International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 25-11-2024, Accepted: 26-12-2024, Published: 10-01-2025
Volume 10, Issue 1, 2025, Page No. 12-16

Leucas aspera: An integrative review of its pharmacological potency and pharmacognostical insights

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Abstract
Leucas aspera is a plant species belongs to the genus Leucas and the family Lamiaceae. Species has different common names depending its location and most commonly known as Tumbai or Thumba, is distributed throughout India from the Himalayas down to Ceylon. It is known for its various uses in the fields of medicine and agriculture. This article aims to provide a comprehensive review on the pharmacognostic, phytochemical, and pharmacological aspects of *Leucas aspera*. Traditionally different parts of the plants are used as an antipyretic, insecticide, stimulant, emmenagogue, expectorant, aperient and diaphoretic. Leaves are found to be useful in chronic rheumatism, chronic skin eruptions specially in psoriasis. In case of snake bite, bruised leaves are applied locally. The plant mainly contains triterpenoids, oleanolic acid, b-sitosterol, diterpenes, ursolic acid, nicotine, sterols, glucoside and phenolic compounds. The plant, flower extract and essential oil shows various activities like antioxidant, anti-microbial, anti-fungal and antinociceptive etc.

Keywords: *Leucas aspera*, phamacognostic, pharmacological, antioxidant, emmenagogue

Introduction

Human beings have used plants as medicine for diverse health issues for thousands of years [1]. Plants are widely used in traditional medicine of different countries and are a source of many potent and powerful drugs [2]. The newly discovered and the existing medicinal plants are being screened for many diseases to identify the significant therapeutic importance. Several medicinal plants have been investigated against mitigation and cure of a variety of devastating diseases such as cancer [3].

In the last few decades, studying medicinal plants and their value in different countries was increasing. The increased interest was due their potent pharmacological benefits, low cost and no toxicity.[4] Nowadays, the term Alternative medicines were more common, based on the idea of use of plants for medicinal purposes [5]. According to WHO, medicinal plants were good source of variety of drugs and almost 80% of people from developing countries use medicinal plants in traditional medicine [6].

Leucas aspera (Willd.) Linn. (Family: Lamiaceae) commonly known as 'Thumbai' [7] is distributed throughout India from the Himalayas down to Ceylon [8]. The plant is used traditionally as an antipyretic and insecticide. Flowers are valued as stimulant, expectorant, aperient, diaphoretic, insecticide and emmenagogue. Leaves are considered useful in chronic rheumatism, psoriasis and other chronic skin eruptions. Bruised leaves are applied locally in snake bites [9].

In India, herbs are always acted as the major source of medicine in Siddha, Ayurveda, Unani, Kabiraji, and Homeopathy treatment system. The plant parts are used traditionally as an anti-pyretic and insecticidal agent, and the flowers are valued as a stimulant, expectorant, and diaphoretic. The leaves of the plants are also useful in chronic rheumatism, psoriasis, and other chronic skin eruptions. It is an aromatic, erect herb widely distributed in tropical Asia, Africa, and grows as a weed in highland crop yields, human settled areas, grasslands, and roadsides [10]. Many phytochemicals that are present in the plant parts belong to the classes of terpenoids, steroids, glycosides, long-chain compounds, favonoids, lignin's, and alkaloids. These varieties of phytochemicals were identified and isolated by different extraction methods.

Vernacular Names [7]:

Table 1: Vernacular names of Leuca aspera

Sanskrit	Dronapushpi, Chitrapathrika, Chitrak-shupa
Punjabi	Guldora
Bengali	Darunaphula, Hulkasha
Gujarati	Kulnnphul
Hindi	Goma madhupati
Sindhi	Kubo
Maharashtra	Bahuphul
Bombay	Tumba
Telugu	Tunni

Taxonomical names [11]:

Table 2: Taxonomical classification

Kingdom	Plantae, plant
Subkingdom	Tracheobionta, vascular plant
Super division	Spermatophyta, seed plant
Division	Angiosperma
Class	Dicotyledonae
Sub-class	Gamopetalae
Series	Bicarpellatae
Order	Tubiflorae
Family	Labiatae or lamiaceae
Genus	Leucas
Species	L. aspera

