID: 14079045), Isoguaicin (CID: 10314441), Lawsoniaside (CID: 135165683), Linolenic acid (CID: 5280934), Lyoniresinol (CID: 10483388), Methyl gallate (CID: 7428), Oxisophrone (CID: 62374), Pinoresinol (CID: 73399), Polygalatinoside (CID: 273763), Protocatechuic acid (CID: 75), Quercetrin (CID: 5280459), Tormentica (CID: 73193). Using an open babel tool that was built into the software, the ligand structures (in SDF format) were then uploaded into PyRx Software. Incorporating charges and optimizing the universal force field allowed for the minimization or optimization of energy. After that, the ligands were converted to AutoDock Ligand format (PDBQT). To determine the binding affinity and learn more about the many ligand-receptor interactions that are responsible for the activity, the PyRx Software with Vina Wizard tool was used to molecularly dock the anticipated key ingredients. The protein and different ligands to be docked were chosen using the Vina Wizard Control feature of the PyRx program. Clicking the "Run Vina" control started the docking process. The Biovia Discovery Studio-2021 Client was used to visualize the docking postures' 2D and 3D interactions [29].

In silico ADMET study

ChemDraw Ultra 8.0 was used to illustrate the structure of the selected compounds from Lumnitzera racemosa for the pharmacokinetics (absorption, distribution, metabolism, and excretion (ADME) studies).The Swiss ADME online server's (http://www.swissadme.ch/) ADME tool was used to evaluate the drug-like and pharmacokinetic properties of the compounds under consideration after the ligands were converted into the SMILES format in accordance with the established protocol [52]. The ProTox-II website (http://tox.charite.de/protox_II) was used to analyze the toxicological profile.It uses a number of parameters, including as immunotoxicity, mutagenicity, cytotoxicity, hepatotoxicity, oral toxicity, and carcinogenicity, to produce predictions.

Results and Discussion

Extractive yields

The choice of solvent plays a crucial role in determining the extraction efficiency of plant materials. The methanol extract was found to have the highest yield (17.6%) when *L. racemosa* leaf extracts were prepared using a variety of solvents. The yields of the petroleum ether, ethanol, and water extracts were 8%, 3%, and 12.2%, respectively (Table 1).

Table 1 Extractive values of plant material

Type of Extract	Extractive values
Petroleum ether extract	8.5%
Ethanolic extract	3%
Methanolic extract	17.6%
Water	12.2%

Phytochemical Screening

All the extracts contained alkaloids, and flavonoids, according to the phytochemical screening of *L. racemosa* leaf extracts. Proteins are not present in this extract and Mucilage and volatile oils are also absent in methanolic extract. These substances merit more research because they may have industrial, nutritional, and medicinal uses [12-18]. Isolated compounds Chebulinic acid, Corilagin, castalagin exhibited hypotensive activity [19]. n-butanol (n-BuOH) fractions of L. racemosa leaves (LR-B-4-11 and LR-B-4-12) of *L. racemosa* exhibited anti-ulcer activity against indomethacin-induced gastric mucosal damage in Wistar rats [20]. Racemolides showed antileishmanial, hepatoprotective, and anti-oxidant activities [21]. Alkaloids, terpenoids, glycosides, phenols, steroids, and saponins have all been shown to have antioxidant potential in recent studies; tannins have been shown to have antibacterial action, while phenols have antioxidant qualities [22]. Terpenes have antimalarial activity, while flavonoids have a variety of therapeutic uses. Proteins, steroids, flavonoids, phenols, alkaloids, and tannins were among the phytoconstituents that were more abundant in the methanolic extract than in other extracts. The existence of several chemicals in *L. racemosa* methanol extracts has also been verified by earlier research, highlighting the plant's diverse phytochemical profile (Table 2).

Table 2 Preliminary Phytochemical analysis of *L. racemosa*

Name of the compound	Type of test performed	Aqueous extract	Methanol extract	Ethanol extract	Petroleum ether extract
Glycoside	Modified Borntrager's test and Lega's test	+ve	+ve	+ve	+ve
Alkaloids	Dragendroff's test and Hager's test	-ve	+ve	+ve	+ve
Triterpenoids	Salkowski's test	+ve	+ve	+ve	+ve
Phenolic acids	Iodine test and Ferric chloride test	-ve	+ve	+ve	+ve
Flavonoids	Alkaline reagent test and Lead acetate test	+ve	+ve	+ve	+ve
Saccharides	Barfoed's test and Molish's test	+ve	+ve	+ve	-ve
Tannins	Gelatin test and Braymer's test	+ve	+ve	+ve	-ve
Phytosterols	Salkowski's test and Libermann-Burchard's test	-ve	+ve	+ve	-ve
Lignans	Labat test	-ve	+ve	+ve	+ve
Coumarins	NaOH paper test	-ve	+ve	+ve	+ve
Anthraquinones	Borntrager's test	+ve	+ve	+ve	+ve
Carotenoids	Carr-Price reaction	+ve	+ve	+ve	+ve
Saponins	Foam test	+ve	+ve	+ve	+ve
Protein estimation	Biuret test and Millon's test	-ve	-ve	-ve	-ve
Mucilage test	Alcohol test	-ve	-ve	-ve	-ve
Volatile oils	Flourescence test	-ve	-ve	-ve	-ve

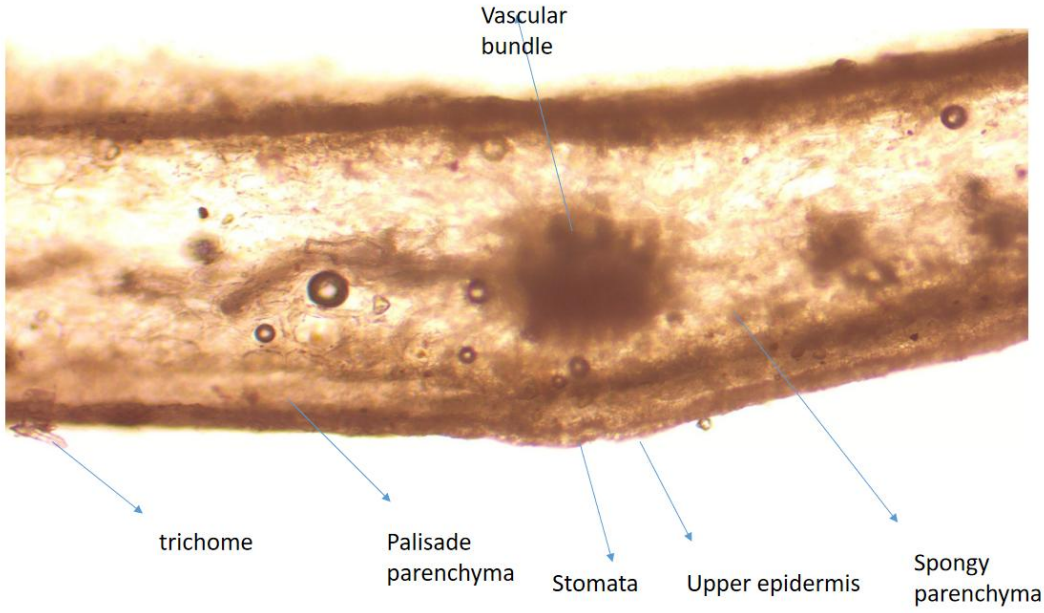
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Pharmacognostic Evaluation

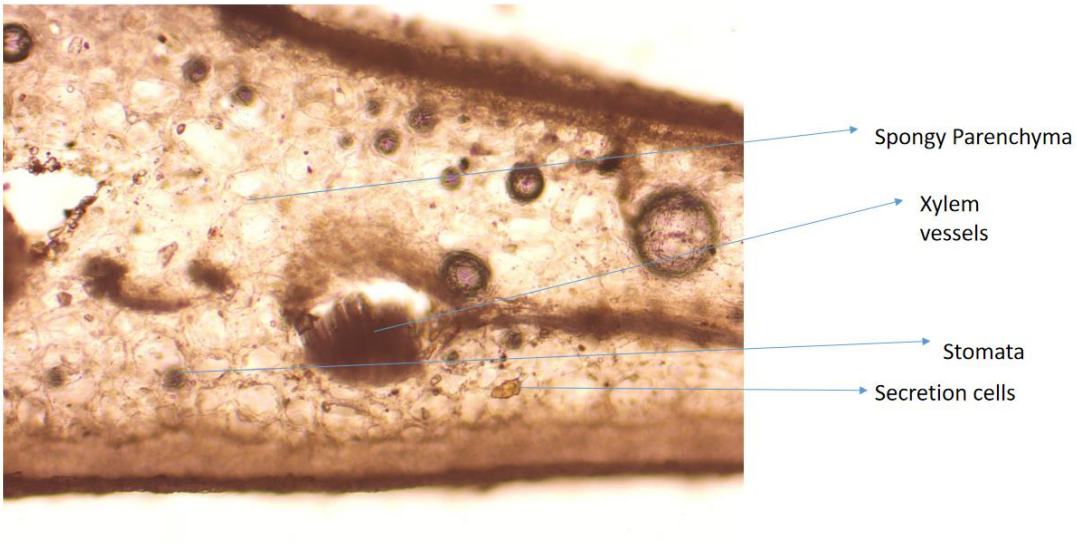
L. racemosa is commonly known as white-flowered black mangrove. For detailed study of the pharmacognostic parameters leave's transverse section was examined under 400X magnification, that revealed various structural elements like Spongy parenchyma, xylem vessels, stomata, secretion cells, trichome, palisade parenchyma, upper epidermis (Figure 2 A, B & C). The fine powder was dyed (phlorogucinol + conc. HCl) and mounted in glycerin. Following microscopic examination under 400X magnification revealed the existence of xylem fibers, stomata, spiral xylem channels, rosettes-shaped calcium oxalate crystals, parenchyma, and cork (Figure 3 A,B,C,D,E,F).



(A)

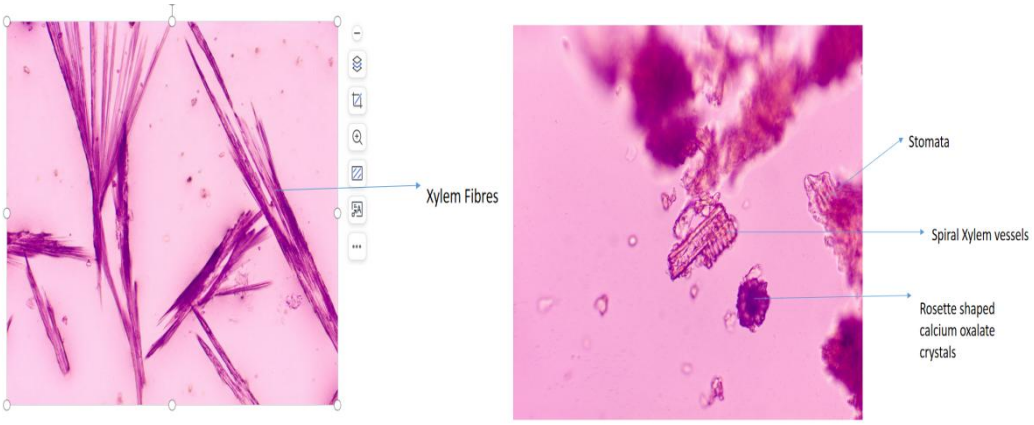


(B)



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Figure 2 A, B & C Transverse section of *L.racemosa* under 400X magnification



