

Ethnobotanical survey of genus *Leucas*

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ABSTRACT

Plants of genus *Leucas* (Lamiaceae) are widely distributed throughout Asia, Africa, and India. The plant is used in traditional medicine to cure many diseases such as cough, cold, diarrhea, and inflammatory skin disorder. A variety of phytoconstituents have been isolated from the *Leucas* species, which include lignans, flavonoids, coumarins, steroids, terpenes, fatty acids, and aliphatic long-chain compounds. Anti-inflammatory, analgesic, anti-diarrheal, antimicrobial, antioxidant, and insecticidal activities have been reported in the extracts of these plants and their phytoconstituents. An overview of the ethnobotanical, phytochemical, and pharmacological investigations on the *Leucas* species is presented in this review.

Key words: Bioactive constituents, ethno medical information, *Leucas*

INTRODUCTION

Plants are indispensable sources of medicine since time immemorial. Studies on natural products are aimed to determine medicinal values of plants by exploration of existing scientific knowledge, traditional uses, and discovery of potential chemotherapeutic agents. Phytochemicals are used as templates for lead optimization programs, which are intended to make safe and effective drugs.^[1] Plants of genus *Leucas* (Lamiaceae) have been widely employed by the traditional healers to cure many diseased conditions, which insinuated that this genus has immense potential for the discovery of new drugs or lead molecules. The genus *Leucas* comprises about 80 species.^[2] The highest species diversity has been found in East Africa.^[3] In India, 43 species are available.^[4] Plants of genus *Leucas* are generally shrubs, subshrubs, annual herbs, or perennial herbs with woody root and/or stem base. Leaves are opposite, entire, or with spiky lobes, oval shaped with tapered end, petiolated, or sometimes without intervening stalk. The axillary or terminal inflorescence is usually with indeterminate augmentation. Bracteoles are roughly

erect. The calyx shape varies within the genus (often tubular shape); sometimes calyx enlarges into fruits. Calyx comprises of five connate sepals (one upper, two lateral, and two lower) and 5–20 secondary lobes.

Whitish hairs are generally present on the outer surface of the upper lip of the corolla, although yellowish cream color or red hair can also be present in some species.^[5,3] The investigated parts of the *Leucas* species include roots, seeds, stem, leaves, and whole plants. The present review not only covers phytochemical progress made on the plants of genus *Leucas* over the past few decades but also incorporates their uses in different formulations and in the treatment of various diseases by the traditional healers across the globe.

Traditional use of selected species

The plants of genus *Leucas* have been used by the tribals in various parts of Asia, Africa, and India. Widely employed different species, their parts, and mode of application/administration in various diseases are presented as follows.

Ethnomedical information

Leucas aspera (Lamiaceae)

Hot water extract of *Leucas aspera* is used orally as stimulant, anthelmintic, laxative, and diaphoretic.^[1] It is also used orally for the treatment of headache, asthma, and bronchitis.^[6] Hot water extract of entire plant is also used to treat inflammation, dyspepsia, and jaundice.^[2] Entire plant extract is used orally to treat scabies, psoriasis, and snake bite.^[7] The plant *Leucas aspera* is externally used as an insect repellent.^[8] *Leucas aspera* and *Ocimum canum* are externally used to fumigate dwellings.^[7] A handful of flowers roasted in ghee are given orally (5–10 g once a day) for treatment of cough and colds.^[7] The flowers are crushed and

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aroma is inhaled in the opposite nostril for the relief of migraine.^[7] The juice of leaves is used aurally for ear pain^[9] and for pus discharge from ear.^[9] The paste of leaves ground with chalk is applied to tooth cavity (periodontal) to prevent decay.^[9] The decoction of leaves is used nasally as an antivenin.^[9] Infusion of leaves is used externally to treat scabies.^[10] Leaf paste mixed with turmeric is used to heal wounds and boils.^[11] The decoction of roots, stem, and inflorescence of *Leucas aspera*, stem of *Phylla nodiflora*, and roots of *Ocimum gratissimum* are used orally for high fevers,^[12] for influenza,^[13] and for malarial fevers.^[7]

