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Review article

A Comprehensive Review of *Leucas aspera*

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ABSTRACT:

Natural In the Indian subcontinent, there are a variety of herbal medicines available, and they play an important role in India's traditional medicine. They are used to treat or cure ailments and find applications in food, agriculture, pharmaceutical, and cosmetic industries. *Leucas aspera* belongs to the Lamiaceae family and can be found in India from the Himalayas down to the Ceylon with names like Dronpushpi, Thumbai, or Goma madhupati. Traditionally this plant is used as an insecticidal or anti-pyretic agent. It is also being suggested to be used as an antidote for snake venom. Medicinally, the plant, flowers, leaves extract and essential oil possess various pharmacological actions like antioxidant, antimicrobial, antifungal, anti-inflammatory, anticancer, antidiabetic, and antinociceptive activities. Further, studies reveal the presence of various important phytochemical constituents in this plant mainly contains glucoside, nicotine, sterols, ß-sitosterol, oleanolic acid, ursolic acid, diterpenes, triterpenoids, and phenolic compounds (4-(24-hydroxy-1-oxo-5-n-propyltetracosanyl)-phenol). The present review provides a comprehensive review of the plant *Leucas aspera*.

Keywords: *Leucas aspera*, Lamiaceae, Herbal Plant, Pharmacological, Antioxidant activity.

1. INTRODUCTION

Traditionally, medicinal plants were the only sources for treating physiological disorders. Peoples of India use medicinal plants from ancient time and they use them for several health-related applications. In the ethnic medical texts, there are approximately 25,000 plant-based formulations are present. In addition, at least 25% of drugs used in modern medicine are made from plants or artificial drugs made from plant-derived original compounds. India is one of the richest granaries of medicinal herbs in the world, with extraordinary modern applications that ensure the health of millions of people [1]. Medicinal herbs are a rich source of lead compounds for novel drug discovery, and so their biological value is increasing rapidly [2-4]. Newly discovered and existing medicinal plants have been investigated for a variety of ailments to determine their therapeutic potential. Several medicinal plants have been studied for the prevention and treatment of a number of life-threatening diseases including cancer [5]. They are used to treat or cure the ailments and find applications in food, agriculture, pharmaceutical, and cosmetic industries. The Indian subcontinent contains a wide variety of herbal plants, which are used as the basis for India's traditional medical systems: Ayurveda and Siddha [6]. *Leucas aspera* is member of the family Lamiaceae and commonly known as Dronpushpi, Thumbai, or *Goma madhupati* is widely distributed throughout India from the Himalayas down to Ceylon. Medicinally, the plant, flowers, leaves extract and essential oil possess various pharmacological actions like antioxidant, antimicrobial, antifungal, anti-inflammatory, anticancer, antidiabetic, and antinociceptive activities. The effectiveness of *L. aspera* whole plant extracts on larvicidal and pupicidal activities against the malarial vector *Anopheles stephensi* has been proven [7]. Leaves of *L. aspera* are useful in chronic rheumatism, chronic skin eruptions, psoriasis, and scabies, and their juices are used as antibacterial agents. The antifungal activity of *L. aspera* is shown by its chloroform and ether extracts [8]. The plant *L. aspera* possesses the property of wound healing and is also used in cobra venom poisoning [9]. Additionally, studies show that this plant contains several significant phytochemical components, including glucoside, nicotine, sterols, ß-sitosterol, oleanolic acid, ursolic acid, diterpenes, triterpenoids, and phenolic compounds (4-(24-hydroxy-1-oxo-5-n-propyltetracosanyl)-phenol) [6]. The family and taxonomical detail are provided in Table 1 and Table2. .

2. PLANT PROFILE

Table 1: Vernacular Names of *Leucas aspera*

Language	Common name
Sanskrit	Dronapushpi, Chitrakshup, Chitrapathrika
Hindi	Guma, Dhurpisag, Goma madhupati
Gujrati	Kulnnphul
Bengali	Darunaphula, Hulkasha, Shwetdron
Maharashtra	Bahuphul
Mumbai	Tumbai
Telugu	Thummichittu, Tunni
Punjabi	Guldora
Assam	Dronaphool
Sindhi	Kubo

Table 2: Taxonomical Classification of *Leucas aspera*

Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Angiosperma
Super division	Spermatophyta
Class	Dicotyledonae
Subclass	Gamopetalae
Family	Lamiaceae
Order	Lamiales
Genus	*Leucas*
Species	*L.aspera*
Series	Bicarpellatae

BOTANICAL DESCRIPTION

PLANT PARTS	DESCRIPTION	PICTURES
ROOTS	Cylindrical, zig-zag, smooth, fine rootlets, size variable, along with numerous wiry, fracture, fibrous, taste, characteristic	
STEM	Light greenish-yellow, rough surface, much branched, hispid or scabrid, thick up to 4 mm, quadrangular with four prominent furrows, hairy, slightly bitter taste	
LEAF	Yellowish-green, 2.5-6 cm long, 1-3 cm wide, linear or narrowly oblong-lanceolate, more or less hairy, crenate, serrate, pungent taste	
SEED	Oblong, trigonous, smooth, dark brown, approximately 0.3 cm long and 0.1 cm wide	
FRUIT	Schizocarpic carcerule, nutlets 2.5 mm smooth, brown, inner face angular and outer face rounded [10]	
INFLORESCENCE AND FLOWER	Sessile, white, dense, approximately 2-3.5 cm in diameter, surrounded by many leaves, 1.2-1.5 cm long and 0.3-0.35 cm wide; thin, lanceolate, pointed, ciliate, slightly convex, 1-2.25 cm long, calyx, tubular, hairy on upper part; corolla, 1.7-2 cm long, white, upper lip is about 4 mm long and hairy; lower lip is nearly twice as long as the upper lip; lateral lobes are small	

3. MICROSCOPIC DESCRIPTION

ROOT

The TS of the root is narrow, elongated, and densely packed epidermal cells with thin walls, whereas the flattened walls are flat. A unicellular head and a short unicellular stalk have been identified in glandular with trichomes.

