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Review Article

A Review of the Botany, Phytochemistry and Pharmacology of Mangrove *Lumnitzera racemosa* Willd.

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ABSTRACT
Traditional system of medicines has heavily relied on plants and plant-based natural products. Phytomedicines have also been the backbone of the drug discovery programmes. Mangroves are unique salt-tolerant plant communities that withstand hostile environments and produce an array of bioactive natural products. *Lumnitzera racemosa* Willd. is a mangrove from the Combretaceae family and has a widespread geographical distribution along the shores of East Africa, Asia, Australia, and Polynesia. Traditional healers have been using parts and extracts of this small sized tree to manage a range of health ailments such as cutaneous disorders, diabetes, and asthma. The plant has been found to be phytochemically rich in tannins, flavonoids, terpenes, terpenoids, phenolic compounds, phytosterols and a number of novel metabolites which have exhibited noteworthy pharmacological activities. The present review aims to retrieve and stack up the information about the taxonomy, botany, phytoconstituents and pharmacological properties reported so far for *L. racemosa* from scientific books, journals, and databases. These findings can provide an authentic basis for the proposed use of this mangrove in standard and complementary medicine.
Key words: Mangroves, Antimicrobial, Anticancer, Phytomedicine, Antidiabetic.

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INTRODUCTION

Mangroves are salt-tolerant plants that grow and form unique, highly productive communities in the intertidal zones of 123 tropical and subtropical countries.[1,2] They offer immense ecological and economical benefits. They produce many novel metabolites to counter their hostile environment and are reported to have applications in folk-medicines to treat a number of diseases.[3]

Combretaceae is a plant-family that includes around 20 genera and 500 species. *Lumnitzera* Willd. is a genus from this family comprising of true mangrove species distributed along the shores of East Africa to Indo-West Pacific. The name of this genus has been derived from István (Stephan) Lumnitzer, a Hungarian botanist.[4,5]

This genus has two main species viz. *L. racemosa* (having white coloured flowers) and *L. littorea* (having red flowers). A third variety *L. rosea* showing intermediate and mixed characters (pink flowers) has been infrequently reported from Philippines, New Guinea, New Caledonia, and Australia, and being sterile, is not considered as a true species but a hybrid encountered in the overlapping regions of *L. racemosa* and *L. littorea*, represented as *L.* x *rosea*.[6-8]

L. racemosa is geographically more widely distributed species and has been used by traditional knowledge healers to address numerous medical complications.[3] Like other mangroves, the species has been found to contain novel compounds, many of which are pharmacologically important. An attempt has been made to compile up-to-date information about the phytochemical and pharamcological investigations on this mangrove to showcase its therapeutic potential since no such review could be found.

Taxonomical and Botanical description

L. racemosa is commonly known as white-flowered mangrove or black mangrove in English. Since the plant is distributed across three different continents, it has a number of region-specific local names as shown in Table 1.[9-24] Synonyms include *L. racemosa* var. *lutea* Gaud., *L. racemosa* var. *racemosa* Willd., *L. racemosa* var. *pubescens* Koord. and Vahl., and *Languncularia rosea* Gaud.[10]

L. racemosa (Figure 1) is a large shrub or a medium-sized, evergreen tree growing to a height of up to 8 m (average 4 m). Twigs are green, smooth but the bark is grayish-brown and roughly fissured. Distinct growth rings can be observed.[25] Leaves are simple, isobilateral, 4-6 cm long, light green, succulent, amphistomatic and show alternate arrangement. They are obovate-elliptic, spoon-shaped with a notch at tips. Mesophyll tissue shows only palisade layer.[26] This species is characterized by white coloured, tiny (2-3 cm long) actinomorphic, sessile and bisexual flowers. Petals are five in number.[27] The species name has been derived from the Latin word 'Racemosa' that

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means 'the one which has racemes' (stalked inflorescence arranged in clusters).[4]

Style is simple, glabrous and centrally placed inside the calyx cup that produces a lot of nectar which attracts day time active pollinating insects.[7] Flowering season varies from region to region. In the Indian sub-continent, flowering is observed from July to early November and fruiting from November to early January.[13,22,28] In Australia, highest flowering has been observed in December followed by the maturation of fruits in February-March whereas in S. Africa, it flowers from December-April and fruiting occurs from February-May.[4,29] Stamens and petals are of equal length. Fruits are small sized (about 1 cm long), ribbed, fibrous and present in clusters. Each fruit drupe is one seeded, falls off as a propagule and can float for an efficient dispersal by water currents. This species does not produce any pneumatophores but at times produces small buttress roots. It shows hypogeal type of germination.[5,7]

L. littorea varies from *L. racemosa* by having red coloured flowers, two times taller stamens than petals, terminal inflorescence, off-centrally positioned style, and a much taller height of up to 25 m.[4]