Leucas cephalotes (Lamiaceae)

The decoction of dried aerial parts of plant (India) is used orally for diarrhea.^[7] The decoction of entire plant (India) is used orally to reduce fever.^[14] The H₂O extract of entire plant (India) is used orally as an appetizer.^[15] The flowers and leaves are applied externally as poultice to treat headache.^[16] The decoction of flower heads in Nepal is used orally to treat jaundice.^[17] The decoction of flowers in India is used orally as an emmenagogue.^[10] Hot water extract of dried flowers in India is used orally for coughs.^[18] Hot water extract of dried flowers in India is used orally for colds.^[19] The juice of unripe fruits (India) is used externally to treat scabies.^[20] The juice of leaves is used nasally as an antivenin.^[21] The juice of leaves is used externally as an antivenin.^[22] The dried leaves are used orally as a blood purifier.^[23]

Leucas indica (Lamiaceae)

The flowers are used orally to treat typhoid fever.^[24] The leaves are pounded with garlic, pepper, and leaves of *Piper longum* and made into pills and used orally to treat typhoid fever.^[25] Leaves along with tender shoots of *Momordica charantia*, pepper, garlic, and common salt are pounded, in equal quantities, made into pills, and taken orally once a day for 9 consecutive days to treat pneumonia.^[10] The leaves with those of *Alternanthera sessilis* in equal quantity are pounded with “ghee” and the extract is applied to eyes, and paste made into pills, which are taken for 40 days orally to treat night blindness.^[26]

Leucas lanata (Lamiaceae)

The plant juice is used orally for treatment of headache.^[27] The plant juice is used orally for treatment of stomach-ache.^[8] Leaves are made into a paste and applied externally for cuts and wounds.^[28] A poultice of leaves is placed on affected area to promote exudation of pus from boils.^[29] The juice is used orally as an antidote for reptile poison.^[30]

Leucas lavandulaefolia (Lamiaceae)

The decoction is used orally for treatment of diarrhea.^[15] The juice of plant mixed with *Rubia cordifolia* and *Nicotiana tabacum* is used externally as an antivenin.^[31] The infusion of plant is used orally to treat fever. The infusion of plant is used orally to treat headache.^[32] One handful of *Leucas linifolia* plants, 50 g *Brassica campestris* seeds, and one average *Curcuma longa* rhizome are ground into a paste, which is applied externally to the forehead daily at sunrise for 7 days to treat migraine.^[33] The infusion of plant is used orally for cough.^[34] The infusion of plant is used externally for skin diseases.

^[11] The infusion of plant is used externally for painful swellings.
^[35] The infusion of plant is used orally for inflammations.^[36] The infusion of plant is used externally for psoriasis.^[6] The infusion of plant is used externally for chronic skin eruptions.^[37]

Leucas martinicensis (Lamiaceae)

Hot water extract is used orally for gastroenteritis, cholera,^[38] malaria,^[39] syphilis,^[40] leprosy,^[41] diarrhea,^[42] and dysentery.^[43] The leaves are also used orally for pain during pregnancy.^[44] The infusion is used ophthalmically for proptosis,^[45] for conjunctivitis,^[44] and for corneal disease.^[46]

Leucas mollissima (Lamiaceae)

The leaf juice is applied externally (rubbed on forehead) in headache.^[43] The decoction is used orally to treat diabetes mellitus.^[31] The decoction is used orally to treat hepatitis.^[47] The hot water extract is used orally to treat liver diseases.^[48]

Leucas plukenetii (Lamiaceae)

The leaves are used orally for curing throat troubles.^[31] The twig is orally used as food.^[49]

Leucas stelligera (Lamiaceae)

The plant is used orally in females as an emmenagogue.^[50]

Leucas urticaefolia (Lamiaceae)

The decoction is used orally to expel placenta after delivery in cows.^[51] The decoction is used orally to expel placenta after delivery in buffalos.^[52]

Leucas zeylanica (Lamiaceae)

The plant is externally rubbed on abdomen after child birth in human pregnant.^[53]

