A comprehensive Review on Phytopharmacological Studies of *Leucas aspera*

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Abstract

The current study presents the phytopharmacological studies of *Leucas aspera* (Lamiaceae) based on the recent research reports. Abundant phytochemicals have been extracted from *L. aspera* including oleanolic acid, ursolic acid and 3-sitosterol, leucasperones A and B, leucasperols A and B, isopimarane as the major active ingredients. The range of compounds extracted from this plant has been investigated to substantiate its pharmacological property. Medicinally, it has been proven to possess various pharmacological activities like antifungal, antioxidant, antimicrobial, antinociceptive and cytotoxic activity. There is enormous potential for the discovery of new medicinal compounds in this species and an immediate need for techniques to facilitate the production of high quality, chemically consistent plant material for drug development and clinical trials. The purpose of this review is to summarize the information concerning the pharmacological significance and biological activities of *L. aspera*.

Key Words

Pharmacognostic, Antinociceptive, Angiosupresive, Parkinson's disease

1.INTRODUCTION

Plants are the main source for treatment of human physiological disorders in ancient days. In India herbs are acted as the primary source of traditional medicine. Medicinal plants are widely used in different countries as a source of potent and powerful curing drugs. *Leucas aspera* belongs to family "Lamiaceae" is commonly called as "Thumbai" found in India from the Himalayas to Ceylon. *Leucas aspera* is a herb erecting to a height of 15-60 cm and widely distributed throughout India as a weeds [1,2] The Plant derived bio-molecules that have been extensively used globally as a therapeutic traditional medicine because of the presence of

terpenoids, fatty acids, nicotine, ursolic acid, glucoside, beta-sitosterol, sterols, diterpene, and phenolic chemicals are the main phytoconstituents found in the plants [3]. Traditionally this plant can be used to treat psoriasis, chronic rheumatism, and chronic skin eruptions. Throughout the world, herbal plants are essential to traditional medicine, and even today, the majority of people living in both rural and urban areas use these plants for a variety of everyday needs. Because of their advantages for the environment, economy, and health, natural chemicals are currently the subject of more research than manufactured ones. Phytochemicals are the various chemical substances that plants manufacture for their biological needs, such as defence mechanisms against insects, bacteria, and herbivorous animals. Herbal plants are utilised extensively in medications and are a natural source of several significant compounds [4]. They serve as the foundation of the Siddha and Ayurvedic traditional medical systems in India. Over the past 100 years, development of chemotherapy and technology for the production of synthetic drugs changed the world scenario in medicine [6,7] today.

2.PHYTOCHEMISTRY OF *LEUCAS ASPERA*

2.1Taxonomical 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
Genus	*L. aspera*
Species	*L. aspera*

2.2Phytochemical studies

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, β-sitosterol, and dotriacontanol.
Root	Leucolactone (I)

3.Pharmacological activities

3.1**Antioxidant activity**

Antioxidant property of *L. aspera* was reported by researchers. The ethanol extract of *L. aspera* leaf showed potent antioxidant activity with IC50 value (40.79µg/ml) against DPPH radical and IC50 value (46.1 µg/ml) against ABTS radicals[8] Phosphomolybdenum method and total antioxidant capacity of crude methanol fraction was found to be 59.40 mg/g of plant extract (expressed as ascorbic acid equivalents) which is the highest antioxidant capacity comparing with other fractions the antioxidant results were compared to the standard gallic acid and found to be effective maximum flavonoid and minimum effect by alkaloid compound and their IC50 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]

3.2Cytotoxic 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 results showed that, at the doses of 250 and 500 mg/kg there was significant inhibition in writhing in mice where could be considered as active for further research.

3.3Anticancer activity

Anticancer activity of *Leucas aspera* was done using ethyl acetate extracts of *L. aspera* aerial parts showed anti-cancer effect and study also established the anti-cancer activity by MTT assay on MCF-7 cell lines with moderate concentration. These activities are attributed to flavonoids in higher amount than alkaloids [12]In this *in vivo* and *in vitro* study, the biochemical and histological results concluded that 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* is comparable to the standard drug 5-Fluro uracil [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. In a dose-dependent study, it was showed that the LC50 value is 52.8 μg/mL.27[14].