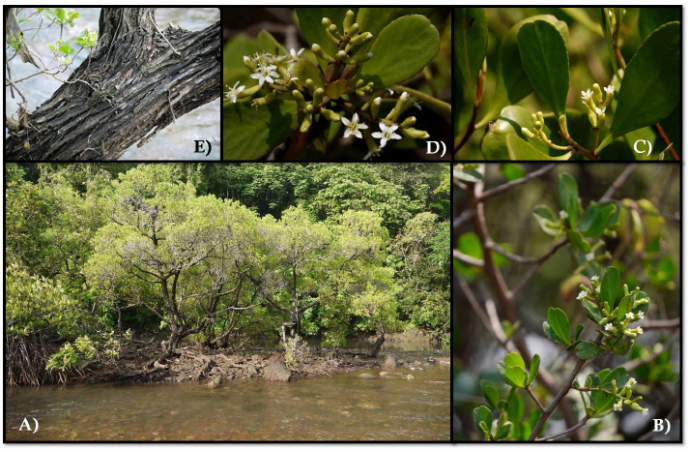

Figure 1: *Lumnitzera racemosa* Willd. A) Small-sized tree in its natural habitat forming communities; B) A flowering branch; C) Fleshy, spoon-shaped leaves with a notch; D) Small, white coloured flowers; E) Fissured, grayish-brown bark (Courtesy: Dinesh Valke)

Table 1: Taxonomical classification, local and vernacular names of *L. racemosa* [9-24]

Taxonomical classification	Country and states-specific local and vernacular names	
Kingdom: Plantae	**China:** *Lan li*	**S. Africa (Zulu):** *Isikhaha-esibomvu*
Subkingdom: Viridiplantae	**Thailand:** *Faad Khao, Fat, Fard dok khao*	**S. Africa (Afrikaans):** *Tonga-wortelboom*
Infrakingdom: Streptophyta	**Japan:** *Hirugimodoki*	**Kenya:** *Kikandaa, mkaa pwani, Mkanda-Mwitu*
Phylum (division): Tracheophyta	**Maldives:** *Burevi*	**Madagascar:** *Lovintso*
Subphylum (subdivision): Spermatophytina	**Indonesia:** *Api-api Balah, Duduk, Teruntum, Adu-adu*	**India** Andhra Pradesh state (Telugu): *Kadivi, Thanduga, Podapa*
Class: Magnoliopsida	**Sri Lanka:** *Bariya, Beriya*	**India** Maharashtra state (Marathi): *Kirpa*
Superorder: Rosanae	**Philippines:** *Kulasi, Solasi, Agnaya*	**India** Tamil Nadu state (Tamil): *Thipparathi, Kaandaa*
Order: Myrtales	**Vietnam:** *Krognyep sor, Krognyep-pkasor*	**India** Odisha state (Oriya): *Churunda, Tunda*
Family: Combretaceae	**Borneo:** *Api-api Jambu*	**India** West Bengal (Bengali): *Kripan*
Genus: Lumnitzera	**Singapore:** *Teruntum putih*	**India** Kerala (Malayalam): *Katakkantal*
Species: *L. racemosa* Willd.	**Cambodia :** *Cóc trâ'ng*	**English:** White-flowered mangrove, Black mangrove

Geographical Distribution

L. racemosa is seen widely distributed along the tropical and subtropical coastal countries of Eastern Africa, Asia, South China to Korea, and Southeast Asia to Northern Australia-Polynesia (Figure 2).[4,10,30,31] It is a native plant of Indo-Malay-West Pacific region and has a broader range than *L. littorea*, the latter being sparsely distributed only in the western hemisphere and is already endangered in countries such as China and Singapore.[32,33] *L. racemosa* has been categorized by IUCN as 'Least Concern' since its numbers are not declining as rapidly as that of *L. littorea*. However, the ever-increasing habitat destruction has been a major concern to the distribution of this mangrove. *L. racemosa* was brought into Florida, USA in 1960s, where owing to its prolific growth, it outnumbered native flora, became an invasive species and had to be eradicated.[34]

Habitat and ecology

L. racemosa is a landward or back mangrove species that prefers hard, muddy or sandy drier sediments with lesser salinities. It is found to be one of the most drought tolerant species, often found growing parallel to estuarine banks, slightly away from the main shore in the mid to high intertidal zones.[35,36] It frequently forms small sized community forests in association with other dominant mangrove species.[8,10]

Traditional ethnomedicinal importance

Owing to its widespread distribution, native people of various countries have been using this plant to treat health ailments since long. The fluid from old bark, juice of young twigs, and fruits of this plant have been mainly found useful in treating skin disorders, herpes, scabies, pruritus (itching), wounds, and thrush arising due to fungal infections in India, Sri Lanka, China, Malaya, Singapore, Thailand, Taiwan, Maldives, and Philippines.[3,11,13,24,37-39] Tribes of Odisha state, India have been using this plant to treat snakebite cases and also as blood purifier. Preparations from *L. racemosa* have been also used to treat sores, asthma, leprosy and as an antifertility agent to prevent pregnancy.[23,40] In China, the juice of

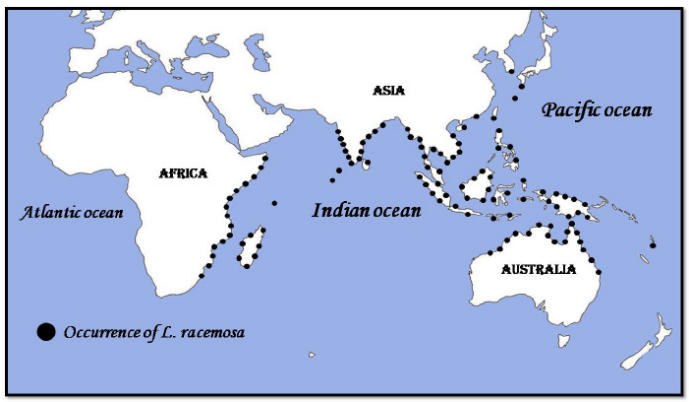

Figure 2: Geographical Distribution of *L. racemosa*.