COMMON COMPOUNDS REPORTED IN GENUS *LEUCAS*

Phenolic compounds

Plant phenolics are a structurally diverse set of compounds responsible for organoleptic properties of plants with a wide range of therapeutic activity. They occur in plants in the form of simple phenolic acids or as complex structures associated with the oxygenated heterocyclic ring, such as benzoic acid derivatives, stilbenes, tannins, lignans, anthocyanins, flavonoids, and coumarins.^[54] In plants of the genus *Leucas*, phenolics are found in abundance, Organic acids, namely, methoxybenzyl benzoate, 4-hydroxy benzoic acid, and urticic acid have been isolated from the chloroform fraction of methanolic extract of whole plant of *Leucas urticifolia*.^[54] Mishra *et al.* reported 4-(24 ϵ -hydroxy-1 ϵ oxo-5 ϵ -propyltetracosanyl) - phenol from the shoots of *Leucas aspera*.^[55] Sadhu *et al.* isolated eight lignans, namely, nectandrin B, (-)-chicanine, meso-dihydroguaiaretic acid, macelignan, myristargenol B, erythro-2-(4-allyl-2, 6- dimethoxyphenoxy)-1-(4-hydroxy-3-methoxy phenyl) propan-1-ol, machilin C, (7R, 8R)-, and (7S, 8S)-licarin from the methanol extract of the whole plant of

Leucas aspera.^[56] Flavonoids, another important class of phenolics featuring the linkage of two benzene rings by a chain of 3 carbon atoms so as to form pyran or pyrone ring, play a predominant role in plant physiology and serve as light screens, antioxidants, enzyme inhibitors, precursors of toxic substances, and pigments.^[56,57] In the genus *Leucas*, many reports reveal the occurrence of flavonoids in the conjugated form (that is with sugar). However, free flavonoid baicalein was reported in the ethereal fraction of hydro-methanolic extract of *Leucas aspera* flower^[58] and a flavone – cirsimaritin were reported in *Leucas mollissima* Wall. var. *Chinensis* Benth.^[59] Sadhu et al. reported acacetin, chrysoeriol, and apigenin from the *Leucas aspera*.^[60] 5-hydroxy-7, 4 ϵ - dimethoxyflavone, pillion, gonzalitosin I, and triclin were reported from *Leucas cephalotes*.^[60] Coumarins, another class of plant phenolics, comprised phenylpropanoid system, are found to be physiologically effective for animals as well as humans.^[61] Natural coumarins such as coumestrol, 8-ethoxycoumestrol, siderin and a novel compound coumarleucasin are isolated from acetone extract of *Leucas inflata* roots.^[62]

Steroids

Sterols structurally comprise of perhydrocyclopenta- (O) phenanthrene ring system, which are widely distributed in higher plants.^[54] Presence of ubiquitous phytosterol such as β -sitosterol, stigmasterol, campesterol, ursolic acid, and their derivatives have been reported in plants of genus *Leucas*.^[62-66] A novel steroid “leucosterol” was reported from the methanol extract of whole plant of *Leucas urticifolia*,^[54] which is similar to stigmasterol, the difference lying in the side chain that is presence of a hydroxyl group at C-20 atom, a double bond at C-22 atom, and S configuration at C-24 atom.