Shows a single-layered epidermis consisting of rectangular, thin-walled cells; the secondary cortex is composed of thin-walled, indirectly elongated with parenchymal cells; the secondary phloem is made up of sieve components and phloem parenchyma; secondary xylem is made up of blood vessels, trachea, fibers, and xylem parenchyma; trachea with simple pits, much-elongated xylem fibers with pointed tips and moderately thick walls, some with simple pits; up to 8 cells long.

STEM

The schematic TS of the young stem is square in outline with four specific collenchymatous ridges that are covered in hairs. It depicts a small cortex and a ring of vessel elements enclosing the wide stele.

Detailed TS shows that the epidermis is covered by a thick layer of cuticle, sometimes transported with stomas, and bears normally. It also shows that the trichomes are multicellular with 3-4 cell heads, uniseriate, and have a sessile structure. It also has a narrow parenchymatous cortex with the exception of under ridges, where it's collenchymatous, a different endoderm, and a distinct parenchymatous pericycle. Most importantly, it shows that the stellar region is made up of a ring of vascular bundles which is connected by an interfascicular sclerenchymatous band. It also shows a very small parenchymatous phloem as well as radially structured xylem tissue.

Trichomes are extremely rare in old stems, phloem tissue is wide and located on each side of a wide band of xylem; the core is parenchymatous, broad, and contains needle-like calcium oxalate crystals.

LEAF

Petiole-It shows a single-layer epidermis composed of unicellular to tricellular trichomes with pointed ends, a cortex comprising of single-layer collenchyma that is round to precise, and the parenchyma is made up of cells with thin walls and prismatic calcium oxalate crystals. It also has four vascular bundles, two smaller ones in the direction of each comer and two larger ones in the middle.

Midrib-The epidermis is made up of one to three-cell trichomes on each side, followed by 1-2 layers of collenchyma on the lower surface, 3-4 layers onthe upper surface, followed by round to oval parenchyma, 4-7 layers of a vascular bundle with curved shaped in the center.

Lamina-The epidermis shows 1-3 cell trichomes on each side and rarely on top of the surface; palisade single-layered, spongy parenchyma 3-5 layers, irregular, thin-walled, stomatal index of the upper surface is 16.6-30.7 and the lower surface is 16.6-40.5; palisade ratio 7-9[11].

PHYTOCHEMICAL CONSTITUENTS

The existence of a wide range of phytochemicals has been investigated in the preliminary study on *L. aspera* including steroids, terpenoids, lignans, alkaloids and flavonoids [12-13] nicotine[9], sterols[14], oleanolic acid, ursolic acid, 3-sitosterol[15-16], galactose and glucoside [16].

The fingerprinting examination of the methanolic extract of the entire plant *L. aspera* by HPTLC revealed two types of alkaloids, two types of steroids, and six types of flavonoids[17]. The use of Gas Chromatography coupled with the Mass Spectrometry (GC-MS) analysis method has recently been used to identify 24 essential phytochemicals during the evaluation of extracts of plant leaves from methanol. Important essential oils were found during the hydro-distillation process of aerial parts with 43 compounds, representing 98.09% of the total essential oil. Other chemicals, such as β-caryophyllene (34.2%), α-pinene (5.8%), epi-α-bisabolol (4.6%), α-humulene (6.3%), 1-octen-3-ol (14.8%) and limonene (4.5%) were identified as the plants primary phytoconstituents using the same method[18]. The chemical constituents of the seed were linoleic acid (48.11%), oleic acid (42.07%), stearic acid (2.84%), and linolenic acid (0.65%). 3-sitosterol and ceryl alcohol are found in the unsaponifiable fraction[19]. Catechin [20] and phytol [21] were found in whole plant extracts. In the GC-MS analysis, the oil is rich in oxygenated monoterpenes (0.6%), oxygenated sesquiterpenes (14.8%), monoterpene hydrocarbons (14.8%), oxygenated LCH and phenyl derivative constituents (20.2%), and sesquiterpene hydrocarbons (47.7%) [22]. Among 25 compounds methanol (11.3%), u-farnesene (26.4%), x-thujene (12.6%)amyl propionate (15.2%), and isoamyl propionate (14.4%) among 10 compounds are major constituents in leaf and flower extracts respectively[23]. Shoot contained β-sitosterol, 5-acetoxytriacontane, nonatriacontane, dotriacontanol, Leucolactone (I), aliphatic ketones (28-hydroxypentatriacontan-7-one, 7-hydroxydotriacontan-2-one), novel phenolic compounds (4-(24- hydroxy-1-oxo-5-n-propyltetracosanyl)-phenol) and long-chain compounds (1-hydroxytetratriacontan-4-one, 32-methyltetratriacontan-8-ol)[24-27]. The constituents can be found in Table 3.

The first time eight lignans and four flavonoids were isolated from the plant *Leucas aspera*. Flavonoids include Acacetin (LA4), Apigenin 7-O-[60-O-(p-coumaroyl)-b -D-glucoside (LA5), Chrysoeriol (LA6), Apigenin (LA7), while lignanes include nectandrin B (LA1), mesodihydroguaiaretic acid (LA2), macelignan(LA3), (-)-chicanine(LA8), Licarin A(LA9),erythro-2-(4-allyl-2,6-dimethoxyphenoxy)-1-(4-hydroxy-3methoxyphenyl)propan-1-ol (LA10), myristargenol B(LA11), machilin C (LA12). Among which LA8 was found to be a new antipode of (+)-chicanine,while LA9 was found to be a combination of two enantiomers of (7R, 8R) and (7S,8S)-licarinA [28].