trunk is used for treating aphtha (mouth or tongue ulcers) whereas the bark is used to control diabetes and for treating kidney stone.[41-43]

Other uses

Like other mangroves, the bark is preferred by the local inhabitants as a firewood, for producing charcoal and for tanning leather.[21,44] Wood is sturdy, long-lasting but being lesser in diameter than *L. littorea,* its use is restricted to small carpentry works such as making poles, house posts, paver blocks, fences.[10,45-47] African fishermen have been using its wood to make parts of boats (masts, paddles, oars, tie rod).[20,48] The leaves are edible and consumed by herbivores of Western Pacific islands in case of food scarcity. In Southern India and Sri Lanka, twigs and branches are used to build broom-like semi-captive type of fish traps called 'brush parks'.[49]

PHYTOCHEMICAL STUDIES

There are numerous studies reporting the phytochemical classes present in *L. racemosa*. Qualitative investigations indicate the presence of sugars, tannins, terpenoids, phenols, flavonoids, steroids, glycosides, alkaloids, essential oils, coumarins, anthraquinones, and saponins in the extracts of leaves, stems and bark. Methanol and water have been found to be the best solvents for extracting the metabolites of this plant, followed by ethanol and acetone.[50-55]

Concentrations of various macro- and micro-molecules, inorganic constituents, organic acids, amino acids have been already documented (Table 2).[56-68] Studying the concentrations of ions such as chlorides, sodium, potassium is crucial for mangroves like *L. racemosa* growing in a saline habitat. These abiotic stress-causing factors are known to be the inducers of novel metabolites in such plants and therefore need to be studied.

Numerous compounds belonging to phytochemical classes of tannins, terpenoids, phytosterol, low molecular weight carbohydrates, fatty alcohols, flavonoids and phenolic compounds have been isolated and structurally characterized (Figure 3). Many of these phytoconstituents are of pharmacological importance and their benefits have been well documented (Table 3). [69-80]

Triterpenoids that are usually found in *L. racemosa* include lupeol, lupenone, betulin, α & β- amyrins, and friedeline whereas stigmasterol, campesterol, and β-sitosterol are the frequently reported phytosterols. Flavonoids like quercetin and myricetin are commonly found in this mangrove and are well-documented for their antioxidant and other bioactivities. Polyphenolic compound like punicalagin, normally found in pomegranate, having a number of pharmaceutical as well as health benefits and a fatty alcohol namely triacontanol, a well known plant growth stimulator have been also reported from *L. racemosa*.[79,81,82]

This plant is known for having long chain rubber-like polyioprenoid alcohols.[83] Total polyisoprenoid content in the leaves and roots was found to be 6.7 and 0.8 mg/g dry weight (dw) respectively comprising of polyprenols (3.0 and 0.2 mg/g dw) and dolichols (3.7 and 0.6 mg/g dw) in leaves and roots which increase significantly with aging.[60]

Based on the habitat and age of the plant, tannin content in the bark varies from 15-19%. Balasooriya *et al*. report hydrolysable type of tannins in the bark at 8.6%.[84] Average gallotannin content in leaves is 0.683 mg/g dry weight whereas non-saponifiable lipid content per leaf tissue is 0.47 mg/g. It is noteworthy that these secondary metabolites are important in conferring resistance and defending the plant against predators and microbial pathogens.[82,85]

Analysis of floral scent has identified molecules which are terpenoids, benzoids, carotenoids or fatty acid-derivatives.[78] These novel molecules are important in attracting pollinating insects. Pollination also maintains genetic diversity in a population.

Table 2: Proximate elemental analysis of phytoconstituents in leaves of *L. racemosa* [56-68]

Element / Phytoconstituent	Concentration
Moisture	77.7-80.8%
Ash	15.67%
Fats	2.4%
Proteins	1.16%
Total Carbon	39.2 % dw
Total Nitrogen	0.66-0.78 % dm; 1.2-1.5 g / 100 g
Total lipids	120.0±12.1 mg/g dw
Polar lipids	9.7 ± 0.9%
Sterol	8.5 ± 1.6%
Triacylglycerols	11.8 ± 0.8%
Wax esters	5.8 ± 0.5%
Sterol esters	17.6 ± 0.9%
Total free amino acids	1.7 mol per m^3 pw
Proline	0.16-0.21 g/100 g fw
Alanine	0.18 mol per m^3 pw
Aspartate	0.34 mol per m^3 pw
Glutamate	0.16 mol per m^3 pw
Gamma amino-butyric acid (GABA)	0.36 mol per m^3 pw
Organic acids	(equ. per m^3 pw)
Oxalate	13.7
Malate	35.1 & 51.5 (Y & O)
Citrate	51.9 & 10.7 (Y & O)
Quinate	15.5 & 2.3 (Y & O)
Carbohydrates	
Reducing Sugars	1.1 g/100 g dw
Total sugars	2.77 g/100 g dw
Starch	5.85 g/100 g dw
(starch + sugars)	8.62 g/100 g dw
Fructose	7.2 & 6.1 mol per m^3 pw
Glucose	7.1 & 6.2 mol per m^3 pw
Sucrose	4.4 & 5.9 mol per m^3 pw
Hexose	101.1 & 91.4 mol per m^3 pw
Myo-inositol	1.0 & 0.4 mol per m^3 pw
Hexitols (Mannitol+ Sorbitol+Dulcitol)	110.0 mol per m^3 pw
Tannins	39.11 % (top leaves), 34.09 % (middle leaves), 8.83 % (bottom leaves)
Anthocyanins	0.049% (top leaves), 0.034% (middle leaves), 0.032% (bottom leaves)
Vitamin C	291.51 (top leaves), 284.10 (middle leaves) and 273.72 mg/100g (bottom leaves)
Alkaloids	0.071% (top leaves), 0.063% (middle leaves), 0.066% (bottom leaves)