Terpenes

Terpenes constitute one of the largest and structurally diverse class of plant secondary metabolites responsible for flavor, fragrance, and bioactivity of the plants.^[67] Plants of genus *Leucas* are found to be rich in terpenes. Chemical structures of some of these terpenes are presented, Vagionas et al. reported the presence of monoterpenes in the essential oil obtained from *Leucas glabrata* by GCMS analysis. It revealed the presence of menthone, pulegone, piperitone, piperitenone, α -thujene, myrcene, α -phellandral, γ -terpinene, terpinen-4-ol, nerolidol, carvone, carvacrol, caryophyllene, cumyl alcohol, α -farnesene, menthol, and E-nerolidol in the oil.^[68] However, the essential oil fraction from the leaves and flowers of *Leucas aspera* were found to contain high amount of α -farnesene, α -thujene, and menthol;^[69,70] whereas, high content of β -cubebene, α -pinene, trans-caryophyllene, limonene, and α -terpineolene were reported in the essential oil from *Leucas milaniana*.^[71] The essential oil fraction of *Leucas deflexa* leaf was reported to have a high amount of sesquiterpene hydrocarbons, namely, germacrene-D, β -caryophyllene, and α -humulene.^[72] A new type of diterpenes, leucasperones A and B; leucasperols A and B, have been reported from *Leucas aspera*.^[66] Miyaichi et al. reported new diterpenes Leucadins A, B, and C, two protostane-type triterpenes named Leucastriins A and B, and oleanolic acid from the methanol extract of whole plant of *Leucas cephalotes* Spreng.^[60]

Glycoside

Two new flavonoidal glucosides leufofin A and B were reported from the ethyl acetate fraction of methanolic extract of whole plant *Leucas urticifolia*.^[73] A novel phenylethanoid glycoside, 3-O-methyl poliumoside and angoroside C, 2-(3-hydroxy-4-methoxyphenyl)- ethyl-O- α -L-rhamnopyranosyl-(1 \rightarrow 3)-O- α -L-rhamnorhamnopyranosyl-(1 \rightarrow 6)-4-O-E-feruloyl-b-D-glucopyranoside, incanoside D, martynoside, and acteoside were reported in the methanolic extract of the whole plant of *Leucas indica*.^[74] A flavonoidal glycoside, baicalin, reported from the fresh flower of *Leucas aspera*.^[58] Further, the isopimarane-type diterpenoidal glycosides leucasperosides A, B, C and linifolioside reported in *Leucas aspera* and *Leucas linifolia*.^[75,66] Flavonoidal glycoside apigenin 7-O-(6 ϵ -O-(p - coumaroyl) - b-D-glucoside) has been isolated from the *Leucas aspera*,^[36] while cosmosin, anisofolin A, and luteolin 4 ϵ -O-b-D-glucuronopyranoside were reported from *Leucas cephalote*.^[60] Chandrasekhar et al. reported the isolation of chrysoeriol-6 ϵ -O-(Ac)-4 ϵ -b-glucoside from ethanolic extract of the aerial parts of *Leucas lavandulaefolia* Rees.^[76]

Fatty acids

Leucas cephalotes and *Leucas urticaefolia* seeds were found to have a high content (28% w/w) of laballanic acid.^[77,78] Varying concentrations of oleic acid (87) and linoleic acid (88) were found in *Leucas aspera*, which was contingent upon crop variation.^[79,75]

Miscellaneous

Leucas aspera is widely used in countryside as foods and also for nutritional requirement. It is reported to have high content (21.3%) of protein.^[79,80] Structures of some glycosides isolated from *Leucas* species. Significant amounts of total carotenoid and β -carotene.^[81] Asperphenamate and alkaloid nicotine have also been reported in *Leucas aspera*.^[70] Long-chain compounds nonatriacontane,^[55] 1-dotriacontanol, 1-hydroxytetraatriacontan-4-one, 32-methyltetraatriacontane were reported in *Leucas aspera*.^[82] Aliphatic ketols, namely, 28-hydroxypentatriacontan-7-one, 7-hydroxy-dotriacontan-2-one, 5-acetoxy-triacontane were isolated from the shoots of *Leucas aspera*.^[83] n-Hentriacontane, 1-dotriacontanol, phytol, and a new diterpene fatty acid ester known as trans-phytyl palmitate were reported from *Leucas nutans*.^[84] Amyl propionate and isoamylpropionate were present in high concentration in the essential oil fraction of the leaf and flower parts of *Leucas aspera*.^[85] Accumulation of heavy metals reported in plants adversely affect the quality, safety, and their medicinal value. Higher concentration of zinc (201 μ g/g), iron (809 μ g/g), and strontium (133 μ g/g), have been reported from *Leucas linifolia* grown in the North Eastern region of India.^[86,87]