Table 3: Phytochemical Classification of *L. aspera*

S. No.	Phytochemical compounds	Secondary metabolites
1.	Terpenoids	Ursolic acid, Oleanolic acid, Menthol, x-thujene, Squalene, Limonene, β-caryophyllene, α-humulene, α-pinene, epi-α-bisabolol, Leucasperone A, B and C
2.	Steroids and Fatty acids	Ceryl alcohol, dotriacontanol, linoleic acid, oleic acid, n- hexadecenoic acid, stearic acid, 3-sitosterol and 9, 12, 15-Octadecatrienoic acid methyl ester
3.	Glycosides	Glucoside, leucasperosides- A, B, C and linifolioside
4.	Flavonoids	Acacetin, apigenin, catechin, and chrysoeriol
5.	Lignans	Chicanine, licarin A, erythro-2-(4-allyl-2,6-dimethoxyphenoxy)-1-(4-hydroxy-3-methoxyphenyl)propan-1-ol, necatandrin, myristargenol B, machilin C, macelignan and meso-Dihydroguaiaretic acid
6.	Long chain phytocompounds	5-acetoxytriacontane, 1-hydroxypentatriaconton-4-one, 7-hydroxydotriacontan-2-one, 28-hydroxypentatriacontan-7-one, 32-methyltetratriacontan-8-ol, and 4-(24-hydroxyl-1-oxo-5-n-propyltetracosanyl)-phenol
7.	Other compounds	Asperphenamate, amyl propionate, isoamyl propionate, 1, 2-benzenedicarboxylic acid bis-2(2-methyl propyl) ester, galactose sugar, nicotine alkaloids, and 1-octen-3-ol

4. PHARMACOLOGICAL ACTIVITY

Anti-asthmatic activity

The whole dried plant of *Leucas aspera* shows an anti-asthmatic effect. This study demonstrated the drugs methanolic extract had considerable bronchodilatory, antihistaminic, anti-inflammatory, mast cell stabilization and anti-cholinergic effects in histamine-induced bronchospasm. The dose used in this study was100mg/kg. Additionally, it showed significant results in models for guinea pig tracheal

chain and ileum preparations, passive paw anaphylaxis, mesenteric mast cell degranulation, and histamine and acetylcholine-induced contraction respectively. However, the anti-allergic activity in milk-induced eosinophilia was not significant. Therefore, further investigation is needed to determine the active antihistaminic component of the methanolic extract from the dried whole plant of *Leucas aspera* [29].

Antihyperglycemic activity

Oral glucose tolerance tests using Swiss albino mice underwent an evaluation of the antihyperglycemic effects of a methanol extract of the leaves and stem of *L. aspera*. It was found that *Leucas aspera* leaf extract was more effective than stem extract at lowering serum glucose levels. Therefore, the chemical components that are more abundant in leaves than stems should be identified and further investigated for their anti-glycemic effect [30].

The *L. aspera* alcoholic extract was found to have a hypoglycemic effect in rats that had been chronically treated for normoglycemia and diabetes, according to another study examining the impact of *Leucas aspera* on blood glucose levels in normoglycemic and diabetic rats. On day 0, a single dosage of the plant extract had no effect on the blood glucose level. At intervals of 30 and 60 minutes, levels increased. However, with prolonged dosing, the extract significantly decreased fasting blood sugar levels (FBL) and was similar to the reference drug, Metformin [31].

Antimicrobial activity

The methanolic extract of *L. aspera* flowers, its fractions, the alkaloidal residue, and expressed flowers had good antimicrobial activity in the zone of inhibition method against the bacteria (*E. coli, P. aeruginosa, Streptococcus pyogenes, S. aureus, Klebsiella pneumonia, Bacillus subtilis*) and fungi (*Cryptococcus neformans, Candid albicans, Aspergillus niger, Trichophyton*) [32].

The antimicrobial properties of methanolic and ethanolic extracts are demonstrated to be effective against the pathogens *E. coli, Klebsiella pneumonia, and Staphylococcus epidermis* respectively [33]. Compared to ethanolic and petroleum ether extracts, the antimicrobial activity of methanolic extracts of leaves was more effective.The antibacterial activity of the ethanol extract of the entire plant was high at higher concentrations depending on time and dose when administered in the Colony forming unit (CFU) method against *E. coli*[34].

Bacillus cereus, Bacillus subtilis, Bacillus megaterium and *S. aureus* are examples of gram-positive bacteria that are more sensitive in comparison with gram-negative bacteria such as *E. coli,Salmonella dysenteriae, Salmonella paratyphi, Salmonella typhi, Pseudomonas aeruginosa*and*Vibrio cholera* in the ethanolic extract [35]. The plant's 80% ethanolic extract showed potent antibacterial activity against *Bacillus subtilis and S. aureus* [36-37].

The essential oils from *L. aspera* had a bacteriostatic effect against *S. typhi, S. aureus, E. coli, Proteus vulgaris, Klebsiella aerogenes, Vibrio cholerae, and Pseudomona pyocyanea*[38].

In this study, it was found that *L. aspera's* essential oils do not have any antibacterial activity against *Candida albicans, E. coli,and P. aeruginosa. L. aspera* oil had good antibacterial activity against *S. aureus, B. cereus,* and *A. niger* which was most likely due to its sesquiterpene content in the oil. (E)-caryophyllene and α-humelene have demonstrated antibacterial activity against *Bacillus cereus* and *Staphylococcus aureus* [39].

Antifungal activity

In an in vitro investigation, chloroform and ether extracts of *L. aspera* showed both fungistatic and fungicidal effects against *Trichophyton* and *Microsporum gypseum* with a minimum inhibitory concentration of 5mg/mL [40].

Anti-inflammatory activity

To determine the anti-inflammatory activity caused by prostaglandin inhibitory effect on prostaglandin-induced contraction in guinea pig ileum, the methanolic extract of the whole plant of *L. aspera* was used and it was found to be effective in Magnus assay method [28, 41].

In a study, the anti-inflammatory effect of *L. aspera* crude extract, alkaloid fraction, and non-alkaloid fraction was tested using a formalin-induced rat paw edema method and compared to Phenylbutazone. The ant-inflammatory activity of Phenylbutazone was determined to be the highest, followed by crude extract and alkaloid fraction. The non-alkaloid fraction didn't show anti-inflammatory activity [42].