Polyphenols	2.21 g /100g fw
Total phenolic content	30-39 mg gallic acid eq. / 100 g sample; 476. 37 µg/ml gallic acid eq.
Total flavonoids content	28-35 mg quercetin eq. / 100 g sample; 24.96 µg/ml gallic acid eq.
Sodium (Na)	2.8 ± 0.34 (g per 100 g dw) / 0.39 %
Potassium (K)	0.98 ± 0.07 (g / 100g dw) / 853.66 ppm
Calcium (Ca)	1.14 ± 0.04 (g / 100g dw) / 0.837 %
Magnesium (Mg)	1.43 ± 0.025 (g / 100g dw) / 1716.22 ppm
Chloride (Cl)	2.9 ± 0.2 g / 100g dw
Manganese (Mn)	221.44 ppm / 29.4 µg/g dw
Phosphorus (P)	1415.63 ppm
Calcium (Ca)	0.837 ppm
Cadmium (Cd)	0.05 ppm
Cobalt (Co)	0.08 ppm / 5.9 µg/g dw
Copper (Cu)	4.1 µg/g dw
Chromium (Cr)	0.03 ppm
Molybdenum (Mo)	29.4 µg/g dw
Iron (Fe)	77.87 ppm
Nickel (Ni)	0.71 ppm
Lead (Pb)	0.391 ppm
Zinc (Zn)	29.4 µg/g dw
Sulphur (S)	1091.72 ppm
Total Chlorophyll	70.68 mg /100 g fw
Chlorophyll a	32.16 mg /100 g fw
Chlorophyll b	38.52 mg /100 g fw

dw: dry weight, fw: fresh weight, ppm: parts per million, dm: dry matter, pw: plant water.

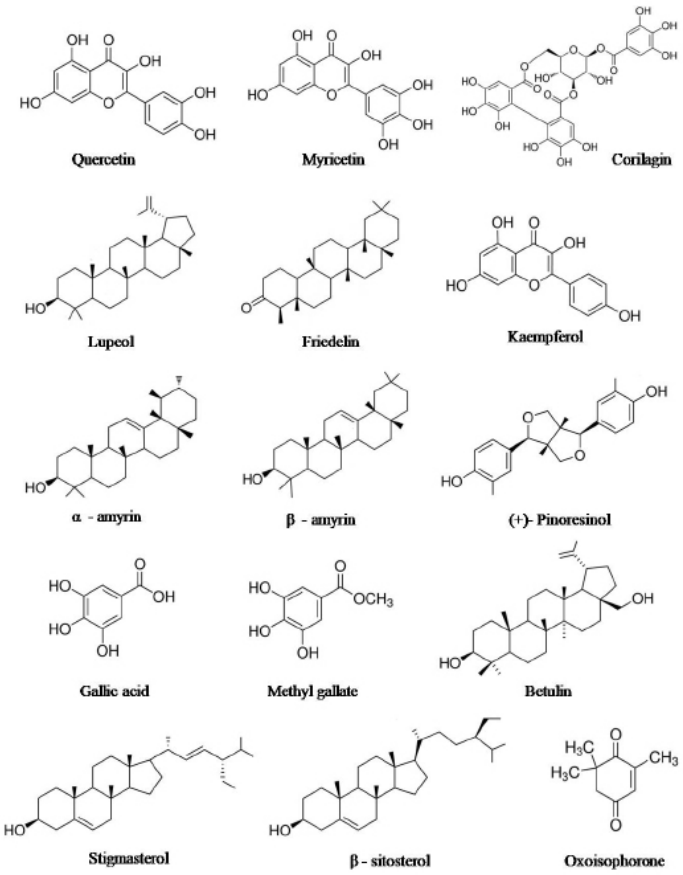

Figure 3: Compounds isolated from *L. racemosa*.

PHARMACOLOGICAL ACTIVITIES

Antibacterial and antifungal activity

There are various reports highlighting antimicrobial activities of leaves, twigs, and bark extracts of this plant. Overall results indicate that the plant has a significant antibacterial and slight antifungal activity (Table 4).

Leaf and twig methanol extracts and purified fractions inhibited the methicillin-resistant clinical isolate as well as multidrug-resistant *Staphylococcus aureus* strain suggesting the potential of *L. racemosa* in tackling antibiotic resistant infections.[76,86] Crude methanolic leaf and bark extracts showed promising inhibition and activity index against bacterial pathogens isolated from silkworm. Values were at par with the standard herbal control used.[87] Flavonoids (quercetin and myricetin) isolated from n-butanol fractions prepared from fresh twigs exhibited encouraging activity against the eight different pathogenic bacteria of clinical significance.[76] Moderate antibacterial activity against gram positive and negative bacteria was reported by crude ethanol leaf extract.[88] Tender and mature leaves extracts exhibited remarkable inhibition of the antibiotic resistant bacterial strains of *Staphylococcus aureus* and *Proteus* sp.[89] Acetone and methanol stem extracts showed promising activity against clinically important drug-resistant and drug-sensitive bacteria.[52] Aqueous leaf extract exhibited significant activity against the bacterium *E. coli* and fungus *Aspergillus niger*.[90] Methanol leaf extracts showed moderate to high inhibition of bacteria whereas fungi viz. *Rhizopus* and *Aspergillus niger* were slightly inhibited.[54] Recently, silver nanoparticles synthesized using the aqueous leaf extract were found to be inhibitory against the bacteria *S. aureus* and *E. coli* with zone of inhibition of 16 and 13 mm respectively.[55]