(A) **(B)**

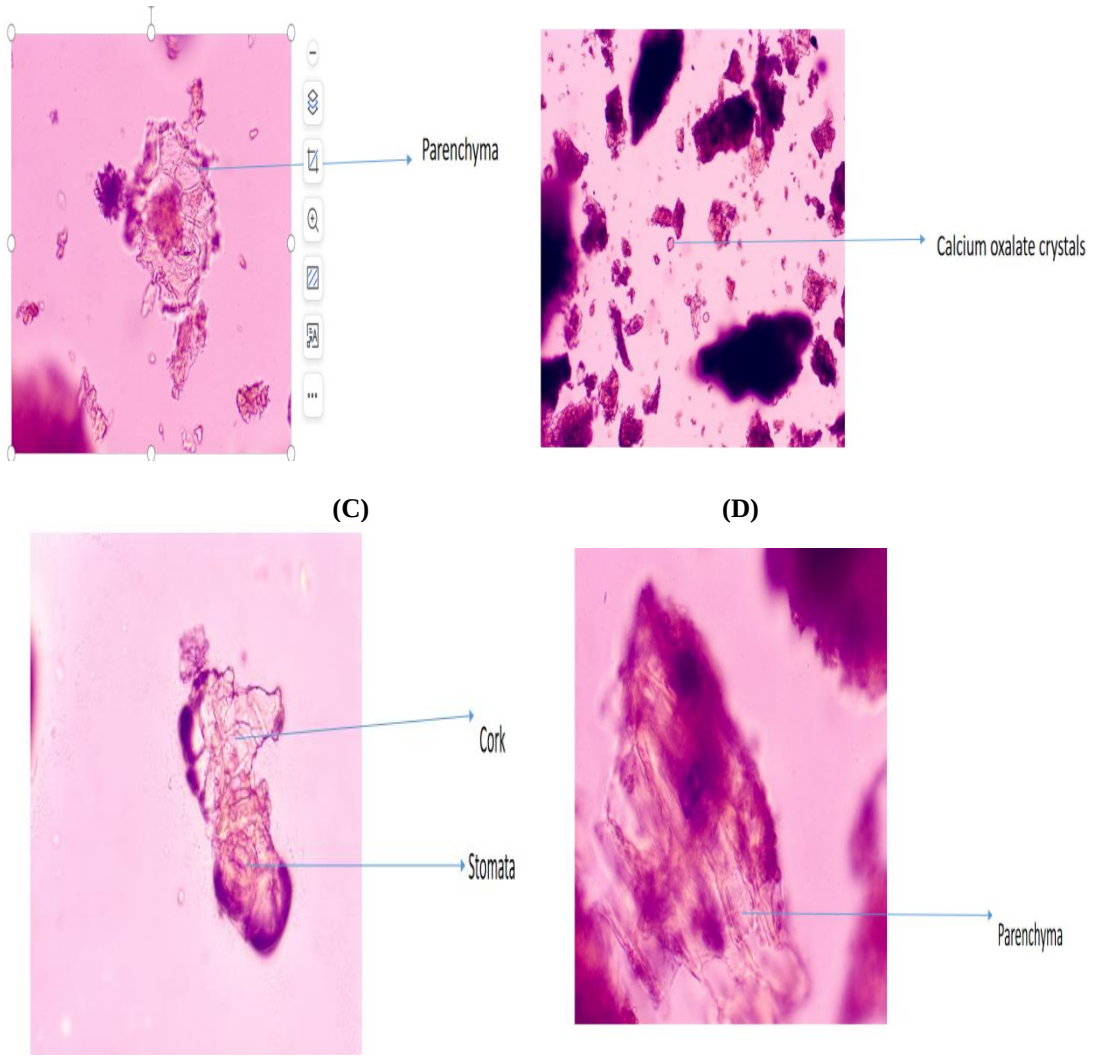


Figure 3: A,B,C,D,E,F Powder characteristics of *L. racemosa* under 400X magnification

Physicochemical Properties

Significant mineral presence is indicated by a high total ash level, which affects the quality of inorganic residues in biomass used to produce energy as well as the nutritional content and processing properties of food products (23,24). It helps in assessment of Purity and nutritional values (25). This indicates the existence of stable, acid-resistant minerals, which is important for quality control and preventing the presence of inert or contaminating compounds (25). It serves as a quality control measure in the pharmaceutical industry, revealing amounts of inorganic compounds during strong oxidation, which may have an impact on the safety and effectiveness of drugs. Additionally, it shows the proportion of organic substances that alcohol can extract, like alkaloids and essential oils, which are significant for their flavor profiles and medicinal qualities. These factors promote product development across industries, optimize extraction and processing techniques, and enable the thorough evaluation of raw materials for safety and quality compliance. They guide crucial decisions about the efficacy, safety, and use of products, ensuring that they fulfill customer expectations and regulatory standards, especially in the food, pharmaceutical, and biomass energy sectors (26-28). The physicochemical parameters and how they affect the analysis of a sample (*L. racemosa*), where this information is essential for determining its usefulness and quality. The *L. racemosa* sample has the following contents: moisture (91.32%), total ash (13.97%), ash soluble in water (6.12%), ash insoluble in acid (3.68%) (Table 3).

Table 3: Physicochemical Parameters

S.NO	Physicochemical Parameter	%W/W
1	Moisture	91.32
2	Total ash	13.9
3	Water soluble ash	6.12
4	Water insoluble ash	3.68

GCMS Profiling

GC-MS analysis of the leaf extract identified bioactive chemicals with potential therapeutic use. The majority of the compounds identified belonging to terpenes, Eicosanoids. Cinnamyl carbanilate exhibited the highest antifungal activity. Terpenes are also well-known for their antimicrobial properties. They disrupt the multilayered structure of polysaccharides, fatty acids, and phospholipids, breach the cell wall, and permeate the cytoplasmic membrane. In bacteria, these events are connected with ion loss and decreasing membrane potential, which leads to proton pump malfunction, ATP pool depletion, and lysis [40]. Citronellol, a monoterpene alcohol identified at 1.08% possessing the pharmacological activities include anti-inflammatory, analgesic, and antioxidant characteristics [41]. Phytol was identified at 0.49% exhibit various pharmacological effects include anxiolytic, metabolism-modulating, cytotoxic, antioxidant, autophagy- and apoptosis-inducing, antinociceptive, anti-inflammatory, immune-modulating, and antimicrobial activity [42]. Isoborneol identified at 0.63% exhibited pharmacological activities such as antimicrobial, anti-inflammatory, analgesic, neuroprotective, and antiepileptic activity [43]. Bornone was identified at 9.86% and the R time is 8.906. 1-Tridecene was identified at 0.62% and the R time is 9.488, Dianhydromannitol was identified at 5.87% and the R time is 10.045. 2-Isopropyl-5-methyl-1-heptanol was identified at 1.77% and the R time is 13.406. Dimethyl(bis[((2Z)-pent-2-en-1-yloxy]) silane was identified at 8.12% and the R time is 13.584. D-Allose was identified at 9.59% and the R time is 14.054. Cervical, hepatocellular, ovarian, head and neck, skin, prostate, and leukemia cancer cell lines have all been proven to be susceptible to D-allose's ability to stop their growth. It works by regulating reactive oxygen species, causing cell cycle arrest, metabolic reprogramming, autophagy, inducing apoptosis, and making cancers more sensitive to chemotherapy and radiation. Because of its anti-inflammatory and antioxidant properties, D-allose may be able to lessen oxidative stress and inflammation. Additionally, D-allose has immunosuppressive, cryoprotective, and anti-hypertensive properties [44,45]. 1-Cyclopentyleicosane was identified at 3.17% and the R time is 14.988. Isochiapin B was identified at 4.07% and the R time is 16.116, which has Anti diabetic and anti-oxidant activities [46]. Isophytol was identified at 0.83% and the R time is 16.735. Neophytadiene was identified at 3.98% and the R time is 17.986. Which has anxiolytic activity [47]. Disparlure was identified at 4.89% and the R time is 18.243. Eicosane was identified at 2.95% and the R time 18.617. It has Anti-inflammatory, analgesic and antipyretic activity [48]. Phytol Isomer was identified at 2.37% and the R time is 20.860. Oleic acid was identified at 16.09% and the R time was 21.103. Oleic acid exhibited anti-microbial, anti-cancer, anti-oxidant and anti-inflammatory activity [49]. Silicone oil was identified at 5.97% and the R time is 24.636.(Table 4, Figure 2 and 3)

Table 4: Compounds identified from the methanolic extract of *L.racemosa by* GC-MS

S.No	R time	Are %	Compound	Molecular Formula	Molecular Weight
1	6.888	1.00	Cinnamyl carbanilate	$C_{16}H_{15}NO_2$	253
2	7.441	2.06	gamma.-Terpinene	$C_{10}H_{16}$	136
3	7.613	1.08	.beta.-Citronellol, Chlorodifluoroacetate	$C_{12}H_{19}ClF_2O_2$	268
4	8.316	0.49	Phytol	$C_{20}H_{40}O$	296
5	8.906	9.86	(±)-2-Bornanone	$C_{10}H_{16}O$	152
6	9.276	0.63	Isoborneol	$C_{10}H_{18}O$	154
7	9.488	0.62	1-Tridecene	$C_{13}H_{26}$	182
8	10.045	5.87	Dianhydromannitol	$C_6H_{10}O_4$	146
9	10.409	1.89	Phytol	$C_{20}H_{40}O$	296
10	11.010	0.49	1-Tridecene	$C_{13}H_{26}$	182
11	13.406	1.77	2-Isopropyl-5-methyl-1-heptanol	$C_{11}H_{24}O$	172
12	13.584	8.12	Dimethyl(bis[((2Z)-pent-2-en-1-yloxy]) silane	$C_{12}H_{24}O_2Si$	228
13	14.054	9.59	D-Allose	$C_6H_{12}O_6$	180
14	14.988	3.17	1-Cyclopentyleicosane	$C_{25}H_{50}$	350
15	16.116	4.07	Isochiapin B	$C_{19}H_{22}O_6$	346
16	16.735	0.83	Isophytol,acetate	$C_{22}H_{42}O_2$	338

17	17.986	3.98	Neophytadiene	$C_{20}H_{38}$	278
18	18.243	4.89	Disparlure	$C_{19}H_{38}O$	282
19	18.617	2.95	Eicosane	$C_{20}H_{42}$	282
20	20.860	2.37	Phytol Isomer	$C_{20}H_{40}O$	296
21	21.103	16.09	Oleic acid	$C_{18}H_{34}O_2$	282
22	23.292	12.21	Hexatriacontyl trifluroacetate	$C_{38}H_{73}F_3O_2$	618
23	24.636	5.97	Silicone oil	$[Si(CH_3)2O)-]n$	9999

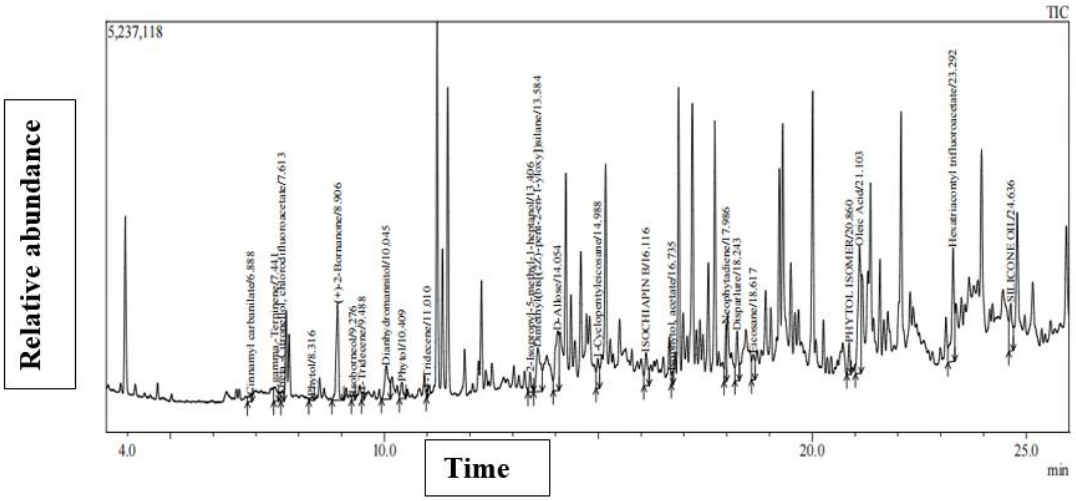
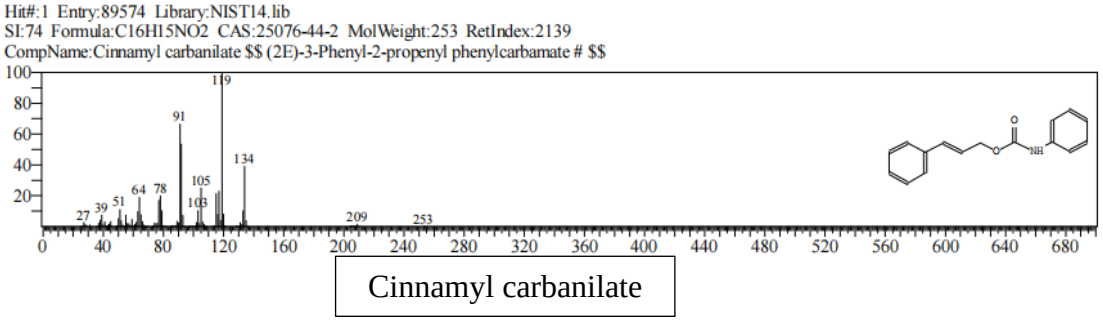
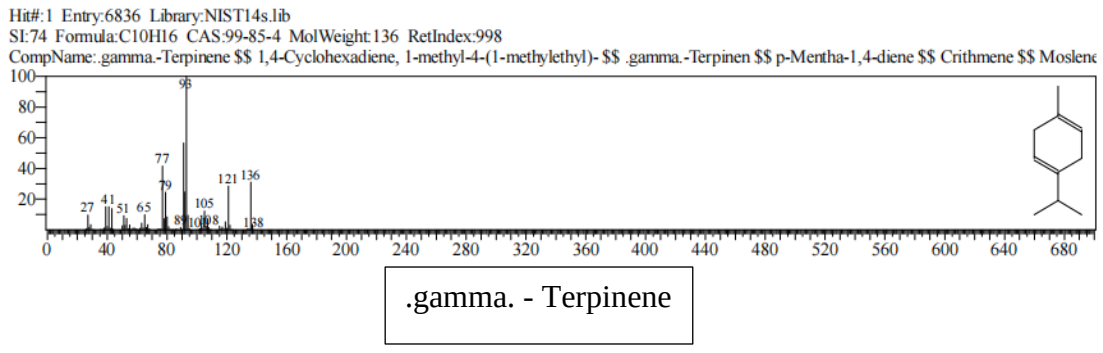
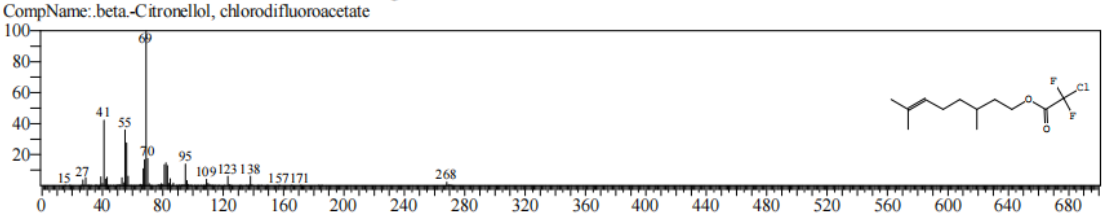