The effects of *Leucas aspera* aqueous and alcoholic extracts on experimental inflammation and mast cell degranulation were studied.In the case of acute and chronic inflammation, both extracts showed significant anti-inflammatory activity. Pretreatment with *Leucas aspera* extract successfully inhibited mast cell degranulation produced by propranolol and Carbachol[43].

In both acute and chronic inflammation experiments, different concentrations of ethanolic extract from leaves (100mg/kg, 200mg/kg, and 400mg/kg) showed a significant anti-inflammatory effect. The 400mg/kg dose produced a percentage inhibition of 60.64% in the carrageenan model, which was comparable to 60.70% in the standard drug Diclofenac, whereas Diclofenac was 60.27% in the cotton pellet method and 50.85%,57.63%, and 58.42% in the three different test doses (100mg/kg,200mg/kg and 400mg/kg) [44].

Antipyretic activity

The antipyretic effects of ethanolic extract of *L. aspera* and *Glycosmis pentaphylla* in rats were investigated using Brewer's yeast-induced pyrexia model. The extract of *L. aspera* (200mg/kg) and standard paracetamol demonstrated effective antipyretic efficacy for the duration of the test (6 hrs) probably by inhibiting prostaglandin synthesis in the

hypothalamus. The researcher proposed additional research to identify the active elements involved in this activity and understand their respective mechanism of action [45]

Anti-helminthic activity

Using Pheretima Posthuma as an experimental model, the anti-helminthic characteristic of *Leucas aspera* was examined. The standard reference was piperazine citrate. When compared to aqueous extract of *L. aspera* it showed substantial anti-helminthic activity against Pheretima Posthuma. The ethanolic extract was also found to be more effective than the usual medication. The ethnomedical claims of *Leucas aspera* as an anti-helminthic herb were supported by this investigation [46].

Antioxidant activity

Oxidative stress is harmful to human health and lack of antioxidants may reduce reactive free radicals, causing degenerative diseases such as cardiovascular disease, cancer, neurodegenerative disorders, Alzheimer's disease, and inflammatory diseases to emerge[47]. To avoid the toxic effects of oxidative stress, a nutritional supplement containing antioxidant compounds can be used, and most herbal plants possess antioxidant properties. Many researchers have reported that *Leucas aspera* has antioxidant properties [48-55].

In another study, the ethanolic extract was tested for antioxidant, antinociceptive, and cytotoxic properties using acetic acid-induced writhing inhibition, brine shrimp lethality bioassay, and DPPH free radical scavenging assay. According to the researchers, the ethanolic extract of *L. aspera* root inhibited acetic acid-induced writhing in mice at doses of 250mg/kg and 500 mg/kg. The extract demonstrated strong free radical scavenging activity with an impact concentration (IC50) of 8 µg/ml and significant toxicity to brine shrimp [51]. The petroleum ether extract of *L. aspera* leaf had significant antioxidant activity and the order of activity is chloroform < ethyl acetate < isopropyl alcohol < ethanol < petroleum ether [54]. They also recommended petroleum ether (non-polar solvent selection) and ethyl alcohol or isopropyl alcohol (polar solvent selection) for better phytochemical extraction. When compared to *in vitro*callus extract, wild leaf extract had higher antioxidant activity. [55]In comparison to ethyl acetate and n-hexane extracts, ethanol extract showed a more significant anti-oxidant effect [48].

Anti-ulcer activity

The study showed that the traditional use of *L. aspera* to treat all gastrointestinal disorders was supported by a combination of antioxidant and histopathological testing, with Methanolic extract from *L. aspera* demonstrating potent antisecretory and protective action against ulcerations in all tested ulcer models [56].

To investigate the antiulcer effect of the alcoholic extract of *Leucas aspera*ALA, two experimental models were used. Significant reductions of acid secretion and ulcer scores were observed in rats after administration of ALA. According to this observation, the combination of anti-secretary and protective effects against gastric mucosa may be associated with ALA's antiulcer action [57].

The study found that the hydroalcoholic extract of *L. aspera* leaves contains saponins, tannins, and flavonoids in a phytochemical analysis. Furthermore, the study revealed that the gastric ulcer-forming effect of the extract was mediated by the killing of bacteria by inhibiting the cell wall biosynthesis of indomethacin-induced gastric ulcers, as well as the relevance of the extract in the reduction of ulcer surface and ulcer score[58].

Cytotoxicity activity

In a brine shrimp lethality test, a crude methanolic extract of the leaves demonstrated cytotoxic activity. The sample LC50 value was 30µg/mL, while vincristine sulfate has a value of 10µg/ml [51]. In the MTT assay, ethyl acetate flower extract demonstrated strong cytotoxic activity with a TC50 value of 631.6µg/ml in HeLa cells [59]. In vitro MTT and Trypan blue assay show that aerial parts of the *L. aspera* plant have cytotoxic effects in Dalton's Ascitic Lymphoma (DAL) bearing Swiss albino mice [60]. In the brine shrimp nauplii bioassay method, 80 % ethanolic extract of *L. aspera* root was found to have a potent cytotoxic effect with 52.8µg/ml LC50[51].

Anti-arthritic activity

A study was performed to evaluate *L. aspera* anti-arthritic activity. Its ethanolic extract demonstrated substantial anti-inflammatory ($p < 0.001$) and antioxidant ($p<0.001$). Up to a dose of 2000 mg/kg body weight, the medication was shown to be safe. EELA2 revealed cartilage repair. Apart from glycosides, phenolic compounds, and tannins, the researcher proposed that the anti-arrhythmic properties of EELA's may be due to the presence of phytosterols (β-sitosterol), catechins (epicatechin, β-epicatechin), and flavonoids (procyanidin) [61].