Classical categorization [12-20]:

Table 3: *L. aspera* Categorization

Bhavaprakasha nighantu	Guduchyadi Varga, Shaka varga
Kaiyadeva nighantu	Osadhi varga
Raja nighantu	Parpatadi varga
Priya nighntu	Shatapushpadi varga
Madanapala nighantu	Abhayadi varga
Nighantu Adrasha	Tulasyadi varga
Shaligrama nighantu	Guduchyadi Varga
Madhava Dravyaguna	Vividaushadi varga

Botanical Description:

Leucas aspera is an annual, branched, herb erecting to a height of 15-60 cm with stout and hispid acutely quadrangular stem and branches. Leaves are sub-sessile or shortly petiolate, linear or linearly lanceolate, obtuse, pubescent up to 8.0 cm long and 1.25 cm broad, with entire or crenate margin; petiole 2.5-6 mm long; flowers white, sessile small, in dense terminal or axillary whorls; bracts 6 mm long, linear, acute, bristle-tipped, ciliate with long slender hairs; calyx variable, tubular, 8-13 mm long; tube curved, contracted above the nutlets, the lower half usually glabrous and membranous, the upper half ribbed and hispid; mouth small, very oblique, not villous, the upper part produced forward; teeth small, triangular, bristle-tipped, ciliate, the upper tooth being the largest. Corolla 1 cm long; tube 5 mm long and pubescent above, annulate in the middle; upper lip 3 mm long, densely white-woolly; lower lip about twice as long, the middle lobe obviate, rounded, the lateral lobes small, subacute. Fruit nutlets, 2.5 mm long, oblong, brown, smooth, inner face angular and outer face rounded [21-22].

Fig 1: *Leucas aspera* plant

Microscopic Description [23]:

- **Stem**

Diagrammatic TS of young stem is quadrangular in outline with four distinct collenchymatous ridges, covered with hairs. It shows a narrow cortex and a ring of vascular tissue encircling the wide stele.

Detailed TS shows an epidermis covered with thick cuticle, traversed occasionally with stomata and bears simple, multicellular (three to four-celled) uniseriate lignifi ed trichomes and sessile, glandular trichomes with multicellular head; narrow parenchymatous cortex, except under the ridges where it is collenchymatous, distinct endodermis and parenchymatous pericycle, especially; stellar region consisting of a ring of vascular bundles connected with interfascicular sclerenchymatous band; very narrow parenchymatous phloem, and radially arranged xylem tissue.

In old stem, trichomes are few, phloem tissue is wide and found on either side of the wide xylem band; pith is parenchymatous, wide and embedded with acicular crystals of calcium oxalate.

- **Leaf**

TS of leaf passing through the midrib is broadly convex on the lower side and slightly grooved or flat on the upper side, a centrally located conjoint and collateral meristele associated with a parenchymatous pericycle layer on lower side, collenchymatous tissue underneath both the epidermis; dorsiventral lamina epidermis covered with thick cuticle, traversed with stomata, bears simple and glandular trichomes of the same type as found on stem, 1 to 2 layered palisade tissue occupying the major area of the section and spongy parenchyma.

Chemical Constituents [24-29]:

In *Leucas aspera*, different types of phytoconstituents are present.

Phytochemical compounds and secondary metabolites of *Leucas aspera* which were identified in the previous studies can be classified in the following manner, such as:

- **Terpenoids**

Oleanolic acid, ursolic acid, squalene, β-caryophyllene, α-humulene, α-pinene, epi-α-bisabolol, limonene, x-thujene, menthol, leucasperone A, leucasperone B, and leucasperone C.

- **Flavonoids**

Catechin, acacetin, apigenin, and chrysoeriol

- **Steroids and Fatty Acids**

3-sitosterol; 9, 12, 15-Octadecatrienoic acid methyl ester, n-hexadecanoic acid, linoleic acid, oleic acid, stearic acid, ceryl alcohol, and dotriacontanol.