Figure 3: Total ion chromatogram of Methanolic extract of *L.racemosa* leaves



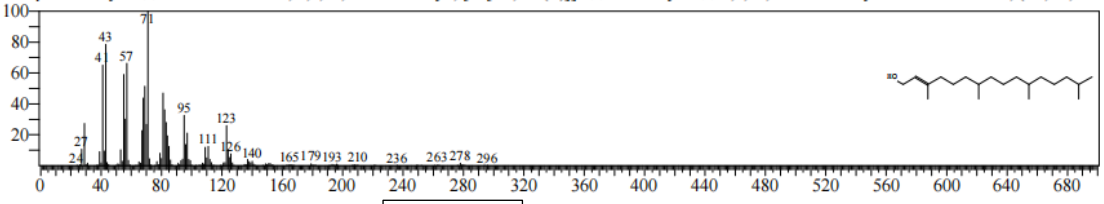


Hit#:1 Entry:102067 Library:NIST14.lib
SI:86 Formula:C12H19ClF2O2 CAS:0-00-0 MolWeight:268 RetIndex:1321
CompName:.beta.-Citronellol, chlorodifluoroacetate



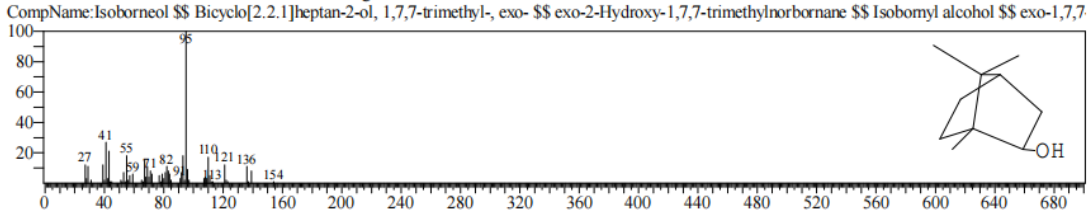
.beta.-Citronellol, Chlorodifluoroacetate

Hit#:1 Entry:28152 Library:NIST14s.lib
SI:78 Formula:C20H40O CAS:150-86-7 MolWeight:296 RetIndex:2045
CompName:Phytol $$ 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, [R-[R*,R*-(E)]]- $$ trans-Phytol $$ 3,7,11,15-Tetramethyl-2-hexadecen-1-ol-, (2E,7R,11R



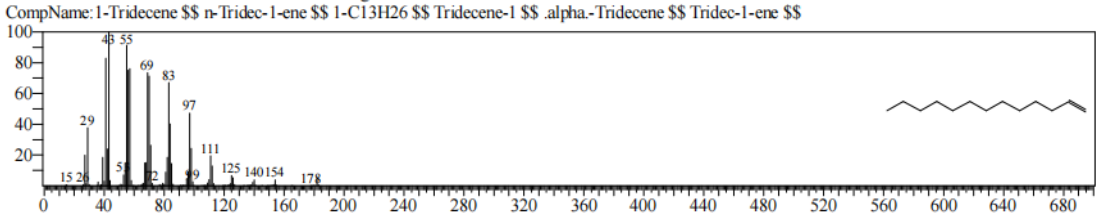
Phytol

Hit#:1 Entry:10399 Library:NIST14s.lib
SI:84 Formula:C10H18O CAS:124-76-5 MolWeight:154 RetIndex:1138
CompName:Isoborneol $$ Bicyclo[2.2.1]heptan-2-ol, 1,7,7-trimethyl-, exo- $$ exo-2-Hydroxy-1,7,7-trimethylnorbornane $$ Isobornyl alcohol $$ exo-1,7,7-



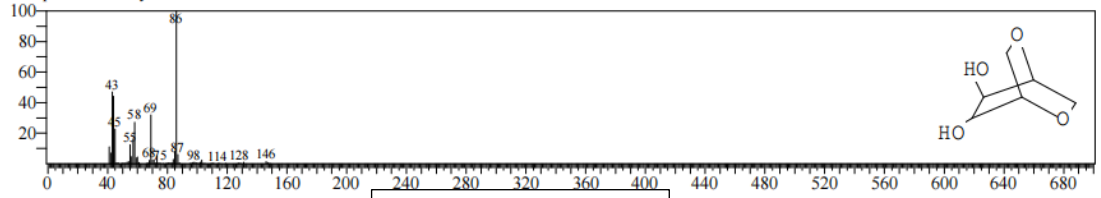
Isoborneol

Hit#:1 Entry:34798 Library:NIST14.lib
SI:89 Formula:C13H26 CAS:2437-56-1 MolWeight:182 RetIndex:1304
CompName:1-Tridecene $$ n-Tridec-1-ene $$ 1-C13H26 $$ Tridecene-1 $$ .alpha.-Tridecene $$ Tridec-1-ene $$



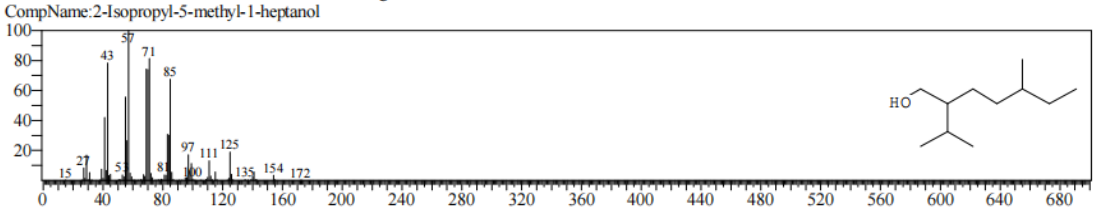
1-Tridecene

Hit#:1 Entry:13875 Library:NIST14.lib
SI:88 Formula:C6H10O4 CAS:0-00-0 MolWeight:146 RetIndex:1216
CompName:Dianhydromannitol



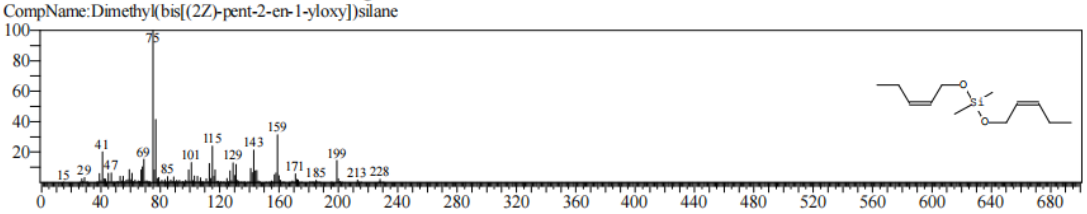
Dianhydromannitol

Hit#:1 Entry:28465 Library:NIST14.lib
SI:89 Formula:C11H24O CAS:91337-07-4 MolWeight:172 RetIndex:1165
CompName:2-Isopropyl-5-methyl-1-heptanol



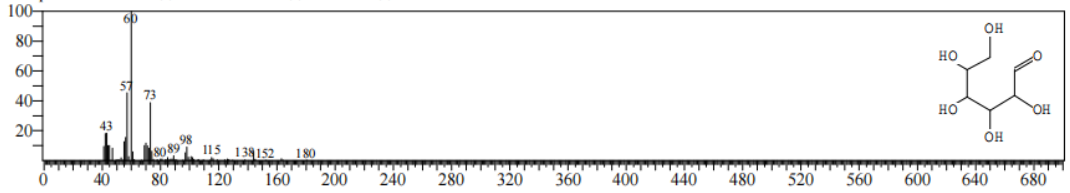
2-Isopropyl-5-methyl-1-heptanol

Hit#:1 Entry:68992 Library:NIST14.lib
SI:73 Formula:C12H24O2Si CAS:0-00-0 MolWeight:228 RetIndex:1292
CompName:Dimethyl(bis[(2Z)-pent-2-en-1-yloxy])silane



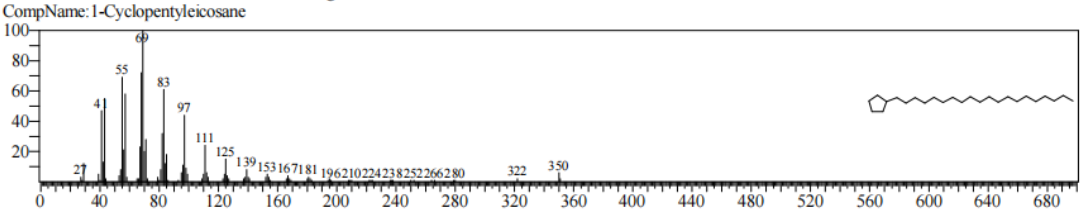
Dimethyl(bis[((2Z)-pent-2-en-1-yloxy]) silane

Hit#:1 Entry:32602 Library:NIST14.lib
SI:94 Formula:C6H12O6 CAS:2595-97-3 MolWeight:180 RetIndex:1698
CompName:D-Allose $$ .beta.-D-Allose $$ Hexose # $$



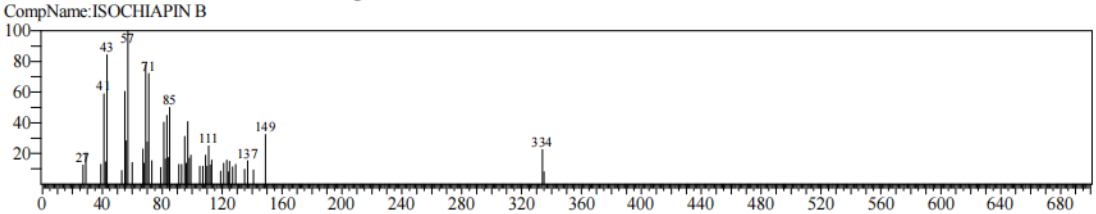
D-Allose

Hit#:1 Entry:175016 Library:NIST14.lib
SI:89 Formula:C25H50 CAS:0-00-0 MolWeight:350 RetIndex:2549
CompName:1-Cyclopentyleicosane



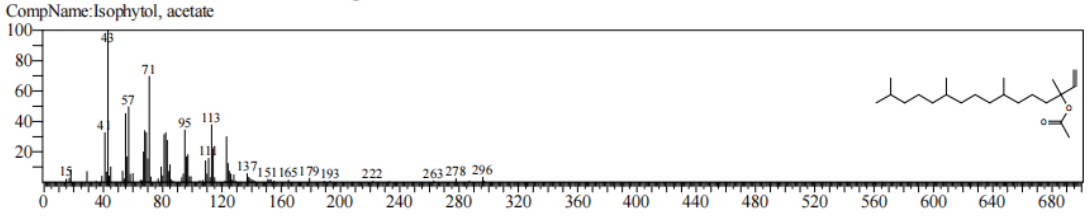
1-Cyclopentyleicosane

Hit#:1 Entry:290772 Library:WILEY8.LIB
SI:80 Formula:C19H22O6 CAS:0-00-0 MolWeight:346 RetIndex:0
CompName:ISOCHIAPIN B



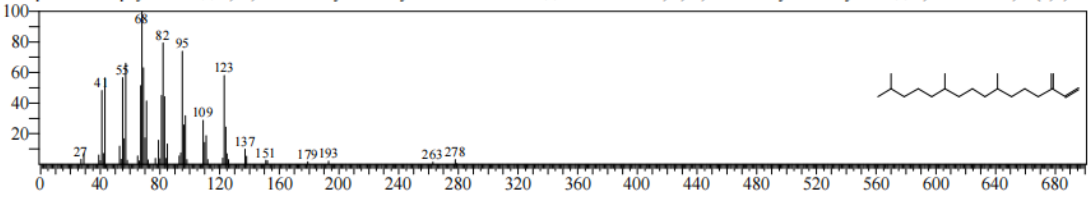
Isochiapin B

Hit#:1 Entry:165113 Library:NIST14.lib
SI:80 Formula:C22H42O2 CAS:0-00-0 MolWeight:338 RetIndex:2089
CompName:Isophytol, acetate