Anticancer activity

In a brine shrimp lethality test, ethanolic extract of the entire plant showed cytotoxic action and the LC50 values were 181.68±2.15 and 181.67±1.65µg/ml[62], compared to 0.76±0.04µg/ml of standard vincristine sulfate. In the brine shrimp nauplii bioassay method, an 80% ethanolic extract of the *L. aspera* root was demonstrated to have effective and dose-dependent cytotoxic action, with an LC50 of 52.8µg/ml [51].

The previous study used the brine shrimp lethality assay, and the results showed that the entire plant was susceptible to cytotoxicity with 80% of ethanolic root decoctions showing cytotoxic activity [63]. The LC_{50} value of the sample and vincristine sulfate was obtained using a brine shrimp lethality bioassay of crude methanolic extract of leaves, which were 30.00µg/ml and 10.44µg/ml respectively [50].

Based on the biochemical and histological results of this in vivo and invitro study, it was concluded that the ethyl acetate extracts of the aerial parts of *L. aspera* exhibited anticancer activity mediated by anti-angiogenesis,

microphage stimulation, and free radical scavenging and this anticancer activity of *L. aspera* ethyl acetate extracts are comparable to the standard drug 5-Fluorouracil [56].

Larvicidal activity

Crude methanolic extracts of *L. aspera* were tested for their larvicidal activity against *Aedes aegypti*, *Anopheles stephensi*, and *Culex quinquefasciatus*. These activities were evaluated against fourth-instar stages. Catechin, which is an isolated compound from the plant, has significant larvicidal activity at very low concentrations. Catechin had LC50 and LC90 values of 3.05 and 8.25 ppm against *Aedes aegypti* larvae, respectively. Similarly, the LC50 and LC90 values for catechin against C. *quinquefasciatus* larvae were 3.76 and 9.8 ppm, respectively. The metabolites from the flower with LC50 and LC90 values of 53.16 3.64 and 233.1825.68 ppm indicated a larvicidal effect on Anopheles subpictus.and on Culex tritaeniorhynchus, with values of 81.24 5.16 and 300.45 31.6 ppm, respectively.[64]Ethanolic extract of the entire plant of *L. aspera* showed larvicidal and pupicidal effects against Anopheles stephensi I, II, III, IV instar larvae with LC50 values of 9.695%, 10.272%. 10.823%, 11.303%, and 12.732% against pupae [65]. In comparison to ethanolic and chloroform extracts, hexene extract was found to have effective larvicidal properties against those vectors [66].

Hepato-protective activity

The hepatoprotective activity of *L. aspera* methanol and petroleum ether extracts was tested using paracetamol and thioacetamide-induced hepatotoxicity models. The findings revealed that *L. aspera* root extracts have hepatoprotective properties [67].

In rats with carbon tetrachloride-induced hepatotoxicity, a cold methanolic extract of the whole plant of *L. aspera* showed considerable hepatoprotective activity [68].

Antinociceptive activity

A model of gastrointestinal pain induced by acetic acid showed in Swiss albino mice that *Leucas aspera* has an antinociceptive effect on the whole plant. At dosages of 50, 100, 200, and 400 mg, the methanolic extract of entire plants of *L. aspera* demonstrated higher antinociceptive action. The study also found that *L. aspera* extract, even at low doses, has antinociceptive action when compared to the standard drug aspirin [69] as seen in Table 4.

Dynamic trajectory analysis against COVID-19 spike protein

To discover the efficient lead molecule, spike protein docking interaction studies were performed on a variety of anti-viral herbal plants such as *Azadirachta indica, Curcuma longa,Corallium rubrum, Leucas aspera, Morinda citrifolia, Piper longum, and Ocimum tenniflorum.* Among these, major phytoconstituent substances are *L. aspera, and Morindacitrifolia* as well as the molecule 4- (24-hydroxy-1-oxo-5—n-propyltetracosanyl)-phenol from the plant*L. aspera,* demonstrated significantly greater dynamic trajectory action for the formation of a stable S- protein complex and for complete denaturing of the spike protein compared to hydroxychloroquine (HCQ) and Remdesivir against COVID-19.

Table 4: Pharmacological value of *Leucas aspera*

S. No.	Tissue	Extracts	Activity
1	Aerial parts	Methanol extract	Ulcer protective [56]
2	Roots	Ethanol extract	Anti-pyretic [45]
3	Leaf	Hydroalcoholic extract	Hepatoprotective [67-68]
4	Flowers	Methanol extract	Antimicrobial [32]
5	Aerial parts	Hydroalcoholic extract	Arthritis, ant-arthritic [61]
6	Whole plant	Ethanol extract	Cytotoxic [51]
7	Whole plant	Aqueous and alcoholic extracts	Anti-inflammatory [43]
8	Whole plant	Methanol extract	Anti-asthmatic [29]
9	Leaf	Triterpenoid from methanol extract	Anti-helminthic [46]
10	Root	Methanol and petroleum ether extracts	Hepatoprotective [67]

CURRENT APPLICATION AND FUTURE SCOPE

According to WHO, the most common victims of snake bites are agricultural workers. As *Leucas aspera* grows into a weed in fields it has the potential to be an antidote for venom poisoning. Drug discovery from medicinal plants continues to yield novel and significant lead compounds against a wide range of pharmacological targets including cancer. In stagnant water bodies, it would be preferable to use locally accessible *L. aspera* extracts as larvicide to control the spread of mosquito vector-borne diseases like malaria, dengue, chikungunya, and yellow fever. Nanoparticles have a wide range of uses in fields such as healthcare, manufacturing, electronics, and the environment. *L. aspera* leaf extract has been employed in the green synthesis of silver and cerium dioxide nanoparticles. It is a low-cost, non-toxic, and environmentally acceptable bio-mediated combustion approach for nanoparticle manufacturing. These phytochemicals can be used in computational and molecular modeling research to develop and identify novel medicines.