Antimalarial activity

Ravikumar *et al*. reported an IC_{50} of 110 µg/ml of *L. racemosa* leaf extract against the chloroquine-sensitive *Plasmodium falciparum* strain indicating its antimalarial potential. Even though this value was quite high compared to the control used; the active principle isolated from this crude extract could significantly enhance the bioactivity.[91] In a recent study, leaf chloroform and methanol extracts exhibited a strong inhibition of chloroquine-sensitive (MRC-2) and chloroquine-resistant (RKL-9) *Plasmodium falciparum* isolates with IC_{50} values ~2 µg/ml.[67]

Insecticidal activity

Reports indicate that this mangrove could present an eco-friendly approach to control vector borne diseases.

LC_{50} values of 1.2833 mg/ml and 1.1957 mg/ml were reported for stem and leaf methanol extracts respectively against the third instar larva of *Aedes aegypti*.[92] Crude acetone extracts prepared from fresh leaves also exhibited a strong mosquito larvicidal activity. The mortality of fourth instar larva of *Aedes aegypti* increased in a concentration dependent manner with LC_{50} of 8 ppm.[93]

Both the crude aqueous flower-bud extract and the synthesized zinc oxide nano-rods were screened for larvicidal activity against *Aedes aegypti*. Flower bud extract exhibited 100% mortality at 2500 µg/ml concentration with LC_{50} of 1333.75 µg/ml. Zinc nano-rods were significantly potent as they showed 100% mortality at a lower concentration of 50 µg/ml with LC_{50} of 24.74 µg/ml.[94]

Table 3: Novel compounds (phytoconstituents) isolated from *L. racemosa*

Sr. no.	Name of the compound and Class	Part, solvent used, and Place of work	Bioactivity	Ref.
1.	Furfural **(aldehyde)**, Benzyle chloride **(organochlorine)**, Hexa decanoic acid - methyl ester **(fatty acid derivative)**	Leaves Methanol extract (India)	Anticancer	[69]
2.	Lupeol and Betulin **(triterpenoids)**	Leaves Chloroform and methanol extracts (India)	Anti-malarial	[67]
3.	Total 8 compounds Racemolide **(macrolactone),** Loliolide **(benzofuran),** protocatechuic acid **(phenolic acid)**, methyl gallate **(galloyl ester),** (+)-lyoniresinol **(lignan),** Myricetin and Quercetin derivatives (**flavonoids**)	Leaves Methanol extract further fractionated (Japan)	Leishmanicidal, Hepatoprotective; Antioxidant	[70]
4.	Racelactone A (**neolignan**), Betulin (**triterpenoid**), 3,4,3'-Tri-O-methyl ellagic acid (**hydrolysable tannin**), methyl gallate (**phenol**), Stigmasterol (**phytosterol**), Myricitrin and Kaempferol (**flavonoids**), and Isoguaiacin (**lignan**)	Twigs and leaves Methanol extract (Taiwan)	Anti-angiogenic and Anti-inflammatory	[71]
5.	Total 10 compounds such as Kaempferol and derivatives of Quercetin and Myricetin (**flavonoids**), 3-O-methylellagic acid (**hydrolysable tannin**), Gallic acid (**phenolic acid**) and a novel glycoside	Leaves Methanol extract further fractionated (Vietnam)	α-glucosidase inhibitory (Antidiabetic)	[72]
6.	Total 8 compounds including one new cyclic compound (U-E-5-3-1) plus seven known compounds such as 3,4-dihydroxybenzoic acid, 3,4,5-trihydroxybenzoic acid methyl ester, Lyoniresinol **(lignan)**, Loliolide **(benzofuran),** Sophoretin, Quercetin-3-O-(2"-O-galloyl)-α-rhamnopyranoside and Myricetin 3-O-(2"-O-galloyl)-α-rhamnopyranoside **(flavonoids)**	Leaves Methanol extract further fractionated (Japan)	Hepatoprotective; Antioxidant	[73]
7.	Total 10 compounds such as Myrcetin 3-*O*-methyl glucuronate **(flavonoid glycoside),** Lumniracemoside **(phenolic glycoside),** *n*-hexanol *O*-rutinoside **(aliphatic alcohol glycoside),** Gallic acid **(phenolic acid),** Corilagin **(gallotannin),** Myricetin & Quercetin derivatives **(flavonoids)**	Leaves Methanol extract further fractionated into n-butanol fraction (Japan)	Hepatoprotective; Antioxidant	[74]
8.	Total 36 compounds such as Perforaphenonoside A **(benzophenone),** (+)-Pinoresinol , Polystachyol, and Alangilignoside C **(lignans),** Quercetine, quercitrin, and myricetin-3-arabinoside **(flavonoids),** Stigmasterol **(phytosterol),** Ginsenoside Re and Ginsenoside Rg1 **(steroid glycosides- triterpene saponins),** Methyl ester gallic acid **(phenol),** ipuranol **(phytosterol glucoside),** linolenic acid **(fatty acid),** tormentic acid, and 20(29) lupen-3-ol **(terpenoids),** Polygalatenoside E **(acid-esterified saccharides)**	leaves Methanol extract further fractionated (Vietnam)	Antioxidant, and Anticancer	[75]
9.	Quercetin and Myricetin (**flavonoids**)	Twigs Methanol extract fractionated into n-butanol fraction (India)	Anti-bacterial	[76]
10.	3-(4-hydroxyphenyl)-propyl-3[1] -(3, 4- dihydroxyphenyl)-propionate **(aromatic ester),** Friedelin, Betulin, and Betulinic acid **(triterpenoids)**	Stem Methylene chloride: methanol (1:1) (India)	Not studied	[77]
11.	*trans*-β-ocimene, 4,8-dimethyl-1,3(*E*),7-nonatriene, α-farnesene **(terpenoids),** oxoisophorone **(Carotenoids),** methyl salicylate **(Benzenoids),** 3(Z)-Hexenol and 3(Z)-Hexenyl acetate **(fatty acid derivatives)**	Scent of flower (Japan)	Not studied	[78]
12.	Punicalagin **(hydrolysable tannin)**	Leaves Aqueous Me_2CO (Taiwan)	Reversing the orthostatic hypotension *in vivo*	[79]
13.	Total 10 compounds such as Corilagin, Castalagin, Chebulagic acid, Chebulinic acid, Neochebulinic acid, Punicalagin **(hydrolysable tannins)** and few Glucopyranose derivatives	Leaves Aqueous Me_2CO extract (Taiwan)	Antihypertensive *in vivo*	[80]