- **Glycosides**

Glucoside, linifolioside, leucasperioside-A, leucasperioside-B, leucasperioside-C

- **Lignans**

Nectandrin B, meso-dihydroguaiaretic acid, (-) chicanine, and erythro-2-(4-allyl-2, 6-dihydroguaiaretic1-(4-hydroxy-3-methoxyphenyl)-propan-1-ol

- **Long Chain Phytocompounds**

4-(24-hydroxyl-1-oxo-5-n-propyltetracosanyl)-phenol
28hydroxypentatriacontan-7-one
7-hydroxydotriacontan-2one
1-hydroxytetratriacontan-4-one
32-methyltetratriacontan-8-ol
5-acetoxytriacontane

- **Other Compounds**

Nicotine alkaloids, 1, 2-benzene dicarboxylic acid bis-(2-methyl propyl) ester, 1-octen-3-ol, amyl propionate, isoamyl propionate, and asperphenamate

Pharmacological Properties:

- **Antimicrobial activity**

The methanol extract of *Leucas aspera* flowers, its fractions, the alkaloidal residue and the expressed flower juice showed good antibacterial activity for methanol extract and methanol fraction with maximum activity for the alkaloidal residue [30]. The essential oils from *Leucas aspera* possessed bacteriostatic activity against Staphylococcus aureus, Vibrio cholerae, Salmonella typhi, Klebsiella aerogenes, Escherichia coli, Proteus vulgaris, Pseudomonas pyocyanea and Dys. Flexneri [31]. Furthermore, in-vitro study of chloroform and ether extracts of *Leucas aspera* revealed its antifungal activity against Trichophyton and Microsporum gypseum. The minimum inhibitory concentration was found to be 5 mg/mL. *Leucas aspera* had both fungistatic and fungicidal actions [32].

- **Prostaglandin inhibitory and antioxidant activities**

Leucas aspera was tested for its prostaglandin (PG) inhibitory and antioxidant activities. The ext. showed both activities, that is, inhibition at 3-4 g/mL against PGE1- and PGE2-induced contractions in guinea pig ileum and a 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging effect. Phytochemical investigation suggested the presence of nectandrin B, meso-dihydroguaiaretic acid, macelignan, acacetin, apigenin 7-O-[6′-O-(p-coumaroyl)-3-D-glucoside], chrysoeriol, apigenin, erythro-2-(4-allyl-2,6-dimethoxyphenoxy)-1-(4-hydroxy-3methoxyphenyl) propan-1-ol, myristargenol B and machilin C, (-)-chicanine, (7R,8R)- and (75,85)-licarin A [33].

- **Hepatoprotective activity**

Methanol extracts of *Leucas aspera* found a good hepatoprotective activity against carbon tetrachloride induced liver damage in Rats [11]. Fresh juice from leaves of *Leucas aspera* had high liver protective activity [34]. Effect of *Leucas aspera* on CCL4 indued hepato-carcinogenesis in rats was studied by Gupta *et al*. On administration with ethanolic and aqueous extracts of *Leucas aspera* exhibited the decreased hepatic cell proliferation and nodulogenesis in tested rats [35]. Hydroalcoholic extracts of *Leucas aspera* leaves at a dose of 400mg exhibited hepatoprotective activities in male albino rats exposed to lead acetate at a dose of 50mg/kg. The study found that there was a significant reduction in liver enzymes in a dose dependent manner ($p<0.05$)

- **Antipyretic activity**

Leucas aspera has been shown to possess antipyretic properties. The plant has been used to treat fever and other febrile conditions. The antipyretic effect of the plant may be due to its ability to inhibit the production of prostaglandins, which are involved in the regulation of body temperature [32].

- **Antinociceptive, antioxidant and cytotoxic activities**

The ethanolic extract of *Leucas aspera* was subjected to acetic acid induced writhing inhibition, 1,1-diphenyl-2-picryl hydrazyl (DPPH) free radical scavenging assay and brine shrimp lethality bioassay for screening of antinociceptive, antioxidant and cytotoxic activity respectively. The ethanolic extract of *Leucas aspera* root produced significant inhibition in acetic acid induced writhing in mice at the doses of 250 and 500 mg/kg. The extract showed a significant free radical scavenging activity with an IC50 of 8 µg/ml. The extract showed significant lethality to brine shrimp [36].