PHARMACOLOGICAL ACTIVITY

Anti-inflammatory activity

The whole plant extract of *Leucas aspera* was reported to have anti-inflammatory activity and caused degranulation of mast cells.^[88] Significant anti-inflammatory activity of the yellow-

colored chromatographic fraction of *Leucas aspera* extract was observed in the chronic and acute models of inflammation. It was observed that the activity was due to the inhibition of histamine and serotonin.^[89] Srinivas *et al.* showed that a dose of 50 mg/kg of *Leucas aspera* dried leaf powder in 2% gum acacia showed significant anti-inflammatory activity, which was found to be better than acetylsalicylic acid in the carrageenin-induced paw edema model and less active than phenylbutazone, when tested in cotton pellet-induced granuloma in rat model.^[90] Goudgaon *et al.* reported that the anti-inflammatory activity of *Leucas aspera* is mainly due to its alkaloidal component, and the tannins present have no role.^[91] Sadhu *et al.* reported that methanol extract of the whole plant at 3×10^{-5} g/mL concentration possesses inhibitory activity against both PGE1- and PGE2-induced contractions in guinea pig ileum, and the isolated compound (3-O-b-D-glucosyl (1 β 2)-b-D-glucoside) was found to be mainly responsible for this activity.^[36,66] Manivannana and Sukumar reported that the bioactive constituents (baicalein and baicalin) of *Leucas aspera* flowers exhibited significant RBC membrane stabilizing activity.^[92] The acetone extract of the roots of this plant was found to possess anti-inflammatory activity in the preliminary studies.^[62] Extract of *Leucas mollissima* Wall also exhibited potent anti-inflammatory activity, which was mainly due to its bioactive constituent, apigenin-7-O-b-D- (6 $\epsilon\epsilon$ -p-coumaroyl) glucoside.^[59]

CENTRAL NERVOUS SYSTEM ACTIVITY

Methanol and acetone extracts of *Leucas inflata* possess dose-dependent antinociceptive activity, which may be mediated by their central and peripheral actions.^[48] In a similar study, ethanolic extract of *Leucas aspera* root showed significant peripheral antinociceptive activity at a dose of 400 mg/kg.^[40] Mukherjee *et al.* reported a yellow-colored fraction from the methanol extract of *Leucas lavandulaefolia*, which exhibited dose-related effects on general and exploratory behavior and muscle relaxant activity in rats and mice.^[50]

COUGH, COLD, AND ANTI-DIARRHEAL ACTIVITIES

Saha *et al.* reported that the semisolid mass from the yellow-colored band obtained from methanol extract of *Leucas lavandulaefolia* showed significant dose-dependant anti-tussive activity. This effect was comparable to codeine phosphate and suggested that this activity was mediated by the CNS.^[93] Mukherjee *et al.* reported that the ethanol extract of aerial part of *Leucas lavandulaefolia* significantly reduced the incidence and severity of diarrhea in the castor oil-induced diarrhea in rats.^[51]

ANTI-DIABETIC ACTIVITY

The methanol extracts of whole plant of *Leucas lavandulaefolia* possess a dose-related strong hypoglycemic activity and have similar potency to that of glibenclamide at an oral dose of 400 mg/kg.^[94]

ANTIMICROBIAL ACTIVITY

Menthone, pulegone, and piperitone-rich essential oil of *Leucas glabrata* possessed significant antimicrobial activity against selected gram positive and negative bacteria and fungi strains at a concentration of 0.45 to 1.14 mg/mL (MIC).^[68] Significant antimicrobial activity was reported for the alkaloidal fraction and the total methanol extracts the *Leucas aspera* flowers.^[95] The methanol extract of *Leucas zeylanica* and 80% ethanolic extract of *Leucas aspera* leaves were found to exhibit potent inhibitory activity against *Staphylococcus aureus* and *Bacillus subtilis*.^[96,39] Interestingly, the volatile oil obtained from the leaves of this plant exhibited high sensitivity for *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *S. aureus*, and *Candida albicans* but practically no sensitivity against *Bacillus subtilis*, *Proteus vulgaris*, *Neisseria gonorrhoea*, *Tricoderma vibriae*, and *A. niger*.^[69]

