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Review Article

# A Comprehensive Review on Phytopharmacological Studies of *Leucas aspera*

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## Abstract

Global health awareness is required for better treatment of human diseases and their medication is necessary and the current study presents the phytopharmacological studies of *Leucas aspera* (Lamiaceae) based on the recent research reports. Most of photosynthetic substances have been extracted from *L. aspera* including oleanolic corrosive, ursolic corrosive and 3 sitosterol, leucasperones A and B, leucasperols A and B, isopimarane is the most active component of aspera. The plant contains abundant bioactives such as alkaloids, flavonoids, phenolics, terpenes and N containing compounds which shows different pharmacological activities such as antidiabetic, anti-inflammatory, antifungal, anticancer and *Leucas aspera* is also used to treat various diseases. This review gives findings from various *in vitro* and *in vivo* activities performed by different researchers and further studies are required to investigate the bioactives present in the plant and development of different therapeutic medicines to treat the diseases by medical validation and bring awareness the usage of leucas aspera as therapeutic agent. This abstract reviews the key potential phytochemical components and encourages further research for its applications for development of different functional health products.

***Keywords:*** *Pharmacognostic; Antinociceptive; Angiosuppressive; Parkinson's Disease; Antidiabetic; CNS Depressant Activity*

## Introduction

Plants are the main source for treatment of human physiological disorders in ancient days. Medicinal plants are widely used in different countries as a source of potent and powerful curing drugs In India herbs are acted as the primary source of traditional medicine. Ayurveda is the oldest system of medicine given by great sages of India, which has influenced all other systems of medicines either directly or indirectly, Leucas aspera belongs to family "Lamiaceae" is commonly called as "Thumbai" and widely distributed across tropical and subtropical regions. This plant is a traditional medicine for its abundant medicinal uses. Various parts of plant such as root, stem, leaves, and flowers have been used in folk remedies to treat disease conditions such as cough, cold, fever, snake bites and skin diseases such as psoriasis, chronic rheumatism, and chronic skin eruptions. Phytopharmacological research into this plant has revealed a wide array of bioactive compounds, including flavonoids, terpenoids, alkaloids, among them 3-sitosterol, leucasperones A oleanolic acid, ursolic acid, B, leucasperols A and B, isopimarane as the major active ingredients which contribute to its broad spectrum of pharmacological activities. These include antifungal, antioxidant, antimicrobial, antinociceptive, analgesic effect and cytotoxic activity. The review of Leucas aspera phytopharmacological properties aims to consolidate current scientific findings, highlighting its potential for further exploration

in modern medicine and drug development. Because of their advantages for the environment, economy, and health, natural chemicals are currently the subject of more research than manufactured ones. Further, research is necessary for better understanding and isolation of the active compounds for potential therapeutic development.

## Botanical description

Leucas aspera is an erect, annual herb that typically grows to a height of 15 - 60 cm. It has a rigid and rough stem, with quadrangular stem and branches (a characteristic feature of Lamiaceae family) leaves of this plant are simple, lanceolate, and are arranged oppositely along the stem. The edges of the leaves are serrated and have rough texture and an aromatic scent when crushed. The plant produces small, tubular, white flowers that are clustered densely in whorls at the upper part of the stem. Each flower has a two -lipped corolla, with the upper lip being hood-shaped and the lower lip divided into three lobes, The calyx is tubular with pointed teeth the inflorescence is a verticillaster, where flowers are grouped in a whorl at the nodes. The plant produces small nutlets as its fruit, these nutlets are smooth and contain the seeds of the plant. It has a fibrous root system which helps it absorb nutrients effectively and hold the soil tightly.