Table 4: Antibacterial and antifungal activity of *L. racemosa*

Sr. No.	Type of compound / extract & concentration	Test organisms	Activity reported	Reference
1.	Aqueous and methanol extracts of leaves (500 µg/disc)	Methicillin resistant clinical isolates of *Staphylococcus aureus*	Moderate antibacterial	[86]
2.	Methanol extracts of leaves and bark (25 mg/disc)	Five bacterial (*Bacillus cereus*, *B. megaterium*, *Proteus vulgaris*, *S. aureus*, *Streptococcus lactis)* & two fungal pathogenic strains (*Aspergillus niger*, *Metarrhizum anisopliae*) isolated from infected silkworm larva	Moderate antibacterial; No antifungal	[87]
3.	Methanol extract of twigs, n-butanol fraction of crude extract, Compounds Quercetin and Myricetin (30, 50 and 500 µg/ml)	*E. coli, Klebsiella pneumoniae, P. mirabilis, Pseudomonas aeruginosa, S. typhi, Shigella flexineri, S. aureus, Vibrio cholera* (bacteria); *Aspergillus fumigatus, Mucor* sp., *Candida albicans* (Fungi); Hepatitis B virus (Virus)	Moderate to strong antibacterial; No antifungal; No antiviral	[76]
4.	Ethanol extracts of leaves (10 mg /100 µl)	*Alcaligens faecalis*, *B. cereus*, *Campylobacter coli*, *E. coli*, *Kl. pneumoniae*, *Pseud. aeuroginosa*, *P. vulgaris*, *Streptococcus mutans* & *S. aureus* (Pathogenic bacteria)	Moderate antibacterial activity against 3 out of 9 pathogens	[88]
5.	Aqueous and ethanol extracts of young leaves, mature leaves, shoot and bark (50 µl / well)	*Shigella* sp. & *Pseudomonas* sp. plus two antibiotic resistant strains of *S. aureus* and *Proteus* sp. (clinical isolates)	Moderate antibacterial	[89]
6.	Stem extracts prepared in eight different solvents (5 to 20 mg /ml)	*E. coli, Kl. pneumonia, B. cereus*, *B. subtilis* & *S. aureus*	Moderate antibacterial	[52]
7.	Dried powder of leaves dissolved in distilled water (1 mg /ml)	*E. coli* & *Aspergillus niger*	Antibacterial; Antifungal	[90]
8.	Methanol, acetone & hexane extracts of leaves (25 to 200 µg)	*Micrococcus luteus, S. aureus, Pseud. aeuriginosa, B. subtilis*, *Kl. pneumonia* (pathogenic bacteria); *Aspergillus niger, Rhizopus* sp.(pathogenic fungi)	Strong antibacterial; Weak antifungal	[54]
9.	Silver nanoparticles prepared from aqueous leaf extract (200 mg/ml)	*E. coli*, *S. aureus*, *B. subtilis* & *Kl. pneumoniae*	Moderate antibacterial	[55]

Anti-leishmanial activity

Racemolide isolated from leaves significantly inhibited cells of the parasite *Leishmania major* at 50 µM concentration. The percent values of inhibition for the isolated compound and positive control miltefosine were found to be of 67.6 and 93.3 respectively indicating leishmanicidal potential of *L. racemosa*.[70]

Antioxidant activity

There are clear evidences about the antioxidant properties of extracts and compounds from *L. racemosa* as depicted in Table 5.

Out of various solvents investigated, polar solvent such as methanol was found to be the best followed by water to extract antioxidants from this plant.[54,59,66] Leaf extracts exhibited higher antioxidant activity than stem extracts.[51,54,95] Seven out of 36 isolated compounds from the leaf methanolic extract, exhibited promising antioxidant power.[70] Darwish *et al*. have reported DPPH radical scavenging activity of isolated compounds from leaves which was at par or higher than the standard control trolox.[70,73-74]

Antidiabetic activity

There are scientific reports available supporting the use of *L. racemosa* by the traditional knowledge healers for treating diabetes.