3.4Anti-fungal activity

Anti-fungal activity of **c**hloroform and ether extracts of *L. aspera* showed its antifungal activity both fungistatic and fungicidal actions against Trichophyton and Microsporum gypsum, In Vitro study and the minimum inhibitory concentration was found to be 5mg/ml. Prostaglandin inhibitory and antioxidant activities *Leucas aspera* acacetin for inhibition of COX and 5-LOX showed both prostaglandin inhibitory and antioxidant activities at 3-4 g/mL in guinea pigs ileum against PGE1- and PGE2- induced contractions and a 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging effect [15] .

3.5Antimicrobial activity

Antimicrobial activity of *Leucas aspera* was reported by many researchers**,** the hexane extract showed remarkably highest activity with IC50 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. Methanol extract of *leucas aspera* showed more zone of inhibition. The antimicrobial activities of extracts of *L aspera* were assessed against three gram negative: Klebsiella pneumonia (MTCC109), Pseudomonas aeruginosa (MTCC2453) and gram positive: Staphylococcus aureus (MTCC96), Bacillus subtilis (MTCC2057) and Mycobacterium smegmatis (MTCC992), Chromobacterium violaceus (MTCC432) [16]. Four compounds, stigmasterol, lupeol, β-sitosterol and menthol, were isolated from methanol extract. Sixteen 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 where noteworthy zone of inhibition was observed against Gram positive B. subtilis and S. aureus, B. megaterium and Gram-negative S. Para typhi, S. typhi, V. mimics, S. dysenteries and V. cholera [17]

3.6Antinociceptive activity

Antinociceptive activity of *Leucas aspera* was reported by many researchers, The ethanolic extract of *L. aspera* root was subjected for screening of antinociceptive activity in acetic acid induced writhing inhibition, 1,1-diphenyl-2-picryl hydroxyl (DPPH) free radical scavenging assay and brine shrimp lethality bioassay respectively. The results showed that, at the 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. The results showed significant lytic activity in vitro study of the aqueous extract of *Leucas aspera* leaves which could be because of the enzyme with an approximate 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).

3.7Anti-ulcer activity

The study of Anti-ulcer activity showed by many researchers is that hydroalcoholic extract of *Leucas aspera* leaves contains flavonoids, tannins and saponins in phytochemical analysis and

also produced gastric ulcer healing effect through the death of the bacteria by inhibiting its cell wall biosynthesis in indomethacin induced gastric ulcer and also showed its significance in reducing the ulcer area and ulcer score [20] In this study the results of antioxidant and histopathological studies justifies the Folklore 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 antisecretory and ulcer protective effect [21].

3.8 Free radicle scavenging and elastase inhibitory activity

The study revealed by the many researchers showed that 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 IC50 of 247.42 µg/ml, at a significant level (α)[22].

3.9Anti –bacterial activity

In this study the anti-bacterial activity was done by disc diffusion method of the synthesized CuO nanoparticles using the aqueous leaf extract of *Leucas aspera* and *Morinda tinctoria* plant material showed remarkable antibacterial activity when compared with the standard values of the reference sample Amikacin against a few Gram-negative and Gram-positive bacteria [23].Bacteriostatic activity was showed by essential oils from *L. aspera* against Staphylococcus aureus, Pseudomonas pyocyanin, Escherichia coli, Vibrio cholerae, Proteus vulgaris, Dys. Flexneri, Salmonella typhi and Klebsiella aerogenes [24] Antibacterial activity was seen in the methanolic extract, it's fraction, alkaloidal residue and the flower juice of *L. aspera*, with maximum activity for the alkaloidal residue [25].

4.0Anti-inflammatory activity

In present study *Heliotropium indicum Linn* and *Leucas aspera Spreng* were tested for anti-inflammatory activity in the carrageenan induced hind paw oedema and cotton pellet 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 [26] The petroleum ether and ethanolic decoction showed anti-inflammatory properties with respect to the standard diclofenac sodium and analgin.25 The extracts are highly effective against acute and chronic inflammations. *L. aspera* showed activity against mast cell degranulation persuaded by propranolol and carbachol.26 Petroleum ether, chloroform,

ethanol, and aqueous raw extracts were previously investigated for the anti-inflammatory property2[27].

4.1 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].

4.2 Hepatoprotective activity

The methanol and petroleum ether extracts of *Leucas aspera* was evaluated for hepatoprotective potential by paracetamol and thioacetamide induced hepatotoxicity models. 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].

4.3Anti-asthmatic activity

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

4.4Analgesic effect

The aqueous extract of *Leucas aspera* was evaluated for the antinociceptive activity in animal models. The study showed significant inhibition of writhing response in the acetic acid induced writhing model. The extract also produced significant increase in the latency in the hot plate test in a dose related manner [32].