5. CONCLUSION

Leucas aspera is a plant with a wide range of medicinal properties and applications. It has been used in traditional systems of medicine for treating various diseases and disorders, such as cough, asthma, fever, skin infections, wounds, snake bites, diabetes, malaria, and cancer. It has

also been reported to have anti-inflammatory, analgesic, antipyretic, antimicrobial, antioxidant, antidiabetic, antimalarial, anticancer, and immunomodulatory effects. The phytochemical analysis of *Leucas aspera* has revealed the presence of various bioactive compounds, such as terpenoids, flavonoids, phenols, alkaloids, steroids, and saponins. These compounds are responsible for the pharmacological activities of the plant and its extracts. However, there is a need for more scientific studies to validate the traditional uses of *Leucas aspera* and to elucidate its mechanisms of action. Moreover, the safety and toxicity profiles of *Leucas aspera* and its constituents should be evaluated in detail before using it for therapeutic purposes. *Leucas aspera* is a promising source of natural drugs and deserves further attention from researchers and practitioners.

6. REFERENCES

1. Enjamoori VK, Nampalli A, Vasudha B, Gangarapu K, Boggula N. A review on Leucas aspera for phytopharmacological studies. INNOSC Theranostics and Pharmacological Sciences. 2019;2(1).
2. Balunas MJ, Kinghorn AD. Drug discovery from medicinal plants. Life sciences. 2005 Dec 22;78(5):431-41.
3. Lahlou M. The success of natural products in drug discovery. Pharmacology & Pharmacy. 2013;4(03):17-31.
4. Katiyar C, Gupta A, Kanjilal S, Katiyar S. Drug discovery from plant sources: An integrated approach. Ayu. 2012 Jan;33(1):10.
5. Desai AG, Qazi GN, Ganju RK, El-Tamer M, Singh J, Saxena AK, Bedi YS, Taneja SC, Bhat HK. Medicinal plants and cancer chemoprevention. Current drug metabolism. 2008 Sep 1;9(7):581-91.Shah M, Prajapati M, Patel J, Modi K. Leucas aspera: A review. Pharmacogn. Rev. 2010;4:85-7.
6. Kovendan K, Murugan K, Vincent S, Barnard DR. Studies on larvicidal and pupicidal activity of Leucas aspera Willd.(Lamiaceae) and bacterial insecticide, Bacillus sphaericus, against malarial vector, Anopheles stephensi Liston.(Diptera: Culicidae). Parasitology research. 2012 Jan;110:195-203.
7. Chew AL, Jessica JJ, Sasidharan S. Antioxidant and antibacterial activity of different parts of Leucas aspera. Asian Pacific Journal of Tropical Biomedicine. 2012 Mar 1;2(3):176-80.
8. Mangathayaru K, Thirumurugan D, Patel P, Pratap D, David D, Karthikeyan J. Isolation and identification of nicotine from Leucas aspera (willd) link. Indian Journal of Pharmaceutical Sciences. 2006 Jan 1;68(1).
9. Srinivasan R, Ravali B, Suvarchala P, Honey A, Tejaswini A, Neeraja P. Leucas aspera-medicinal plant: a review. International Journal of Pharma and Bio Sciences. 2011;2(1):153-9.
10. G. Vijay kumar et al. Ijsrm.Human, 2016; Vol. 5 (1): 485-503.
11. Latha B, Rumaisa Y, Soumya CK, Shafeena S, Sadhiya N. Phytochemical studies on Leucas aspera. Journal of chemical and pharmaceutical research. 2013;5(4):222-8.
12. Kamat M, Singh TP. Preliminary chemical examination of some Compounds in the different parts of the Genus Leucas R. Br. GEOBIOS-JODHPUR-. 1994;21:31-.
13. Khalique A, Hug ME, Huq MS, Mansoor MH. Chemical investigations on Leucas aspera. I. Isolation of compound-A, 3-sitosterol and et-sitosterol from the aerial parts. J Sci Res. 1970;7:125.
14. Chaudhury NA, Ghosh D. Insecticidal plants: Chemical examination of Leucas aspera. J Indian Chem Soc. 1969;46:95.
15. Chatterjee SK, Majumdar DN. Chemical investigation of Leucas aspera. J Inst Chem. 1969;41:98-101.
16. Karthikeyan S, Sivakumar A, Anbalagan M, Nalini E, Gothandam KM. Finger printing of alkaloids, steroids and flavonoids using HPTLC of Leucas aspera L. Whole plant methanolic extract. Journal of Pharmaceutical sciences and Research. 2013 Mar 1;5(3):67.
17. Choudhury S, Ghosh P, Sarkar T, Poddar S, Sarkar A, Chatterjee S. Morphological features, phytochemical, and pharmacological study of Leucas aspera (Lamiaceae): A brief review. Intl J Pharmacogn Phytochem Res. 2020;12(3):132-7.
18. Jam MP, Nath HB. Examination of the component fatty acids of the oil from the seeds of Leucas aspera. Lab dev. 1968;6:34-6.
19. Elumalai D, Hemavathi M, Hemalatha P, Deepaa CV, Kaleena PK. Larvicidal activity of catechin isolated from Leucas aspera against Aedes aegypti, Anopheles stephensi, and Culex quinquefasciatus (Diptera: Culicidae). Parasitology research. 2016 Mar;115:1203-12.
20. Basarkar UG. Phytol–A chemical constituent of Leucas aspera through HPTLC. Am Int J Res Form Appl Nat Sci. 2014;8:44-6.
21. Joshi RK. Leucas aspera (Willd.) Link Essential oil from India: β-caryophyllene and 1-octen-3-ol chemotypes. Journal of chromatographic science. 2016 Mar 1;54(3):295-8.
22. Kalachaveedu M, Ghosh A, Ranjan R, VedamVenkat K. Volatile constituents of Leucas aspera (WilId.). J Essent oil res. 2006;18:104-5.
23. Misra TN, SINGH S, Pandey HS. A NOVEL PHENOLIC COMPOUND FROM LEUCAS ASPERA SPRENG. Indian journal of chemistry. Sect. B: Organic chemistry, including medical chemistry. 1995;34(12):1108-10.
24. Misra TN, Singh RS, Prasad C, Singh S. Two aliphatic ketols from Leucas aspera. Phytochemistry. 1992 Dec 23;32(1):199-201.