Four different solvents were used to prepare extracts from the leaves and tested for antidiabetic potential by evaluating the percent inhibition of enzymes α-amylase and α-glucosidase. The extracts showed a concentration-dependant increase in the activity for both the assays. Methanol extract reported the highest inhibition of both the enzymes with a percent inhibition of 84.47 and 78.02 for α-amylase and α-glucosidase respectively which was close to the inhibition shown by standard antidiabetic drug acarbose.[53] Nguyen *et al*. prepared 4 different extracts by fractionating the crude leaf methanol extract and also isolated 10 different compounds. Promising antidiabetic potential in terms of α-glucosidase inhibitory activity of all the extracts as well as of the compounds was reported. IC_{50} was found to be better than the positive control acarbose. Compounds 2, 5, 6, 7 and 8 (flavonoids and phenolic acids) exhibited potent inhibition of the enzyme.[72] Crude methanol extract prepared using soxhlet was found to have mild anti-hyperglycemic activity in sucrose-loaded male albino wistar rats.[96]

Anti-angiogenic activity

Yu *et al*. reported suppression of capillary-tube formation in human circulating endothelial progenitor cells (EPCs) by compound racelactone A isolated from *L. racemosa* extract. With an increase in the concentration of the test compound, tube length was observed to be decreased. Lactic dehydrogenase levels in the treated cells also indicated

Table 5: *In vitro* Antioxidant activity of *L. racemosa*

Sr. No.	Part used & place of work	Extract / fraction / phytoconstituent tested and method	Concentration	Result / activity	Ref.
1.	Leaves (Tamil Nadu, India)	Crude aqueous extract DPPH and ABTS radical scavenging assays	20-100 µg/ml	IC_{50} extract 38.89 µg/ml, standard 21.71 µg/ml for DPPH assay; and IC50 extract 44.38 µg/ml, standard 19.93 µg/ml for ABTS assay	[66]
2.	Leaves and Stems (Maharashtra, India)	Crude aqueous methanol DPPH radical scavenging assay and Reducing power assay	25-500 µg/ml; 0-525 µg/ml	IC_{50}: extract- leaf 23.31 µg/ml, stem 111.5 µg/ml, standard 14.99 µg/ml for DPPH assay Maximum absorbance for reducing power assay at 525 µg/ml for the leaves was 1.67 and 0.793 for stem extracts; Standard ascorbic acid showed absorbance of 2.5 and 2.05.	[51]
3.	Leaves (Vietnam)	36 compounds isolated from methanolic extract Peroxyl radical scavenging assay and reducing power assay	1-10 µM	Compounds 4, 8, 11, 18, 20, and 22 showed Trolox equivalent (TE) values of 8.55, 8.96, 7.74, 8.60, 5.28, and 7.13 µM TE, respectively for Peroxyl scavenging assay. Compounds 8, 9, 18, and 20 to 23 exhibited promising reducing power, with 36.02, 34.09, 12.49, 10.73, 32.87, 17.23, and 52.12 µM of generated copper (I) ions	[75]
4.	Leaves (Japan)	Methanolic extract further fractionated into ethanol and butanol fractions to isolate 8 compounds DPPH radical scavenging assay	6.25, 12.5 & 25 µM	Compounds 2, 3, 4, 5, 6 and 8 showed IC_{50} of 14.74, 18.88, 5.93, 7.17, 7.38 and 15.72 µM, respectively IC_{50} standard trolox 5.93 µM Results indicate high antioxidant activity	[73]
5.	Leaves (Japan)	Methanolic extract further fractionated into ethanol and butanol fractions to isolate 10 compounds DPPH radical scavenging assay	6.25, 12.5 & 25 µM	Out of the 10 isolated compounds, 6 showed more than 50 percent inhibition of DPPH radical at 25 µM Compound 4, 6, 7 and 9 showed % inhibition of 93.4, 93.5, 94.4, and 91% respectively which was higher than the standard Trolox that showed 89.2% inhibition	[74]
6.	Leaves (Japan)	Methanolic extract further fractionated into ethanol and n-butanol fractions to isolate 8 compounds DPPH radical scavenging assay	25 µM	Compound and % inhibition of DPPH radical at 25 µM : Compound 4 - 91.1, No. 6 - 91.5, No. 7 - 91.9 and Compound 8 - 86.5 % Trolox (standard) - 89.2 %	[70]
7.	Leaves (Andhra Pradesh, India)	Crude methanol extract DPPH radical scavenging assay	50-200 µg/ml	Maximum scavenger activity 95.62% at 200 µg/ml. At the same concentration, standard ascorbic acid showed the activity of around 98% indicating strong antioxidant activity.	[54]
8.	Leaves (Terengganu, Malaysia)	Crude hexane, water and methanol extracts DPPH radical scavenging assay	100 µg/ml	Mean percent inhibition of DPPH radicals was 99.28% for water, 99.33% for methanol and 93% for hexane extracts. Standard ascorbic acid showed 99.5% inhibition.	[59]
9.	Leaves (Tamil Nadu, India)	Crude extract prepared in 95% ethanol-water mixture DPPH assay Hydroxyl radical scavenging (HRSA) Nitric oxide radical scavenging (NO) Lipid peroxide radical scavenging (LPO) Ferric reducing antioxidant power (FRAP) Superoxide radical scavenging (SOD)	1.9-500 µg/ml	IC50 values (µg/ml) for extract and for standard vitamin C DPPH assay: 56.37 and 2.87 HRSA: 57.68 and 44.24 NO assay: 64.14 and 4.98 LPO assay: 94.53 and 31.79 FRAP assay: 61.94 and 56.69 SOD assay: 69.70 and 24.31	[95]

non-toxicity of this compound in EPCs.[71] This report of anti-angiogenic activity implies the efficacy against combating late-stage tumors.