## Phytochemistry of *Leucas aspera*

| | |
|---|---|
| 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 |
| Genus | *L. aspera* |
| Species | *L. aspera* |

***Table 1:*** *Taxonomical classification.*

| Tissue | Phytochemicals |
|---|---|
| Whole plant | Oleanolic acid, ursolic acid, 3-sitosterol. |
| Aerial part | Nicotine, sterols, reducing sugars, glucoside, diterpenes, linifolioside, licarin A. |
| Leaf | Volatiles such as u-farnesene, X-thujene. |
| Flower | Amyl propionate, isoamyl propionate |
| Seed | Stearic acid, linoleic acid, oleic acid, palmitic acid, ceryl alcohol. |
| Shoot | Novel phenolic compounds, aliphatic ketols, long-chain compounds, nonatriacontane, 5-acetoxytriacontane, βsitosterol, and dotriacontanol. |
| Root | Leucolactone (I) |

***Table 2:*** *Phytochemical studies.*

## Pharmacological activities

### Antioxidant activity

Antioxidant property of *L. aspera* was reported by researchers. The ethanolic extract of *L. aspera* leaf exhibited high antioxidant activity having $IC_{50}$ value (40.79 µg/ml) against DPPH radical and $IC_{50}$ value (46.1 µg/ml) against ABTS radicals [8]. Phosphomolybdenum method and total antioxidant capacity of crude methanol fraction has showed to be 59.40 mg/g of plant extract. which has the highest antioxidant capacity compared with other fractions. The antioxidant results were compelled to the standard gallic acid and showed to be effective maximum flavonoid and minimum effect by alkaloid and their $IC_{50}$ concentration [9]. The plant extracts also significantly increased the antioxidant enzymes, such as superoxide dismutase, catalase, and glutathione peroxides, whereas the lipid peroxides levels in the liver become decreased, the crude methanolic decoctions of the plant leaves were observed with strong 1, 1-diphenyl-2-picrylhydrazyl (DPPH) and superoxide radical scavenging properties compared to other polarity based extracted fractions [10].

### Cytotoxic activity

The ethanolic extract of *L. aspera* root was subjected for screening of cytotoxic activities in acetic acid induced inhibition in mice, *in vitro* cytotoxic activity was performed by using 3-(4, 5-dimetylthiazol-2-yl)-2 and 5-diphenyltetrazolium bromide (MTT) assay using MCF-7 cell lines was done cell line also exhibited maximum flavonoids compare to alkaloids an adequate amount of cytotoxicity showed in brine shrimp [11]. The findings concluded the doses of 250 and 500 mg/kg was having significant inhibition in writhing in mice where this results could be considered as active for further research.

### Anticancer activity

Anticancer activity of *Leucas aspera* was done using ethyl acetate extracts of *L. aspera,* aerial parts showed anti-cancer effect and further MTT assay on MCF-7 cell lines with minimum concentration was done. These activities were attributed to flavonoids in higher amount than alkaloids [12]. In this *in vivo* and *in vitro* study, the biological results concluded the effect is mediated through macrophage stimulation, anti-angiogenesis and free radical scavenging and also concluded that this anti-cancer effect of the ethyl acetate extracts of *L. aspera* was more effective against the standard drug [13]. The cancer study reveals that Seo Nanoparticles are effective in anticancer therapeutics by inducing the apoptosis process. The study results observed that the hydroalcoholic decoctions of the whole plant showed cytotoxicity and this activity was more in 80% ethanolic root decoctions. Dose-dependent study, was done it has showed that the $LC_{50}$ value is 52.8 µg/mL [14].

### Anti-fungal activity

The extract of chloroform and ether extracts of *L. aspera* showed its antifungal activity against Trichophyton and Microspore gypsum was fungistatic, *in vitro* study of antifungal with the minimum inhibitory concentration was showed to be 5 mg/ml. Prostaglandin inhibitory and antioxidant activities *Leucas aspera* acacetin for inhibition of COX and 5-LOX showed both prostaglandin inhibition at 3 - 4 g/mL in guinea pigs ileum against PGE1- and PGE2- induced contractions and a 1, DPPH radical scavenging effect this experiment proved as antifumigatus [15].