25. Misra TN, Singh RS, Pandey HS. Long-chain compounds from Leucas aspera. Phytochemistry. 1992 May 1;31(5):1809-10.
26. Pradhan BP, Chakraborty DK, Subba GC. A triterpenoid lactone from Leucas aspera. Phytochemistry. 1990 Jan 1;29(5):1693-5.
27. Sadhu SK, Okuyama E, Fujimoto H, Ishibashi M. Separation of Leucas aspera, a medicinal plant of Bangladesh, guided by prostaglandin inhibitory and antioxidant activities. Chemical and pharmaceutical bulletin. 2003;51(5):595-8.
28. Limbasiya KK, Modi VR, Tirgar PR, Desai TR, Bhalodia PN. Evaluation of Anti asthmatic activity of dried whole plant extract of Leucas aspera using various experimental animal models. International Journal of Phytopharmacology. 2012;3(3):291-8.
29. Mannan A, Das H, Rahman M, Jesmin J, Siddika A, Rahman M, Rahman S, Chowdhury MH, Rahmatullah M. Antihyperglycemic activity evaluation of Leucas aspera (Willd.) Link leaf and stem and Lannea coromandelica (Houtt.) Merr. bark extract in mice. Advances in Natural and Applied Sciences. 2010 Sep 1;4(3):385-8.
30. Adiga S, Sagar V, Vasantha RR. Evaluation of the effect of Leucas aspera alcoholic extract on blood glucose level in normoglycemic and diabetic rats. Pharmacologyonline. 2011 Dec 1;3:1046-50.
31. Mangathayaru K, Lakshmikant J, Sundar NS, Swapna RG, Grace XF, Vasantha J. Antimicrobial activity of Leucas aspera flowers. Fitoterapia. 2005 Dec 1;76(7-8):752-4.
32. Ilango K, Ramya S, Gopinath G. Antibacterial activity of Leucas aspera spreng. Int. J. Chem. Sci. 2008;6(2):526-30.
33. Saritha K, Rajesh A, Manjulatha K, Setty OH, Yenugu S. Mechanism of antibacterial action of the alcoholic extracts of Hemidesmus indicus (L.) R. Br. ex Schult, Leucas aspera (Wild.), Plumbago zeylanica L., and Tridax procumbens (L.) R. Br. ex Schult. Frontiers in microbiology. 2015 Jun 9;6:577.
34. Rahman MA, Islam MS. Antioxidant, antibacterial and cytotoxic effects of the phytochemicals of whole Leucas aspera extract. Asian Pacific journal of tropical biomedicine. 2013 Apr 1;3(4):273-9.
35. Rajakaruna N, Harris CS, Towers GH. Antimicrobial activity of plants collected from serpentine outcrops in Sri Lanka. Pharmaceutical Biology. 2002 Jan 1;40(3):235-44.
36. Valsaraj R, Pushpangadan P, Smitt UW, Adsersen A, Nyman U. Antimicrobial screening of selected medicinal plants from India. Journal of ethnopharmacology. 1997 Oct 1;58(2):75-83.
37. Rao BG, Narasimha GV. Antimicrobial action of some essential oils. IV. Effect of organic compounds. Riechstoffe, Aromen, Koerperp. egemittel. 1971;21:10-2.
38. Schmidt JM, Noletto JA, Vogler B, Setzer WN. Abaco bush medicine: Chemical composition of the essential oils of four aromatic medicinal plants from Abaco Island, Bahamas. Journal of herbs, spices & medicinal plants. 2007 Feb 1;12(3):43-65.
39. Thakur DK, Misra SK, Choudhuri PC. In vitro trials of plant extracts and chemicals for their antifungal activity. Indian J Animal Health. 1987;26:31-5.
40. Sadhu SK, Okuyama E, Fujimoto H, Ishibashi M. Diterpenes from Leucas a spera Inhibiting Prostaglandin-Induced Contractions. Journal of Natural Products. 2006 Jul 28;69(7):988-94.
41. Saundane AR, KM HU, Satyanarayan ND. Antiinflammatory and analgesic activity of various extracts of Leucas aspera Spreng (Labiatae).
42. Reddy MK, Viswanathan S, Sambantham PT, Ramachandran S, Kameswaran L. Effect of Leucas aspera on experimental inflammation and mast cell degranulation. Ancient Science of Life. 1986 Jan;5(3):168.
43. Parida A, malalur C, kotian RP. Evaluation of anti-inflammatory activity of alcoholic extract of leaves of Leucas Aspera in albino rats.
44. Gupta N, Subhramanyam EV, Jha S, Bhatia V, Narang E. A comparative antipyretic activity of the crude extracts of the plant Leucas aspera and Glycosmis pentaphylla. J. Chem. Pharm. Res. 2011;3(1):320-3.
45. Agarwal S, Jacob S, Chettri N, Bisoyi S, Badarinath DK, Vedamurthy AB, Krishna V, Hoskeri HJ. Evaluation of in vitro anthelminthic activity of Leucas aspera extracts. Pharmacognosy Journal. 2011 Aug 1;3(24):77-80.
46. Krishnaiah D, Sarbatly R, Nithyanandam R. A review of the antioxidant potential of medicinal plant species. Food and bioproducts processing. 2011 Jul 1;89(3):217-33.
47. Das BK, Das B, Arpita FK, Morshed MA, Uddin A, Bhattacherjee R, Hannan JM. Phytochemical screening and antioxidant activity of Leucas aspera. International Journal of Pharmaceutical Sciences and Research. 2011 Jul 1;2(7):1746.
48. Nagarasan S, Boominathan M. Perspective pharmacological activities of Leucas aspera: An indigenous plant species. Indo American Journal of Pharmaceutical Research. 2016;6(09):6567-72.
49. Ali MS, Sayeed MA, Nabi MM, Rahman MAA. In vitro antioxidant and cytotoxic activities of methanol extract of Leucas aspera leaves. J Pharmacogn Phyto-chem. 2013;2(1):8-13.
50. Rahman MS, Sadhu SK, Hasan CM. Preliminary antinociceptive, antioxidant and cytotoxic activities of Leucas aspera root. Fitoterapia. 2007;78(7-8):552-5.