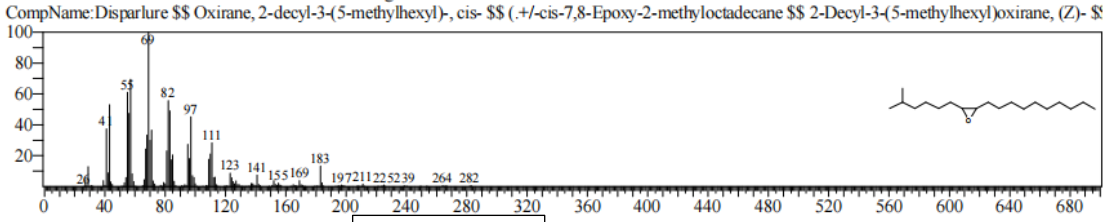
Isophytol,acetate

Hit#:1 Entry:111732 Library:NIST14.lib
SI:94 Formula:C20H38 CAS:504-96-1 MolWeight:278 RetIndex:0
CompName:Neophytadiene $$ 7,11,15-Trimethyl-3-methylenehexadec-1-ene $$ 1-Hexadecene, 7,11,15-trimethyl-3-methylene- $$ 1,3-Butadiene, 2-(4,8,12-



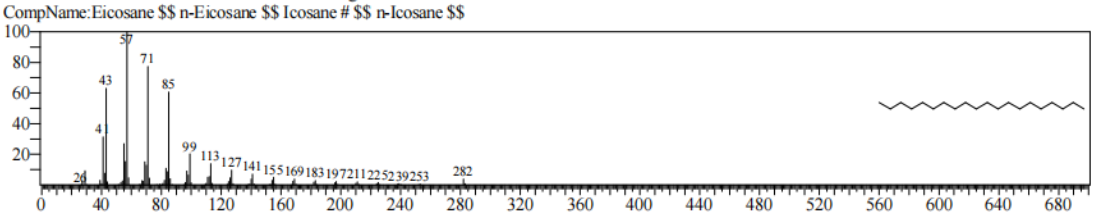
Neophytadiene

Hit#:1 Entry:27126 Library:NIST14s.lib
SI:86 Formula:C19H38O CAS:29804-22-6 MolWeight:282 RetIndex:1898
CompName:Disparlure $$ Oxirane, 2-decyl-3-(5-methylhexyl)-, cis- $$ (.+/-cis-7,8-Epoxy-2-methyloctadecane $$ 2-Decyl-3-(5-methylhexyl)oxirane, (Z)- $$



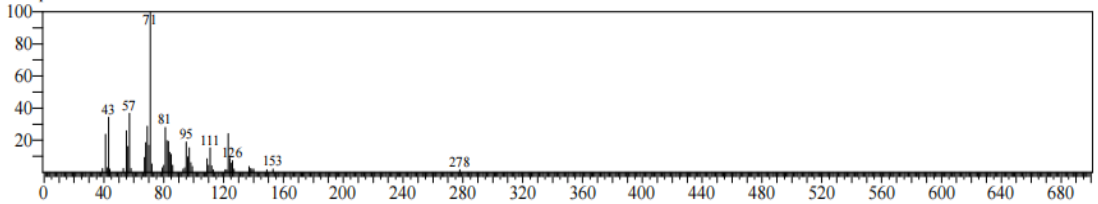
Disparlure

Hit#:1 Entry:115221 Library:NIST14.lib
SI:86 Formula:C20H42 CAS:112-95-8 MolWeight:282 RetIndex:2009
CompName:Eicosane $$ n-Eicosane $$ Icosane # $$ n-Icosane $$



Eicosane

Hit#:1 Entry:235603 Library:WILEY8.LIB
SI:89 Formula:C20H40O CAS:0-00-0 MolWeight:296 RetIndex:0
CompName:PHYTOL ISOMER



Phytol Isomer

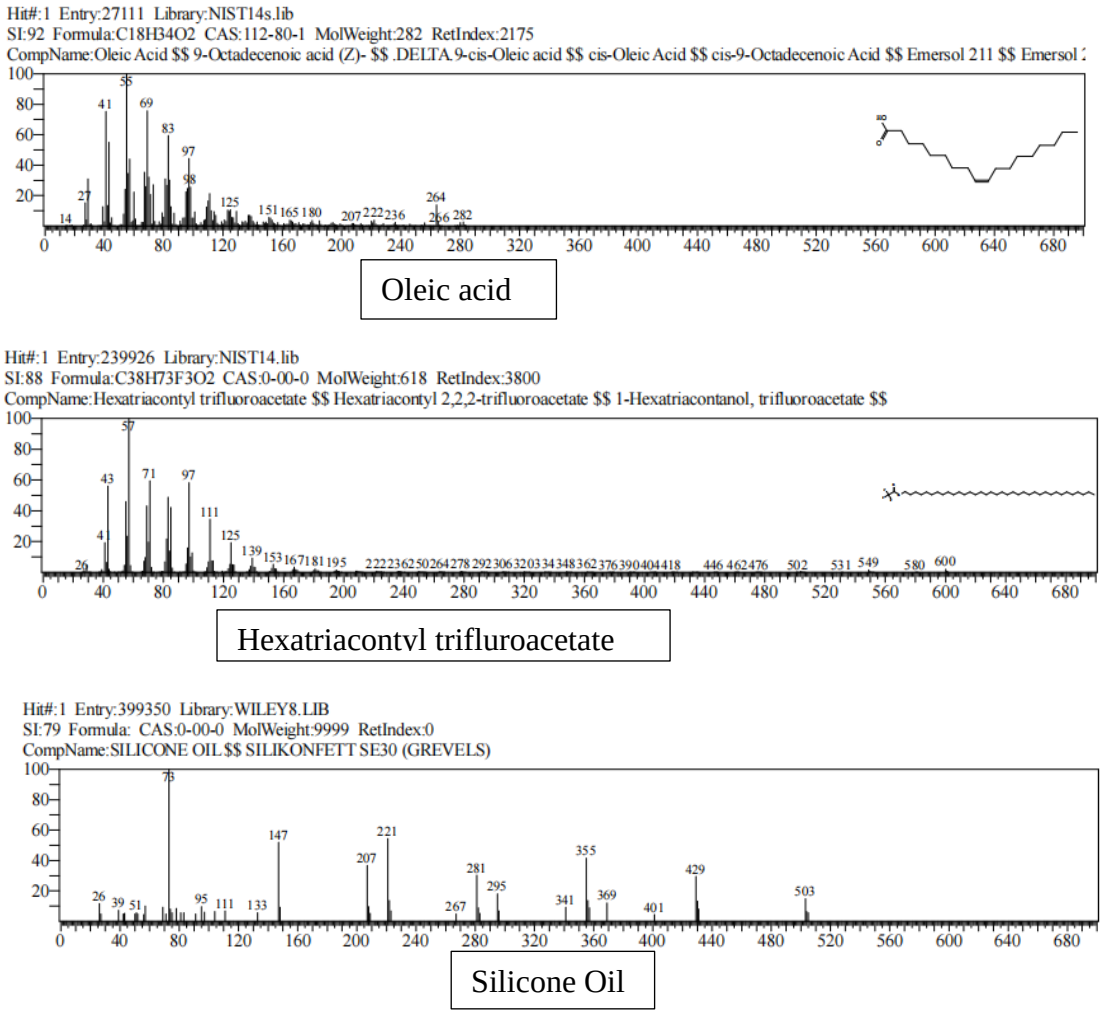


Figure 4: Mass fragmentation pattern and molecular structure for some most abundant phytochemicals identified in *L.racemosa* leaf.

Molecular docking

The bioactive compounds of *L. racemosa* methanolic extract exhibited potential binding capacity with specific proteins selected. These phytochemicals are further investigated for their potential to physically bind to the Estrogen α receptors (Estrogen α, PDB:1x7e,1x7r) and estrogen β (Estrogen β, PDB: 1U9e,1x7b,1x7j,1x76,1x78) receptors. It will suppress many symptoms because Estrogen plays major role Menopause. Osteoporosis development is directly linked to the deficiency of estrogen during perimenopause and menopause which weakens bones and raises the possibility of unexpected and abrupt fractures. A member of the tumor necrosis factor (TNF) cytokine family, which is a ligand for osteoprotegerin and essential for osteoclast activation and differentiation, is encoded by this gene. This protein is involved in the control of the T cell-dependent immune response and has been demonstrated to be a dendritic cell survival factor. It has been documented that T cell activation increases osteoclastogenesis and bone loss by inducing the expression of this gene [35]. TNF, which causes inflammation and joint degradation in inflammatory disorders like rheumatoid arthritis, also inhibits osteoclast production. The mechanism Animal research indicates that serotonin (5-HT) is crucial for thermoregulation and that an excess of serotonin receptor sites in the hypothalamus may be the cause of the temperature rises connected to hot flushes and flushing. The 5-HT(2A) receptor subtype in particular might be crucial to the development of hot flashes [36]. HIF (Hypoxia-Inducible Factor) is a transcription factor that detects low oxygen levels (hypoxia). During menopause, variable hormone levels can cause variations in oxygen levels in various tissues, which may influence sleep patterns. HIF may be involved in the body's adaptation to these changes, regulating sleep quality and duration. The control of sleep-wake cycles is one of the numerous biological processes that depend on CAMP (Cyclic Adenosine Monophosphate), a secondary messenger. Menopausal hormonal changes may affect CAMP levels, which may cause sleep disturbances. Because they can identify infections and trigger immunological responses, TLRs (Toll-like Receptors) are a class of proteins that are essential to the immune system. Sleep quality may be impacted by alterations in inflammation and immunological function after menopause. Because TLRs affect inflammatory responses that interfere with regular sleep cycles, they may be a factor in sleep disorders

[50]. During menopause, women with bipolar disorder may have more manic/hypomanic and depressed episodes [51]. Among the selected phytochemical constituents of *L. racemosa*, Castalagin (-9.7 kcal/mol), Lumnitzera lactone (-9.6) and Phellingridine (-9.3 kcal/mol) exhibited binding affinity which is almost similar to standard 17 β-estradiol (-10.784 kcal/mol) (Table 5,6). Poly galatinoside (-10.9 kcal/mol) binding affinity equal to the standard 17 β-estradiol (-10.943 kcal/mol) with ER β system. Castalagin exhibited the binding affinity of (-9.5 kcal/mol & -8.0 kcal/mol) with 1s55 and 2eqo targets for osteoporosis. Castalagin exhibited best binding affinity with 2lxt target for determining depression (Table 7). Castalagin (-10.8kcal/mol), ellagic acid (-10.1kcal/mol) for GABA A systems 5osc and 1bnd respectively. The binding capacity of α-amyrin for anti-anxiety activity determination is -9.7kcal/mol (Table 8). Binding affinity of Castalagin (-9.8kcal/mol) and Lumnitzeralactone (-9.2kcal/mol) for sleep disturbances targeting 1h2n and 5k8s. Tormentic acid exhibited best binding affinity (-8.3 kcal/mol) against 6COA for bipolar disorders (Table 9).