### Antimicrobial activity

Antimicrobial activity of *Leucas aspera* was reported by many researchers, the hexane extract showed remarkably highest activity with $IC_{50}$ value was 247.42 µg/ml, at a significant level (α), methanolic extract of whole plant showed the highest amount of phenolic (124.62 ± .552 mg GAE/g) and flavonoid (98.23 ± 0.41 mg QE/g) contents after quantitative observation. Methanol extract of *Leucas aspera* showed more zone of inhibition against microbes. The antimicrobial activities of extracts of *L. aspera* were assessed against three gram negative and gram positive was showing effective antimicrobial activity [16]. Four compounds, stigmasterol, lupeol, β-sitosterol and menthol, were isolated from methanol extract. Different microorganisms were used for investigating antimicrobial activity of the different extracts of

*L. aspera* methanolic extract exhibited higher zone of inhibition against three bacteria i.e. *P. aeruginosa, M. smegmatis* and *K. pneumonia* showed zone of inhibition was observed against three gram positive and gram-negative *B. subtilis* and *S. aureus, B. megaterium, S. Para typhi, S. typhi, V. mimics, S. dysenteries* and *V. cholera* [17].

### Antinociceptive activity

Antinociceptive activity of *Leucas aspera* was reported by many researchers. The ethanolic extract of *L. aspera* root was subjected in acetic acid induced writhing inhibition, 1,1-diphenyl-2-picryl hydroxyl free radical scavenging assay and brine shrimp lethality bioassay was done. The results showed that, at these doses of 250 and 500 mg/kg there was significant inhibition in writhing in mice, producing a significant free radical scavenging activity with an IC50 of 8 µg/ml and also there was significant lethality to brine shrimp [18]. Protease and thrombolytic activity of *Leucas aspera* leaves showed significant lytic activity in these plants *in vitro* study of the aqueous extract of *Leucas aspera* leaves was because of the enzyme with molecular weight, 19.89 KDa [19]. The ethanolic decoctions of these plant parts have significant peripheral antinociceptive effects at a particular dose of (400 mg/kg).

### Anti-ulcer activity

The study of anti-ulcer activity showed by many researchers is that hydroalcoholic extract of *Leucas aspera* leaves showed gastric ulcer healing effect through the death of the bacteria by inhibiting its cell wall biosynthesis and also showed its significance in reducing the ulcer area and ulcer score [20]. In this study justifies the use of *L. aspera* in all gastric disorders where study concluded that the methanolic extract of *L. aspera* in all the tested ulcer models showed significant ulcer protective effect [21].

### Free radicle scavenging and elastase inhibitory activity

The study revealed by the many researchers showed that the use of *Leucas aspera* was supported by the anti-elastase assay found. The hexane extract showed remarkably highest activity with $IC_{50}$ of 247.42 µg/ml, at a significant level (α) [22].

### Anti-bacterial activity

The study of anti-bacterial activity was done by disc diffusion method using the aqueous leaf extract of synthesized CUO nanoparticles of *Leucas aspera* and *Morinda tinctoria* plant showed remarkable antibacterial activity when compared with the standard values of the reference sample against a few Gram-negative and Gram-positive bacteria [23]. Bacteriostatic activity was showed by essential oils from *L. aspera* against different strains of bacteria including gram positive and negative bacteria [24]. Antibacterial activity was seen in the methanolic extract, the flower juice of *L. aspera*, with maximum activity for the alkaloidal residue [25].

### Anti-inflammatory activity

In present study induced granuloma models in albino rats. The result showed *Leucas aspera* was more efficacious than acetyl salicylic acid but in subacute inflammation, the plant extract was less beneficial than phenylbutazone and exhibited the antiinflammation [26]. The petroleum ether and ethanolic showed anti-inflammatory properties with respect to the standard diclofenac sodium and analgin. The extracts are highly effective against acute and chronic inflammations. *L. aspera* showed activity against mast cell degranulation persuaded by propranolol and carbachol. Petroleum ether, chloroform, ethanol, and aqueous raw extracts were previously investigated for the anti-inflammatory property [27].

### Photocatalytic activity

The SeO nanoparticles absorbed the dye molecules from this way the water purification occurs during the addition of nanoparticles in dye containing water. It indicates that the SeO nanoparticles have capacity to degrade dye Fastly [28].

### Hepatoprotective activity

The methanol and petroleum ether extracts of *Leucas aspera* was evaluated for hepatoprotective potential. The result showed that the root extracts of *Leucas aspera* possess hepatoprotective potential [29]. Cold methanolic decoctions of the whole plant of *L. aspera* was evaluated for the hepato-protective property. The results showed that the plant part has a significant hepato-protective effect on liver damage. Fresh juice of the leaves was tested for carbon tetrachloride-induced liver damage as well [30].