ANTIOXIDANT ACTIVITY

Methanol extract of the whole plant of *Leucas mollissima* showed insignificant free radical and superoxide anion scavenging activity.^[97] However, significant activity was found in the ethanolic extract of *Leucas aspera* root (IC₅₀ = 7.5 μ g/ml).^[40]

HEPATO-PROTECTIVE ACTIVITY

The chloroform extract of *Leucas lavandulaefolia* whole plant, obtained after defatting with petroleum ether, was found to have hepato-protective activity in D (+) galactosamine-intoxicated rat mode.^[98] The cold methanolic extract of the whole plant of *Leucas aspera* was found to exhibit significant hepato-protection in CCl₄ induced liver damage.^[99]

CYTOTOXICITY

Various studies using Brine shrimp lethality assay model showed that the hydroalcoholic extract of *Leucas aspera* whole plant exhibited cytotoxicity (LC₅₀ = 1900 μ g/mL)^[100] and this activity was more in the root extract (LC₅₀ = 52.8 μ g/mL).^[40]

INSECTICIDAL AND REPELLANT ACTIVITY

Leucas aspera leaves are used as mosquito repellent and as insecticide.^[101] These claims were vindicated by extensive studies, which indicated that *Leucas aspera* leaf extract exhibited significant larvicidal activity against first, second, third, and fourth instar larvae of *Culex quinquefasciatus*.^[102] *Leucas aspera* leaf extract (4% solution) showed 90% death of the fourth instar larvae^[103] and 100% death after 24 h were recorded for the third instar larvae of *Anopheles stephensi*.^[104] The petroleum ether extract of the leaves of *Leucas aspera* exhibited LC₅₀ between 100 to 200 ppm against the fourth instar larvae of *C. quinquefasciatus*, *A. stephensi*, and *Aedes aegypti*.^[105] *A. stephensi* larval treatment with *Leucas aspera*

leaf extract resulted in significant fall of its carbohydrate and DNA profile.^[104] Further, the highest mortality was seen during the moulting, melanization, and tanning processes, which are controlled by hormones.^[106] Hence, the above findings suggest that the larvicidal activity of the plant may be due to disturbance in hormonal and metabolic process of larvae. The seed oil obtained from *Leucas cephalotes* and *Leucas urticifolia* failed to show repellent/anti-feedant activity against adult *Tribolium castaneum* Herbst insect.^[107]

MISCELLANEOUS ACTIVITY

Mukherjee *et al.* reported that yellow-colored chromatographic fraction of the methanol extract of *Leucas lavandulaefolia* showed effects on general behavior pattern of experimental mice and also exhibited tranquilizing effect.^[50] Saha *et al.* reported wound healing activity of methanol extract of *Leucas lavandulaefolia* in the excision and the incision wound models in rats.^[24] They also observed significant contracting ability, wound closure time, tensile strength, and regeneration of tissues at the wound sites.^[24] In another study, the protective role of *Leucas aspera* against the snake (cobra) venom poisoning was studied in mice. This study revealed that *Leucas aspera* alcoholic extract treatment significantly improved the survival time, which may be due to the stabilization of mast cells and inhibition of the secretion of platelet activating factor and histamine.^[38]

CONCLUSION

The following manifestations can be made on the basis of this comprehensive perusal of literature of the plants belonging to genus *Leucas* being used traditionally due to their immense therapeutic potential to treat/cure various diseases. Phenolics and triterpenes are present in plants and exhibit significant biological activity. Many studies demonstrated significant anti-inflammatory activity of the extracts and some isolated constituents obtained from the plants of this genus. This vindicated the use of certain species in the chronic and acute inflammatory diseases including psoriasis, dermatitis, and other skin disorders. A variety of phytoconstituents have been isolated from the different species of the genus *Leucas*. However, only a few species have been explored exhaustively for their chemical constituents and pharmacological activities. Thus, there remains a tremendous scope for further scientific exploration of this genus to establish their therapeutic efficacy and commercial exploitation.

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