Table 5 Docking results of the compounds in ERα system with 2 targets

	Docking score (kcal/mol)	
Compound	**1x7e**	**1x7r**
Lumnitzeralactone	-9.6	-8.7
Zingerone	-6.5	-6.4
Phellingridine	-9.2	-9.3
β-stigmasterol	-9.1	-8.3
Epigallocatechin	-7.5	-8.6
Isoquercetin	-8.5	-8.2
Kaempferol	-8.5	-7.5
Luteol	-8.7	-8.8
Methyl ellagic acid	-8.5	-8.9
Myricetin	-8.5	-6.7
Quercetin	-8.5	-8.5
Stigmasterol	-7.7	-8.9
Adenosine	-7.5	-8.2
α-amyrin	-9	-7.5
Benzyl β arabinosyl	-7.7	-7.4
β-amyrin	-8.9	-7.5
Castalagin	-9.7	-7.4
Corilagin	-9.1	-8.6
Di methoxy xanthone	-8.2	-8.4
Fridelin	-6.8	-7.9
Galactopyranosyl glycerol	-6.3	-7.4
Gallic acid	-7.8	-5.1
Ginsenoside	-7.7	-5.9
Hyderagenin arabinosyl	-8.3	-7.4
Icariside	-7.6	-7.3
Iso guaicin	-7.8	-7.4
Lawsoniaside	-8.7	-7.4
Linolenic acid	-5.5	-6.4
Lyoresinol	-7.5	-8.1
Methoxy xanthene	-8	-5.6
Methyl gallate	-6.5	-6.3
Oxisophrone	-6.5	-7.3
Pinoresinol	-8.1	-6.1
Poly galatinoside	-11.3	-6
Proto catechuicacid	-6.2	-7.7
Quercetrine	-9.3	-5.9
Tormentic acid	-8.7	-6.8

Table 6: Docking results of the compounds in ER β system with 5 targets

	Docking score (kcal/mol)				
Compound	**1U9E**	**1x7b**	**1x7j**	**1x78**	**1x76**
Lumnitzeralactone	-8.6	-8.8	-9.7	-7.5	-9.6
Zingerone	-6.3	-6.4	-5.3	-5.7	-6.3
Phellingridine	-9.3	-9.4	-9.1	-7.9	-7.3
β-stigmasterol	-6.7	-8.2	-7.1	-6.7	-7.6
Ellagicacid	9.4	-7.5	-8.4	-9.5	-8.4
Epigallocatechin	-7.7	-6.8	-7.4	-7.0	-6.6
Isoquercetin	-6.4	-7.4	-7.3	-7.0	-6.8
Kaempferol	-8.1	-7.1	-7.0	-6.7	-7.2
Luteol	-8.6	-7.5	-9.5	-8.3	-7.2
Methyl ellagic acid	-8.7	-7.1	-8.3	-6.5	-6.9
Myricetin	-8	-7.7	-7.0	-8.4	-7.3
Quercetin	-6.2	-7.5	-9.4	-8.0	-7.2
Stigmasterol	-7	-7.8	-6.8	-7.1	-7.4
Adenosine	-7.5	-7.7	-7.5	-7.7	-6.1
α-amyrin	-7.5	-7.8	-7.8	-7.6	-8.8
Benzyl β arabinosyl	-7.4	-5.7	-7.4	-6.0	-5.8
β-amyrin	-7.2	-8.9	-7.9	-7.7	-8.9
Castalagin	-7.6	-9.6	-9.4	-8.7	-9.0
Corilagin	-7.6	-8.6	-8.2	-8.7	-8.6
Di methoxy xanthone-	-8.5	-6.7	-8.4	-6.0	-6.5
Fridelin	-7.3	-9.5	-7.8	-7.9	-7.3
Galactopyranosyl glycerol	-5.9	-5.8	-6.6	-5.9	-5.6
Gallic acid	-5.8	-6.4	-5.8	-5.9	-6.1
Ginsenoside	-6.9	-6.3	-7.6	-7.1	-8.3
Hyderagenin arabinosyl	-7	-7.5	-8.7	-7.6	-8.4
Glycopyranoside	6.9	-6.2	-6.7	-6.7	-6.5
Icariside	-7.3	-6.9	-7.1	-7.0	-7.0
Iso guaicin	-5.7	-6.5	-6.7	-7.2	-6.4
Lawsoniaside	-7.1	-8.6	-6.9	-7.4	-7.7
Linolenic acid	-4.5	-4.3	-4.6	-5.0	-7.8
Lyoresinol	-5.6	-6.7	-6.8	-7.1	-6.8
Methoxy xanthene	-8.2	-6.8	-8.4	-6.7	-8.2
Methyl gallate	-5.9	-5.1	-6.0	-6.1	-6.1
Oxisophrone	-6.1	-5.8	-6.0	-6.3	-4.9
Pinoresinol	-6.2	-7.3	-7.2	-6.4	-7.3
Poly galatinoside	-6.3	-8.7	-10.9	-10.1	-10.3
Proto catechuicacid	-6	-5.9	-6.0	-6.1	-6.0
Quercetrine	-7	-7.9	-8.4	-7.4	-7.2
Tormentic acid	-6.7	-8.0	-7.5	-7.7	-7.9

Table 7: Docking results of the compounds in TNFSF 11 system with 1s55 target, IP2 system with 2eqo target for Osteoporosis & Depression CREB1 system with 2lxt target

	Docking score (kcal/mol)		
Compound	**TNFSF 11:1s55**	**IP2:**2eqo	**CREB1:**2lxt
Lumnitzeralactone	-8.0	-6.4	-5.6
Zingerone	-5.9	-5.0	-4.5
Phellingridine	-8.0	-6.9	-5.4
β-stigmasterol	-8.7	-6.6	-6.2
Ellagicacid	-7.7	-6.5	-5.5
Epigallocatechin	-6.9	-6.0	-5.7
Isoquercetin	-7.1	-6.5	-5.4
Kaempferol	-7.2	-6.1	-5.2
Luteol	-7.5	-6.6	-5.8
Methyl ellagic -aid	-7.4	-6.1	-5.7

Myricetin	-7.5	-6.5	-5.3
Quercetin	-7.6	-6.6	-5.4
Stigmasterol	-8.5	-6.3	-6.1
Adenosine	-6.4	-5.6	-4.5
α-amyrin	-9.4	-6.9	-6.1
Benzyl β arabinosyl	-9.4	-5.1	-4.7
β-amyrin	-9.2	-6.9	-6.3
Castalagin	-9.5	-8.0	-6.7
Corilagin	-8.5	-7.3	-5.9
Di methoxy xanthone-	-6.6	-6.4	-4.9
Fridelin	-8.4	-7.2	-6.6
Galactopyranosyl glycerol	-6.6	-5.7	-3.9
Gallic acid	-5.9	-5.0	-4.1
Ginsenoside	-8.5	-6.6	-6.5
Hyderagenin arabinosyl	-8.3	-6.9	-6.0
Glycopyranoside	-7.3	-6.0	-4.9
Icariside	-7.3	-6.1	-5.4
Iso guaicin	-6.8	-6.0	-5.5
Lawsoniaside	-7.8	-6.5	-5.8
Linolenic acid	-6.2	-4.2	-3.8
Lyoresinol	-7.2	-5.7	-5.3
Methoxy xanthene	-7.0	-6.3	-5.1
Methyl gallate	-5.5	-4.9	-4.2
Oxisophrone	-5.1	-4.7	-3.8
Pinoresinol	-7.1	-5.9	-5.9
Poly galatinoside	-6.5	-6.6	-6.2
Proto catechuicacid	-5.7	-4.9	-3.9
Quercetrine	-7.4	-6.3	-5.3
Tormentic acid	-8.1	-6.6	-6.1

Table 8: Docking results of the compounds in GABA A system with 5osc,1bnd ,CaMKIV system with 2w4o , Egr-1 system with 4x9j, CREB system with 5zko targets for Anxiety

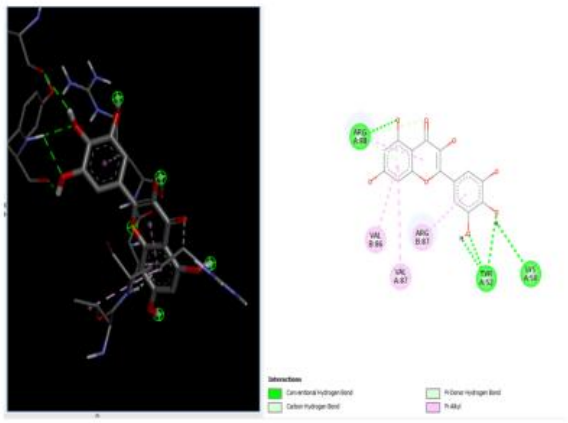
	Docking score (kcal/mol)				
Compound	**GABA A:**5osc	**GABA A:**1bnd	**CaMKIV:** 2w4o	**Egr-1:**4x9j	**CREB:**5zko
Lumnitzeralactone	-8.5	-7.7	-8.6	-6.3	-6.0
Zingerone	-6.4	-5.8	-6.2	-5.4	-4.8
Phellingridine	-8.9	-5.1	-8.6	-6.6	-6.1
β-stigmasterol	-8.8	-6.7	-9.5	-6.7	-7.3
Ellagicacid	-8.7	-10.1	-8.8	-6.8	-6.1
Epigallocatechin	-8.3	-7.6	-8.3	-5.9	-6.3
Isoquercetin	-7.8	-7.1	-8.7	-6.4	-5.9
Kaempferol	-8.1	-10.1	-7.9	-6.1	-6.0
Luteol	-8.4	-7.6	-8.5	-9.1	-6.1
Methyl ellagic -aid	-8.6	-7.0	-8.7	-6.6	-5.7
My-rcetin	-8.3	-9.2	-8.6	-9.4	-5.7
Quercetin	-8.3	-7.3	-7.6	-6.3	-6.0
Stigmasterol	-8.8	-6.7	-8.7	-6.7	-7.3
Adenosine	-7.9	-7.1	-6.4	-5.5	-5.3
α-amyrin	-9.6	-7.5	-9.7	-6.7	-7.6
Benzyl β arabinosyl	-7.3	-6.4	-6.9	-5.3	-5.5
β-amyrin	-9.0	-7.9	-9.2	-6.9	-7.3
Castalagin	-10.8	-9.1	-8.9	-7.9	-7.0
Corilagin	-9.6	-8.6	-8.6	-6.9	-6.7
Di methoxy xanthone-	-8.3	-6.8	-8.4	-6.0	-5.7
Fridelin	-9.9	-8.0	-8.8	-7.2	-7.8
Galactopyranosyl glycerol	-6.7	-5.2	-7.4	-4.8	-4.3
Gallic acid	-6.2	-6.5	-5.5	-2.8	-4.8

Ginsenoside	-8.6	-7.5	-8.7	-6.5	-6.1
Hyderagenin arabinosyl	-9.2	-7.0	-7.9	-7.5	-7.2
Glycopyranoside	-7.5	-6.7	-6.9	-5.9	-5.8
Icariside	-7.8	-7.2	-7.8	-6.0	-5.6
Iso guaicin	-7.7	-6.7	-7.3	-5.8	-6.6
Lawsoniaside	-8.0	-7.7	-8.8	-6.7	-6.2
Linolenic acid	-5.8	-4.3	-5.8	-3.6	-4.1
Lyoresinol	-7.7	-7.3	-7.3	-5.7	-5.4
Methoxy xanthene	-8.5	-7.2	-7.9	-6.3	-5.8
Methyl gallate	-5.7	-5.7	-8.6	-4.9	-4.7
Oxisophrone	-6.2	-5.0	-5.4	-4.6	-4.7
Pinoresinol	-7.5	-6.7	-8.6	-6.6	-6.2
Poly galatinoside	-6.4	-6.3	-6.7	-6.5	-6.1
Proto catechuicacid	-6.8	-5.7	-5.6	-4.9	-4.7
Quercetrine	-7.9	-7.9	-8.6	-6.3	-6.1
Tormentic acid	-8.8	-7.2	-7.8	-7.1	-6.3

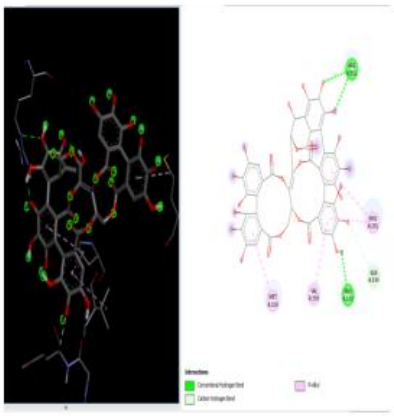
Table 9: Docking results of the compounds in HIF-1a system with 1h2n,CAMP system with 5k8s targets for Sleep disturbances (Serotonergic synapse CAMP,HIF-1a) & Catechol-o-aminotransferase,brain derived neurotrophic factor,Voltage dependent Ca+2 channel α-1 subunit system with 6COA target for Bipolar disorders

	Docking score (kcal/mol)		
Compound	HIF-1a:1h2n	CAMP:5k8s	6COA
Lumnitzeralactone	-8.2	-9.2	-6.5
Zingerone	-6.1	-7.1	-5.2
Phellingridine	-7.8	-9.6	-6.5
β-stigmasterol	-7.8	-8.6	-7.1
Ellagicacid	-7.7	-7.7	-6.3
Epigallocatechin	-7.4	-7.8	-6.1
Isoquercetin	-8.4	-8.1	-6.2
Kaempferol	-6.2	-8.2	-6.3
Luteol	-9.1	-7.6	-6.3
Methyl ellagic -aid	-7.4	-7.2	-6.2
My-rcetin	-8.4	-7.9	-6.0
Quercetin	-8.5	-8.1	-6.2
Stigmasterol	-8.3	-8.4	-7.7
Adenosine	-6.6	-6.9	-5.6
α-amyrin	-8.6	-8.5	-7.4
Benzyl β arabinosyl	-7.1	-8.9	-5.7
β-amyrin	-8.6	-9.1	-7.4
Castalagin	-9.8	-8.3	-7.3
Corilagin	-8.9	-7.7	-7.4
Di methoxy xanthone-	-7.3	-7.1	-6.1
Fridelin	-9.0	-8.8	-7.6
Galactopyranosyl glycerol	-6.6	-7.2	-4.6
Gallic acid	-6.1	-6.6	-4.7
Ginsenoside	-8.8	-8.1	-6.7
Hyderagenin arabinosyl	-7.3	-7.6	-7.6
Glycopyranoside	-8.2	-7.2	-6.5
Icariside	-7.2	-7.5	-6.1
Iso guaicin	-6.9	-7.0	-6.5
Lawsoniaside	-9.2	-7.7	-5.1
Linolenic acid	-6.2	-6.4	-5.0
Lyoresinol	-8.2	-6.6	-6.1
Methoxy xanthene	-6.0	-7.8	-6.2
Methyl gallate	-6.0	-6.8	-4.7
Oxisophrone	-6.0	-6.1	-5.0
Pinoresinol	-7.7	-7.4	-6.9
Poly galatinoside	-6.8	-6.5	-6.7
Proto catechuicacid	-6.1	-6.4	-4.7
Quercetrine	-8.7	-7.6	-7.1
Tormentic acid	-8.3	-8.4	-8.3