4.5 Immonomodulatory activity

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

4.6 Anthelmintic and cytotoxic activity

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

4.7Anti-diabetic activity

The study concluded that *Leucas aspera* leaf extract has shown antidiabetic potential in streptozotocin-induced diabetic Wistar albino rats in-vivo model [35]. 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 [36]

4.8 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 IC50 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]

4.8 CNS depressant activity

In this study *Leucas 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 early stage and duration of sleeping time was also lengthened. The results concluded that Methanolic leaf extract of *Leucas aspera* has CNS depressant activity [38] .

4.9 Anti-pyretic activity

In this study *Leucas aspera* showed Ethanolic extract of *Leucas aspera* and *Glycosmis pentaphylla* were studied for anti-pyretic activities in rats using Brewer's yeast induced pyrexia

model. Extract of *Leucas aspera* (200mg/kg) and standard paracetamol group showed the maximum antipyretic activity throughout the test period of 6 hours probably by inhibiting the synthesis of prostaglandin in hypothalamus [39] . In this study the ethyl acetate extracts of *Leucas aspera* showed significant antipyretic activity than methanolic extracts in baker's yeast induced pyrexia method. These results confirm its traditional antipyretic activity of a plant and among different parts of plant bud has shown maximum activity [40] .

5.0 Angiosupresive Activity

The study concluded that Angiogenesis promotes growth of tumours by providing nutrients and oxygen, and facilitating tumour invasion and metastasis. So, it was a target for cancer chemotherapy. Different solvent extracts of Leucas aspera leaf and stem was studied for Angiosupresive activity using Chicken Chorioallantoic Membrane (CAM)Methanol extract of leaf revealed high angiosuppresive activity. This plant can be used in designing the drugs to cure anti-angiogenesis [41].

5.1 SeO Nanoparticles as stabilizing agents

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

5.2 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 (PD) causing alphasynuclein was evaluated. [44] Molecular docking using Pyrex and BIOVIA revealed that Baicalein and Leucasperones A were the best antagonists for 3Q25 Parkinson’s causing alpha-synuclein. the plant *L. aspera* contains the phytochemicals Baicalein in their flowers and Leucasperones A in their ariel parts, which can be used to create PD medications.

5.3 Biochemical defence for treating crude soil sample

In this study of *Leucas aspera* showed the present investigation of enzymatic defence of *Leucas aspera* in the crude oil polluted soil has been studied. In addition, phytoremediation potential of the herb was investigated in terms of dissipation in total oil and grease contents, changes in soil physicochemical and enzyme profiles and beneficial bacterial population. the species have ability to counter the stress imposed due to hydrocarbon contaminations. The species have potential to lessen the total oil and grease concentrations and could uptake/metabolize hydrocarbon components from the oil contaminated soil [45]

5.4. antilarvicidal activity

This study aimed to identify a novel antilarval combination from the endophytic fungi present in *Leucas aspera* leaves. The objectives include the isolation of endophytic fungi from leaf samples, selection of potent antilarval endophyte, and characterization of its bioactive compound. Crude methanolic decoctions of plant leaf was examined for its larvicidal property against Culex quinquefasciatus, Aedes aegypti, and Anophelesstephensi. These activities tested against fourth-instar stages. Catechin, an isolated compound from the plant, showed noticeable larvicidal activity in a very low concentration.[46].

5.5 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. The result of the study showed that these plant parts possess significant properties on the central nervous system.[47]

5.6 Antivenom Activity

In this study of *Leucas aspera* showed Triterpenoid extracted from *Leucas aspera* Linn. was tested for antivenom activity against Naja Naja induced toxicity in mice .1-hydroxytetratriacontane-4-one (C34H68O2), 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]

5.7 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 12th day rapid healing process was observed. Baicalin isolated from flowers of L. aspera has better wound healing activity [49]

5.8Angiosupresive Activity

In this study of *Leucas aspera* Angiogenesis promotes growth of tumours by providing nutrients and oxygen, and facilitating tumour invasion and metastasis. So, it was a target for cancer chemotherapy. Different solvent extracts of *Leucas aspera* leaf and stem was studied for Angiosupresive activity using Chicken Chorioallantoic Membrane (CAM). Methanol extract of leaf revealed high Angiosupresive activity. By this the plant can be used in designing the drugs to cure anti-angiogenesis [50]

5.9 Source of Essential oils 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, liginins, terpenoids, fatty acids, ursolic acid, betasitosterol, diterpene,

olenolic 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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