### Anti-asthmatic activity

In this study the methanolic extract of whole plant of *Leucas aspera* showed significant antihistamine, bronchodilatory, in various *in-vivo* and *in-vitro* anti-asthmatic models and thus concluded its significant anti-asthmatic activity [31].

### Analgesic effect

The aqueous extract of *Leucas aspera* was examined for the antinociceptive activity in animal models. The study showed significant inhibition in the acetic acid induced writhing model. The extract also produced fast analgesic effect in a dose related manner [32].

### Immunomodulatory activity

In the study ethyl extract of *Leucas aspera* was showing for immunomodulatory activity which showed that EALA is a potent immunostimulant, stimulating both the specific and non-specific immune mechanism [33].

### Anthelmintic and cytotoxic activity

In this study the methanolic crude extract of *Leucas aspera* have shown significant cytotoxic activity and against study also showed mild anthelmintic activity against the *Pheretima posthuma* in comparison with standard albendazole [34].

### Anti-diabetic activity

The study showed *Leucas aspera* leaf extract has shown antidiabetic potential in diabetic Wistar albino rats *in-vivo* model by streptozotocin-induced [35]. The study was done to evaluate the effect of leaves of the plant on experimental diabetic rats. Similarly, the diabetic rats were induced with methanolic extract of the plant to reduce the blood glucose level reduced after injecting into rats. The study was done by considering both biological and chemical parameters, ethanolic extract of *Leucas aspera* leaves with different dose was injected in the albino rats reduced the blood glucose level [36].

### Anti elastase activity

The study concluded that *Leucas aspera* leaf extract has shown elastase inhibitory activity The traditional use of *Leucas aspera* was supported by the anti elastase assay where it revealed that among all the extracts, the hexane extract showed remarkably highest activity with $IC_{50}$ of 247.42 µg/ml, at a significant level (α), methanolic extract of whole plant showed the highest amount of phenolic (124.62 ± .552 mg GAE/g) and flavonoid (98.23 ± 0.41 mg QE/g) contents after quantitative observation [37].

### NS depressant activity

In this study *Leucas aspera* showed remarkable decrease in locomotor activity of open field and whole cross tests, the methanolic leaves extract of *Leucas aspera* notably induced the sleep at early stage and duration of sleeping time was also lengthened [38].

### Anti-pyretic activity

Antipyretic activity study was done using ethanolic extract of *Leucas aspera* and *Glycosmis pentaphylla* with concentration (200 mg/kg) in rats and exhibited the maximum antipyretic activity throughout the test period due to the presence of paracetamol group this

inhibited the synthesis of prostaglandin in hypothalamus of albino rats [39]. The study of the ethyl acetate extracts of *Leucas aspera* showed significant antipyretic activity than methanolic extracts in albino rats by using baker's yeast induced pyrexia method. These results showed that plant bud has maximum Antipyretic activity [40].

### Angiosuppressive activity

The study gives that the solvent extracts of *Leucas aspera* leaf and stem using Chicken Chorioallantoic Membrane (CAM), high angiosuppressive activity was observed in leaf so this plant leaf can be used in the treatment of cancer, where supresses the growth of abnormal cells and metastasis of the cell is inhibited [41]. Therefore this plant can be a boon to research field.

### SeO nanoparticles as stabilizing agents

In this study *Leucas aspera* showed that the study of green synthesis of copper oxide (Cuco) nanoparticles mediated by aqueous leaf extracts of *Leucas aspera* and *Morinda tinctoria* plant which acted as reducing agents [42]. *In vivo* activity was done using SeO nanoparticles, they showed lower degree of toxicity compared to biochemical agents [43].

### Parkinson's disease

The bioactive phytocompounds from *Leucas aspera* were examined to establish their inhibitory activity against alpha-synuclein protein. In this study, ten phytocompounds were selected from *L. aspera* and their efficacy to counteract Parkinson's disease causing alpha synuclein was evaluated [44]. Molecular docking studies revealed that Baicalein and Leucasperones A were the best antagonists for Parkinson's causing alpha-synuclein. This plant contains the phytochemicals Baicalein in their flowers and Leucasperones A in their ariel parts, which can be used to treat PD.