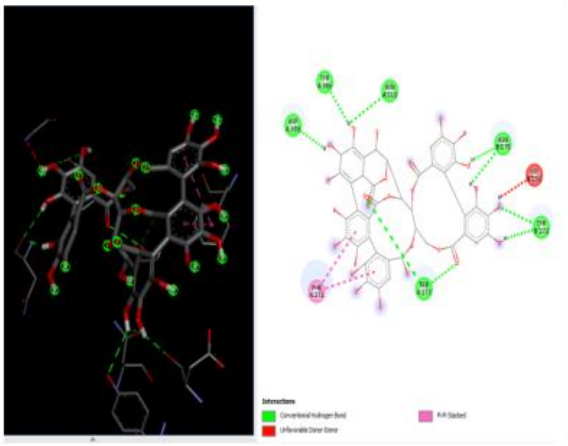
(A)1bnd-Myricetin



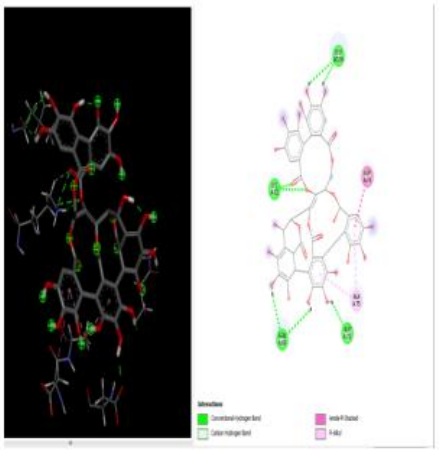
(B)1h2n-Castalagin



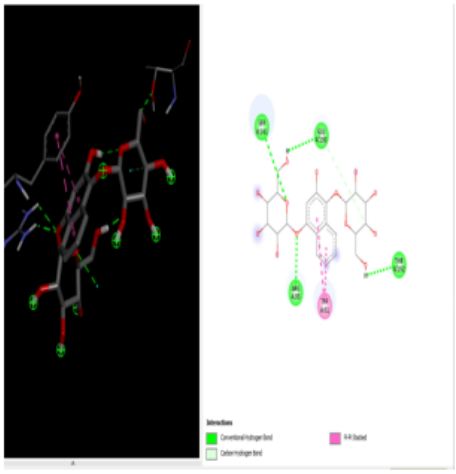
(C)1s55-Catalagin



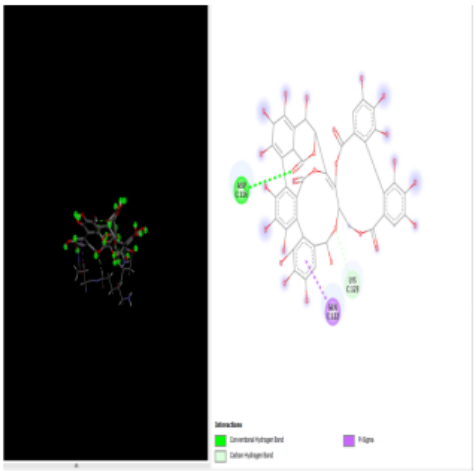
(D)2eqo- Castalagin



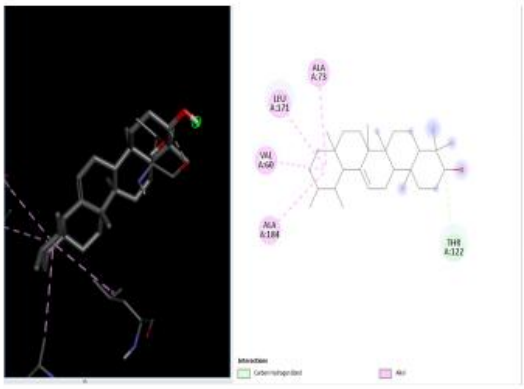
(E)2F34-Isoguaicin



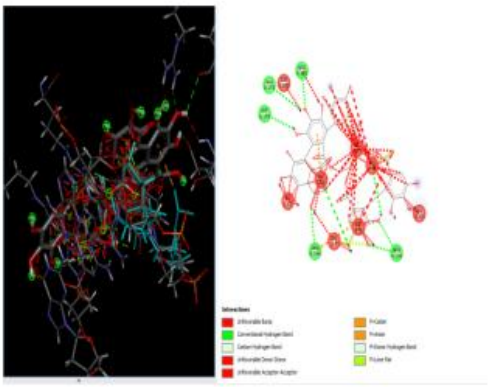
(F) 2lxt-Castalagin



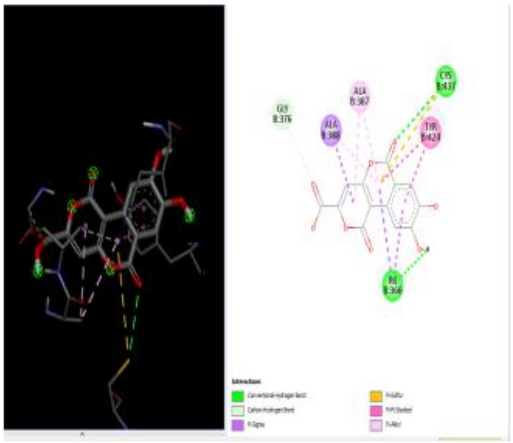
(G)2W4o-α Amyrin



(H)4x9j-Castalagin



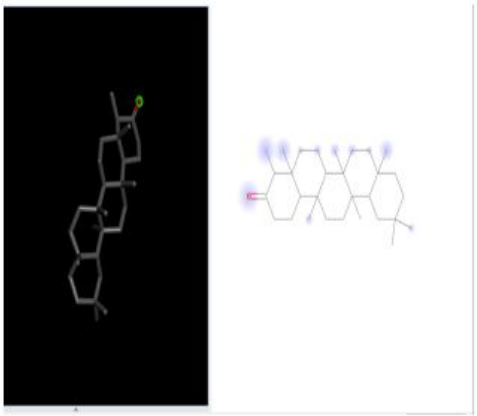
(I)5k8s-Phellingridine



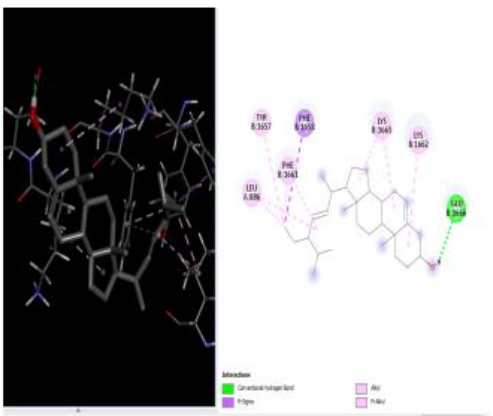
(J)5osc-Friedelin



(K)5ZKo- Friedelin



(L)6Coa-β-Sitosterol



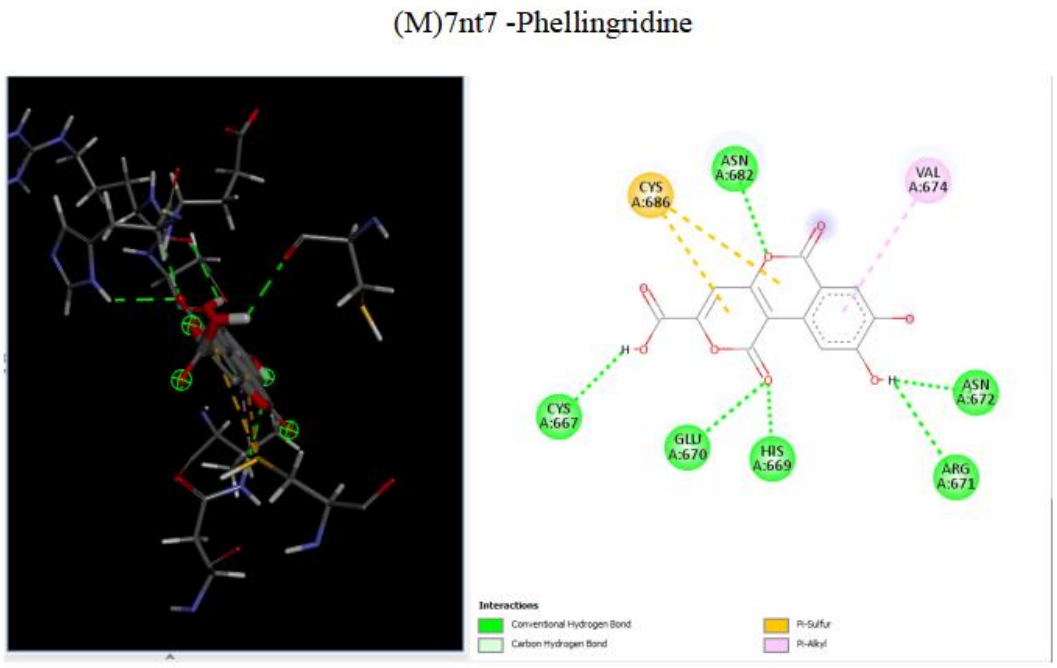


Fig 5: (A-M) 2D interaction diagram of molecules in various binding cavities with least binding energies. The complexes are (A)1bnd-Myricetin (B)1h2n-Castalagin (C)1s55-Catalagin (D) 2eqo- Castalagin (E) 2F34-Isoguaicin (F) 2lxt-Castalagin(G) 2W4o-α Amyrin (H) 4x9j-Castalagin (I) 5k8s-Phellingridine(J) 5osc-Friedelin (K)5ZKo- Friedelin (L) 6Coa-β-Sitosterol (M)7nt7 -Phellingridine

The best binding compounds for each target was depicted in the Figure 4. The best docked pose of Myricetin with 1bnd exhibited 3 pi-alkyl interactions and 3 conventional hydrogen bond interactions, Castalagin with 1h2n exhibited 2 conventional hydrogen bond interactions, 2 pi-alkyl interactions and 1 carbon hydrogen bond. Castalagin with 1s55 exhibited 2 pi-sigma bonds interactions, 1 pi-alkyl bond interactions and 1 conventional hydrogen bond interactions. Castalagin with 2eqo exhibited 1 amide pi stacked bond interaction, 4 conventional hydrogen bonds, 1 pi-alkyl bond interactions. 2F34 with Isoguaicin exhibited 2 pi-alkyl bond interactions, 3conventional hydrogen bond interactions, 1 pi-pi stcked and T shaped bond interactions. Castalagin with 2lxt exhibited 1 pi-sigma bond interaction, 1 conventional hydrogen bond interaction and 1 carbon hydrogen bond. α Amyrin with 2W4o exhibited 4 alkyl bond interactions and 1 carbon hydrogen bond interaction. Castalagin with 4x9j exhibited 5 conventional hydrogen bond interactions, 1 pi-cation,1 pi- anion and 1-pi lone pair interactions. Phellingridine with 5k8s exhibited 1 pi-sulfur, 2 conventional hydrogn bond interactions, 1 pi-alkyl, 1pi-pi stacked, 1 pi-alkyl and 1 carbon hydrogen bond interactions. Friedelin with 5osc exhibited 1 alkyl bond interaction. Friedelin with 5ZKo exhibited 1 alkyl bond interaction. β-Sitosterol with 6Coa exhibited 6 pi-alkyl bonds, 1 conventional hydrogen bond interaction and 1 pi-sigma and 5 pi-alkyl bond interactions. Phellingridine with 7nt7 exhibited 1 pi-sulfur bond interaction, 1 pi-alkyl bond interaction and 6 conventional hydrogen bond interactions.

ADMET analysis

The chosen compounds' ADME (absorption, distribution, metabolism, and excretion) characteristics, including their pharmacokinetic and drug-like traits, have been predicted using the SwissADME online server (http://www.swissadme.ch, viewed on May 19, 2023). The laws that define a drug's properties, such as Lipinski's [53], Egan's [54], and Veber's [55], were followed. Molecular weight (MW) < 500, topological surface area (TPSA) < 140, number of H-bond acceptors (nOHA) ≤ 7, number of H-bond donors (nOHD) ≤ 5, water partition coefficient (WLOGP) ≤ 5.88, and number of rotatable bonds (nRB) ≤ 10 are the criteria that the compound should not violate in accordance with the >1 Lipinski rule.