- **Anti-Cancer Property**

The previous research investigation conducted the brine shrimp lethality assay and the study results observed that the hydroalcoholic decoctions of the whole plant showed cytotoxicity and this activity was more in 80% ethanolic root decoctions [37]. In a dose-dependent study, it was showed that the LC50 value is 52.8 µg/mL.27 Brine shrimp lethality assay was also used to study the crude methanolic leaves extract of the plant. The study results showed the LC50 value of the sample and vincristine sulfate as 30 and 10.44 µg /mL, respectively [38].

- **Antifungal activity**

In vitro study of chloroform and ether extracts of *Leucas aspera* revealed its antifungal activity against *Trichophyton* and *Microsporum gypseum*. The minimum inhibitory concentration was found to be 5mg/mL. *Leucas aspera* had both fungistatic and fungicidal actions [32].

- **Anti-Diabetic Property**

In an earlier study, the ethanolic and petroleum ether extracts showed significant anti-hyperglycaemic effects in alloxan-induced and streptozotocin-induced diabetic rats.30 The study was done to evaluate the effect of leaves of the plant on experimental diabetic rats. Similarly, the methanolic extract of the plant was directed in streptozotocin-induced diabetic rats to reduce the blood glucose level.31 Ethanolic extract of this plant leaves reduced the blood glucose levels in the dose-dependent study and restrained the biochemical parameters in the animal model [39].

- **Anti-Venom activity**

The present concluded that methanolic extract of *Leucas aspera* showed anti-venom activity and it can be potential source for the anti-ophidian metabolites [40].

- **Anti -psoriatic activity**

Petroleum ether extract of C. juncea and ethanol extract of L. aspera were studied for anti-psoriatic activity, results showed the good skin keratinocyte antiproliferative activity by in habiting nitric oxide production and lipid peroxidation, suggesting the anti-oxidant mediated anti-psoriatic activity [41]. The skin diseases treatments with plant extracts and natural products has been reported since ancient civilizations [42].

- **CNS depressant activity**

In this study Leuca aspera showed remarkable decrease in locomotor activity of open field and whole cross tests and significant increase in the duration of immobility time of force swimming and tail suspension tests. In thiopental sodium-induced sleeping time test, the methanolic leaves extract of *Leucas aspera* notably induced the sleep at earlystage extract of *Leucas aspera* has CNS depressant activity [43].

Dynamic trajectory analysis against COVID-19 spike protein

Docking interaction of spike protein study was done on anti-viral herbs like Curcuma longa, Morinda citrifolia, Ocimum tenniflorum, Leucasaspera, Piper longum, Azadirachta indica and Corallium rubrum to identify the effective lead molecule. Among these, major phytoconstituents of M. Citrifolia and L. aspera, plus the molecule 4-(24-hydroxy-1-oxo-5—n-propyltetracosanyl)-phenol from Leucasaspera showed significant dynamic trajectory activity of forming the stable complex with S- protein and complete denaturation of spike protein than HCQ and Remdesivir against COVID-19 [44].

Conclusion

Leucas aspera, commonly known as "Thumbai," is a versatile medicinal herb with profound pharmacological and therapeutic potential. Widely used in traditional medicine, it has demonstrated an array of bioactivities, including antimicrobial, anti-inflammatory, antioxidant, hepatoprotective, antipyretic, cytotoxic, antifungal, and antidiabetic properties. These effects are attributed to its diverse phytochemical composition, comprising flavonoids, alkaloids, terpenoids, steroids, phenolics, glycosides, and essential oils. Pharmacognostical studies have provided crucial insights into its botanical characteristics, aiding in identification, standardization, and quality control.

While the traditional uses and pharmacological benefits of *Leucas aspera* are well-documented, there is a significant need for advanced research to bridge the gap between ethnobotanical knowledge and modern medical applications. Molecular studies are required to elucidate its mechanisms of action, while rigorous clinical trials are necessary to confirm its safety, efficacy, and therapeutic potential. Additionally, exploring its bioactive compounds through advanced isolation and drug development approaches can pave the way for new pharmaceutical innovations.

Leucas aspera stands out as a promising candidate for the development of plant-based drugs, offering immense potential to address global health challenges. Further interdisciplinary research could significantly enhance its role in both traditional and modern medicine, establishing it as a cornerstone in phytopharmaceutical advancements.

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