### Biochemical defence for treating crude soil sample

This study of *Leucas aspera* shows the enzymatic defence of *Leucas aspera* in the crude oil polluted soil. In addition, phytoremediation potential of the herb was experimented in terms of depletion in total oil and grease contents, the changes in dissolution of grease and oil were seen. This species have potential to lessen the total oil and grease concentrations and could metabolize hydrocarbon components from the oil contaminated soil [45].

### Antilarvicidal activity

This study of antilarvicidal crude methanolic decoctions of plant leaf was examined for its larvicidal property against *Culex quinquefasciatus*, *Aedes aegypti* and *Anopheles stephensi*. These activities tested against fourth-instar stages. Catechin, an isolated compound from the plant, showed noticeable larvicidal activity in a very low concentration [46].

### Central nervous system effect

This study aimed to identify the crude ethanolic extract of plant root of *Leucas aspera* was investigated for its effect on the central nervous system, using pentobarbitone-induced sleeping time test, the open field test, and the hole cross test in Swiss albino mice was done. The result of the study showed that these plant parts possess significant effects on the central nervous system [47].

### Antivenom activity

In this study of *Leucas aspera* showed Triterpenoid extracted from *Leucas aspera* Linn. was tested for antivenom activity against induced toxicity in mice. 1-hydroxytetratriacontane-4-one ($C_{34}H_{68}O_2$), was isolated from methanol extracts of *Leucas aspera* plant was compared with commercial presence of sterols, flavonoids, galactose, ursolic acid, oleanolic acid, Beta-sitosterol, alpha-sitosterol, cardiac glycosides, saponins and tannins. Total antioxidant and phenol were 190.00 ± 7.95 mg/g and 15.36 ± 0.512 GAE/g dry weight of extract respectively [48].

### Wound healing activity

In this study of *Leucas aspera* showed Baicalein-7-O-β-D-glucuronide (baicalin) isolated from methanol extracts of *Leucas aspera* flowers was investigated for wound healing activity in albino rats. And it was found that earlier there was slow healing process but after the 12$^{th}$ day rapid healing process was observed. Baicalin isolated from flowers of *L. aspera* has better wound healing activity [49].

### Source of essential oils

In this study of *Leucas aspera* aerial parts of Leucas aspera by hydro-distillation for isolation of essential oil and chemical composition of oil was done by gas chromatography. It was identified 43 compounds, accounts for 98.1% of total oil. βcaryophyllene (34.2%), epi-α-bisabolol (4.6%), 1-octen-3-ol (14.8%), α-humulene (6.3%), α-pinene (5.8%), and limonene (4.5%) were the main constituents of the oil. The oil was also rich in sesquiterpene hydrocarbons (47.7%), followed by others (long chain hydrocarbons (LCH), oxygenated LCH and phenyl derivative constituents) (20.2%), monoterpene hydrocarbons (14.8%), oxygenated sesquiterpenes (14.8%) and oxygenated monoterpene (0.6%) [51].

## Conclusion

The literature review revealed that *Leucas aspera* is an important medicinal plant easily available weed, less cost effective and widely available in various parts of the world.

Medicinally it has been proven that plant possess various pharmacological, phytochemical, and pharmacognostic activities like antifungal, antioxidant, antimicrobial, antinoceptive, antidiabetic, anti-inflammatory and cytotoxic activities. Phytochemical screening reveals the presence of various phytochemical constituents such as phenolics, alkaloids, flavonoids, glycosides, steroids, lignins, terpenoids, fatty acids, ursolic acid, beta sitosterol, diterpene, oleanolic acid, tannins, saponins and carbohydrates. The research on the pharmacological value of this plant proves that it has valuable compounds for curing many diseases asthma, chronic rheumatism, psoriasis, scabies, chronic skin eruptions. and thus, it is a promising plant for future advanced medicine. We suggest studies on this plant must be carried out to explore other important and unknown benefits and Further research may help validate and expand the use of this herb in modern medicine.

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## Conflict of Interest

There is no conflict of interest and the authors declare the same.

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