All of the compounds taken into consideration, according to the current research, complied with the Lipinski, Egan, and Verber rules, indicating the compounds advantageous drug-like properties. A higher degree of bioactivity in the molecule was indicated by the bioavailability score of 0.55 for each of the compounds that were taken into consideration. Compounds with a TPSA values of less than 30.2 Å2 exhibit good lipophilicity behavior and brain penetration. The range of the consensus Log Po/w is 0.42 to 3.70 (Table 10). Good intestinal absorption was seen in compounds with no P-glycoprotein (P-gp) substrate. Most of the compounds exhibited high GI absorption except Adenosine, α and β amyrin,

Corilagin and β sitosterol. Glycopyranosyl, Icariside, Isoguaicine, Linolenic acid, oxisoprone, Pinoresinol exhibited good penetration through blood brain barrier. Some compounds interacted with CYP isoenzyme may cause little hazard. The bioavailability radar graph (Fig. 6) is used to show the drug like characteristics and GI absorption of the selected compounds of *L.racemosa*.

The toxicity parameters of selected phytocompounds were predicted using the web server ProTox II. The compounds with LD_{50} 2000mg/kg are therapeutically effective and less toxic. All the data regarding toxicity of the compounds was depicted in Table 11.

Table 10 In silico ADMET analysis of important constituents of *Lumnitzera racemosa*

Compounds	**1**	**2**	**3**	**4**	**5**	**6**	**7**
TPSA* (A2)	139.54	106.84	17.07	20.23	310.66	107.22	141.34
Consensus* Log Po/w	1.44	2.11	7.44	6.89	-0.90	0.99	1.00
Mol wt (g $mol^{-1)}$	267.24	406.43	426.72	412.69	634.45	288.25	302.19
nRB	2	7	0	0	3	1	0
nOHA	7	8	1	1	18	6	8
nOHD	4	3	0	1	11	4	4
WLOGP	2.30	2.10	8.46	7.78	-0.30	1.16	1.31
Water Solubility	Soluble	Moderately soluble	Poorly soluble	Poorly soluble	Soluble	Soluble	Soluble
GI absorption**	Low	High	Low	Low	Low	High	High
BBB permeation***	No	No	No	No	No	No	No
P-gp substrate**	No	Yes	No	No	Yes	No	No
CYP1A2 inhibitor**	No	No	No	No	No	No	Yes
CYP2C19 inhibitor**	No	No	No	No	No	No	No
CYP2C9 inhibitor**	No	No	No	No	No	No	No
CYP2D6 inhibitor**	No	Yes	No	No	No	No	No
CYP3A4 inhibitor**	No	No	No	No	No	No	No
Log Kp (cm/s) skin permeaion	-8.68	-7.25	-1.94	-2.70	-10.12	-7.13	-7.36
Lipinski***	Yes	Yes	Yes	Yes	No	Yes	Yes
Lipinski violation	0	0	1	1	3	0	0
Bioavailability score***	0.55	0.55	0.55	0.55	0.17	0.55	0.55

Compounds	**8**	**9**	**10**	**11**	**12**	**13**	**14**
TPSA* (A2)	130.61	111.13	97.99	60.69	57.53	77.76	20.23
Consensus* Log Po/w	0.42	1.73	0.21	5.53	1.32	5.34	1.41
Mol wt (g $mol^{-1)}$	306.27	286.24	170.12	446.71	210.27	472.70	108.14
nRB	1	1	1	4	2	2	1
nOHA	7	6	5	3	3	4	1
nOHD	6	4	4	3	2	3	1
WLOGP	0.93	2.28	0.50	6.11	1.21	6.21	1.03
Water Solubility	soluble	Soluble	Soluble	Moderately soluble	Soluble	Moderately soluble	Soluble
GI absorption**	High	High	High	High	High	High	High
BBB permeation***	No	No	No	No	No	No	Yes
P-gp substrate**	No	No	No	No	No	Yes	No
CYP1A2 inhibitor**	No	Yes	No	No	No	No	Yes

CYP2C19 inhibitor**	No	No	No	No	No	No	No
CYP2C9 inhibitor**	No	No	No	No	No	No	No
CYP2D6 inhibitor**	No	Yes	No	No	No	No	No
CYP3A4 inhibitor**	No	Yes	Yes	No	No	No	No
Log Kp (cm/s) skin permeaion	-8.17	-6.25	-6.84	-4.20	-7.14	-4.34	-6.18
Lipinski***	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lipinski violation	1	0	0	1	0	1	0
Bioavailability score***	0.55	0.55	0.56	0.55	0.55	0.56	0.55

Compounds	**15**	**16**	**17**	**18**	**19**	**20**	**21**
TPSA* (A2)	58.52	111.13	111.13	111.13	37.30	138.18	111.13
Consensus* Log Po/w	3.70	1.73	1.73	1.83	5.09	0.84	1.73
Mol wt (g $mol^{-1)}$	328.40	286.24	286.24	286.24	278.43	290.18	286.24
nRB	3	1	1	1	13	1	1
nOHA	4	6	6	6	2	8	6
nOHD	2	4	4	4	1	3	4
WLOGP	4.08	2.28	2.28	2.28	5.66	1.01	2.28
Water Solubility	Moderately soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble
GI absorption**	High	High	High	High	High	High	High
BBB permeation***	Yes	No	No	No	Yes	No	No
P-gp substrate**	No	No	No	No	No	No	No
CYP1A2 inhibitor**	No	Yes	Yes	Yes	Yes	No	Yes
CYP2C19 inhibitor**	Yes	No	No	No	No	No	No
CYP2C9 inhibitor**	No	No	No	No	Yes	No	No
CYP2D6 inhibitor**	Yes	Yes	Yes	Yes	No	No	Yes
CYP3A4 inhibitor**	No	Yes	Yes	Yes	No	No	Yes
Log Kp (cm/s) skin permeaion	-5.12	-6.25	-6.25	-6.25	-3.41	-7.61	-6.25
Lipinski***	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lipinski violation	0	0	0	0	1	0	0
Bioavailability score***	0.55	0.55	0.55	0.55	0.85	0.56	0.55

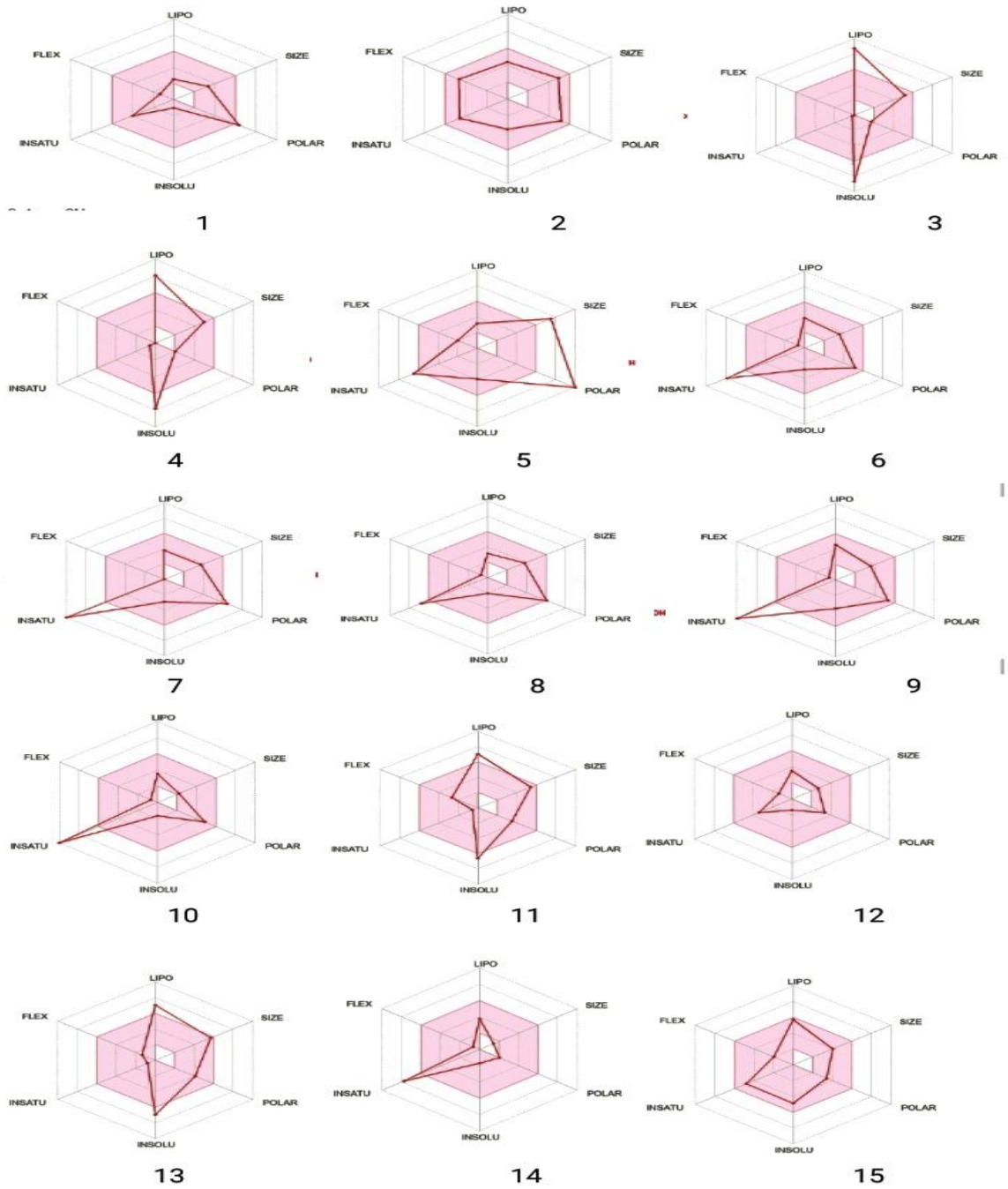
Compounds	**22**	**23**	**24**	***25***	**26**	**27**	**28**
TPSA* (A2)	100.13	108.34	86.99	111.13	34.14	138.18	58.92
Consensus* Log Po/w	1.49	2.16	0.57	1.83	1.47	0.84	3.63
Mol wt (g $mol^{-1)}$	274.23	344.27	184.15	286.24	152.19	290.18	354.44
nRB	1	3	2	1	0	1	2
nOHA	6	8	5	6	2	8	4
nOHD	3	1	3	4	0	3	2
WLOGP	2.07	2.22	0.59	2.28	1.52	1.01	3.92
Water Solubility	Soluble	Moderately	Soluble	Soluble	Soluble	Soluble	Moderatel