51. Banu S, Bhaskar B, Balasekar P. Hepatoprotective and antioxidant activity of Leucas aspera against D-galactosamine induced liver damage in rats. Pharmaceutical Biology. 2012 Dec 1;50(12):1592-5.
52. Emran TB, Rahman MA, Zahid Hosen SM, Saha D, Chowdhury S, Saha D, Dey TK. Antioxidant property of ethanolic extract of Leucas aspera Linn. Bull. Pharm. Res. 2012;2(1):46-9.
53. Annapandian VM, Rajagopal SS. Phytochemical evaluation and in vitro antioxidant activity of various solvent extracts of Leucas aspera (Willd.) Link leaves. Free Radicals and Antioxidants. 2017 Mar 1;7(2):166-71.
54. Dharishini MP, Radha A, Balasubramanian K, Dinesh S, Narasimman M. In Vitro Micropropagation and Comparative Free Radical Scavenging Activity of Wild Plant and Callus Extract of Leucas aspera. Journal of Academia and Industrial Research (JAIR). 2014 Jun;3(1):16.
55. Augustine BB, Pitta S, Lahkar M, Dash S, Samudrala PK, Thomas JM, et al. Asian Pacific Journal of Tropical Disease. 2014;4:395-02.
56. Reddy MK, Viswanathan S, Thiugnanasambhantham P, Kameshwaran L. Anti-ulcer activity of Leucas aspera spreng. Ancient science of Life. 1992 Jul;12(1-2):257.
57. Kumar S, Patel N, Budholiya P, authors. Evaluation of anti-ulcer activity of hydroalcoholic leaves extract of Leucas aspera. IJPBA 2021;9(2):7-13.
58. Kamaraj C, Kaushik NK, Rahuman AA, Mohanakrishnan D, Bagavan A, Elango G, Zahir AA, Santhoshkumar T, Marimuthu S, Jayaseelan C, Kirthi AV. Antimalarial activities of medicinal plants traditionally used in the villages of Dharmapuri regions of South India. Journal of Ethnopharmacology. 2012 Jun 14;141(3):796-802.
59. Augustine BB, Dash S, Lahkar M, Sarma U, Samudrala PK, Thomas JM. Leucas aspera inhibits the Dalton's ascitic lymphoma in Swiss albino mice: A preliminary study exploring possible mechanism of action. Pharmacognosy magazine. 2014 Apr;10(38):118.
60. Kripa KG, Chamundeeswari D, Thanka J, Reddy CU. Modulation of inflammatory markers by the ethanolic extract of Leucas aspera in adjuvant arthritis. Journal of ethnopharmacology. 2011 Apr 12;134(3):1024-7.
61. Rahman MA, Sultana R, Bin Emran T, Islam MS, Rahman MA, Chakma JS, Rashid HU, Hasan CM. Effects of organic extracts of six Bangladeshi plants on in vitro thrombolysis and cytotoxicity. BMC complementary and alternative medicine. 2013 Dec;13:1-7.
62. Krishnaraju AV, Rao TV, Sundararaju D, Vanisree M, Tsay HS, Subbaraju GV. Assessment of bioactivity of Indian medicinal plants using brine shrimp (Artemia salina) lethality assay. International Journal of Applied Science and Engineering. 2005 Oct;3(2):125-34.
63. Kamaraj C, Bagavan A, Rahuman AA, Zahir AA, Elango G, Pandiyan G. Larvicidal potential of medicinal plant extracts against Anopheles subpictus Grassi and Culex tritaeniorhynchus Giles (Diptera: Culicidae). Parasitology research. 2009 Apr;104:1163-71.
64. Kovendan K, Murugan K, Vincent S, Barnard DR. Studies on larvicidal and pupicidal activity of Leucas aspera Willd.(Lamiaceae) and bacterial insecticide, Bacillus sphaericus, against malarial vector, Anopheles stephensi Liston.(Diptera: Culicidae). Parasitology research. 2012 Jan;110:195-203.
65. Maheswaran R, Sathish S, Ignacimuthu S. Larvicidal activity of Leucas aspera (Willd.) against the larvae of Culex quinquefasciatus Say. and Aedes aegypti L. Int J Integr Biol. 2008;2(3):214-7.
66. Shelke SS, Chandanam S, Chandrasekhar KB. Hepatoprotective potential of root extract of Leucas aspera. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS). 2015;4(2):708-38.
67. Mangathayaru K, Grace XF, Bhavani M, Meignanam E, Karna SR, Kumar DP. Effect of Leucas aspera on hepatotoxicity in rats. Indian journal of pharmacology. 2005 Sep 1;37(5):329.
68. Hossan AN, Zaman F, Barman MR, Khatoon S, Zaman M, Khatun F, Mosaiab T, Mostafa F, Sintaha M, Jamal F, Rahmatullah M. Antinociceptive activity of Xanthium indicum J. Koenig ex Roxb.(Asteraceae) leaves and Leucas aspera (Willd.) Link (Lamiaceae) whole plants. Advances in Natural and Applied Sciences. 2011 Apr 1;5(2):214-7.
69. Navabshan I, Sakthivel B, Pandiyan R, Antoniraj MG, Dharmaraj S, Ashokkumar V, Khoo KS, Chew KW, Sugumaran A, Show PL. Computational lock and key and dynamic trajectory analysis of natural biophors against COVID-19 spike protein to identify effective lead molecules. Molecular biotechnology. 2021 Oct; 63(10):898-908.

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