Anti-inflammatory activity

Racelactone A, methyl gallate, and myricitrin isolated from *L. racemosa* exhibited a potent inhibition of superoxide anion generation in the human neutrophils signifying strong anti-inflammatory activity.[71] This finding could play a crucial role against the onset as well as control of cancers.

Reversing the induced *in vivo* hypotension

Punicalagin isolated from leaves was intravenously administered into male wistar rats to check its possible effect in reversing the drug and mechanical tilt-induced orthostatic hypotension. A dose-dependent elevation of mean arterial blood pressure for 10 min followed by steady blood pressure readings clearly indicated the utility of this compound. Histological studies suggested that the compound affected the noradrenergic nerve terminals thereby releasing norepinephrine.[74]

Anti-hypertensive activity

Corilagin, chebulinic acid, and castalagin exhibited promising activity by lowering the systemic blood pressure in rats which had a spontaneously high blood pressure above 180 mmHg. Chebulinic acid was found to exhibit most promising anti-hypertensive activity in the study.[80]

Hepatoprotective activity

In vivo liver protecting effect of ethanol leaf extract of *L. racemosa* was reported. Male wistar albino rats were first administered with hepatotoxin and adverse changes in the serum parameters were recorded. This was followed by administration of the leaf extract at a dosage of 75, 150, and 300 mg/kg of body weight. Significant improvement in the serum parameters and liver function enzymes were observed post this treatment which was confirmed by histopathological studies that clearly showed a reduction in necrosis.[95]

Human liver hepatoma cells (HepG2) were incubated with the test compounds lyoniresinol and myricetrin isolated from *L. racemosa* leaves which were found to be highly hepatoprotective in action against the possible oxidative damage caused by the analgesic acetoaminophen. The results are of significance since the values were at par with the standard drug glycyrrhizin used as a positive control.[73-74] Racemolide isolated from leaves was also found to have moderate hepatoprotective activity.[70]

Sperm immobilization abiliity

Antifertility activity of *L. racemosa* mentioned in the traditional medicine was investigated. Leaf methanol extract was used for evaluating the time (15 to 240 sec) and concentration (0.15 to 50 µg) dependent sperm immobilization activity on human semen samples. Extract exhibited 90% inhibition of the sperm motility at 5 µg concentration and 100% inhibition at 10 µg and 50 µg concentration at 120 sec exposure. This activity was attributed to the disruption the plasma membrane of sperms suggesting that *L. racemosa* has a potential to be developed as an antifertility agent and could be consumed for birth control, as practiced in the folk-medicine.[97]

Anticancer activity

Soxhlet-prepared crude methanol leaf extract drastically reduced the cell viability and changed the cellular morphology in a concentration-dependent manner in MCF-7 (breast cancer) and HeLa (cervical cancer) cell lines.[69] IC_{50} of 26.05 and 195.1 µg/ml were reported for the aqueous and methanol leaf extracts against HepG2 (Human hepato-carcinoma) with a promising cytotoxicity and apoptosis inducing ability.[66,98] Villacorta *et al*. photoactivated the crude ethanol extract prepared using aerial parts and observed cytotoxic and apoptotic effect against MCF-7 with an IC_{50} of 11.63 µg/ml which was comparable with that shown by the standard drug doxorubicin (2.16 µg/ml).[99]

Methanol extract, methylene chloride and n-butanol fractions along with 36 isolated compounds were screened against HL-60 (human leukaemia cell line) and HEL-299 (human embryoid lung carcinoma). All the tested samples were found to be cytotoxic against either or both the cancerous cell lines. n-butanol fraction exhibited potent anticancer activity with IC_{50} of 1.27 and 3.94 µM for HL-60 and HEL-299 respectively. Compound 1 and 14 also exhibited strong cytotoxicity comparable to the drug mitoxantrone, used as a positive control.[75]

All these results imply that phytoconstituents of *L. racemosa* could play a crucial role against an array of cancers such as breast, cervical, leukaemia, lung and further screening against more cancerous cell lines is therefore suggested.

Anti-coagulant activity

Prolongation of clotting time post treatment with the aqueous leaf extract suggested a weak anticoagulant activity of *L. racemosa* crude extract.[66]

CONCLUSION

This review evidently indicates the pharmacological and therapeutic potential of *Lumnitzera racemosa*. An array of bioactivity exhibited has been attributed to the various phytoconstituents and secondary metabolites present. Purification of crude extracts to isolate bioactive principles is recommended. New drugs could be developed by coupling the active principles isolated from this mangrove with synthetic analogues. Studies in animal models are warranted to investigate the use of this plant in treating wounds and skin disorders as practiced by traditional knowledge healers. Toxicity studies should be performed to vindicate the safety of extracts or compounds from this plant before any therapeutic use.

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CONFLICT OF INTEREST

The author declares no conflict of interests.

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