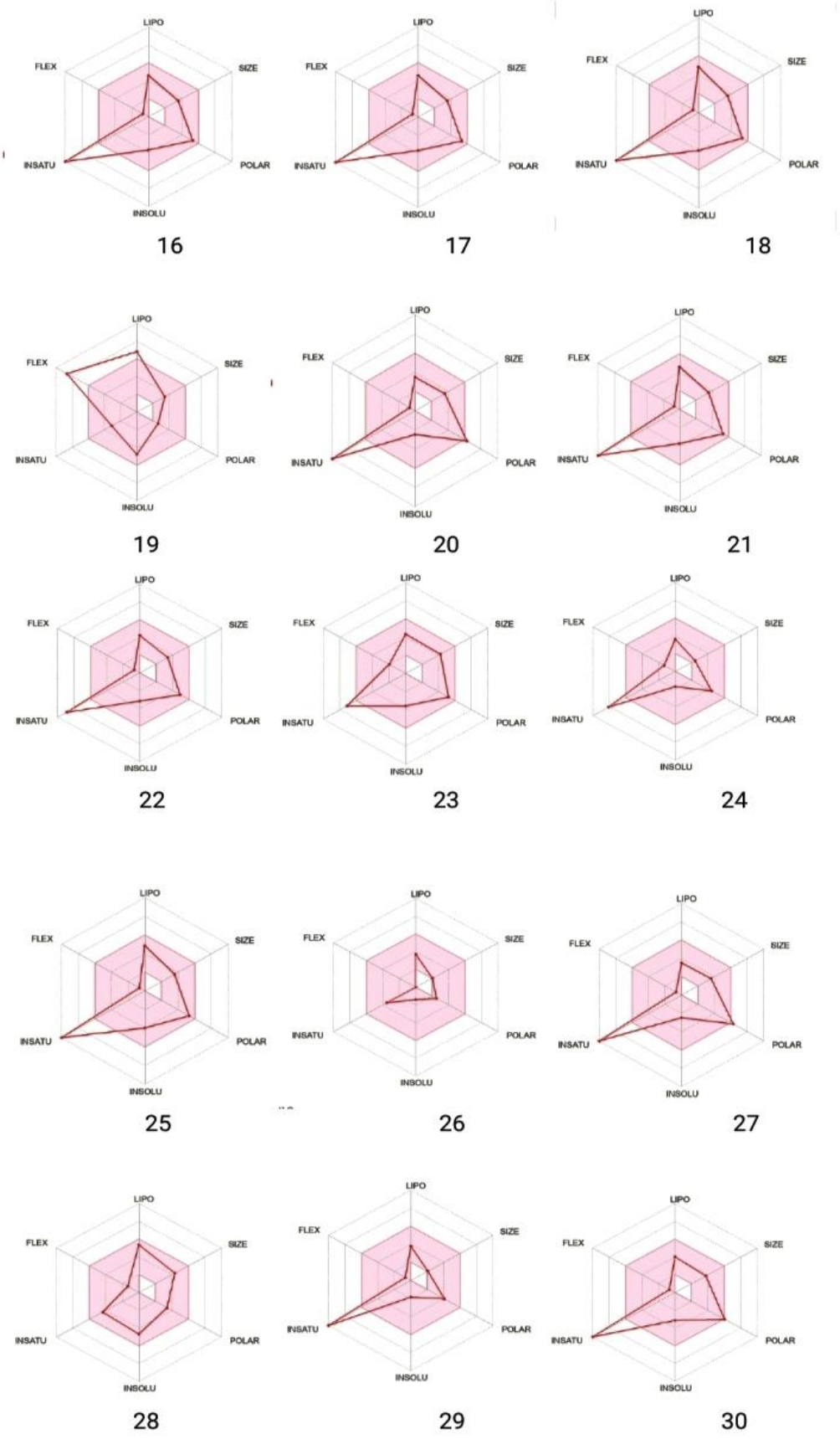
		soluble					y Soluble
GI absorption**	High	High	High	High	High	High	High
BBB permeation***	No	No	No	No	Yes	No	Yes
P-gp substrate**	No	No	No	No	No	No	yes
CYP1A2 inhibitor**	Yes	Yes	No	Yes	No	No	No
CYP2C19 inhibitor**	No	No	No	No	No	No	No
CYP2C9 inhibitor**	No	Yes	No	No	No	No	No
CYP2D6 inhibitor**	Yes	No	No	Yes	No	No	Yes
CYP3A4 inhibitor**	Yes	Yes	No	Yes	No	No	No
Log Kp (cm/s) skin permeaion	-6.65	-6.92	-6.81	-5.95	-6.52	-7.61	-5.72
Lipinski***	Yes	yes	Yes	Yes	Yes	Yes	Yes
Lipinski violation	0	0	0	0	0	0	0
Bioavailability score***	0.55	0.55	0.55	0.55	0.55	0.56	0.55

Compounds	**29**	**30**	**31**	***32***	**33**
TPSA* (A2)	77.76	131.36	127.45	111.13	20.23
Consensus* Log Po/w	0.65	1.23	0.63	1.73	6.75
Mol wt (g $mol^{-1)}$	154.12	302.24	304.25	286.24	412.69
nRB	1	1	1	1	0
nOHA	4	7	7	6	1
nOHD	3	5	5	4	1
WLOGP	0.80	1.99	0.86	2.28	7.63
Water Solubility	Soluble	Soluble	Soluble	Soluble	Poorly soluble
GI absorption**	High	High	High	High	Low
BBB permeation***	No	No	No	No	No
P-gp substrate**	No	No	No	No	No
CYP1A2 inhibitor**	No	Yes	No	Yes	No
CYP2C19 inhibitor**	No	No	No	No	No
CYP2C9 inhibitor**	No	No	No	No	No
CYP2D6 inhibitor**	No	Yes	No	Yes	No
CYP3A4 inhibitor**	Yes	Yes	No	Yes	No
Log Kp (cm/s) skin permeaion	-6.42	-7.05	-7.48	-6.25	-2.80
Lipinski***	Yes	Yes	Yes	Yes	Yes
Lipinski violation	0	0	0	0	1
Bioavailability score***	0.56	0.55	0.55	0.55	0.55

ADMET: Absorption, Distribution, Metabolism, Excretion and Toxicity, Lipophilicity*, Pharmacokinetics**, Drug likeness***, TSPA: Topological Polar surface area, nRB: no. of rotable bonds, nOHA: no. of H-bond acceptor, nOHD: no. of H-bond donor, WLOGP: water partition coefficient, GI absorption: gastrointestinal absorption, BBB: blood–brain barrier, P-gp: permeability glycoprotein, CYP: cytochrome P450, Entry 1:Adenosine, 2: Alagilinoside, 3: α-amyrin, 4: β-amyrin, 5: Corilagin, 6: Dimethoxy xanthone, 7: Ellagic acid, 8: Epigallocatechin, 9:Friedelin, 10: Gallic acid, 11:Ginsenoside, 12: Glycopyranosyl, 13: Hederagenin, 14: Icariside, 15: Isoguaicine, 16: Isoquercetine, 17:Kaempferol, 18:

Lawsoniaside, 19:Linolenic acid, 20: Lumnitzera lactone, 21: Luteolin, 22: Methoxy xanthone, 23: Methyl ellagic acis, 24: Methyl gallate, 25: Myricetin, 26: Oxisoprone, 27:Phellingridine, 28:Pinoresinol, 29: Protocatechuic acid, 30: Quercetine, 31:Quercetrine, 32: Zingerone, 33: β-sitosterol.




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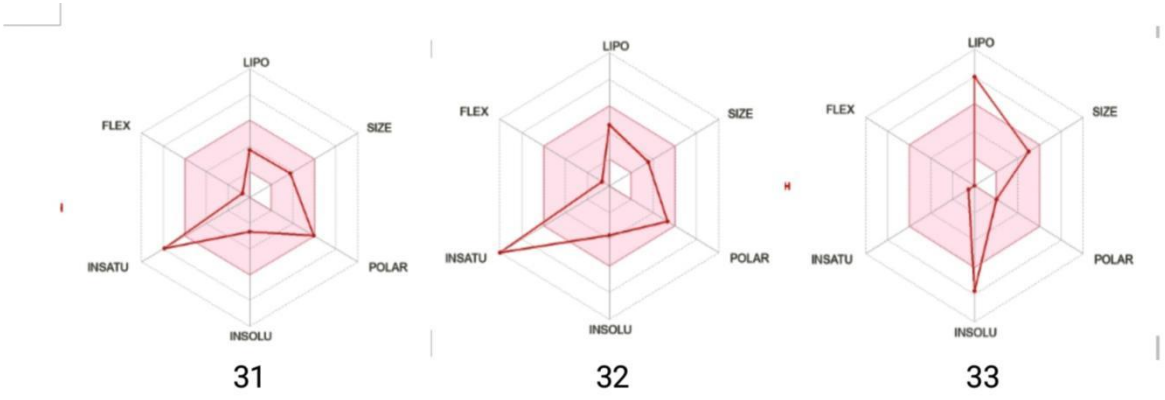


Fig 6: Bioavailability radar of the selected compouns from *L.racemosa* extract (Pink area represents the drug likeness properties of selected compounds) Entries 1-33 same like in Table 10.

Table 11: Toxicological Properties of selected compounds from *L.racemosa*

Compound	Hepatotoxicity		Carcinogenicity		Cytotoxicity		Immunotoxicity		Mutagenicity		Neurotoxicity		Cardiotoxicity		Predicted LD 50 (mg/kg)	Toxicity class
	Pr	Pb	Pr	Pb	Pr	Pb	Pr	Pb	Pr	Pb	Pr	Pb	Pr	Pb		
Adenosine	In	0.84	In	0.71	Ac	0.74	In	0.99	In	0.87	Ac	0.65	In	0.89	8	II
β-Sitosterol	In	0.87	In	0.60	In	0.94	Ac	0.99	In	0.98	Ac	0.54	In	0.85	890	IV
β-amyrin	In	0.75	In	0.60	In	0.96	Ac	0.96	In	0.96	Ac	0.57	In	0.86	667	IV
Castalagin	In	0.84	In	0.59	In	0.77	Ac	0.74	In	0.65	In	0.9	In	0.96	2170	V
Corilagin	In	0.85	In	0.72	In	0.62	Ac	0.72	In	0.56	In	0.89	In	0.81	2260	V
Ellagic acid	In	0.83	Ac	0.59	In	0.90	In	0.81	In	0.84	In	0.91	In	0.76	2991	IV
Epigallocatechin	In	0.72	In	0.51	In	0.84	In	0.92	In	0.55	In	0.90	In	0.99	10000	VI
Gallic acid	In	0.61	Ac	0.56	In	0.91	In	0.99	In	0.94	In	0.88	In	0.89	2000	IV
Ginsenoside	In	0.86	In	0.54	In	0.98	Ac	0.94	In	0.80	In	0.61	In	0.55	2260	V
Hederagenin	In	0.86	In	0.67	In	0.97	Ac	0.67	In	0.80	In	0.90	Ac	0.65	2000	IV
Icariside	In	0.95	In	0.91	In	0.74	In	0.65	In	0.84	In	0.92	Ac	0.78	4000	V
Isoquercetine	In	0.82	In	0.85	In	0.69	Ac	0.66	In	0.76	In	0.88	In	0.67	5000	V
Kaempferol	In	0.68	In	0.72	In	0.98	In	0.96	In	0.52	In	0.89	In	0.91	3919	V
Lawsoniaside	In	0.88	In	0.85	In	0.61	In	0.73	In	0.64	In	0.91	Ac	0.57	4000	V
Lumnitzeralactone	In	0.83	Ac	0.59	In	0.90	In	0.97	In	0.84	In	0.91	In	0.76	1000	IV
Methyl gallate	In	0.62	In	0.63	In	0.93	In	0.98	In	0.91	In	0.83	In	0.73	1700	IV
Myrecetin	In	0.69	Ac	0.68	In	0.99	In	0.86	Ac	0.51	In	0.89	In	0.99	159	III

Phellingridine	Ac	0.69	In	0.62	In	0.93	Ac	0.96	In	0.97	Ac	0.87	In	0.77	1190	IV
Pinoresinol	In	0.86	In	0.51	In	0.98	Ac	0.89	In	0.77	In	0.86	Ac	0.52	1500	IV
Procatechuic acid	In	0.59	Ac	0.72	In	0.90	In	0.99	In	0.97	In	0.86	In	0.90	2000	IV
Quercetine	In	0.69	Ac	0.68	In	0.99	In	0.86	Ac	0.51	In	0.89	In	0.99	159	III
Stigmasterol	In	0.87	In	0.60	In	0.94	Ac	0.99	In	0.98	Ac	0.54	In	0.85	890	IV
Tormentic acid	In	0.65	Ac	0.63	In	0.89	Ac	0.97	In	0.87	In	0.85	Ac	0.70	2000	IV
Gingerone	In	0.51	In	0.73	In	0.89	In	0.90	In	0.89	In	0.64	In	0.83	2580	V
Linolic acid	In	0.54	In	0.63	In	0.71	In	0.99	In	0.95	In	0.92	In	0.98	10000	VI

Conclusion:

All the findings in the present research meticulously characterized *L. racemosa* leaf through pharmacognostic parameters, GC-MS profiling, Molecular docking, ADMET studies. The highest extraction yield was obtained with Methanol. Various bioactive compounds including tannins, flavonoids, alkaloids, steroids, lignans, carotenoids, phytosterols and phenolic compounds were identified in the methanolic extract. These findings were combined with the acceptable physio chemical parameters of moisture, ash content and extractive values. Molecular docking studies suggested that the compounds present in *L. racemosa* extract could reduce the symptoms like sleep disturbances, Osteoporosis, anxiety, Depression and Bipolar disorders. These compounds also exhibited good binding affinity for estrogen α and β receptors as evident from their interactions with the relevant protein targets. The overall safety of the selected compounds was shown by ADMET studies. This gives the important information on the mangrove *L. racemosa*. Additional in vivo research is necessary to fully assess the safety and effectiveness of these active ingredients.

CRediT authorship:

Amala Masa: Writing- review & editing, Writing original draft, validation, Methodology, Investigation, formal analysis, Data curation. **Samriti Faujdar:** Writing-review & editing, Validation, Supervision, Project administration, Methodology, Formal analysis, Conceptualization. **Saraswati Patel:** Writing- original draft, Investigation, Formal analysis, Supervision.
Venkata Ramana Juvvala: Writing -original draft, Investigation, Formal analysis. **Nagasen Dasari:** Writing- original draft, Investigation, Formal analysis.

Acknowledgments

The authors acknowledge the Nanotechnology Research Centre (NRC), SRMIST for providing the research facilities for GC-MS analysis of the plant extract, Krishna University, Andhra Pradesh for providing infrastructure to complete research work.

Declaration of competing interest

Authors declare that they have no conflict of interest.

Funding

This research work did not receive any funding.

Data Availability

Not Applicable

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